NATIONALE VERSORGUNGS LEITLINIEN

Nationale VersorgungsLeitlinie

Typ-2-Diabetes

Recherchedokumentation + Evidenztabellen
zum Kapitel Nicht-medikamentöse Therapie

Ergänzung zu Version 3

AWMF-Register-Nr. nvl-001

Träger:

Bundesärztekammer

Kassenärztliche Bundesvereinigung

Arbeitsgemeinschaft der Wissenschaftlichen
Medizinischen Fachgesellschaften

BUNDESÄRZTEKAMMER KBV AWMF

Aufbau des Recherche-/Evidenz-Dokuments

Zur leichteren Handhabung der umfangreichen Evidenzrecherchen werden die Recherchedokumentationen und Evidenztabellen in verschiedenen Teilen dargestellt:

- Teil 1
  - Evidenzbasis des Kapitels Nicht-medikamentöse Therapie
  - Themenübergreifende systematische Recherche
  - Themenverwandte AWMF-Leitlinien
  - Nationale und internationale Konsensuspapiere (von der Leitliniengruppe eingebrachte Literatur)
- Teil 2
  - Systematische Recherche zum Gewichtsmanagement
  - Systematische Recherche zu Formuladiäten
  - Systematische Recherche zu Mediterraner Diät
- Teil 3
  - Systematische Recherche zu körperlicher Aktivität und strukturierten Bewegunsprogrammen
- Teil 4
  - Systematische Recherche Alkoholkonsum und Neuropathie
  - Systemtische Recherche Interventionen zur Stressbewältigung

Die Seitennummerierung und Nummerierung der Inhalts- und Literaturverzeichnisse sind nicht fortlaufend, sondern beginnen in jedem Teil neu.

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Inhaltverzeichnis

1 Aufbau der Recherche-/Evidenz-Dokumente

Zur leichteren Handhabung der umfangreichen Evidenzrecherchen werden die Recherchedokumentationen und Evidenztabellen in verschiedenen Teilen dargestellt:

- Teil 1 (vorliegendes Dokument)
  - Evidenzbasis des Kapitels Nicht-medikamentöse Therapie
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  - Systemtische Recherche Interventionen zur Stressbewältigung

2 Evidenzbasis des Kapitels Nicht-medikamentöse Therapie

Die hier veröffentlichten Recherchestrategien und Evidenztabellen beziehen sich auf die aktuelle Bearbeitung des Kapitels Nicht-medikamentöse Therapie, das nach Bekanntgabe der Auflösung des ÄZQ zum 31.12.2024 als Ergänzung zur Version 3 der NVL Typ-2-Diabetes [1] veröffentlicht wurde [2]. Die Recherchestrategien für die in der 2. Auflage (2021) und der Version 3 (2023) der NVL Typ-2-Diabetes veröffentlichten Kapitel sind im Leitlinienreport der 2. Auflage [3] und Leitlinienreport der Version 3 [4] dargestellt. Recherchedokumentationen und Evidenztabellen der vorherigen NVL zum Themenbereich Diabetes sind in dem jeweiligen Leitlinienreport dokumentiert (siehe www.leitlinien.de/themen/diabetes/archiv).

Für das Kapitel Nicht-medikamentöse Therapie erfolgte eine themenübergreifende systematische Recherche zu Schlagwörtern wie „Diabetes“ in der Cochrane-Datenbank, bei der U.S. Agency for Healthcare Research and Quality (AHRQ), bei NICE (National Institute for Health and Care Excellence) und beim IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen). Zum Nutzen des Gewichtsmanagements, verschiedener Ernährungsinterventionen, körperlicher Aktivität und von strukturierten Bewegungsprogrammen, Alkoholkonsum und Interventionen zur Stressbewältigung erfolgten weitere systematische Recherchen. Die vorherigen Auflagen der NVL zum Themenbereich Diabetes, insbesondere die 1. Auflage der NVL Therapie des Typ-2-Diabetes [5] und die NVL Diabetes – Strukturierte Schulungsprogramme [6] wurden in die Erwägungen miteinbezogen.

Grundlage der Diskussion für das Kapitel Nicht-medikamentöse Therapie bildeten demnach die Ergebnisse der systematischen Recherchen, die vorherigen Auflagen der NVL zum Themenbereich Typ-2-Diabetes, themenverwandte AWMF-Leitlinien sowie nationale und internationale Konsensuspapiere, die klinische Erfahrung der Leitliniengruppe, sowie gute klinische Praxis.

3 Recherchedokumentation - Themenübergreifende systematische Recherche

Einleitung

Es wurden systematische Übersichtsarbeiten (bereits publizierte sowie Protokolle) zum Thema Typ-2-Diabetes gesucht, die als primäre Evidenzquelle für die Aktualisierung/Überarbeitung der NVL Typ-2-Diabetes dienen sollten. Es erfolgte ein zweizeitiges TiAb-Screening, um die Recherche bzw. die Screening-Ergebnisse auch für die Überarbeitung zukünftiger Themenbereiche und die Aktualisierung bestehender Kapitel nutzen zu können. In einem

ersten Schritt wurden alle Reviews ohne Relevanz für die NVL ausgeschlossen. Alle verbleibenden Übersichtsarbeiten wurden auf inhaltliche Relevanz für das Kapitel Nicht-medikamentöse Therapie geprüft.

Die eingeschlossenen Treffer aus dem TiAb-Screening aus der übergeordneten Recherche, die für ausstehende Kapitel oder die Aktualisierung bereits bestehender Kapitel relevant sein können, werden im Folgenden bei der Cochrane-Recherche, aber für die weiteren Recherchen nicht separat als Treffer, sondern bei den Ausschlüssen aufgeführt.

PICO-Fragestellung (themenübergreifende Recherche)

Population: erwachsene Personen mit Typ-2-Diabetes (oder erhöhtem Risiko für Diabetes, Personen mit intermediärer Hyperglykämie)*

Intervention: jegliche diagnostische, nicht-medikamentöse, medikamentöse Intervention

Kontrolle: jegliche diagnostische, nicht-medikamentöse, medikamentöse Vergleiche

Outcome: in der themenübergreifenden Recherche im ersten TiAb-Screening keine Einschränkungen

Study: systematische Übersichtsarbeiten, HTA

Sprache: deutsch, englisch

Publikationstyp: aggregierte Evidenz

Zeitraum: Siehe jeweilige Recherchestrategie (für Themenbereiche, die bereits in einer der vorherigen NVL bearbeitet wurden, wurde der Beginn des Suchzeitraums auf den Zeitpunkt der Veröffentlichung dieser NVL festgelegt).

*Nur für ausgesuchte Fragestellungen, wie z. B. Diagnostik, Screening

Recherchequellen

Als Quellen für die themenübergreifende systematische Suche nach hochwertigen systematischen Übersichtsarbeiten wurden folgende Institutionenen aufgrund ihrer evidenzbasierten Vorgehensweise, ihrer hohen Berichtsqualität, ihrer wissenschaftlichen Unabhängigkeit, eines weitergehenden Einblicks in Studiendossiers sowie ggf. ihres Bezugs zum deutschen bzw. europäischen Versorgungskontext ausgewählt:

- Cochrane Library
- AHRQ (Agency for Healthcare Research and Quality)
- NICE (National Institute for Health and Care Excellence)
- IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)

Recherchestrategien und -ergebnisse

Die Recherchestrategien (z. B. Datenbanksuche, Schlagwortsuche, einfaches Screening) richteten sich nach den Möglichkeiten der jeweiligen Recherchequelle.

3.1 Cochrane Library

PICO- Fragestellung

Fragestellung: Cochrane-Reviews zum Thema Typ-2-Diabetes

Population: erwachsene Personen mit Typ-2-Diabetes, (für den Bereich Diagnostik/Screening auch Personen mit erhöhtem Risiko für Diabetes, Personen mit intermediärer Hyperglykämie)

Intervention: jegliche diagnostische, nicht-medikamentöse, medikamentöse Intervention

Kontrolle: jegliche Vergleiche

Outcome: im ersten TiAb-Screening (themenübergreifend): keine Einschränkungen; Kapitel Nicht-medikamentöse Therapie: Gesamtmortalität, kardiovaskuläre Morbidität und Mortalität, diabetesbedingte Folgemorbidität und Mortalität, Lebensqualität, Diabetesremission, (HbA1c-Senkung, wenn dadurch Medikamente eingespart werden konnten), Sicherheit und unerwünschte Wirkungen, für Stressbewältigung: auch Diabetes-related distress, Depression (siehe dort).

Study Cochrane Reviews (Systematische Übersichtsarbeiten und Metaanalysen) und Protokolle

Sprache: deutsch, englisch

Zeitraum: 2014-2023 (Zeitpunkt der letzten Recherche 21.08.2023)

Vorüberlegungen

Das Title-Abstract-Screening erfolgte zweizeitig, um die Recherche bzw. die Screening-Ergebnisse auch für die Überarbeitung zukünftiger Themenbereiche nutzen zu können. In einem ersten Schritt wurden alle Reviews ohne Relevanz für die NVL ausgeschlossen. Hierin enthalten waren auch zurückgezogene Arbeiten und Protokolle zu Reviews ohne Relevanz für die NVL. Protokolle mit thematischer Relevanz für die NVL wurden in diesem Schritt eingeschlossen, so dass im Verlauf geprüft werden kann, ob der entsprechende Review mittlerweile veröffentlicht wurde. Die verbleibenden Reviews wurden auf Ihre inhaltliche Relevanz für das aktuell zu bearbeitende Kapitel geprüft.

Im Februar 2021 war eine strukturierte Recherche zur Vorbereitung der ersten Sitzung der Arbeitsgruppe Nicht-medikamentöse Therapie erfolgt. Im August 2023 wurde eine Update-Recherche durchgeführt.

3.1.1 Recherchestrategie

Datenbanken der Cochrane Library (21. August 2023):

Nr.	Suchfrage	Anzahl
#3	#1 OR #2	546
#2	MeSH descriptor: [Diabetes Mellitus] explode all trees (Reviews and Protocols)	226
#1	Diabet*:ti,ab,kw in Cochrane Reviews (Reviews and Protocols), word variations have been searched	546

Cochrane Reviews • Review • Protocol	 489 57
Other Reviews	Nicht gesucht
Trials	Nicht gesucht
Methods Studies	Nicht gesucht
Technology Assessment	Nicht gesucht
Economic Evaluations	Nicht gesucht
Cochrane Groups	Nicht gesucht

Anzahl der Treffer: 546

in den Jahren 2014-2023: 391

3.1.2 TiAb-Screening

Ein- und Ausschlusskriterien (übergeordnetes TiAb-Screening)

Einschluss (E)	**Population:** Erwachsene Personen mit Typ-2-Diabetes, oder Menschen mit erhöhtem Risiko für die Entwicklung eines Diabetes **Intervention:** jegliche therapeutische oder diagnostische Intervention (ggf. inklusive sich aus den Ergebnissen ergebende Therapie), Screening **Outcome:** alle Protokolle mit relevanter Fragestellung
Ausschluss (A)	- Thematisch nicht passend: andere Erkrankung/Fragestellung/Thema (z. B. Schwangerschaft, nur Typ-1-Diabetes, Fragestellung für NVL nicht relevant), - zurückgezogene Reviews, oder aktuellerer Review vorhanden - Protokoll für thematisch nicht relevante Reviews

Ein- und Ausschlusskriterien (TiAb-Screening Nicht-medikamentöse Therapie)

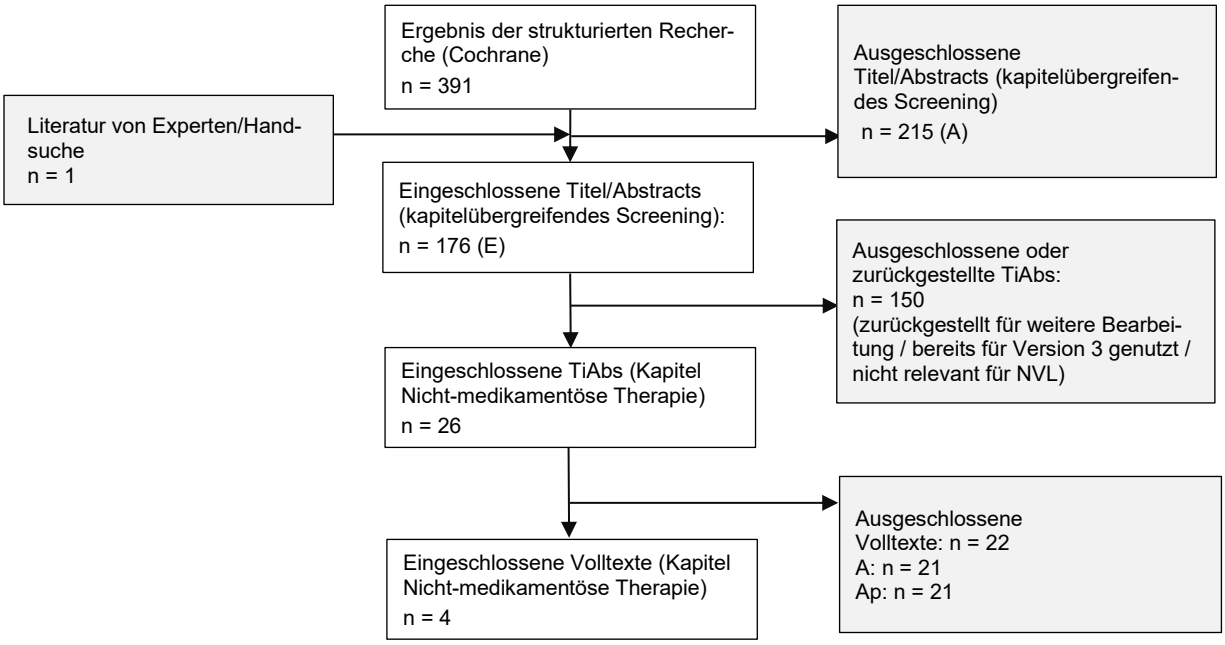
Einschluss (E)	**Population:** Erwachsene Personen mit Typ-2-Diabetes **Intervention:** Nicht-medikamentöse Interventionen **Kontrolle:** andere oder keine nicht-medikamentösen Interventionen **Outcome:** Gesamtmortalität, kardiovaskuläre Morbidität und Mortalität, diabetesbedingte Folgemorbidität und Mortalität, Lebensqualität, Sicherheit und unerwünschte Wirkungen, - zunächst im TiAB-Screening der themenübergreifenden Recherche großzügiger Einschluss unabhängig von den betrachteten Endpunkten. Später bei Bearbeitung der jeweiligen Themen im Kapitel nicht-medikamentöse Therapie Ein- oder Ausschluss der Artikel im Volltextscreening entsprechung der priorisierten Endpunkte.	
Zurückgestellt (Z)	Zurückgestellt: Themenbereiche, die in den nächsten Bearbeitungsrunden bearbeitet werden (unabhängig vom Publikationstyp, z. B. Protokoll oder Review)	
Ausschluss (A)	**Aa**	Thematisch nicht passend: andere Erkrankung/Fragestellung/Thema (z. B. Schwangerschaft, nur Typ-1-Diabetes, Fragestellung für NVL nicht relevant)
	Aw	Zurückgezogen, oder Update vorhanden; aktuellere Reviews, die den Themenbereich abdecken vorhanden, falscher Zeitraum (Veröffentlichung vor 2013)
	Ap	Protokoll für thematisch nicht relevante Reviews

3.1.3 Flowchart

Legende für das Volltextscreening:

A: Thematisch nicht passend, nicht Fragestellung in der aktuellen Überarbeitung.

Ap: Protokoll



Anmerkungen

- Es wurde ein Protokoll mit passender Fragestellung zum Thema Stressbewältigung identifiziert. Die Rücksprache mit den Autor*innen ergab, dass eine Veröffentlichung 2024 nicht zu erwarten ist: Ee CC, Armour M, Piya MK, et al. Mindfulness-based interventions for adults with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2021(12):CD014881. DOI: 10.1002/14651858.CD014881. http://dx.doi.org/10.1002/14651858.CD014881.
- Ein Review aus der NVL Diabetes – Strukturierte Schulungsprogramme von 2012 wird im Kapitel Nicht-medikamentöse Therapie zusätzlich zitiert (Deakin et al., 2005).

Eingeschlossene Reviews

n=4 (+ Deakin et al., 2005)

- Chew BH, Vos RC, Metzendorf MI, et al. Psychological interventions for diabetes-related distress in adults with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2017(9):CD011469. DOI: 10.1002/14651858.CD011469.pub2. http://dx.doi.org/10.1002/14651858.CD011469.pub2.
- Attridge M, Creamer J, Ramsden M, et al. Culturally appropriate health education for people in ethnic minority groups with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2014(9):CD006424. DOI: 10.1002/14651858.CD006424.pub3. http://dx.doi.org/10.1002/14651858.CD006424.pub3.
- Naude CE, Brand A, Schoonees A, et al. Low-carbohydrate versus balanced-carbohydrate diets for reducing weight and cardiovascular risk. Cochrane Database of Systematic Reviews 2022(1):CD013334. DOI: 10.1002/14651858.CD013334.pub2. http://dx.doi.org/10.1002/14651858.CD013334.pub2.
- Allaf M, Elghazaly H, Mohamed OG, et al. Intermittent fasting for the prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2021(1):CD013496. DOI: 10.1002/14651858.CD013496.pub2. http://dx.doi.org/10.1002/14651858.CD013496.pub2.
- Deakin, T.; McShane, C. E.; Cade, J. E.; Williams, R. D. (2005): Group based training for self-management strategies in people with type 2 diabetes mellitus. In: Cochrane Database Syst Rev (2), CD003417.

3.2 AHRQ (Agency for Healthcare Research and Quality)

Suche zuletzt am 26.02.2024 auf der Seite www.ahrq.gov

3.2.1 Recherchestrategie

→ Research → Evidence-based Practice Center (EPC) Reports → Research findings and reports:

Kategorien	Suchbegriffe/ Filter (Keine Einschränkung des Zeitraums)	Treffer	Eingeschlossene Treffer im TiAb (nicht-medikamentöse Therapie)
Search All EPC Reports (n=866)	Endocrine conditions	n=27	2
Technology Assessment Program (completed)	Sichtung der Ergebnisliste ohne Eingabe von Suchbegriffen (https://www.ahrq.gov/research/findings/ta/index.html#tacomplete)	n=5 (ab 2020)	0

TiAb: Ausgeschlossene Treffer: n=32, eingeschlossene Treffer: n=2

3.2.2 TiAb-Screening

Ein- und Ausschlusskriterien (Kapitel Nicht-medikamentöse Therapie)

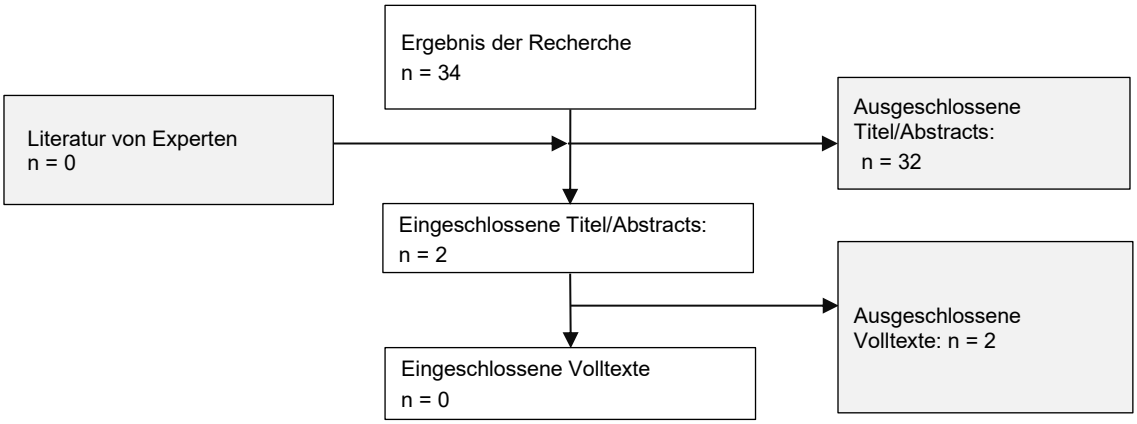
Einschluss (E)	**E**	**Einschluss: Fragestellung passend, Studientyp passend** Population: Erwachsene Personen mit Typ-2-Diabetes Intervention: nicht-medikamentöse Therapie Kontrolle: andere oder keine nicht-medikamentöse oder medikamentöse Intervention Outcome: Gesamtmortalität, kardiovaskuläre Morbidität und Mortalität, diabetesbedingte Folgemorbidität und Mortalität, Lebensqualität, Sicherheit und unerwünschte Wirkungen; - im übergeordneten TiAb-Screening großzügiger Einschluss, je nach Themenbereich erfolgte eine Festlegung der priorisierten Endpunkte durch die Gruppe vor Betrachtung der Studien
Ausschluss (A)	**A**	Thematisch nicht passend: andere Erkrankung/Fragestellung/Thema (z. B. Kinder/Jugendliche, Schwangerschaft, nur Typ-1-Diabetes, Fragestellung für NVL insgesamt, oder für das Kapitel Nicht-medikamentöse Therapie nicht relevant), Suchzeitraum des Reviews zu alt für den Themenbereich; zurückgezogene Artikel

Suchergebnisse

Volltextscreening:

- Behavioral Programs for Diabetes Mellitus, 2015; Ein-/Ausschluss: A (Recherche zu alt)
- Mobile Health Applications for Self-Management of Diabetes, 2018; Ein-/Ausschluss: A (nicht relevant; in der AG Nicht-medikamentöse Therapie wurde in der 4. Zoom-Konferenz beschlossen, für digitale Gesundheitsanwendungen (DiGAs) auf das DiGA-Verzeichnis des BfARM zu verweisen. Recherche für das Thema zu alt)

3.2.3 Flowchart



3.3 NICE (National Institute for Health and Care Excellence)

3.3.1 Recherchestrategien

Die Suche wurde im Verlauf der Bearbeitung aktualisiert. Dargestellt ist die Anzahl der Treffer der aktuellen Recherche.

Suche unter **www.nice.org.uk/guidance** > View all guidance	
Filter by title	"diabetes"
Filter by last updated data	keine Einschränkung
Filter by type	keine Einschränkung
Zeitpunkte der Suche	26.10.2023; 26.02.2024
Treffer (Anzahl) 26.02.2024	
Published: n=32	
In Consultation: n=0	
In development: n=5	
Awaiting development: n=6	

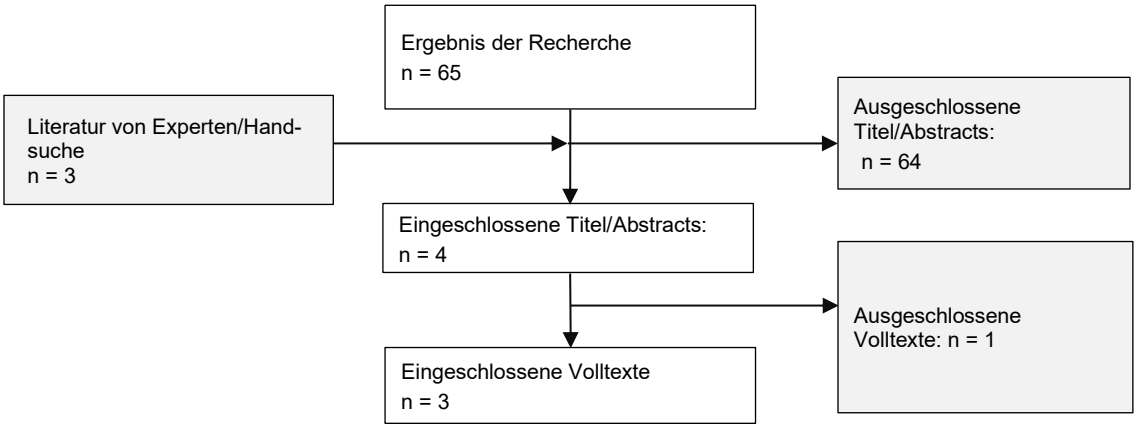
Suche unter **www.nice.org.uk/guidance** > View all guidance	
Filter by title	"diabetic"
Filter by last updated data	keine Einschränkung
Filter by type	alles ausgewählt
Zeitpunkt der Suche	26.10.2023; 26.02.2024
Treffer (Anzahl) 26.02.2024	
Published: n=18	
In Consultation: n=0	
In development: n=3	
Awaiting development: n=1	

3.3.2 TiAb-Screening

Ein- und Ausschlusskriterien (Kapitel Nicht-medikamentöse Therapie)

Einschluss (E)	**Einschluss: Fragestellung passend, Studientyp passend**
	Population: Erwachsene Personen mit Typ-2-Diabetes **Intervention:** Nicht-medikamentöse Therapie **Kontrolle:** andere oder keine nicht-medikamentöse oder medikamentöse Intervention **Outcome:** Gesamtmortalität, kardiovaskuläre Morbidität und Mortalität, diabetesbedingte Folgemorbidität und Mortalität, Lebensqualität, Sicherheit und unerwünschte Wirkungen; - im TiAb-Screening großzügiger Einschluss, je nach Themenbereich erfolgte eine Festlegung der priorisierten Endpunkte durch die Gruppe vor Betrachtung der Studien
Ausschluss (A)	• Thematisch nicht passend: andere Erkrankung/Fragestellung/Thema (z. B. Kinder/Jugendliche, Schwangerschaft, nur Typ-1-Diabetes, Fragestellung für NVL insgesamt, oder für das Kapitel Nicht-medikamentöse Therapie nicht relevant) • Zurückgezogen, oder Update vorhanden; aktuellere Reviews, die den Themenbereich abdecken vorhanden, falscher Zeitraum (Veröffentlichung vor 2013) • Kein Systematischer Review

3.3.3 Flowchart



Über die Surveillance Summary der NICE guideline NG28 (Type 2 diabetes in adults: management NICE guideline [NG28], Published date: 02 December 2015, Last updated: 16 December 2020 https://www.nice.org.uk/guidance/ng28) wurden die Artikel von Meng et al., 2017; Korsmo-Haugen et al., 2019 und Huntriss et al., 2018 identifiziert.

Eingeschlossene Treffer

- Meng Y, Bai H, Wang S, Li Z, Wang Q, Chen L (2017) Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes research and clinical practice 131:124–31 11. https://pubmed.ncbi.nlm.nih.gov/28750216/
- Korsmo-Haugen H-K, Brurberg KG, Mann J, Aas A-M (2019) Carbohydrate quantity in the dietary management of type 2 diabetes: A systematic review and meta-analysis. Diabetes, Obesity & Metabolism 21(1):15–27 https://pubmed.ncbi.nlm.nih.gov/30098129/

- Huntriss R, Campbell M, Bedwell C (2018) The interpretation and effect of a low carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. European Journal of Clinical Nutrition 72(3):311–25 12. https://pubmed.ncbi.nlm.nih.gov/29269890/.

3.4 IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)

3.4.1 Recherchestrategien

Suche auf www.iqwig.de nach IQWiG-Projekten und Ergebnissen.

Erste Suche am 21.08.2023, letzte Aktualisierung 19.02.2024

	Suchfrage
www.iqwig.de Projekte und Ergebnisse	Filter: - Ressort/Bereich: Alle - Anwendungsgebiet: Alle - Status: Alle - Jahr: Alle
Suchzeitraum	Keine Einschränkungen
Suchbegriffe: Diabetes, diabetische, diabetisch	
Treffer	109
Ergebnis-Link	https://www.iqwig.de/projekte/projekte-und-ergebnisse/#searchQuery=query=Diabetes&page=1&rows=10&sortBy=score&sortOrder=desc&facet.filter.language=de https://www.iqwig.de/projekte/projekte-und-ergebnisse/#searchQuery=query=diabetische&page=1&rows=10&sortBy=score&sortOrder=desc&facet.filter.language=de
Eingeschlossene Treffer	4
IQWiG-Themencheck https://www.iqwig.de/sich-einbringen/themencheck-medizin/ → Übersicht ThemenCheck Berichte	
Treffer	35
Eingeschlossen	1 zur Aktualisierung PEF-Kapitel (Bericht aktuell noch in Bearbeitung, HT22-01, Stand 05/2024, vorläufiger Bericht vorhanden)

3.4.2 TiAb-Screening

Ein- und Ausschlusskriterien (Kapitel Nicht-medikamentöse Therapie)

Einschluss (E)	**E**	**Einschluss: Fragestellung passend, Studientyp passend** **Population:** Erwachsene Personen mit Typ-2-Diabetes **Intervention:** nicht-medikamentöse Interventionen **Kontrolle:** andere oder keine nicht-medikamentöse Intervention **Outcome:** Gesamtmortalität, kardiovaskuläre Morbidität und Mortalität, diabetesbedingte Folgemorbidität und Mortalität, Lebensqualität, Sicherheit und unerwünschte Wirkungen - im TiAb-Screening großzügiger Einschluss, je nach Themenbereich erfolgte eine Festlegung der priorisierten Endpunkte durch die Gruppe vor Betrachtung der Studien
Ausschluss (A)	**Aa**	Thematisch nicht passend: andere Erkrankung/Fragestellung/Thema (z. B. Kinder/Jugendliche, Schwangerschaft, nur Typ-1-Diabetes, Fragestellung für NVL insgesamt, oder für das Kapitel Nicht-medikamentöse Therapie nicht relevant)

	Aw	Zurückgezogen, oder Update vorhanden; aktuellere Reviews, die den Themenbereich abdecken vorhanden, falscher Zeitraum (Veröffentlichung vor 2013)
	As	Kein Systematischer Review

Suchergebnisse

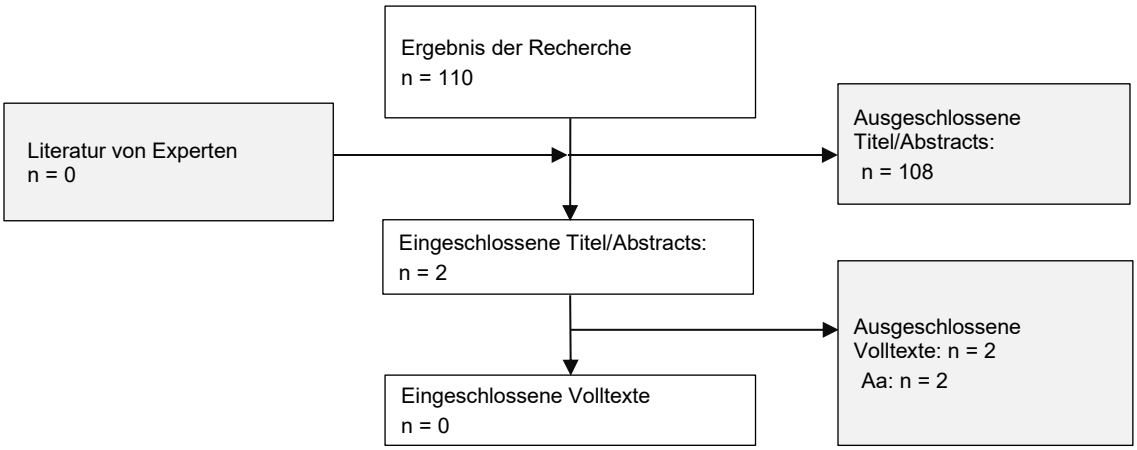
n=110 Treffer

Die Treffer wurden auf der Internetseite gescreent (Titel zu medikamentöser Therapie, Typ-1-Diabetes oder anderen nicht-relevanten Themen wurden direkt bei der Sichtung ausgeschlossen). Titel mit möglicher Relevanz für die aktuelle Bearbeitung (Kapitel Nicht-medikamentöse Therapie) werden hier aufgeführt:

- Nutzenbewertung nichtmedikamentöser Behandlungsstrategien bei Patienten mit Diabetes mellitus Typ 2: Steigerung der körperlichen Aktivität - Rapid Report, Letzte Aktualisierung 19.07.2012, Ein-/Ausschluss: Aa (relativ alt, wurde in der letzten NVL Therapie des Typ-2-Diabetes (2014) bereits berücksichtigt.
- Behandlung der Adipositas bei Patientinnen und Patienten mit Diabetes mellitus Typ 2 - Leitliniensynopse und ergänzende Recherche und Bewertung systematischer Übersichtsarbeiten, Letzte Aktualisierung 10.07.2012, Ein-/Ausschluss: Aa (relativ alt, Recherche bis 2011; es liegen aktuellere S3-Leitlinien hu Adipositas vor; Recherche zu Gewichtsmanagement wird für die NVL erfolgen)

Legende: Aa: Ausschluss (Thema für das Kapitel nicht passend, für die NVL nicht relevant), E: Einschluss

3.4.3 Flowchart



3.5 Zusammenfassung

	Cochrane	AHRQ	NICE	IQWiG
Einschlüsse	4 (+1)	0	3	0

4 Recherche im AWMF-Leitlinienregister

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)

Gezielte Recherche nach themenverwandten AWMF-Leitlinien: Leitliniensuche unter www.awmf.org/leitlinien/leitlinien-suche.html bei Anmeldung der Leitlinie und intermittierende während der Bearbeitung der einzelnen Themenbereiche.

- Zeitpunkt der letzten Suche: 19.02.2024
- Suchbegriff: Diabetes
- Status: alle
- Dokumententyp: alle
- Entwicklungsstufe: alle
- Gesellschaft: alle
- Organisation: alle
- Sortieren nach: Relevanz

Eingeschlossene Leitlinien

Siehe 6 Themenverwandte AWMF-Leitlinien und vorherige NVL zum Themenbereich Diabetes.

5 Evidenztabellen - Themenübergreifende systematische Recherche

5.1.1 Schulung

Attridge et al. (2014)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Attridge M, Creamer J, Ramsden M, et al. Culturally appropriate health education for people in ethnic minority groups with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2014(9):CD006424. DOI: 10.1002/14651858.CD006424.pub3. http://dx.doi.org/10.1002/14651858.CD006424.pub3	**Suche:** 2007 - July/September 2013, update of existing review **Fragestellung:** effectiveness of culturally appropriate health education for people in ethnic minority groups with T2DM. **Population:** people >16 years with T2DM from named ethnic minority groups residing in upper-middle-income or high-income countries **Intervention:** culturally appropriate health education*. **Comparator:** 'conventional' diabetes health education ('any mode of delivery of health education that does not take into account the cultural background and context of the individual or group to whom the intervention is directed).' **Primary outcomes:** - HbA1c - Health-related quality of life - Adverse events **Secondary outcomes:** unter anderem - All-cause and specific mortality. - Complications of diabetes. - Measures of participant empowerment and self-efficacy. - Measures of attitude. - Measures of knowledge of disease. - Blood pressure. - Body mass index (BMI). **Studies:** RCTs and quasi-RCTs	- total of 33 trials included (including 11 from the original 2008 review) n= 7453 participants - 28 trials providing suitable data for meta-analysis. - interventions provided in these studies were very different (participant numbers, duration of intervention, group versus individual intervention, setting), - most studies were caried out in the USA (African American populations (12 studies), or people of Hispanic identity (14 studies)), for others see review. - Most studies were set in deprived areas of four countries (USA, UK, Netherlands, Canada), in rural or inner city urban settings. **Glycaemic control (HbA1c)**: showed improvement following culturally appropriate health education compared with control groups who received 'usual care' - At 3 months post intervention: mean difference (MD) -0.4% (95% confidence interval (CI) -0.5 to -0.2); 14 trials; 1442 participants; high-quality evidence - 6 months post intervention: MD -0.5% (95% CI -0.7 to -0.4); 14 trials; 1972 participants; high-quality evidence. - at 12 months post intervention (MD -0.2% (95% CI -0.3 to -0.04); 9 trials; 1936 participants) - at 24 months post intervention (MD -0.3% (95% CI -0.6 to -0.1); 4 trials; 2268 participants; moderate-quality evidence) **Other Outcomes** - Neutral effects on **health-related quality of life measures**, blood pressure, body mass index, self-efficacy and empowerment compared with control groups. - general lack of reporting of **adverse events** in most studies - **Knowledge scores** showed improvement in the intervention group at three (standardised mean difference (SMD) 0.4 (95% CI 0.1 to 0.6), six (SMD 0.5 (95% CI 0.3 to 0.7)) and 12 months (SMD 0.4 (95% CI 0.1 to 0.6)) post intervention.	High y-y-n-y-y-y-y-y-y-y-y-y-y-y-y	- Heterogene Populationen und Interventionen (fraglich auf deutschen Versorgunskontext übertragbar)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	*Culturally appropriate' health education is defined here as education that is tailored to the cultural or religious beliefs and linguistic skills of the community being approached, taking into account likely literacy skills (Overland 1993).	- Data on the secondary outcomes of **diabetic complications, mortality** and health economics were lacking or were insufficient. **Authors' conclusions (Review)** Culturally appropriate health education has short- to medium-term effects on glycaemic control and on knowledge of diabetes and healthy lifestyles.		

Deakin 2005

Referenz	Jahr	Studiencharakteristika	Kommentar
Deakin, T.; McShane, C. E.; Cade, J. E.; Williams, R. D. (2005): Group based training for self-management strategies in people with type 2 diabetes mellitus. In: Cochrane Database Syst Rev (2), CD003417	2005	Objectives: To assess the effects of group-based, patient-centred training on clinical, lifestyle and psychosocial outcomes in people with type 2 diabetes. Search strategy: Date of last search was February 2003. Selection criteria: Randomised controlled and controlled clinical trials which evaluated group-based education programmes for adults with type 2 diabetes compared with routine treatment, waiting list control or no intervention. Studies were only included if the length of follow-up was six months or more and the intervention was at least one session with the minimum of six participants.	Aus der NVL Diabetes – Strukturierte Schulungsprogramme 2012 übernommen.

5.1.2 Gewichtsmanagement / Ernährung

Die ausführliche Extraktion der Reviews ist bei der Recherche zu dem jeweiligen Themenbereich zu finden.

Referenz	Jahr	Studiencharakteristika	Kommentar
Naude CE, Brand A, Schoonees A, et al. Low-carbohydrate versus balanced-carbohydrate diets for reducing weight and cardiovascular risk. Cochrane Database of Systematic Reviews 2022(1):CD013334. DOI: 10.1002/14651858.CD013334.pub2. http://dx.doi.org/10.1002/14651858.CD013334.pub2.	2022	Objectives To compare the effects of low-carbohydrate weight-reducing diets to weight-reducing diets with balanced ranges of carbohydrates, in relation to changes in weight and cardiovascular risk, in overweight and obese adults without and with type 2 diabetes mellitus (T2DM). Search: up to 25 June 2021 Selection criteria We included randomised controlled trials (RCTs) in adults (18 years+) who were overweight or living with obesity, without or with T2DM, and without or with cardiovascular conditions or risk factors. Trials had to compare low-carbohydrate weight-reducing diets to balanced-carbohydrate (45% to 65% of total energy (TE)) weight-reducing diets, have a weight-reducing phase of 2 weeks or longer and be explicitly implemented for the primary purpose of reducing weight, with or without advice to restrict energy intake.	

Referenz	Jahr	Studiencharakteristika	Kommentar
Allaf M. Intermittent fasting for the prevention of cardiovascular disease. Cochrane Database Syst Rev 2021; 1(1):CD013496. https://www.ncbi.nlm.nih.gov/pubmed/33512717.	2021	OBJECTIVES To determine the role of IF in preventing and reducing the risk of CVD in people with or without prior documented CVD. SEARCH: 12 December 2019 SELECTION CRITERIA We included randomised controlled trials comparing IF to ad libitum feeding (eating at any time with no specific caloric restriction) or continuous energy restriction (CER). Participants had to be over the age of 18 and included those with and without cardiometabolic risk factors.	
Meng Y, Bai H, Wang S, Li Z, Wang Q, Chen L (2017) Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes research and clinical practice 131:124–31 11. https://pubmed.ncbi.nlm.nih.gov/28750216/ Identifiziert über NICE NG28	2017	OBJECTIVE of this systematic review and meta-analysis is to assess the efficacy of Low Carbohydrate Diet (LCD) compared with a normal or high carbohydrate diet in patients with type 2 diabetes. METHODS: We searched MEDLINE, EMBASE, and Cochrane Library database for randomized controlled trials. Research-es which reported the change in weight loss, blood glucose, and blood lipid levels were included.	
Huntriss R, Campbell M, Bedwell C (2018) The inter-pretation and effect of a low carbohydrate diet in the management of type 2 dia-betes: a systematic review and meta-analysis of ran-domised controlled trials. European Journal of Clini-cal Nutrition 72(3):311–25 12. https://pubmed.ncbi.nlm.nih.gov/29269890/ Identifiziert über NICE NG28	2018	OBJECTIVES Recently, the role of a low-carbohydrate diet in diabetes management has generated interest with claims being made re-garding its superiority over the traditional high-carbohydrate, low-fat dietary approach. This systematic review and meta-analysis evaluated the interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes. SUBJECTS/METHODS Randomised controlled trials were searched for which included adults with type 2 diabetes aged 18 years or more. The intervention was a low-carbohydrate diet as defined by the author compared to a control group of usual care. MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, ISRCTN, ProQuest and opengrey.eu were searched. Independent experts were contacted and reference lists of selected papers were checked. Results were analysed descriptively and meta-analyses were completed to include trials that presented data at 1 year.	

Referenz	Jahr	Studiencharakteristika	Kommentar
Korsmo-Haugen H-K, Brurberg KG, Mann J, Aas A-M (2019) Carbohydrate quantity in the dietary man-agement of type 2 diabetes: A systematic review and meta-analysis. Diabetes, Obesity & Metabolism 21(1):15–27 https://pubmed.ncbi.nlm.nih.gov/30098129/ Identifiziert über NICE NG28	2019	OBJECTIVES This systematic review and meta-analysis (registration number: CRD42013005825) compares the effects of low carbohy-drate diets (LCDs) on body weight, glycaemic control, lipid profile and blood pressure with the effects of higher carbo-hydrate diets (HCDs) in adults with type 2 diabetes. METHODS MEDLINE, EMBASE, CENTRAL, CINAHL, Food Science Source and SweMed+ databases were systematically searched to identify randomized controlled trials (duration ≥3 months) investigating the effects of an LCD compared to an HCD in the management of type 2 diabetes. Data were extracted and pooled using a random effects model and were expressed as mean differences and risk ratio. Subgroup analyses were undertaken to examine the effects of duration of intervention, extent of carbohydrate restriction and risk of bias. The certainty of evidence was assessed using GRADE.	

Lohner 2020

Darstellung zur Information. Zitat wurde nicht eingeschlossen und wird nicht im Hintergrundtext zitiert.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Lohner S, Kuellenberg dG, Toews I, et al. Non-nutritive sweeteners for diabetes mellitus. Cochrane Database of Systematic Reviews 2020(5):CD012885. DOI: 10.1002/14651858.CD012885.pub2. http://dx.doi.org/10.1002/14651858.CD012885.pub2.	**Zeitpunkt der Suche:** last search of all databases (except for Scopus) May 2019. Scopus: January 2019. **Fragestellung:** effects of non-nutritive sweeteners in people with diabetes mellitus. **Population:** individuals with type 1 or type 2 diabetes **Intervention:** any type of NNS Trials with concomitant behaviour-changing interventions, such as diet, exercise, or both, were eligible for in-clusion, given that the concomitant interventions were the same in the intervention and comparator groups. **Control:** usual diet, no intervention, pla-	included 9 RCTs that randomised a total of 979 people with type 1 or type 2 diabetes. - intervention duration ranged from 4 to 10 months. - we judged none of these trials as at low risk of bias for all 'Risk of bias' domains; most of the included trials did not report the method of randomisation. **Vergleich: dietary supplement containing NNS versus sugar:** - 3 trials - HbA1c was 0.4% higher in the NNS group (95% CI −0.5 to 1.2; P = 0.44; 3 trials; 72 participants; very low-certainty evidence). - weight change: MD −0.1 kg (95% CI −2.7 to 2.6; P = 0.96; 3 trials; 72 participants; very low-certainty evidence). - None of the trials with sugar as comparator reported on adverse events. **Vergleich: NNS versus placebo:** - 5 trials - HbA1c: MD 0%, 95% CI −0.1 to 0.1; P = 0.99; 4 trials; 360 participants; very low-certainty evidence. The 95% prediction interval ranged between −0.3% and 0.3%. - body weight: MD −0.2 kg, 95% CI −1 to 0.6; P = 0.64; 2 trials; 184 participants; very	High y-y-n(?)-y-y-y-y-y-y-y-y-y-y-y-y	The included trials did not report data on health-related quality of life, diabetes complications, all-cause mortality, or socioeconomic effects. Für HbA1c keine statistisch signifikant positiven Effekte. Thema des Reviews war nicht

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	cebo, water, a different NNS, or a nutritive sweetener **Studies:** RCTs with a duration ≥ 4 weeks **Subgroup-analysis:** Type 1 diabetes or Type 2 diabetes	low-certainty evidence. - 3 trials reported the numbers of participants experiencing at least one non-serious adverse event: 36/113 participants (31.9%) in the NNS group versus 42/118 participants (35.6%) in the placebo group (RR 0.78, 95% CI 0.39 to 1.56; P = 0.48; 3 trials; 231 participants; very low-certainty evidence). **Vergleich: NNS versus nutritive low-calorie sweetener (tagatose):** - 1 trial - HbA1c was 0.3% higher in the NNS group (95% CI 0.1 to 0.4; P = 0.01; 1 trial; 354 participants; very low-certainty evidence). - This trial did not report body weight data and adverse events. **The included trials did not report data on health-related quality of life, diabetes complications, all-cause mortality, or socioeconomic effects.** „We did not perform subgroup analyses because there were not enough trials to estimate effects in various subgroups“„One trial included only individuals with type 1 diabetes (Chantelau 1985); two trials included both individuals with type 1 and 2 diabetes (Barriocanal 2008; Nehrling 1985), whilst all other trials (6) included participants with type 2 diabetes only.“ Authors' conclusions (Review): There is inconclusive evidence of very low certainty regarding the effects of NNS consumption compared with either sugar, placebo, or nutritive low-calorie sweetener consumption on clinically relevant benefit or harm for HbA1c, body weight, and adverse events in people with type 1 or type 2 diabetes. Data on health-related quality of life, diabetes complications, all-cause mortality, and socioeconomic effects are lacking.		Fragestellung in der Überarbeitung des Kapitels. Für Informationen hinsichtlich kalorienfreier oder kalorienarmer Süßungsmittel verweist die Leitliniengruppe auf die S3 Leitlinie „Prävention und Therapie der Adipositas“ [7].

5.1.3 Stressbewältigung

Die ausführliche Extraktion der Reviews ist bei der Recherche zu dem jeweiligen Themenbereich zu finden.

Referenz	Jahr	Studiencharakteristika	Kommentar
Chew BH. Psychological interventions for diabetes-related distress in adults with type 2 diabetes mellitus. Cochrane Database Syst Rev 2017; 9(9):CD011469.	2017	OBJECTIVES: To assess the effects of psychological interventions for diabetes-related distress in adults with T2DM. SEARCH: December 2014 for BASE and 21 September 2016 for all other databases. SELECTION CRITERIA We included randomised controlled trials (RCTs) on the effects of psychological interventions for DRD in adults (18 years and	

Referenz	Jahr	Studiencharakteristika	Kommentar
https://www.ncbi.nlm.nih.gov/pubmed/28954185		older) with T2DM. We included trials if they compared different psychological interventions or compared a psychological intervention with usual care. Primary outcomes were DRD, health-related quality of life (HRQoL) and adverse events. Secondary outcomes were self-efficacy, glycosylated haemoglobin A1c (HbA1c), blood pressure, diabetes-related complications, all-cause mortality and socioeconomic effects.	

6 Themenverwandte AWMF-Leitlinien und vorherige NVL zum Themenbereich Diabetes

Zitat	Kommentar
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2014): Nationale VersorgungsLeitlinie Therapie des Typ-2-Diabetes - Langfassung, 1. Auflage. Version 4. Online verfügbar unter http://doi.org/10.6101/AZQ/000213, zuletzt geprüft am 12.01.2017.	NVL Therapie des Typ-2-Diabetes (2014)
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissen-schaftlichen Medizinischen Fachgesellschaften (AWMF (2012): Nationale VersorgungsLeitlinie Diabetes. Strukturierte Schulungsprogramme - Langfassung, 1. Auflage. Version 4. Online verfügbar unter http://doi.org/10.6101/AZQ/000295, zuletzt geprüft am 13.07.2016.	NVL Diabetes – Strukturierte Schulungsprogramme
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2013): Nationale VersorgungsLeitlinie Diabetes - Strukturierte Schulungsprogramme - Leitlinienreport, 1. Auflage. Version 3. Online verfügbar unter http://doi.org/10.6101/AZQ/000310, zuletzt geprüft am 01.08.2016.	Leitlinienreport NVL Diabetes - Strukturierte Schulungsprogramme
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): Nationale VersorgungsLeitlinie Typ-2-Diabetes – Langfassung, Version 3.0. Online verfügbar unter https://doi.org/10.6101/AZQ/000503, zuletzt geprüft am 24.01.2024.	NVL Typ-2-Diabetes Version 3, Langfassung
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): Nationale VersorgungsLeitlinie Typ-2-Diabetes – Leitlinienreport. Version 3.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000500, zuletzt geprüft am 15.05.2023	Leitlinienreport NVL Typ-2-Diabetes Version 3
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2021): Nationale VersorgungsLeitlinie COPD – Langfassung, 2. Auflage. Version 1. Online verfügbar unter http://doi.org/10.6101/AZQ/000477, zuletzt geprüft am 17.08.2021.	NVL COPD
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2022): Nationale VersorgungsLeitlinie Chronische KHK – Langfassung. Version 6.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000491, zuletzt geprüft am 15.09.2022.	NVL Chronischen KHK
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): Nationale VersorgungsLeitlinie Chronische Herzinsuffizienz – Langfassung, Version 4.0. Online verfügbar unter	NVL Chronische Herzinsuffizienz

Zitat	Kommentar
http://doi.org/10.6101/AZQ/000510, zuletzt geprüft am 12.12.2023.	
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): Nationale VersorgungsLeitlinie Hypertonie - Langfassung. Version 1.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000502, zuletzt geprüft am 29.06.2023.	NVL Hypertonie
Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF); Deutsche Gesellschaft für Psychiatrie, Psychotherapie und Nervenheilkunde (DGPPN); Deutsche Gesellschaft für Suchtforschung und Suchttherapie (DG-Sucht); Zentralinstitut für Seelische Gesundheit (ZI) (2021): S3-Leitlinie Rauchen und Tabakabhängigkeit: Screening, Diagnostik und Behandlung. Registernummer 076-006, Version 2021-01. Online verfügbar unter https://www.awmf.org/leitlinien/detail/ll/076-006.html, zuletzt geprüft am 11.03.2021	Tabak-LL
Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie (DGPM); Deutsches Kollegium für Psychosomatische Medizin (DKPM) (2020): S3-Leitlinie Screening, Diagnose und Behandlung alkoholbezogener Störungen. Registernummer 076-001. Version 2021-02. Online verfügbar unter https://www.awmf.org/leitlinien/detail/ll/076-001.html, zuletzt geprüft am 20.06.2022.	Alkoholbezogene Störungen
Deutsche Gesellschaft für Sportmedizin und Prävention (DGSP); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2024): S2k-Leitlinie Sportmedizinische Vorsorgeuntersuchung. Registernummer 066 - 002, Version 1.0. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/066-002, zuletzt geprüft am 01.07.2024.	Sportmedizinische Vorsorgeuntersuchung
S3-Leitlinie Adipositas - Prävention und Therapie, AWMF-Register-Nummer 050/001, Version 5.0, Oktober 2024. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/050-001, zuletzt geprüft am 19.11.2024	Adipositas-LL
S3-Leitlinie Chirurgie der Adipositas und metabolischer Erkrankungen, AWMF-Register-Nummer 088 – 001, Version 2.0, Stand 01.02.2018, in Überarbeitung	

Weitere themenverwandte AWMF-Leitlinien und vorherige NVL sind im Leitlinienreport der Version 3 aufgeführt [4].

7 Von der Leitliniengruppe eingebrachte nationale und internationale Konsensuspapiere/Leitlinien

Zitat	Kommentar
Skurk, Thomas; Bosy-Westphal, Anja; Grünerbel, Arthur; Kabisch, Stefan; Keuthage, Winfried; Kronsbein, Peter et al. (2023): Empfehlungen zur Ernährung von Personen mit Typ-2-Diabetes mellitus. In: Diabet Stoffw 18 (S 02), S270-S304. DOI: 10.1055/a-1997-7924.	Praxisempfehlung Ernährung DDG
DGE Gut essen und trinken – Die DGE-Empfehlungen (https://www.dge.de/gesunde-ernaehrung/gut-essen-und-trinken/dge-empfehlungen/)	DGE-Empfehlungen
Deutsche Gesellschaft für Ernährung (DGE). DGE-Ernährungskreis: Der DGE-Ernährungskreis zeigt auf einen Blick wie eine gesunde und ökologisch nachhaltige Ernährung aussieht. 2024 [cited: 2024-10-15]. https://www.dge.de/gesunde-ernaehrung/gut-essen-und-trinken/dge-ernaehrungskreis/. #34569	DGE-Ernährungskreis
Schäfer AC, Boeing H, Conrad J, et al. Wissenschaftliche Grundlagen der lebensmittelbezogenen Ernährungsempfehlungen für Deutschland: Methodik und Ableitungskonzepte. Ernahrungs Umschau 2024; 71(3):M158–66. e5–7. DOI: 10.4455/eu.2024.009. # 34566	DGE Wissenschaftliche Grundlagen
Deutsche Gesellschaft für Ernährung (DGE). Am besten null Promille – neues DGE-Positionspapier zu Alkohol. 2024 [cited: 2024-09-27]. https://www.dge.de/presse/meldungen/2024/dge-positionspapier-zu-alkohol/. Darüber identifiziert: Canadian Centre on Substance Use and Addiction (CCSA). Canada's guidance on alcohol and health: Final report. Ottawa, Ont.: Canadian Centre on Substance Use and Addiction; 2023. https://www.ccsa.ca/canadas-guidance-alcohol-and-health.	DGE-Positionspapier Alkohol
World Health Organization (WHO) (2020): WHO guidelines on physical activity and sedentary behaviour. Online verfügbar unter https://apps.who.int/iris/rest/bitstreams/1315866/retrieve, zuletzt geprüft am 23.02.2023.	Über die systematische Recherche identifiziert
World Health Organization (WHO) (2024): Global levels of physical inactivity in adults. Off track for 2030. Geneva: WHO. Online verfügbar unter https://www.who.int/publications/i/item/9789240096905.	
Şat, Sebahat; Aydınkoç-Tuzcu, Kadriye; Berger, Faize; Barakat, Alain; Danquah, Ina; Schindler, Karin; Fasching, Peter (2023): Diabetes und Migration. In: Diabetol Stoffwechs 18 (2 Suppl), S428–S448. DOI: 10.1055/a-2076-0328.	DDG Diabetes und Migration

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2. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie Typ-2-Diabetes, Ergänzung zu Version 3: Kapitel Nicht-medikamentöse Therapie. 2024 [cited: 2024-11-20]. DOI: 10.6101/AZQ/000518. https://register.awmf.org/de/leitlinien/detail/nvl-001.
3. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie Typ-2-Diabetes – Leitlinienreport, 2. Auflage. Version 1. 2021 [cited: 2021-03-25]. DOI: 10.6101/AZQ/000476. http://doi.org/10.6101/AZQ/000476.
4. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie Typ-2-Diabetes – Leitlinienreport. Version 3.0. 2023 [cited: 2023-05-15]. DOI: 10.6101/AZQ/000500. http://doi.org/10.6101/AZQ/000500.
5. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie Therapie des Typ-2-Diabetes - Langfassung, 1. Auflage. Version 4. 2014 [cited: 2017-01-12]. DOI: 10.6101/AZQ/000213. http://doi.org/10.6101/AZQ/000213.
6. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF. Nationale VersorgungsLeitlinie Diabetes. Strukturierte Schulungsprogramme - Langfassung, 1. Auflage. Version 4. 2012 [cited: 2016-07-13]. DOI: 10.6101/AZQ/000295. http://doi.org/10.6101/AZQ/000295.
7. Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF), Deutsche Adipositas-Gesellschaft (DAG). S3-Leitlinie Prävention und Therapie der Adipositas: Registernummer 050 - 001, Version 5.0. 2024 [cited: 2024-10-14]. https://register.awmf.org/de/leitlinien/detail/050-001.

NATIONALE VERSORGUNGS LEITLINIEN

Nationale VersorgungsLeitlinie

Typ-2-Diabetes

Recherchedokumentation + Evidenztabellen
zum Kapitel Nicht-medikamentöse Therapie
Teil 2: Gewichtsmanagement / Ernährung

Ergänzung zu Version 3

AWMF-Register-Nr. nvl-001

Träger:

Bundesärztekammer

Kassenärztliche Bundesvereinigung

Arbeitsgemeinschaft der Wissenschaftlichen
Medizinischen Fachgesellschaften

BUNDESÄRZTEKAMMER KBV AWMF

Inhaltverzeichnis

1 Aufbau der Recherche-/Evidenz-Dokumente

Zur leichteren Handhabung der umfangreichen Evidenzrecherchen werden die Recherchedokumentationen und Evidenztabellen in verschiedenen Teilen dargestellt:

- Teil 1
  - Evidenzbasis des Kapitels Nicht-medikamentöse Therapie
  - Themenübergreifende systematische Recherche
  - Themenverwandte AWMF-Leitlinien
  - Nationale und internationale Konsensuspapiere (von der Leitliniengruppe eingebrachte Literatur)
- Teil 2 (vorliegendes Dokument)
  - Systematische Recherche zum Gewichtsmanagement
  - Systematische Recherche zu Formuladiäten
  - Systematische Recherche zu Mediterraner Diät
- Teil 3
  - Systematische Recherche zu körperlicher Aktivität und strukturierten Bewegunsprogrammen
- Teil 4
  - Systematische Recherche Alkoholkonsum und Neuropathie
  - Systemtische Recherche Interventionen zur Stressbewältigung

2 Recherchedokumentation Gewichtsmanagement / Ernährung

2.1 Systematische Recherche: Gewichtsmanagement

2.1.1 PICO-Fragestellung

Fragestellung 1: Welchen Nutzen hat die tatsächlich erreichte Gewichtsreduktion bei übergewichtigen und/oder adipösen Personen mit Typ-2-Diabetes auf patientenrelevante Langzeitendpunkte?

P	übergewichtige und/oder adipöse, erwachsene Menschen mit Typ-2-Diabetes
I	erreichte Gewichtsreduktion durch weight loss-Interventions (Ernährung, Lebensstil)
C	Vergleich zu weniger / mehr / keiner Gewichtsreduktion
O	kardiovaskuläre Morbidität /Mortalität, Gesamtmortalität, Lebensqualität, Notwendigkeit einer medikamentösen Therapie (Diabetesremission)
S	Systematische Reviews von RCTs ab 2014

Sprache: deutsch, englisch

Fragestellung 2: Welchen Nutzen haben Interventionen zur Gewichtsreduktion bei übergewichtigen und/oder adipösen Personen mit Typ-2-Diabetes auf patitentenrelevante Langzeitendpunkte?

P	übergewichtige und/oder adipöse, erwachsene Menschen mit Typ-2-Diabetes
I	Interventionen zur Gewichtsreduktion
C	jegliche Vergleiche (z. B. usual care)
O	kardiovaskuläre Morbidität / Mortalität, Gesamtmortalität, Lebensqualität, Notwendigkeit einer medikamentösen Therapie (Diabetesremission)
S	Systematische Reviews von RCTs ab 2014

Sprache: deutsch, englisch

Betrachtete Interventionen (gemäß 1. Sitzung der Arbeitsgruppe), insbesondere:

- Low Carbohydrate Diets,
- Very low carbohydrate diets,
- Intervallfasten,
- Formula-Diäten und
- Mediterrane Diät.

Zu den Themen „Low carbohydrate diet“ und „Intervallfasten“ waren in der themenübergreifenden systematischen Recherche zum Schlagwort „diabetes“ (bei Cochrane, NICE, IQWiG und AHRQ) Übersichtsarbeiten identifiziert worden. Diese sind an den entsprechenden Stellen ebenfalls aufgeführt.

Zu Formuladiäten und mediterraner Diät erfolgte eine gezielte systematische Recherche bei PubMed, Epistemonikos und in der Cochrane-Library, da in den Recherchen keine ausreichende Evidenz identifiziert worden war.

2.1.2 Recherchestrategien

Medline via Pubmed (www.pubmed.gov) (29.06.2021)

Search	Most Recent Queries	Result
#19	**#16 AND #17 Filters: from 2014/1/1 - 29/06/21**	**976**
#18	#16 AND #17	1,531
#17	("systematic review"[Title] OR "meta-analysis"[Publication Type] OR "meta-analysis"[Title] OR "systematic literature review"[Title] OR "this systematic review"[Text Word] OR "pooling project"[Text Word] OR ("systematic review"[Title/Abstract] AND "review"[Publication Type]) OR "meta synthesis"[Title] OR "meta analy*"[Title] OR "integrative review"[Text Word] OR "integrative research review"[Text Word] OR "rapid review"[Text Word] OR "umbrella review"[Text Word] OR "consensus development conference"[Publication Type] OR "practice guideline"[Publication Type] OR "drug class reviews"[Title] OR "cochrane database syst rev"[Journal] OR "acp j club"[Journal] OR "health technol assess"[Journal] OR "evid rep technol assess summ"[Journal] OR "jbi database system rev implement rep"[Journal] OR ("clinical guideline"[Text Word] AND "management"[Text Word]) OR (("evidence based"[Title] OR "evidence based medicine"[MeSH Terms] OR "best practice*"[Title] OR "evidence synthesis"[Title/Abstract]) AND ("review"[Publication Type] OR "diseases category"[MeSH Terms] OR "behavior and behavior mechanisms"[MeSH Terms] OR "therapeutics"[MeSH Terms] OR "evaluation studies"[Publication Type] OR "guideline"[Publication Type] OR "pmc-book"[All Fields])) OR (("systematic"[Text Word] OR "systematically"[Text Word] OR "critical"[Title/Abstract] OR "study selection"[Text Word] OR ("predetermined"[Text Word] AND "criteri*"[Text Word]) OR "exclusion criteri*"[Text Word] OR "main outcome measures"[Text Word] OR "standard of care"[Text Word] OR "standards of care"[Text Word]) AND ("survey"[Title/Abstract] OR "surveys"[Title/Abstract] OR "overview*"[Text Word] OR "review"[Title/Abstract] OR "reviews"[Title/Abstract] OR "search*"[Text Word] OR "handsearch"[Text Word] OR "analysis"[Title] OR "critique"[Title/Abstract] OR "appraisal"[Text Word] OR ("reduction"[Text Word] AND ("risk"[MeSH Terms] OR "risk"[Text Word]) AND ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields] OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]))))) AND ("literature"[Title/Abstract] OR "articles"[Title/Abstract] OR "publications"[Title/Abstract] OR "publication"[Title/Abstract] OR "bibliography"[Title/Abstract] OR "bibliographies"[Title/Abstract] OR "published"[Title/Abstract] OR "pooled data"[Text Word] OR "unpublished"[Text Word] OR "citation"[Text Word] OR "citations"[Text Word] OR "database"[Title/Abstract] OR "internet"[Title/Abstract] OR "textbooks"[Title/Abstract] OR "references"[Text Word] OR "scales"[Text Word] OR "papers"[Text Word] OR "datasets"[Text Word] OR "trials"[Title/Abstract] OR "meta analy*"[Text Word] OR ("clinical"[Title/Abstract] AND "studies"[Title/Abstract]) OR	534,804

Search	Most Recent Queries	Result
	"treatment outcome"[MeSH Terms] OR ("outcome"[Text Word]) OR "pmcbook"[All Fields])))) NOT ("letter"[Publication Type] OR "newspaper article"[Publication Type])	
#16	#5 AND #15	29,546
#15	#6 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	644,185
#14	Obesit*[tiab] AND management*[tiab]	19,764
#13	"Obesity management"[Mesh]	29,058
#12	Reducing diet*[tiab]	979
#11	"Diet, Reducing"[Mesh]	11,263
#10	"Weight reduction programs"[Mesh]	2,615
#9	#7 AND #8	588,970
#8	Weight[tiab]	872,811
#7	Loss[tiab] OR losses[tiab] OR management*[tiab] OR decreas*[Title/Abstract] OR control*[Title/Abstract] OR maint*[Title/Abstract] OR reduc*[tiab] OR losing[tiab] OR watch*[tiab] OR change[tiab] OR lower*[tiab]	11,350,143
#6	"Body weight changes"[Mesh]	75,501
#5	#3 AND #4	111,737
#4	Obese[tiab] OR adipos*[tiab] OR obesit*[tiab] OR overweight[tiab] OR overweight[Mesh]	463,497
#3	#1 OR #2	739,971
#2	"Diabetes Mellitus"[Mesh]	448,374
#1	diabet*[tiab]	680,657

Epistemonikos (www.epistemonikos.org) (30.06.2021)

Search	Most Recent Queries	Result
#2	**Publication year: from 2014 to 2021** **Publication type: Systematic review**	**519**
#1	(title:(((title:(obesit*) OR abstract:(obesit*)) AND (title:(management*) OR abstract:(management*))) OR ((title:(diet) OR abstract:(diet)) AND (title:(reducing) OR abstract:(reducing))) OR ((title:(weight) OR abstract:(weight)) AND (title:(Loss OR losses OR management* OR decreas* OR control* OR maint* OR reduc* OR losing OR watch* OR change OR lower*) OR abstract:(Loss OR losses OR management* OR decreas* OR control* OR maint* OR reduc* OR losing OR watch* OR change OR lower*)))) OR abstract:(((title:(obesit*) OR abstract:(obesit*)) AND (title:(management*)	1.994

Search	Most Recent Queries	Result
	OR abstract:(management*))) OR ((title:(diet) OR abstract:(diet)) AND (title:(reducing) OR abstract:(reducing))) OR ((title:(weight) OR abstract:(weight)) AND (title:(Loss OR losses OR management* OR decreas* OR control* OR maint* OR reduc* OR losing OR watch* OR change OR lower*) OR abstract:(Loss OR losses OR management* OR decreas* OR control* OR maint* OR reduc* OR losing OR watch* OR change OR lower*))))) AND (title:((title:(obese OR adipos* OR obesit* OR overweight) OR abstract:(obese OR adipos* OR obesit* OR overweight)) AND (title:((title:(diabetes OR diabet*) OR abstract:(diabetes OR diabet*))) OR abstract:((title:(diabetes OR diabet*) OR abstract:(diabetes OR diabet*))))) OR abstract:((title:(obese OR adipos* OR obesit* OR overweight) OR abstract:(obese OR adipos* OR obesit* OR overweight)) AND (title:((title:(diabetes OR diabet*) OR abstract:(diabetes OR diabet*))) OR abstract:((title:(diabetes OR diabet*) OR abstract:(diabetes OR diabet*))))))	

2.1.3 Übersicht der eingeschlossenen Treffer

	Medline	Epistemonikos	Summe
Aggregierte Evidenz	976	519	**1495**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 415

A2 (nicht englisch/deutsch): 20

A3 (Conference Abstract): 1

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 1059

2.1.4 TiAb-Screening

Kategorie		Beschreibung
Ausschluss	Aa	Population nicht passend: Kinder / Jugendliche, andere Erkrankungen (non-alcoholic fatty liver disease, PCOS), gleichzeitige Auswertung von Patient*innen mit Typ-1-DM und Typ-2-DM. Diabetes in der und um die Schwangerschaft, Gestationsdiabetes, besondere Patientengruppen (nach NTX, severe mentally ill)
		Intervention: andere Interventionen*, anderes Thema, keine Interventionen betrachtet
	As	Studientyp: kein systematischer Review von RCTs, Leitlinie ohne Evidenzbeschreibung, Qualität der Methodik nicht ausreichend (Hochwertige Umbrella-Reviews können zur Überprüfung der eigenen Rechercheergebnisse genutzt werden)
	Ap	Protokoll (thematisch nicht relevant für NVL)
	Aw	Zurückgezogen (withdrawn)
Einschluss	**Population:** Erwachsene mit Typ-2-Diabetes und Übergewicht (BMI 25-29,9kg/m^2) oder Adipositas (BMI ≥30kg/m^2)	
	Intervention:	
	E1	**erreichte Gewichtsreduktion** (unabhängig von der Intervention)
	E2	Reviews zur Beurteilung des Nutzens von Interventionen, die für das Kapitel Gewichtsmanagement/Ernährungstherapie interessant sind (intermittierendes

Kategorie		Beschreibung
		Fasten, mediterrane Diät, very low calorie diets (VLCD), ketogenic diet…), aber für die erste Fragestellung nicht passend sind (Gewichtsverlust als ein Endpunkt und nicht als Intervention/Faktor)
	Vergleich: jeglicher Vergleich, je nach Fragestellung (Fragestellung 1 oder Fragestellung 2 z. B. usual care, Intervention ohne Gewichtsreduktion/Kontrolle, Vergleich zu Baseline-daten (bei HbA1c).	
	Endpunkte: Mortalität, kardiovaskuläre Morbidität, HbA1c mit Auswirkung auf Medikation, Diabetesremission, Lebensqualität	
	Ez (A)	Zurückgestellte Themen: - non-nutritive sweetener (Studie von Lohner et al., 2020 aus der the-menübergreifenden Recherche (Cochrane) wurde später in der Leitlinien-gruppe betrachtet), - breakfast cereal consumption, - physical activity measures, - fermented dairy products, - tea and tea extracts, chinese herbal medicine, sickeldod-samen (Cas-siae semen), Yerba mate, Gymnema sylvestre, Safran, Melatonin

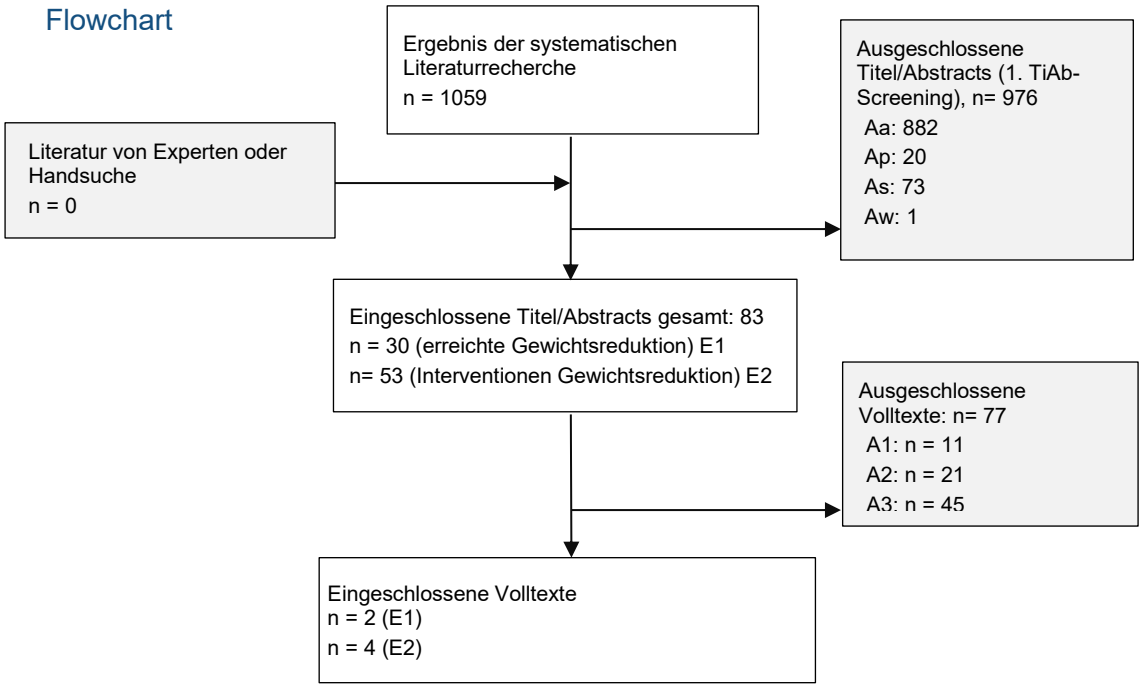
* **Ausgeschlossen:**

- Gewichtsreduktion durch bariatrische Chirurgie/Adipositaschirurgie/metabolische Chirurgie wird nicht im Rahmen der NVL behandelt. Es steht eine S3-LL zur Verfügung. Diese wird aktuell überarbeitet (S3-Leitlinie Chirurgie der Adipositas und metabolischer Erkrankungen, AWMF-Register-Nr: 088-001, Version 2.0, Stand 01.02.2018, aktuell in Überarbeitung).
- Gewichtsreduktion durch (glukosesenkende) Medikamente (GLP-1-RA und SGLT-2-I), ggf. auch andere Medikamente (wie Locaserin).
- Schwingshackl L. Impact of different dietary approaches on glycemic control and cardiovascular risk factors in patients with type 2 diabetes: A protocol for a systematic review and network meta-analysis. Syst Rev 2017; 6(1):57. https://www.ncbi.nlm.nih.gov/pubmed/28320464. Protokoll für interessanten Review. Untersucht die verschiedenen Ernährungsformen, die im Rahmen des NVL-Kapitels betrachtet werden. -> In der Recherche zur mediterranen Diät/Handsuche 01/2024 identifiziert: Schwingshackl L. A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. Eur J Epidemiol 2018; 33(2):157–70. https://www.ncbi.nlm.nih.gov/pubmed/29302846

Handsuche/Update 01/2024: Über die Recherche zu mediterraner Diät identifiziert:

- Goldenberg JZ, Day A, Brinkworth GD, et al. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: Systematic review and meta-analysis of published and unpublished randomized trial data. BMJ 2021; 372:m4743. DOI: 10.1136/bmj.m4743. http://www.ncbi.nlm.nih.gov/pubmed/33441384. (per Altert und über die Recherche zur mediterranen Diät identifiziert (wurde im Umbrella-Review von Szczerba 2023 genannt)).
- Silverii, G. A.; Botarelli, L.; Dicembrini, I.; Girolamo, V.; Santagiuliana, F.; Monami, M.; Mannucci, E. (2020): Low-carbohydrate diets and type 2 diabetes treatment. A meta-analysis of randomized controlled trials. In: Acta Diabetol 57 (11), S. 1375–1382. DOI: 10.1016/S0939-4753(04)80052-8. (nicht in der Recherche zu Gewichtsmanagement gefunden, da „adipös/overweight“ nicht im TiAb enthalten (siehe Zeile #4 der PubMed-Recherche).
- Szczerba E. Diet in the management of type 2 diabetes: Umbrella review of systematic reviews with meta-analyses of randomised controlled trials. BMJ Med 2023; 2(1):e000664. (in der Fragestellung des Reviews nicht speziell nach adipösen oder übergewichtigen Personen mit Typ-2-Diabetes gesucht). https://www.ncbi.nlm.nih.gov/pubmed/38027413
- Churuangsuk C. Diets for weight management in adults with type 2 diabetes: An umbrella review of published meta-analyses and systematic review of trials of diets for diabetes remission. Diabetologia 2022; 65(1):14–36. https://www.ncbi.nlm.nih.gov/pubmed/34796367.
- Schwingshackl L. A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. Eur J Epidemiol 2018; 33(2):157–70. https://www.ncbi.nlm.nih.gov/pubmed/29302846

2.1.5 Flowchart



TiAb-Legende:

Aa: Thema nicht passend, Population nicht passend

Ap: Protokoll

As: methodisch nicht ausreichend, kein SR

Aw: zurückgezogen

Legende Volltextscreening:

A1: Population nicht passend

A2: Endpunkte nicht passend, Fragestellung nicht passend (Assoziationsstudien ohne Intervention)

A3: kein systematischer Review, Review qualitativ von der Methodik her nicht ausreichend, Recherche für Fragestellung zu alt, Sprache: nicht englisch oder deutsch.

Eingeschlossene Artikel

E1: Martenstyn 2020, Gummesson 2017

E2: Naude 2014/2022 , Brown 2017 (nicht im Text zitiert), Huang 2020, Ross 2021

Betrachtete Literatur aus anderen systematischen Recherchen und der themenübergreifenden systematischen Recherche: z. B. Goldenberg 2021, Churuangsuk 2022, Silverii 2020, Szczerba 2023, Schwingshackl 2018, Korsmo-Haugen 2019, Huntriss 2018, Meng 2017, Allaf 2021, (Gregg 2012, Lean 2018 und Taheri 2020 zitiert nach Churuangsuk 2022), siehe auch weitere Recherchen unten.

2.1.6 Evidenzzusammenfassung

Siehe Kapitel Nicht-medikamentöse Therapie (Ergänzung zu Version 3) [1].

2.2 Systematische Recherche Formuladiäten

2.2.1 PICO-Fragestellung

P: Erwachsene Patient*innen mit Typ-2-Diabetes

I: Intervention: Formula-Diäten

C: jegliche Vergleiche (z. B. usual care)

O: 1. Kardiovaskuläre Morbidität / Mortalität, Gesamtmortalität

2. Lebensqualität

3. ggf. HbA1c, wenn dadurch eine medikamentöse Therapie verhindert wird

S: Systematische Übersichtsarbeiten von RCTs ab 2017

Sprache: deutsch, englisch

Suchzeitraum der Recherche wurde entsprechend der Publikation der 1-Jahres Daten der DiRECT-Studie (Landmark study) gewählt.

2.2.2 Recherchestrategien

Medline via Pubmed (www.pubmed.gov) (04.11.2021)

Search		
#11	**Search: #8 AND #9 Filters: from 2017/1/1 - 3000/12/12**	**36**
#10	Search: #8 AND #9	87
#9	Search: ("systematic review"[Title] OR "meta-analysis"[Publication Type] OR "meta-analysis"[Title] OR "systematic literature review"[Title] OR "this systematic review"[Text Word] OR "pooling project"[Text Word] OR ("systematic review"[Title/Abstract] AND "review"[Publication Type]) OR "meta synthesis"[Title] OR "meta analy*"[Title] OR "integrative review"[Text Word] OR "integrative research review"[Text Word] OR "rapid review"[Text Word] OR "umbrella review"[Text Word] OR "consensus development conference"[Publication Type] OR "practice guideline"[Publication Type] OR "drug class reviews"[Title] OR "cochrane database syst rev"[Journal] OR "acp j club"[Journal] OR "health technol assess"[Journal] OR "evid rep technol assess summ"[Journal] OR "jbi database system rev implement rep"[Journal] OR ("clinical guideline"[Text Word] AND "management"[Text Word]) OR (("evidence based"[Title] OR "evidence based medicine"[MeSH Terms] OR "best practice*"[Title] OR "evidence synthesis"[Title/Abstract]) AND ("review"[Publication Type] OR "diseases category"[MeSH Terms] OR "behavior and behavior mechanisms"[MeSH Terms] OR "therapeutics"[MeSH Terms] OR "evaluation studies"[Publication Type] OR "guideline"[Publication Type] OR "pmc-book"[All Fields])) OR (("systematic"[Text Word] OR "systematically"[Text Word] OR "critical"[Title/Abstract] OR "study selection"[Text Word] OR ("predetermined"[Text Word] AND "criteri*"[Text Word]) OR "exclusion criteri*"[Text Word] OR "main outcome measures"[Text Word] OR "standard of care"[Text Word] OR "standards of care"[Text Word]) AND ("survey"[Title/Abstract] OR "surveys"[Title/Abstract] OR "overview*"[Text Word] OR "review"[Title/Abstract] OR "reviews"[Title/Abstract] OR "search*"[Text Word] OR "handsearch"[Text Word] OR "analysis"[Title] OR "critique"[Title/Abstract] OR "appraisal"[Text Word] OR ("reduction"[Text Word] AND ("risk"[MeSH Terms] OR "risk"[Text Word]) AND ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields] OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]))))) AND ("literature"[Title/Abstract] OR "articles"[Title/Abstract] OR "publications"[Title/Abstract] OR "publication"[Title/Abstract] OR "bibliography"[Title/Abstract] OR "bibliographies"[Title/Abstract] OR "published"[Title/Abstract] OR "pooled data"[Text Word] OR "unpublished"[Text Word] OR "citation"[Text Word] OR "cita-	557,947

Search		
	tions"[Text Word] OR "database"[Title/Abstract] OR "internet"[Title/Abstract] OR "text-books"[Title/Abstract] OR "references"[Text Word] OR "scales"[Text Word] OR "pa-pers"[Text Word] OR "datasets"[Text Word] OR "trials"[Title/Abstract] OR "meta analy*"[Text Word] OR ("clinical"[Title/Abstract] AND "studies"[Title/Abstract]) OR "treatment outcome"[MeSH Terms] OR ("outcome"[Text Word]) OR "pmcbook"[All Fields])))) NOT ("letter"[Publication Type] OR "newspaper article"[Publication Type])	
#8	Search: #3 AND #7	1,583
#7	Search: #4 OR #5 OR #6	29,531
#6	Search: "Food, Formulated"[Mesh]	11,069
#5	Search: Meal[tiab] AND replacement*[tiab]	1,605
#4	Search: Formula*[tiab] AND diet*[tiab]	18,801
#3	Search: #1 OR #2	709,336
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	148,471
#1	Search: diabet*[tiab]	697,272

Am 09.11.2021 wurde die Recherche mit den zusätzlichen Suchbegriffen: liquid[tiab] AND (diet*[tiab] OR supplement*[tiab]) durchgeführt. Die 6 zusätzlichen Treffer wurden ausgeschlossen (Thema nicht passend).

Epistemonikos (www.epistemonikos.org) (04.11.2021)

Advanced search

Search	Most Recent Queries	Result
#2	**Publication year: from 2017 to 2021** **Publication type: Systematic review**	**16**
#1	(title:(diabet*) OR abstract:(diabet*)) AND (title:((title:((title:(formula*) OR abstract:(for-mula*)) AND (title:(diet*) OR abstract:(diet*))) OR abstract:((title:(formula*) OR ab-stract:(formula*)) AND (title:(diet*) OR abstract:(diet*)))) OR (title:((title:(meal) OR ab-stract:(meal)) AND (title:(replacement*) OR abstract:(replacement*))) OR abstract:((ti-tle:(meal) OR abstract:(meal)) AND (title:(replacement*) OR abstract:(replacement*))))) OR abstract:((title:((title:(formula*) OR abstract:(formula*)) AND (title:(diet*) OR ab-stract:(diet*))) OR abstract:((title:(formula*) OR abstract:(formula*)) AND (title:(diet*) OR abstract:(diet*)))) OR (title:((title:(meal) OR abstract:(meal)) AND (title:(replace-ment*) OR abstract:(replacement*))) OR abstract:((title:(meal) OR abstract:(meal)) AND (title:(replacement*) OR abstract:(replacement*))))))	128

Cochrane Datenbank (www.cochranelibrary.com) 04.11.2021

Search	Most Recent Queries	Result
#13	**#3 AND #12 in Cochrane Reviews, Cochrane Protocols, Publication date: 2017-2021**	**8**
#12	#4 OR #7 OR #10 OR #11	8833
#11	#5 AND #8	2896
#10	#8 AND #9	957
#9	(Meal):ti,ab,kw	19574
#8	(Replac*):ti,ab,kw	41176
#7	#5 AND #6	5423
#6	(Formul*):ti,ab,kw	46909
#5	(Diet*):ti,ab,kw	97944

Search	Most Recent Queries	Result
#4	MeSH descriptor: [Food, Formulated] explode all trees	1449
#3	#1 OR #2	101779
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	19039
#1	(Diabet*):ti,ab,kw	101779

2.2.3 Übersicht der eingeschlossenen Treffer

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	**36**	**16**	**8**	**60**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 15

A2 (nicht englisch/deutsch): 0

A3 (Conference Abstract): 0

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 45

2.2.4 TiAb-Screening

TiAb-Tabelle		
	Einschluss	**Ausschluss**
Population	Erwachsene mit Typ 2 Diabetes	- Studien, die nicht zwischen Typ-1- und Typ-2-Diabetes unterscheiden - Diabetes bei besonderen Patientengruppen (Cystische Fibrose, nach Transplantation); Alter < 18 Jahre, Diabetes in und um die Schwangerschaft
Intervention	- Formula-Diäten	- Sondenernährung bei Patient*innen mit Schluckstörungen
Comparison	Any	- Vergleich verschiedener Formula-Diäten
Outcome	- Mortalität - Kardiovaskuläre und diabetische Morbidität - Lebensqualität - (Glykämische Kontrolle (HbA1c), wenn dadurch Medikamente eingespart werden können, Diabetesremission.)	- *Andere Laborwerte* - *Lipide* - *Andere Stoffwechselparameter (HOMA-Index)* - *Körpergewicht, Änderung Körpergewicht* - *RR*

2.2.5 Flow-Chart

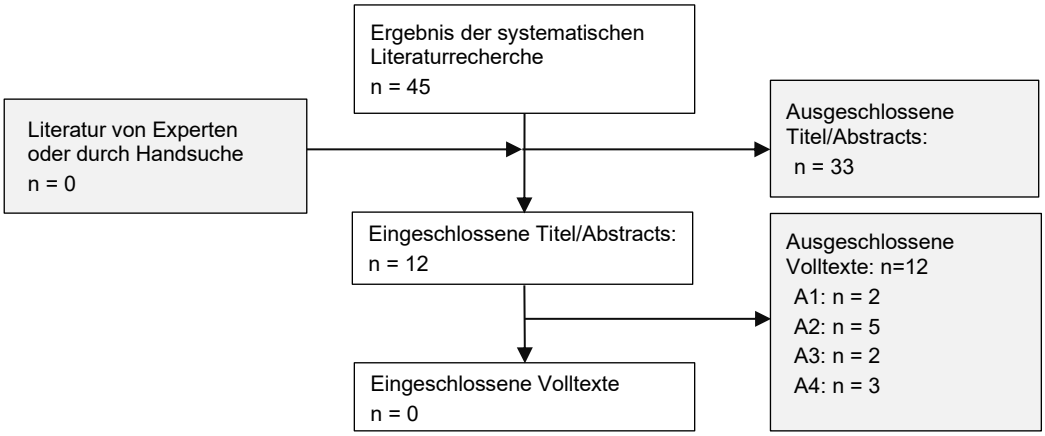
Legende:

A1: Ausschluss, Thema nicht passend, Population nicht passend

A2: Endpunkte nicht passend

A3: Vergleich zweier Formula-Diäten

A4: Methoden nicht ausreichend beschrieben, kein systematischer Review von RCTs, Guideline ohne Beschreibung der Rechercheergebnisse.



2.2.6 Evidenzzusammenfassung

Es erfolgte eine gezielte systemtische Recherche nach aggregierter Evidenz zum Nutzen von Formula-Diäten bei Menschen mit Typ-2-Diabetes in Bezug auf Mortalität, kardiovaskuläre Erkrankungen, Lebensqualität und Change in Medication ab 2017 bei PubMed, Cochrane und Epistemonikos. Identifizierte systematische Reviews betrachteten nicht die in der Recherche festgelegten Endpunkte (z. B. Noronha, et al. 2019, https://www.ncbi.nlm.nih.gov/pubmed/30923163 {Noronha 2019: 31839}).

In der Arbeitsgruppe war bezüglich Formula-Diäten in der ersten Konferenz die DiRECT-Studie {Lean 2018: 27789; Lean 2019: 31846} genannt und diskutiert worden. Die Studien DiRECT und DIADEM wurden auch in einem Review identifiziert (Churuangsuk et al., 2022), weswegen sie in den Evidenztabellen dargestellt werden.

2.3 Systematische Recherche Mediterrane Diät

Es erfolgte eine Recherche im November 2021 und eine Update-Recherche im Dezember 2023. Beide Recherchen werden hier zusammen dargestellt.

2.3.1 PICO-Fragestellung

P: Erwachsene Patient*innen mit Typ-2-Diabetes

I: Mediterrane Diät

C: jegliche Vergleiche (z. B. usual care)

O: 1. Kardiovaskuläre Morbidität / Mortalität, Gesamtmortalität

2. Lebensqualität

3. ggf. HbA1c, wenn dadurch eine medikamentöse Therapie verhindert wird

S: Systematische Übersichtsarbeiten von RCTs* ab 2014 (Update-Recherche: ab 11/2021)

* methodisch hochwertige Umbrella-Reviews wurden zum Abgleich der Rechercheergebnisse herangezogen.

Sprache: deutsch, englisch

2.3.2 Recherchestrategien

2.3.2.1 Recherche 2021

Medline via Pubmed (www.pubmed.gov) (17.11.2021)

Search	Most recent Queries	Result
#10	**Search: #8 AND #7 Filters: from 2014/1/1 - 3000/12/12**	**123**
#9	Search: #8 AND #7	156
#8	Search: (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation study[pt] OR validation study[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	549,584
#7	Search: #6 AND #3	1,773
#6	Search: #4 OR #5	45,508
#5	Search: "Diet, Mediterranean"[Mesh]	4,260
#4	Search: Mediterranean[tiab]	45,020
#3	Search: #1 OR #2	711,002
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	148,934
#1	Search: diabet*[tiab]	698,921

Epistemonikos (www.epistemonikos.org) (17.11.2021)

Advanced search

Search	Most Recent Queries	Result
#2	**Publication year: from 2014 to 2021** **Publication type: Systematic review**	**71**
#1	(title:((title:(diabet*) OR abstract:(diabet*))) OR abstract:((title:(diabet*) OR abstract:(diabet*)))) AND (title:(mediterranean) OR abstract:(mediterranean))	279

Cochrane Datenbank (www.cochranelibrary.com) 17.11.2021

Search	Most Recent Queries	Result
#7	**#3 AND #6 in Cochrane Reviews, Cochrane Protocols, Publication date: 2017-2021**	**3**
#6	#4 OR #5	2359
#5	(Mediterranean):ti,ab,kw	2359
#4	MeSH descriptor: [Diet, Mediterranean] explode all trees	565
#3	#1 OR #2	101780
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	19039
#1	(Diabet*):ti,ab,kw	101780

2.3.2.2 Recherche 2023

Medline via Pubmed (www.pubmed.gov) (01.12.2023)

Search	Most Recent Queries	Result
#10	**Search: #7 AND #8 Filters: from 2021/11/1 - 3000/12/12**	**55**
#9	Search: #7 AND #8	203
#8	Search: (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation study[pt] OR validation study[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	688,01
#7	Search: #6 AND #3	2,177
#6	Search: #4 OR #5	52,789
#5	Search: "Diet, Mediterranean"[Mesh]	5,412
#4	Search: Mediterranean[tiab]	52,288
#3	Search: #1 OR #2	810,274
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	174,809
#1	Search: diabet*[tiab]	797,461

Epistemonikos (www.epistemonikos.org) (01.12.2023)

Advanced search

Search	Most Recent Queries	Result
#2	**Publication year: from 2021 to 2024** **Publication type: Systematic review**	**54**
#1	(title:(diabet*) OR abstract:(diabet*)) AND (title:(mediterranean) OR abstract:(mediterranean))	569

Cochrane Datenbank (www.cochranelibrary.com) 01.12.2023

Search	Most Recent Queries	Result
#7	**#3 AND #6 in Cochrane Reviews, Cochrane Protocols; Publication date: from 01/11/2021**	**0**
#6	#4 OR #5	2999
#5	(Mediterranean):ti,ab,kw (Word variations have been searched)	2999
#4	MeSH descriptor: [Diet, Mediterranean] explode all trees	792
#3	#1 OR #2	118698
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	23568
#1	(Diabet*):ti,ab,kw (Word variations have been searched)	118698

2.3.3 Übersicht der eingeschlossenen Treffer

2.3.3.1 Recherche 2021

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	**123**	**71**	**3**	**197**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 65

A2 (nicht englisch/deutsch): 2

A3 (Conference Abstract): 3

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 127

2.3.3.2 Recherche 2023

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	**55**	**54**	**0**	**109**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten + Doubletten zu Recherche von 2021): 28

A2 (nicht englisch/deutsch): 4

A3 (Conference Abstract): 1

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 76

2.3.4 TiAb-Screening

TiAb-Tabelle		
	Einschluss	**Ausschluss**
Population	Erwachsene mit Typ 2 Diabetes	- Studien, die nicht zwischen Typ-1- und Typ-2-Diabetes unterscheiden - Diabetes bei besonderen Patientengruppen (Cystische Fibrose, nach Transplantation); Alter < 18 Jahre, Diabetes in und um die Schwangerschaft
Intervention	- Mediterrane Diät	
Comparison	Any	
Outcome	- Mortalität - Kardiovaskuläre und diabetische Morbidität - Lebensqualität - (Glykämische Kontrolle (HbA1c), wenn dadurch Medikamente eingespart werden können, Diabetesremission.)	- *Andere Laborwerte* - *Lipide* - *Andere Stoffwechselparameter (HOMA-Index)* - *Körpergewicht, Änderung Körpergewicht* - *RR*

2.3.5 Flow-Chart

2.3.5.1 Recherche 2021

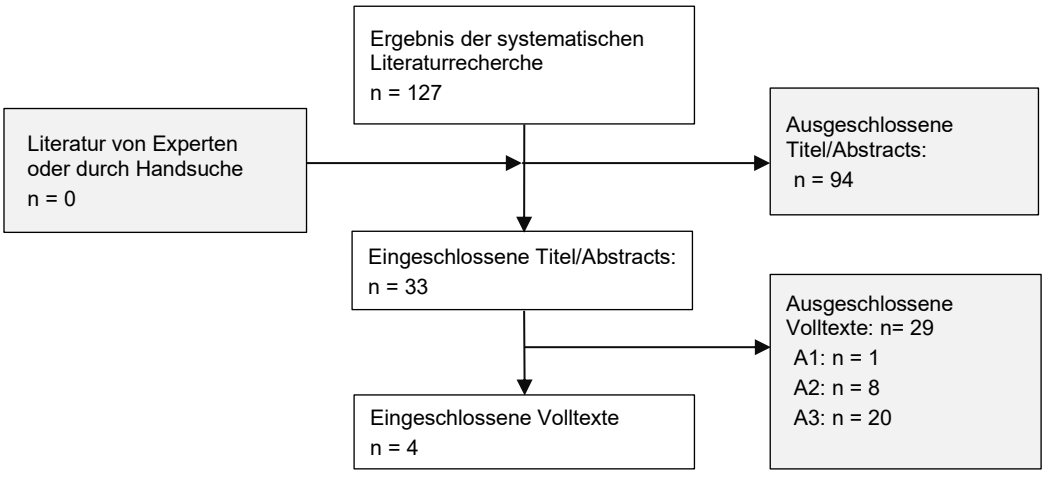
Legende

A1: Ausschluss, Thema nicht passend, Population nicht passend

A2: Endpunkte nicht passend

A3: Methodisch nicht ausreichend

Ap: Protokoll



Eingeschlossene Studien aus der Recherche:

- Dow 2018
- Wong 2018

- Becerra-Tomas 2020
- Bloomfield 2015

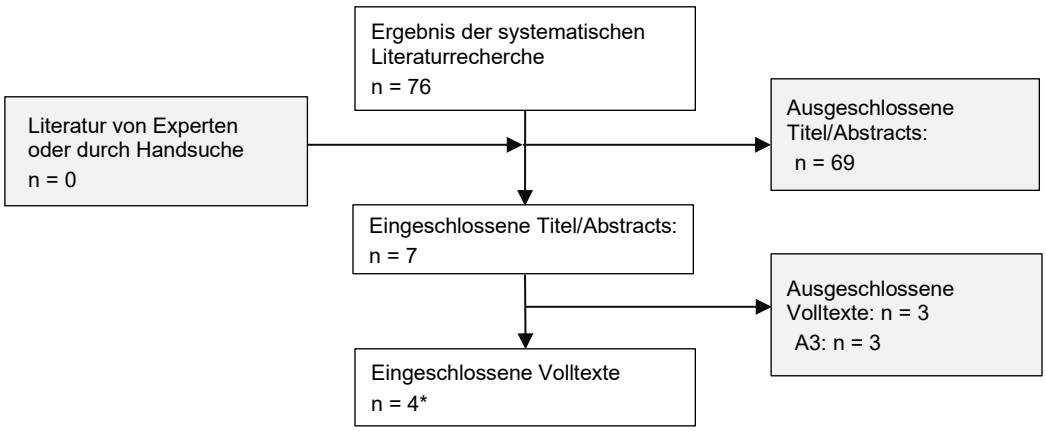
2.3.5.2 Recherche 2023

Legende:

A1: Ausschluss, Thema nicht passend, Population nicht passend

A2: Endpunkte nicht passend

A3: methodisch nicht ausreichend, methodisch hochwertigerer Review zu dem Thema vorhanden



*ein Umbrella-Review

Eingeschlossene Literatur aus der Recherche:

- Churuangsuk 2022
- Shah 2022
- Wu 2023
- Szczerba 2023 (Umbrella-Review)

Von der Leitliniengruppe eingebrachte ergänzende Literatur zur PREDIMED-Studie:

- Salas-Salvadó, Jordi; Bulló, Mònica; Estruch, Ramón; Ros, Emilio; Covas, Maria-Isabel; Ibarrola-Jurado, Núria et al. (2014): Prevention of diabetes with Mediterranean diets. A subgroup analysis of a randomized trial. In: Ann Intern Med 160 (1), S. 1–10. DOI: 10.7326/M13-1725.
- Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: N Engl J Med 378 (25), e34. DOI: 10.1056/NEJMoa1800389.
- Basterra-Gortari, F. Javier; Ruiz-Canela, Miguel; Martínez-González, Miguel A.; Babio, Nancy; Sorlí, José V.; Fito, Montserrat et al. (2019): Effects of a Mediterranean Eating Plan on the Need for Glucose-Lowering Medications in Participants With Type 2 Diabetes. A Subgroup Analysis of the PREDIMED Trial. In: Diabetes Care 42 (8), S. 1390–1397. DOI: 10.2337/dc18-2475.
- Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2022): Nationale VersorgungsLeitlinie Chronische KHK – Langfassung. Version 6.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000491, zuletzt geprüft am 15.09.2022.

2.3.6 Evidenzzusammenfassung

Die Aussagesicherheit der Ergebnisse aus den identifizierten systematischen Übersichtsarbeiten zur mediterranen Diät ist insbesondere durch das Verzerrungsrisiko der Einzelstudien eingeschränkt. Überwiegend wurden Daten aus der PREDIMED-Studie einbezogen, bei deren Betrachtung Bedenken hinsichtlich der Randomisierung als auch

die Vergleichsintervention zu berücksichtigen sind. Zur Evidenzbeschreibung siehe Kapitel Nicht-medikamentöse Therapie (Ergänzung zu Version 3) [1].

3 Evidenztabellen: Gewichtsmanagement / Ernährung

3.1 Weight loss interventions allgemein

3.1.1 Evidenz aus der systematischen Recherche zu Gewichtsmanagement

Martenstyn 2020 (Weight loss interventions)

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
Martenstyn J. Impact of weight loss interventions on patient-reported outcomes in overweight and obese adults with type 2 diabetes: A systematic review. J Behav Med 2020; 43(6):873–91. https://www.ncbi.nlm.nih.gov/pubmed/32060765 #31420 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31420.pdf	**Suchzeitraum:** inception to March 2018 **Fragestellung:** effect of weight loss interventions on weight loss and PROs in overweight and obese adults with T2D. **Population:** overweight and obese (according to BMI) adults aged ≥ 18 years with T2D. **Intervention:** weight loss intervention (diet, surgery, pharmacological, and multi-component lifestyle interventions) **Endpunkte:** changes in PROs from baseline **Ausschluss:** if weight loss or PRO data for the overweight and/or obese adult T2D sample was combined with data for other BMI groups (e.g., normal weight) or comorbid conditions without presenting subgroup results.	19 RCTs, n=9271 - 58% female, 16 trials (84,2%) western or european countries, 2 trials (10,5%) asian countries, 1 (10,5%) in multiple countries. - Interventions: 5 trials (26,3%) dietary modification alone, 4 trials (21,1%) surgical procedure, 3 trials (15,8%) pharmacological agents, 7 trials (36,8%) multicomponent lifestyle interventions, sometimes in combination with diet modification, pharmacological agents, and/or counselling No metaanalysis, narrative synthesis: heterogeneity in weight loss interventions, time intervals and PRO instruments. **Dietary Interventions:** 5 trials, n= 1120 Two high quality trials: greater weight loss in Intervention groups - **Lean 2017** (n=306, assessment baseline and 6 months): Intervention: weight management programme (Counterweight Plus) Control: standard diabetes care - HRQOL (EQ-5D instrument): Intervention better than standard diabetes care at 12ms. - **Holland-Carter 2017** (n=563, assessment 6 and 12 months): Intervention: modified weight watchers diet Control: Standard diabetes care - HRQOL (SF-36 instrument): no significant difference between groups - Impact of Weight on Quality of Life-Lite (IWQOL-Lite): Intervention: better obesity-specific HRQOL compared to standard care - Diabetes distress scale: greater reductions in diabetes related emotional distress in Intervention group - Patient Health Questionnaire-9: no significant difference between groups Two moderate quality trials (n=105, n=115; assessment up to 12 months) similar weight loss between groups (**Davis 2012, Brinkworth 2016**): Interventions: low carbohydrate	Critically low y-n-n-py-y-y-n-n-py-n-noMa-noMa-y-y-n?-y (kein Protokoll, ausgeschlossene Studien nicht genannt, Betrachtung des Publikationsbias nicht in der Methodik beschrieben, aber in der Diskussion diskutiert) Suche scheint verlässlich: Recherche in 3 Datenbanken, Suchstrategie angegeben	

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
	Studien: RCTs **Qualitätsbewertung:** 2010 CONSORT checklist (37 items assessing the design and general reporting of RCTs) (Schulz et al., 2010) and the 2013 CONSORT-PRO Extension (14 items assessing the quality of PRO reporting of RCTs) **Abkürzungen (PRO measure):** - POMS: Profile of Mood States - BDI-II: Beck Depression Inventory II - STAI: State-Trait Anxiety Inventory - D-39: Diabetes-39 (Diabetes-specific quality of life) - PAID: Problem Areas in Diabetes - SF-36: 36-Item Short Form Survey - IWQOL-Lite: Impact of Weight on Quality of Life-Lite - DDS: Diabetes Distress Scale - IIEF-5: International Index of Erectile Function-5 - DTSQ: Diabetes Treatment Satisfaction Questionnaire - POMSb: Profile of Mood States Brief Form - Modified WOMAC: Modified Western Ontario and McMaster Universities Osteoarthritis Index - BMA 2.0: Body Morph Assessment Version 2.0	Control: high carbohydrate HRQOL Diabetes-39: no significant difference between groups Brinkworth 2016: also assessed POMS, BDI-II, STAI, PAID: no sig. difference 1 moderate quality trial (**Khoo 2011**), n=31, assessment baseline, 8 weeks, greater weight loss in intervention group Intervention: meal replacement low-caloric diet Control: high protein diet Abridged IIEF-5 (erectile function assessment): no signifficant difference between groups at 8 weeks **Surgical Interventions:** 4 trials, n=233, see review **Pharmacological interventions:** 3 trials, n=1705 - **Kaukua 2004**, moderate quality trial, n=236, assessment up to 12 months, greater weight loss in intervention group Intervention: 15mg sibutramine/d Control: non-active placebo control HRQOL (SF-36): no significant difference in 8 domains between groups at 3, 6, 9 and 12 months. - **Kipneset 2010**, low reporting quality, n= 623, assessment up to 12 months, more weight loss in intervention groups Intervention: 0,5mg, 1mg or 2mg taranabant/d Control: non-active placebo SF-36: results not reported IWQOL-Lite: results not reported POMSb: no significant differences in global mood at 12 months o Anger-hostility and depression-dejection scales deteriorated with 2 mg taranabant daily compared to placebo (at 12 months). o 0.5 mg and 1 mg taranabant daily, but not 2 mg taranabant daily, produced higher confusion-bewilderment scores compared to placebo at 12 months - **Davies 2015**, high quality study, n=846, more frequent weight loss in intervention groups, assessment up to 56 weeks Intervention: liraglutide 1,8 or 3,0mg/d Comparator: placebo IWQOL-Lite and DTSQ: satisfaction with diabetes treatment and obesity specific HRQOL greater in 3,0mg liraglutid group than placebo (not significant für 1,8mg liraglutide). No sig. differences between liraglutid groups and placebo for self-esteem, sexual life, public distress or work domains. **Multi-component lifestyle interventions (including a physical activity component):** 6 trials, n=6055 - **Look AHEAD**, moderate to high quality evidence, n=5145, assessment up to 96 months, more weight-loss in intervention group Intervention: intensive lifestyle intervention (ILI) Control: general diabetes support and education (DSE) SF-36: greater improvements in physical functions in ILI group compared to DSE (at 12 and 96 ms), no		

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
		significant differences mental components (12 months) BDI-II at 12 ms: larger reduction in ILI group compared to DSE Stewart et al., 2011: moderate quality study: BMA 2.0: perceived current body size, but not perceived ideal body size (Body Morph Assessment Version 2.0) greater in ILI compared to DSE at 12 months (n = 157). **Wing et al., 2010**: better erectile function in ILI than DSE at 12ms (IIEF-5). Among older men (n=372). **Foy et al., 2011**, high quality study, n=2203, subset of Look AHEAD sample with knee pain, reduced pain and improved physical funciton in ILI group at 12 months (modified WOMAC), self reported knee stiffness did not differ. Two studies: intervention exercise as primary component of 16 week multi-component weight loss program - **Wycherley 2014**: greater weight-loss in energy-restricted diet plus resistance training exercise program compared to an energy-restricted diet alone at 16 weeks (n = 106); moderate quality study. HRQOL (Diabetes-39) and PAID: no differences between groups - **Mensberg 2017**: low quality study, n=34, 16 weeks; no difference in weight loss Intervention: exercise (spin classes and resistance training) plus liraglutide Control: exercise alone HRQOL (SF-36 total score): no difference between groups - **Moncrieft 2016**, high quality study, n=111, 12 months, no difference in weight-loss Patients with significant depressive symptoms (BDI-II ≥ 11) Intervention: lifestyle intervention Control: standard diabetes care Depressive symptoms decreased more in the intervention group. Two studies: combination of pharmacological agents and lifestyle interventions: - **Woo 2007**, low quality study, n=55, Intervention group lost significantly more weight Intervention: 360mg Orlistat/d for 6ms, then 6ms lifestyle interventions Control: non-active control HRQOL (SF-36 total score): intervention group better HRQOL Obesity-related HRQOL: no significant group differences - **O´Neil 2012**, moderate quality study, n=604, 12 months, greater weight loss in intervention group Intervention: Lorcaserin 10 or 20mg plus lifestyle intervention Control: lifestyle intervention alone IWQOL-Lite instrument total score: better with 10mg but not 20mg lorcaserin plus lifestyle compared to lifestyle intervention alone. BDI-II: no signifficant differences between lorcaserin plus lifestyle groups and control. **Multi-component lifestyle interventions (no physical activity component):** 1 trial, n=158 - **Berk 2018**, moderate quality study, assessment up to 24 months, similar weight loss between groups		

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Intervention: standard diabetes care plus 12 group cognitive-behavioural therpy sessions Control: standard diabetes care HRQOL (EQ-5D): better HRQOL in intervention group at 12 ms. HADS, RSES, CIS, EDE-Q: no significant differences between groups **Anmerkungen aus Review:** - PROs typically secondary or tertiary outcomes, and reporting quality of PROs was low and likely prone to publication bias (negative findings unlikely to report, PROs not reported at all time points, not reporting numerical data, not reporting minimal clinically important differences). „The results from this review suggest that weight loss itself does not translate to improved PROs; rather, interventions targeting multiple components, for example, weight loss, lifestyle, and psychosocial well-being had the greatest impact on improving PROs." **Quality appraisal:** - less than 50% of the included studies identified their study as a RCT in the title and failed to provide thorough descriptions of results for all primary and secondary outcomes, including lack of reporting of effect sizes and confidence intervals. There was little association within studies between the quality of general RCT reporting (total scores ranged from 49 to 86%) and PRO-specific reporting (total scores ranged from 18 to 82%) (Spearman correlation coefficient = .05; scatterplot shown in Fig. 4). --- Eine Bewertung der Aussagesicherheit der Evidenz zur Beeinflussung von PROs ist aufgrund der schlechten Berichtsqualität des Reviews nicht ausreichend möglich. **Soweit beurteilbar wäre diese am ehesten sehr niedrig. Erläuterung (NVL):** RoB: -1 bis -2 (z. B. Allocation concealment, blinding, reporting of effect sizes) Konsistenz: -1 (Heterogenität sowohl bei den Studien/Interventionen, als auch bei den Ergebnissen. Eine Bestimmung der statistischen Heterogenität nicht möglich, da keine absoluten Zahlen angegeben) Direktheit: 0 Präzision: nicht ausreichend beurteilbar, da nummerische Angaben zu den Effekten und der minimal klinisch relevanten Differenz fehlen. Publication-bias: -1 (prone to publicatoin bias)		

Brown 2017 (Multicomponent intervention)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Brown TJ. Exploring the evidence base	**Suchzeitraum:** 01/2005 to 03/2016 with supplementary searches.	**Ergebnisse:** 14 studies: 1 RCT, 3 controlled and 10 observational studies.	Critically low	- limited to UK-based studies

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
for Tier 3 weight management interventions for adults: A systematic review. Clin Obes 2017; 7(5):260–72. https://www.ncbi.nlm.nih.gov/pubmed/28695579. #31682 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31682.pdf	**Population:** Adults with a BMI of ≥40 kg/m^2, or ≥35 kg/m^2 with comorbidity or ≥30 kg/m^2 with T2DM **Intervention:** multicomponent interventions (diet, physical activity and behaviour change), in any UK or Ireland setting, delivered by a specialist multidisciplinary team. Intervention could include anti-obesity drugs, low-energy liquid diets (LELD) or pre-/post-bariatric surgery care **Comparator:** With and without comparator, no restriction on type of comparator. **Outcome:** No restriction. **Studies:** any design (RCTs, non-RCTs and uncontrolled before and after studies). **Qualitätsbewertung der Studien**: JBI appraisal tools **Begriffserläuterungen:** Tier 3: specialist multidisciplinary weight management service (WMS); multidisciplinary team (MDT) of specialists, led by clinician and typically including: physician (consultant or GP with special interest); specialist nurse; specialist dietitian; psychologist or psychiatrist; and physiotherapist/physical activity specialist/physiology	- studies heterogeneous. No metaanalyses. - keine Subgruppenauswertung für DM. - Multidisciplinary team composition and eligibility criteria varied; dropout rates were high (43–62%). **Extraktion des RCTs (adults with T2DM on insulin therapy)** (Cheyette C et al. 2007) - Intervention: Weight No More programme: 8-session programme run on a fortnightly basis (alle 2 Wo, insgesamt 16 Wo); Control: usual care for DM. **Insulin usage (Units):** End of intervention (ca. 16 Wo): - intervention group (IG) (randomized n=29, assessed n=21): mean average reduction 10.1±16.4 U (p<0,01) to 58.7±28.5 U. - Control group (CG) (20 randomized, 18 assessed), no reduction. At 6 months/12 months: - IG: increased to 63.1±31.4 from 58.7±28.5 U at end of programme (p<0,01) and to 62±30.4 U at 12 months. - CG: increase from end of intervention with mean insulin use of 55.1±25 U (p=0.06), which was maintained at 12 months. Anmerkung ÄZQ: keine weiteren Daten angegeben. (weight: intervention Baseline 93,4 ± 13,2kg, 6 months: 92,8 ±13,2kg, 12 months: 93,4 ± 14,2kg, control: 91,8 ± 15,7kg, 6 months: 92,5 ±15,6kg, 12 months: 92,9 ±16,1kg mean weight change from baseline: 4 months: Intervention -2,2 (2,7), n=29; 12 months: 0,0 (not reported), n=21; Control: 4 months -0,3 (nr), 6 months +1,1 (nr), n=18 HbA1c: intervention group end of intervention: -0,9 ±1% (p<0,01), control -0,3 ±0,6% (p<0,05), increased to 8,3 ±1,2%, 6 months, 8,1 ±1,3% at 12 months in the intervention group) **The Audit of Diabetes-Dependent Quality of Life (ADDQoL) scores:** Present QoL: - Baseline: IG: 0.81±1.1, CG: 0.83±0.9 - after intervention: IG: 1.2±1.1 (p=0.08), CG: 1.3±0.6 (p<0,05) (significant for control group only). „slightly more positive response was seen in the control group.“ Impact of diabetes on QoL score: - Baseline: IG: -1.7±1, CG: -1.6±1.3. - After intervention: IG: -1.2±1 (p<0,05), CG: -1.2±1.2 (p=0.32).	(Suche: keine Schlagworte angegeben, Publication bias nicht berichtet, ausgeschlossene Studien nicht angegeben, Selection-Kriterium fraglich)	- limitierte Angaben zu den von uns betrachteten Endpunkten (Tabelle im Supplement). - nur ein RCT identifiziert (n=49, nur diese Ergebnisse extrahiert) - Ungleichgewicht der Baselinedaten - Der Artikel wurde in der Gruppe betrachtet, aber aufgrund der geringen methodischen Qualität und geringen Aussagesicherheit nicht im Hintergrundtext zitiert.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Quality assessment of trial: Cheyette 2007 - Random assignment?: U (unknown) - Participant blinded?: U - Concealed allocation: U - Attrition (described and includedin analysis): U - comparable treatment groups?: No - Were groups treated identically other than for the named interventions?: Yes - Outcomes mearsure reliable: Yes - Was appropriate statistical analysis used?: No ---------- GRADE-Bewertung: sehr niedrig RoB: -1 bis -2 Konsistenz: keine Heterogenität, da nur eine Studie identifiziert. Direktheit: -1 (es geht ausschließlich um Personen mit Insulintherapie, spezifisches Programm aus England und Irland. Nur Studien aus England/Irland eingeschlossen) Präzision: -1 (nur eine kleine Studie) Publication-bias: ± 0		

3.1.2 Evidenz aus der systematischen Recherche zu Mediterraner Diät

Szczerba et al., 2023 (Umbrella Review)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Szczerba E. Diet in the management of type 2 diabetes: Umbrella review of systematic reviews with meta-analyses of randomised controlled trials. BMJ Med 2023; 2(1):e000664.	**Suchzeitraum:** up to 06/2022. **Fragestellung:** effect of diet on the management of type 2 diabetes and prevention of complications **Population:** individuals with type-2-Diabetes	88 publications with 312 meta-analyses of RCTs included. Methodological quality high to moderate in 23% and low to very low in 77% of the included publications. Im Folgenden nur Informationen zu den, in den bisherigen NVL-Recherchen priorisierten Endpunkten (kardiovaskuläre Morbidität/Mortalität, diabetesassoziierte Morbidität und Mortalität, Gesamtmortalität, Lebensqualität, Diabetesremission bzw. Einsparung von Medikamenten), unabhängig von der Intervention extrahiert. Für weitere Endpunkte siehe Originalpublikation. Characteristics and results of included meta-analyses of RCTs on the effect of diet on health outcomes in type-2-diabetes	In Anlehnung an AMSTAR 2 (Umbrella-Review): high Umbrella review: y-py-y-py-y-y-n.a.-n.a.-	- Umbrella-Review - methodisch hochwertig durchgeführte Übersicht zu SR von RCTs zu Effekten von Ernäh-

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
https://www.ncbi.nlm.nih.gov/pubmed/38027413	**Intervention:** dietary factors (dietary patterns, food groups, and dietary supplements) **Vergleich:** No intervention/ minimal intervention/ placebo/ other dietary interventions/ high versus low intake/ dose-response associations. Siehe auch “Ausschluss” **Ausschluss:** meta-analyses of RCTs with exclusively active control groups (comparing two intervention arms with each other). **Endpunkte:** any health outcome (eg, mortality, incidence of cardiovascular disease, body weight, levels of HbA1c, and heath related quality of life); **Studien:** SR von RCTs, duration ≥ 12 weeks **Qualitätsbewertung der Studien:** AMSTAR 2, GRADE	**Patient relevant outcomes:** - **Serious adverse events:** low carbohydrate (<26% total energy (TE)), Reference: Goldberg 2021, 8 RCTs (n=448), RR 0,79 (0,14; 4,46), Intervention time: 12-36 weeks, Study quality (AMSTAR-2): high*, **Certainty of evidence (CoE): very low** (RoB. Imprecision -2) - **Constipation:** Very low carbohydrate (<15 % TE); Referenz: Naude 2022, 2 RCTs, (n=177); RR 1,37 (0,87; 2,17), intervention time: 24 weeks; study quality: high; **CoE: very low** (RoB, imprecision -2) - **HbA1c Remission <6,5%:** low carbohydrate (<26%), Referenz: Goldenberg 2021, 8 RCTs, (n=264); RR 1,87 (1,18; 2,97), intervention time: 12-36 weeks; study quality: high*; **CoE: low** (imprecision -2) - **HbA1c Remission <6,5% + no medication:** low carbohydrate (<26% TE), Referenz: Goldenberg 2021, 5 RCTs, (n=199); RR 1,24 (0,65; 2,37), intervention time: 12-36 weeks; study quality: high*; **CoE: low** (imprecision -2) - **Medication reduction:** low carbohydrate (<26% TE), Referenz: Goldenberg 2021, 7 RCTs, (n=240); RD 0,24 (0,12; 0,35), intervention time: 12-36 weeks; study quality: high*; **CoE: moderate** (imprecision -1) - **Quality of life SF36– mental domain:** all types of carbohydrate restriction (<55%): Referenz: Silverii 2020, 4 RCTs, (n=577), MD 1,09 (-1,09; 3,28); intervention time: 24-108 weeks, study quality moderate, **CoE: very low** (RoB, imprecision -2) - **Quality of life:** low carbohydrate (<26% TE), Referenz: Goldenberg 2021, 4 RCTs, (n=169), MD -0,97 (-2,67; 0,73), intervention time: 12-36 weeks, study quality: high*, **CoE: low** (imprecision -2) - **Quality of life SF 36 – physical domain:** Referenz Silverii 2020, 3 RCTs, (n=552), MD -0,10 (-1,6; 1,39), intervention time 24-108 weeks, study quality: moderate, **CoE: low** (RoB, imprecision -1) *Anmerkung ÄZQ: Der SR von Goldenberg 2021 war in der AMSTAR 2-Bewertung aufgrund der fehlenden Auflistung von ausgeschlossenen Studien in der NVL-Recherche mit low bewertet worden (hier mit high). Zu der Intervention **mediterrane Diät** wurden keine Studien identifiziert, die patientenrelevante Langzeitendpunkte berichteteten. - weitere im Umbrella-Review genannte SR zu mediterraner Diät, die in der NVL-Recherche zur mediterranen Diät nicht betrachtet wurden: - Ajala 2013: vor dem Suchzeitraum der NVL-Recherche veröffentlicht, - Ajala 2013, Huo 2015, Neuenschwander 2019: betrachteten intermediäre Endpunkte, die in der NVL-Recherche nicht priorisiert worden waren, - Schwingshackl 2018 (intermediäre Endpunkte, Netzwerkmetaanalyse) Aus den „Strengths and limitations … Furthermore, low compliance with the assigned dietary regimens and high dropout rates were commonly seen in randomised controlled trials, especially for low carbohydrate and ketogenic diets, 60 potentially resulting in underestimation of their actual effect.“	n.a.-y-n-y-n.a.-y-y n.a.: nicht anwendbar, da kein SR, sondern Umbrella-Review.	rung bei Menschen mit Typ-2-Diabetes Zum Endpunkt Diabetesremission siehe auch SR von Churuangsuk 2022, in dem nach RCTs und nicht SR gesucht wurde. - Identifiziert über die systematische Recherche zu mediterraner Diät 2023

Churuangsuk et al., 2022

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Churuangsuk C. Diets for weight management in adults with type 2 diabetes: An umbrella review of published meta-analyses and systematic review of trials of diets for diabetes remission. Diabetologia 2022; 65(1):14–36. https://www.ncbi.nlm.nih.gov/pubmed/34796367.	**Suchzeitraum:** up to 05/2021 **Fragestellung 1 (Umbrella-review of diets for weight loss):** dietary approaches for weight loss Anmerkung ÄZQ: Endpunkt Gewichtsreduktion nicht passend zu den priorisierten Endpunkten der NVL-Recherche. **Population:** Adult participants, either sex, with T2D **Intervention:** any type of diets **Comparison:** any control diet or usual/routine care **Outcome:** a weight loss outcome (primary outcome) and/or changes in HbA1c (secondary) as mean difference between the two diet interventions, or mean difference from baseline, at any length of follow-up **Ausschluss:** if the diet intervention (or comparators) included additional components (e.g., drugs, bariatric surgery, exercise, or education) **Studies:** Metaanalyses of RCTs **Qaulity assessment:** AMSTAR-2, GRADE ---------- **Fragestellung 2 (SR of diets for T2DM remission):** type 2 diabetes remission with weight-loss diets **Population:** Adults with type 2 diabetes	Hier nur Darstellung der Ergebnisse des SR zur Diabetesremission: RESULTS: We identified 19 meta-analyses of weight-loss diets, involving 2-23 primary trials (n = 100-1587), published 2013-2021. Twelve were 'critically low' or 'low' AMSTAR 2 quality, with seven 'high' quality. Greatest weight loss was reported with very low energy diets, 1.7-2.1 MJ/day (400-500 kcal) for 8-12 weeks (high-quality meta-analysis, GRADE low), achieving 6.6 kg (95% CI -9.5, -3.7) greater weight loss than low-energy diets (4.2-6.3 MJ/day [1000-1500 kcal]). Formula meal replacements (high quality, GRADE moderate) achieved 2.4 kg (95% CI -3.3, -1.4) greater weight loss over 12-52 weeks. Low-carbohydrate diets were no better for weight loss than higher-carbohydrate/low-fat diets (high quality, GRADE high). High-protein, Mediterranean, high-monounsaturated-fatty-acid, vegetarian and low-glycaemic-index diets all achieved minimal (0.3-2 kg) or no difference from control diets (low to critically low quality, GRADE very low/moderate). **Diabetesremission:** 14 studies eingeschlossen, davon 6 RCTs. ▪ **Lean 2018** DiRECT (total diet replacement, n=298), low RoB ▪ **Taheri 2020** DIADEM-I (total diet replacement, n=147), low RoB ▪ **Gregg 2012** Look AHEAD (Formular meal replacement, n=5145)), RoB: some concerns (selection of reported results) ▪ **Gutierrez-Mariscal 2021** CARDIOPREV Study (Mediterranean diets and LFDs, Analysis in a subset cohort of CHD with T2D in CARDIOPREV study (n=183/1002), RoB: some concerns (selection of reported results) ▪ **Esposito 2014** (Mediterranean diets and LFDs, extended postcore RCT follow up, MD n=108, LFD n=107), RoB: some soncerns (selection of reported results) ▪ **Mollentze 2019** Pilot-RCT (standard energy diet n=9 vs. standard medical nutrition n=9), high risk of bias (randomization process, deviation from intended interventions, selection of the reported results) Only 2 RCTs of total diet replacement were conducted with T2D remission as a primary or secondary outcome. Remaining RCTs were ancillary analysis of available original trial data or extended follow-up period to evaluate remission. **Definition of T2DM remission:** All included studies defined remission as a diagnostic test result, without glucose lowering medication, below the WHO threshold for diagnosis of type 2 diabetes (HbA1c < 48 mmol/mol [6.5%], or fasting plasma glucose <7mmol/L. ▪ **TDR:** Remission at 12 months: 2 RCTs (Lean 2018 DiRECT, Taheri 2020 DIADEM), n=445 with induction phase of 'total diet replacement' (low risks of bias RCTs), diabetes duration <6 and <2 years, mean weight loss 10 and 12 kg in intervention group, 1-4 kg in control.	low* Für den SR: y-py-y-py-y-y-y-y-y-y-py-py-y-NoMa-NoMa-y-y-y/n?-y *Publication bias: "the publication bias or reporting bias was assessed using the domain 'Selection of the reported result' in the Cochrane Risk of Bias and the ROBINS-I tools" Anmerkung ÄZQ: die Bewertung, ob das Publication-bias ausreichend erhoben wurde, macht den Unterschied zwischen den Bewertungen "high" oder "low" aus.	SR und Umbrella-Review mit insgesamt guter Berichtsqualität. Fraglich ist, wie strikt die Autor*innen des Reviews die Kriterien zum Studienausschluss gefolgt sind: "intervention (or comparators) included additional components (e.g. …exercise or education…". In einigen der eingeschlossenen Studien war eine Steigerung der körperlichen Aktivität Teil der Intervention. Der zweite RCT zu mediterraner Diät wird nicht in der Summary of findings tabelle aufgeführt, wahrscheinlich aufgrund der Angabe der Effekte nach 5 und nicht nach einem Jahr. Der SR von Goldenberg 2021 und

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	Intervention: any type of diet, using either food-based or formula diets **Comparator:** any control diet or usual/routine care **Outcome:** proportion/percentage/rate of T2D remission after dietary intervention **Studies:** a.) RCTs b.) NRSsa as following: (1) non-RCTs; and (2) single arm intervention without control group of any type of diets **Ausschlusskriterien:** Studies were excluded if: diet intervention (or comparators) included additional components (e.g., drugs, bariatric surgery, exercise or education) observational studies of self-reported dieters, without intervention provided **Quality assessment:** Cochrane Risk of Bias tool 2.0 and Risk Of Bias In Non-randomised Studies – of Interventions [ROBINS-I] GRADE (Certainty of evidence)	○ remission at 12 months from baseline: standard care: 4–12% vs. intervention median 54% (range 46-61%) (**GRADE: high certainty of evidence**), ▪ **Meal replacement** (1 RCT, Gregg 2012, n=4503; 2 meal replacements/day during 0–20 weeks and 1/day there after): post hoc analyses for remission rates: ○ Remission at 1 year (prevalance estimates): standard care + diabetes education 2% (43/2170) vs. Intervention 11% (247/2157), with mean weight loss 8.6 % in the intervention group, 0,7 % in control (**GRADE: moderate certainty of evidence**, with some concern over risk of bias). ▪ **Mediterranean diet** 1 RCT, Esposito 2014, n=215, mediterranean diet or LFD over 12 months ○ Remission prevlancecontrol LFD arm 4% (4/97) with mean weight loss 4,2kg vs. 15% (15/102) with mean weight loss 6,2kg. (**GRADE: low certainty of evidence;** some concerns over risk of bias). 1 RCT, Gutierrez-Mariscal 2021, mediterranean (n=80) or Low fat diet (LFD) (n=103), ○ T2DM remission 5 years: control (LFD) 38,8% (40/103), weight -1,4kg, versus intervention 41,3% (33/80), weight -1,16kg. (keine GRADE-Bewertung, ggf. da Angabe der Diabetesremission nach 5 Jahren) ▪ **Low fat diet (LFD)**: 1 Pilot-RCT Mollentze 2019, n=18: ○ T2DM remission 6 months: usual care (diet advice) 0% (0/9) weight loss 1,5% vs. LFD 22,2% (2/9), weight -9,6%. (Anmerkung ÄZQ: Keine GRADE-Bewertung, ggf. wegen Anzahl der Teilnehmenden, RoB und Angabe der Remissionsrate nach 6 Monaten)		die darin enthaltenen Studien wurden nicht für low carbohydrate diets eingeschlossen. Begründung: “Unclear remission data of source RCTs; a systematic review.” Es wird nicht für alle bei Goldenberg betrachteten Studien erläutert, warum diese ausgeschlossen wurden. Identifiziert über die systematische Recherche zu mediterraner Diät 2023

3.1.3 Ausgewählte ausgeschlossene Artikel

Aus der systematischen Recherche zu Gewichtsmanagement.

Franz 2015

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Franz MJ. Lifestyle weight-loss	**Suchzeitraum:** 2000-2014 studies published before 2000 are included in the 2013 American Heart Association/American College	11 trials (22 study groups), n= 6 754, - 8 trials: compared 2 weight-loss interventions	Critically low	- Ausgeschlossen wegen unzureichender Qualität

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
intervention outcomes in overweight and obese adults with type 2 diabetes: A systematic review and meta-analysis of randomized clinical trials. J Acad Nutr Diet 2015; 115(9):1447–63. https://www.ncbi.nlm.nih.gov/pubmed/25935570. #31405 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31405.pdf	of Cardiology/The Obesity Society Guideline for the Management of Overweight and Obesity in Adults. **Fragestellung:** outcomes on HbA1c from lifestyle weight-loss interventions resulting in weight losses > or < 5% at 12 months? **Population:** overweight or obese adults with T2DM **Intervention:** Lifestyle weight-loss interventions, ie diet and/or physical activity **Vergleich:** mean baseline data, Weight-loss trials divided into studies with <5%, or ≥5% mean weight loss at 12 months, and usual care/control studies. **Endpunkte:** primary end points: - weighted mean differences (WMD) in weight loss, and resulting effect on HbA1c. Secondary end points: - total cholesterol, LDL-C, HDL-C, and TG - blood pressure (SPB and DBP) - Weight-loss interventions implementing differing macronutrient compositions and their weighted mean differences in weight loss and HbA1c outcomes **Auschluss:** weight-loss medications or bariatric surgery **Studien:** RCTs, study duration ≥12-months, 70% completion rate, HbA1c-level reported at 12 months. **Qualitätsbewertung:** no formal assessment (only RCTs).	- 3 trials: weight-loss intervention versus usual care/control group 19 weight-loss intervention study groups (SG) with 10 categories of weight-loss intervention (see review), 3 study groups (SG) usual care/control **Changes in glucose-lowering, lipid or BP medications medications:** - 7 trials: general decreases in medications at 12months; 1 study: increase in medications at 12 months; Look AHEAD control study group reported increase in lipid medications. - 4 trials: no report on medication changes. Keine weiteren Informationen im Review. Keine Qualitätsbewertung der Studien, daher Betrachtung der Einzelstudien, in denen laut Reviews über medication change berichtet wurde (siehe unten) - Look AHEAD Trial, 2007 - Wolf et al, 2004 - Li et al, 2005 - Davis et al, 2009 - Esposito et al, 2009 - Larsen at al, 2011 - Guldbrand et al, 2012 **Zusammenfassung (SR):** - majority of lifestyle weight-loss interventions in overweight or obese adults with type 2 diabetes resulted in weight loss <5% and did not result in beneficial metabolic outcomes. - weight loss of >5%, beneficial effects on HbA1c, lipids, and blood pressure.	(unzureichende Angaben zum Protokoll, ausgeschlossene Studien nicht genannt, keine Qualitätsbewertung der Einzelstudien, Publication bias nicht erhoben) Recherche: 2 Datenbanken, nur einige Mesh-terms angegeben, Recherche nicht reproduzierbar, keine weitere Bemühungen (Referenzen nicht durchsucht, clinicaltrials nicht durchsucht, Experten nicht befragt).	des Reviews (Einzelstudien siehe unten) - selektive Ergebnisdarstellung (teils Daten aus Meta-Analyse nicht signifikant, dann Bericht von Daten aus Einzelstudien) - Darstellungen im Forest plot nicht nachvollziehbar (Figure 3) und verzerrend (Signifikanz der Effekte, Konfidenzintervalle) - Angegebene I^2-Werte nicht schlüssig: 1652%, I^2=777%?

Kurzübersicht der Einzelstudien aus Franz et al 2015 (Change of Diabetes-Medication)

Link zu den ausführlichen Evidenztabellen der Einzelstudien im Anhang: auf Autorennamen klicken.

Zitat	Intervention / Vergleich	Baseline medication	Change in Medication
Look AHEAD, 2007	n= 5,145, intervention 4 years, follow up planned 11.5 years Intervention: Intensive lifestyle intervention (ILI) (n=2496) Control: Diabetes support Education (DSE) (n=2463)	**Use of Diabetes medicines (%)** Baseline: ILI 86,5% (0,7) vs. DSE 86,5% (0,7), p= 0,93	**Use of Diabetes medicines (%)** Year 1: ILI 78,6% (0,8) vs. DSE 88,7% (0,6), p=<0,001 Change: ILI -7,8 (0,6) vs. DSE 2,2 (0,5), p<0,001 Daten nach 4 Jahren: siehe Beschreibung der Einzelstudie (unten)
Wolf 2004 **#31764**	N= 144, 12 months intervention Intervention: Case management group (CM) n=73 Control: usual care group (UC) n=71,	Number of prescription medications/day (at baseline): CM 6,3 ±2,9 UC 5,8 ±2,6 Number of diabetes medications/day (atbaseline): CM 1,8 ±0,92 UC 1,8 ±0,85	At 6 months (CM n=58, UC n=65): - Individuals **decreasing** total medications CM 45% vs. UC 28%, - Individuals **increasing** total medications: CM 19% vs. UC 35%, P=0,03 At 12 months: UC n=64, CM n=54 - Individuals **decreasing** total medications CM 57% vs. UC 39%, - Individuals **increasing** total medications: CM 17% vs. UC 32%, P=0,13 By 12 months, participants in the CM group were taking 0.8 (0.05–1.1) fewer total medications per day than those in the UC group (P 0.03). (Absolute Zahlen aus Figure 2B nicht extrahierbar). **Diabetes Medications:** By 12 months, the CM group reduced diabetes medications 0.46 medications per day more than those in the UC group (P 0.001).
Li 2005 **#31765**	N=104, 52-week intervention Intervention: soy-based meal replacement (MR) plan (n=46) Control: individualized diet plan (IDP) (n=36) - All study subjects ≥1 oral hypoglycaemic agent at study entry, medication profiles campatible between groups - Drop-out rate 26% over study period, majority o f loss during screening and initial visit. (ITT-Analyse)		- At 12 months: MR group: significant number of subjects hat reduction in Sulfonylurea (p<0,0002) and metformin (p<0,05) use - Nur Darstellung in Figure 2 ohne Angabe absoluter oder prozentualer Zahlen.
Davis 2009	N=105, Intervention 1 year	**Baseline Medications:**	participants using insulin: dose reduced by mean ±SD of 10 ±14 units in LC arm and increased by 4 ±19 units in the LF arm (P = 0.12) at 12 months.

Zitat	Intervention / Vergleich	Baseline medication	Change in Medication
#31766	**Intervention:** low carbohydrate diet (LC) (n=55) **Control:** low-fat diet (LF) (n=50) ITT-Analyse, - prerandomization: adjusted diabetes medication to minimize side effects	Metformin: LC 43/55 (78%), LF 43/50 (86%) Sulfonylurea: LC 29/55 (44%9, LF 26/50 (52%) Insulin LC 19/55 (35%), LF 12/50 (24%) Cholesterol lowering medication: LC 34/55 (62%), LF 28/50 (56%).	Participants using sulfonylurea: 26% had reduction in dose at 12 months. Dose reduction: 1.6 ± 3,6mg in both arms.
Esposito 2009 **#31767**	n=215, 4 year intervention and follow-up **Intervention:** Mediterranean-style diet, n=108 **Control:** low fat diet, n=107 **Population:** newly diagnosed T2DM, never treated with antihyperglycemic drugs **Primary outcome:** Start of antihyperglycemic drug therapy, defined by protocol as indicated for follow-up HbA1c level > 7%.	Baseline HbA1c (%): MED: 7,75 (0,9), LF: 7,71 (0,9)	Anahl der Patienten in den Gruppen: Year 1: MED: n=102, LF: n=97 Year 4: MED: n=50, LF: n=29 Patients requiring treatment: Year 1: MED: 5,5%, LF 9,4% (Difference -3,9 (95% CI -7,8; 1,2) Year 4: MED 44%, LF 70% (Difference -26 (95% CI -31; -20,1) HR (unadjusted): HR 0,63 (0,51; 0,86) HR (adjusted for weight change): HR 0,70 (0,59; 0,9) HR (adjusted for using HbA1c >7% as outcome): HR 0,64 (0,5; 0,82)
Larsen 2011 #31768	N= 108, 12 months intervention Intervention: High-protein diet (HP) Control: High carbohydrate diet (HC) ITT Analyse	Diabetes treatment, n (%) (at baseline) None: HP: 5 (9%), HC: 5 (11%) Insulin: HP: 10 (10%), HC: 7 (15%) Tablets: HP: 38 (72%), HC: 34 (74%)	**Change in diabetes medication** (Weighted %change in diabetes medication), HP n=48, HC n=41 3 months: HP -8,71 vs. HC 0,68, Difference between groups: -9,38 (95% CI -17,85; -0,92) 12 months: HP -8,17 vs. HC 4,56, Difference between groups: -12,72 (95% CI -28,18; 2,73) trend for improved glycaemic control in HP, statistical adjustment for the change in medications did not modify the outcome for the change in HbA1c.

Zitat	Intervention / Vergleich	Baseline medication	Change in Medication
Guldbrand 2012 #31769	N= 61, intervention 2 years Intervention: Low fat diet (LFD) Control: Low carbohydrate diet (LCD)	Medication at baseline - Diet only: LFD 2 patients, LCD 2 - oral glucose-lowering medication only: LFD 13, LCD: 15 - combination of insulin and oral medication LFD 11, LCD: 10	Insulin dose baseline: LFD: 39±51 E vs. LCD 42±65 E, p=0,86 (between groups) Insulin dose 24 m: LFD 36 ±44 (p=0,5), vs. LCD 35 ±56 (p=0,14) P value for change over all time points between groups 0,83 Metformin dose baseline (mg): LFD 1,435 ±946 vs. LCS 1,375 ±950, p=0,8 (between groups) Metformin dose 24 m: LFD 1,306±901 (p=0,28) vs. 1,292±911 (p=0,38), P value for change over all time points between groups 0,93 P-Werte in Klammern: Vergleich zu baseline Glibenclamid: LFD vs. LCD, P value for change over all time points between groups 0,56 Für weitere Details siehe Beschreibung Einzelstudien.

3.2 Evidenz zum Nutzen der erreichten Gewichtsreduktion

3.2.1 Evidenz aus der systematischen Recherche zu Gewichtsmanagement

Siehe auch Martenstyn 2020 (Weight loss interventions) unter 3.1.1 Evidenz aus der systematischen Recherche zu Gewichtsmanagement.

Gummesson 2017

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Gummesson A. Effect of weight reduction on glycated haemoglobin in weight loss trials in patients with type 2 diabetes. Diabetes, obesity & metabolism 2017; 19(9):1295–305.	**Suchzeitraum:** 1990 - December 2012 **Fragestellung:** To quantify effect of weight loss on HbA1c at group level in overweight and obese patients with T2D **Population:** adults, overweight (BMI ≥25kg/m^2) or obese (BMI ≥30kg/m^2) patients with T2DM. **Intervention:** - any energy-reduced weight loss diet;	58 articles, 124 treatment groups, 17 204 subjects - 18 RCTs: mainly dietary interventions. - 30 RCTs: obesity drugs. All but one trials included dietary advice of reduced energy intake in all treatment groups. - 10 studies: bariatric surgery, (3 RCTs, 7 prospective single-arm studies). (Anmerkung ÄZQ: passt nicht zu den Einschlusskriterien randomized controlled weight loss trials). **Changes in Diabetes medication:** 27/53 studies: sufficient information to categorize according to change in diabetes medication (Daten der Einzelstudien werden im SR nicht gezeigt).	Critically low (kein Protokoll, Vorgehen bei Selektion und Extraktion nicht beschrieben, keine Darlegung ausgeschlossener Studien, Funding der Studien nicht berichtet, Studiendetails	- Daten wenig belastbar - Recherche alt: 2012 - Qualitätsbewertung der Studien für „change in diabetes medication“ nicht berichtet oder anderweitig

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
https://www.ncbi.nlm.nih.gov/pubmed/28417575. #31412 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31412.pdf	- pharmacological treatment for weight loss included. Trials evaluating diabetes drugs for weight loss (eg. GLP-1-RA and SGLT2-I) not included (high likelihood of weight loss-independent effects on HbA1c.) - surgical trials aiming at weight loss. **Endpunkte:** weight loss dependent reduction in HbA1c. Data extraction: change in diabetes medication **Studien:** Weight loss RCTs **Qualitätsbewertung:** 5-point Jadad scale **Methodik:** model-based analyses	Proportions of study groups with decrease, increase or no change (number of treament groups): - <5kg weight loss (n=34): decrease in diab.-medication 56% (n=19), no change 35% (n=12), increase 9% (n=3) - 5-10kg weight loss (n=11): decrease in diab.-medication 73% (n=8), no change 18% (n=2), increase: 9% (n=1) - >10 kg weight loss (n=13): decrease in diab.-medication 100%. - ÄZQ: Nicht nachvollziehbar, welche Studien betrachtet wurden, Qualitätsbewertung der Studien im Rahmen dieser Auswertung nicht berichtet. **Results:** Model-based analyses indicated a linear relationship between weight loss and HbA1c reduction with an estimated mean HbA1c reduction of 0,1 percentage point for each 1kg of reduced body weight. **Attrition rates** zwischen 0 und 58%. Qualitätsbewertung der Einzelstudien (durch die Review-Autoren): Jadad-Bewertung zwischen 0 und 5. Sensitivitätsanalysen nach Attrition-Rate und Studienqualität laut Review: keine große Beeinflussung des Models.	im Artikel nicht ausreichend beschrieben, No MA (Entwicklung eines Models), Heterogenitäten in den Studien nicht bewertet oder beschrieben) Suche in MEDLINE, EMBASE und Cochrane Datenbanken mit angegebener Suchstrategie, keine weitere Suche.	nachvollziehbar.

3.2.2 Ausgewählte ausgeschlossene Artikel

Aus der systematischen Recherche zu Gewichtsmanagement.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Chen Y. Weight loss increases all-cause mortality in overweight or obese patients with diabetes: A meta-analysis. Medicine (Baltimore) 2018; 97(35):e12075. https://www.ncbi.	**Suchzeitraum:** inception to 02/2017 **Fragestellung:** relationships between weight loss and all-cause mortality in overweight or obese individuals with diabetes **Population:** overweight or obese adults with diabetes **Intervention:** weight loss	18,887 patients, 8 studies (cohort studies), mean follow-up period of 9.5 years, Newcastle-Ottawa-Scale der Studien: 7-8. **Baseline:** - Patients: 5 studies: DM (Diabetes-Typ nicht angegeben), 1 study: NIDDM, 1 Study: T2DM, 1 Study: T2DM; CVD - **Manner of loosing weight:** 4 studies: Not assessed, 2 studies: Unintentional weight loss/intentional weight loss, 1 study: Dieting, 1 study: attempted to lose weight - Studie used **different measurments of weight change** (numer of studies): For example: 2 kg/m^2 (1), 1 lb (2), 10 lb (1), 1% (2), 1 kg/year (2),	low (formell viele Dinge gut beschrieben, aber es fehlen Informationen über die Studien und es ist fraglich, warum bei Heterogenitäten von 98% Meta-analysen gerechnet wurden)	- Daten nicht belastbar, nur Kohortenstudien identifiziert. - Diabetes-Typ nicht in allen Studien eindeutig angegeben. - Art des Gewichtsverlusts

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
nlm.nih.gov/pubmed/30170423. #31416 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31416.pdf	**Vergleich:** control groups (weight stable/steady) **Endpunkte:** all cause mortality data **Studien:** prospective studies (RCT or observational study), follow-up period ≥2 years **Qualitätsbewertung:** Newcastle–Ottawa scale. A high-quality study: score ≥7, score from 4 to 6: moderate-quality study. Heterogeneity assessed using the I^2 statistic; results for each study were extracted for maximally adjusted models.	**Weight loss group** (compared to stable weight): **all-cause mortality:** overall pooled RR: 1.15 (95% CI, 1.04 to 1.28), I^2=49%, 8 studies, p=0,006 - Sensitivity analysis (exclusion of self reported weight loss, 2 studies): RR: 1.24 (95% CI, 1.10 to 1.39), significant decrease in heterogeneity (Q test, P=0.36, I^2=9%). - all-cause mortality **(intentional weight loss):** RR, 0.90 (95% CI, 0.67 to 1.22), 3 studies, I^2=86%, p=0,0009 **CVD mortality:** RR, 1.15 (95% CI, 1.02 to 1.29), 5 studies, I^2=98%, p<0,00001 **Weight gain group:** **all-cause mortality**: Overall pooled RR: 1.17 (95% CI, 0.87 to 1.58), 6 studies, p=0,31, I^2=97% **CVD mortality**: pooled overall RR: 0.97 (95% CI, 0.93 to 1.01), 4 studies, I^2=0%, p=0,59. 1 lb (Pfund) entspricht 0,4536 kg Studienqualität laut Review-Autoren: high.	Suche: Suchstrategie (MEDLINE) angegeben, ähnliche Suche in EMBASE.	nicht in allen Studien angegeben (in 4 studies manner of loosing weight not assessed). - Definition des Gewichtsverlustes unterschiedlich und teilweise geringer Gewichtsverlust ausreichend z. B. -1lb. Differenz ist klinisch nicht relevant - Studien heterogen.

3.3 Very low-calorie diets

3.3.1 Evidenz aus der systematischen Recherche zu Gewichtsmanagement

Huang 2020 (very low-energy diets)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Komment
Huang YS. Efficacy of Intermittent or Continuous Very Low-Energy Diets in Overweight and Obese Individuals with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analyses. J Diabetes Res 2020; 2020:4851671. https://www.ncbi.nlm.nih.gov/pubmed/32090119. #31699 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31699.pdf	**Suchzeitraum:** from inception until July 2019 **Fragestellung:** efficacy of a very low-energy diet (VLED) in overweight and obese individuals with T2DM. **Population:** overweight and obese adults with T2DM **Intervention:** intermittent or continuous VLEDs comprising ≤800 kcal/day **Vergleich:** control arm receiving other energy control methods, including low-energy diets (LEDs) (800-1600 kcal/day), bariatric surgery, and mild energy restriction (MER) **Endpunkte:** - weight loss (kg), - fasting plasma glucose levels (mmol/l) - change in medication, - others: triglycerides (TG), HOMA-IR level, dropout, side effects, and rebound. **Studies**: controlled studies **Qualitätsbewertung**: RCTs: Cochrane Collaboration's tool, non-RCTs according to the Risk Of Bias In Nonrandomised Studies of Interventions (ROBINS-I) tool **Abkürzungen:** - low-energy diets (LEDs) - very low-energy diet (VLED) - mild energy restriction (MER) - mean difference (MD)	18 studies (11 RCTs, 7 nonrandomized controlled trials (observational studies)), n=911 - 7 RCTs (583 participants): VLEDs vs. LEDs - 6 studies (3 randomized, 3 non-randomized, 204 participants): VLEDs vs. MER, - 5 studies (1 randomized, 4 non-randomized, 124 participants): VLEDs vs. bariatric surgery. **Changes in Medication:** - Im Review narrativer Bericht ohne Darstellung absoluter Werte. → Betrachtung der Einzelstudien (RCTs) (siehe unten) - ÄZQ: Keine GRADE-Bewertung im Rahmen des Reviews für diesen Endpunkt. Qualitätsbewertung kann den Einzelstudien nicht zugeordnet werden **Risk of bias Bewertung:** None of the RCTs had an overall low risk of bias. Most RCTs had unclear risk of bias for sequence generation, allocation concealment, blinding of participants, blinding of outcome, and selective reporting because no detailed information was provided. **Studien (RCTs):** 1.) Anderson 1994 (VLED vs. LED) 2.) Carter 2016 (VLED vs. LED) 3.) Carter 2018 (VLED vs. LED 4.) Carter 2019 (VLED vs. LED) 5.) Harvey 1993 (VLED vs. LED) 6.) Wing 1991 (VLED vs. LED) 7.) Wing 1994 (VLED vs. LED) 8.) Steven 2016 (VLED vs. Bariatric surgery) 9.) Li 2017 (VLED vs. MER) 10.) Williams 1998 / Williams 1998a (VLED vs. MER 11.) Laakso 1988 (VLED vs. MER)	Critially low (kein Protokoll, ausgeschlossene Studien nicht angegeben) Suche: 8 Datenbanken durchsucht, Key-Words nicht angegeben, keine weitere Recherche (graue Literatur, Referenzen, Clinical trials)	Ergebnisdarstellung mit Unsicherheiten. Zahlen in Hintergrundtexten und Abbildungen stimmen teils nicht überein. Studie von Lean et al. 2018 wird erwähnt, war aber nicht eingeschlossen (DiRECT-Study), wahrscheinlich, da kcal/d zu hoch („825–853 kcal/day formula diet for 3–5 months)

Kurzübersicht Einzelstudien (RCTs) aus Huang et al., 2020 (Change in Medication)

Link zu den ausführlichen Evidenztabellen der Einzelstudien im Anhang: auf Autorennamen klicken.

Zitat	Studiencharakteristika	Baseline Medication	Medication change
Risk of bias Bewertung: None of the RCTs had an overall low risk of bias. Most RCTs had unclear risk of bias for sequence generation, allocation concealment, blinding of participants, blinding of outcome, and selective reporting because no detailed information was provided.			
VLED vs. LED			
Anderson 1994 **#31829**	N=40, 12-week intervention, follow-up 1 year 800-kcal diet Group A: liquid supplements only Group B: supplement plus evening meal - Both groups received intensive behavioral education program - Weekly group classes - Emphasis on increase in physical activity	**Baseline (n=39)** (nur von allen Teilnehmern zusammen angegeben) Insulin: 5 subjects Insulin and oral hypoglycemic agents: 3 subjects Oral hypoglycemic agents: 24 subjects Diet alone 7 subjects	**At 12 weeks (n=39)** (nur von allen Teilnehmern zusammen angegeben) Insulin 2 subjects Oral hypoglycemic agents 7 subjects Diet alone: 30 subjects
Carter 2016 http://www.ncbi.nlm.nih.gov/pubmed/27833048. #31770	N= 63, 12-week intervention Intervention: intermittent energy restriction (IRG) Control: continuous energy restriction (CRG)	**Baseline:** MES for OHA: CRG: 1,5 ±0,8, IRG 1,2 ±0,7 MES for Insulin: CRG 1,5 ±1,1, IRG 2,4 ± 1,2 Total MES for OHA & Insulin: CRG 1,9 ±1,2, IRG 1,6 ±1,2	**Change in Medication effect score:** MES for OHA: CRG: -0,4 ±0,6, vs. IER -0,2 ± 0,4, p-value by time by treatment: 0,3 MED for Insulin CER: -0,3 ±0,3 vs. IRG -0,9 ±0,4, p-value by time by treatment:0,06 Total MED: CRG -0,4 ±0,6 vs. IRG -0,4 ±0,5, p-value by time by treatment: 0,7
Carter 2018 http://www.ncbi.nlm.nih.gov/pubmed/30646030 #31771 Betrachtung zusammen mit Carter 2019 http://www.ncbi.nlm.nih.gov/pubmed/30902672	N=137, 24-month follow up, 12-month intervention **Intervention:** intermittent energy restriction (IRG) **Control:** continuous energyy restriction (CRG) **MES:** medication effect score (calculated as (actual drug dose/maximum drug dose) × drug mean adjustment factor. Higher MES corresponded to higher dose of diabetes medication, and reduction in MES corresponded to reduction in diabetes medication.	**Baseline medication:** MES (Medication effect score): Oral hypoglycemic agents (OHA): CRG 1,4 (0,8) vs. IRG 1,3 (0,8) Insulin: CRG 1,5 (1,1) vs. IRG 1,8 (1,1) Total: CRG 1,8 (1,1) vs. IRG 1,7 (1,3)	**From Baseline to 12 months** **Total mean (SEM) MES:** CRG -0,3 (0,1), IRG -0,6 (0,2), p for diet by time: 0,11 **Mean MES for OHA**: CRG -0,2 (0,1) vs. IRG -0,3 (0,1), p for diet by time 0,45 **Mean MED (SEM) for insulin**: CRG -0,3 (0,1) vs. IRG -1,2 (0,2), p for diet by time 0,006 **From Baseline to 24 months** **Total MES (Mean (SEM))**: CER -0,2 (0,1) [95% CI -0,5; 0,1] vs. -0,4 (0,2) [-0,7; -0,1], p value for diet by time 0,15 **MES OHA (MEAN (SEM))**: CER -0,2 (0,1) [-0,4; 0,03] vs IRG -0,2 (0,2) [95% CI -0,5; -0,001], p value for diet by time 0,49

Zitat	Studiencharakteristika	Baseline Medication	Medication change
#31772			**MES Insulin (Mean (SEM)):** CER -0,2 (0,1) [95% CI -0,5; 0,02] vs. IRG -0,6 (0,2) [95% CI -1,2; -0,1], p value for diet by time 0,002
Harvey 1993 **#31830**	J. Harvey, R. R. Wing, and M. Mullen, "Effects on food cravings of a very low calorie diet or a balanced, low calorie diet," Appetite, vol. 21, no. 2, pp. 105–115, 1993. - Substudy within the study of Wing et al. 1994 (#31773), first 6 months of the program - outcome: food cravings		
Wing 1991 http://www.ncbi.nlm.nih.gov/pubmed/2064484 #31831	N=36, 20-week intervention program, follow-up 1 year **Intervention:** behavior therapy program plus 8-week period of very low calorie diet (VLCD) (balanced diet before and after) **Control:** standard behavior therapy (BT) program, balanced diet of 4200-6300kJ/d throuout 20-week programm	**Baseline medication:** BT (n=16), VLCD (n=17) Medication (n) Diet: BT 3/16, VLCD 3/17 Oral: BT 10/16, VLCD 10/17 Insulin: BT 3/16, VLCD 4/17	**Medication after treatment (posttreatment)** Diet alone: BT 8/16 (50%), VLCD: 16/17 (94%), p<0,01 **Medication after 1-year follow-up (n/total)** Diet alone: 8/16 (50%) vs. VLCD 11/17 (53%), p= not significant
Wing 1994 **https://pubmed.ncbi.nlm.nih.gov/7942937/** #31773	N=93, 50 weeks treatment, follow-up 2 years **Intervention:** VLCD (very low calorie diet): balanced low calorie diet with 2x 12 weeks VLCD (insgesamt 50 weeks) **Control:** LCD (low calorie diet) for 50-week intervention Diabetes medication discontinued at start of treatment. Algorithm for restart medication.	**Baseline Medication:** Numbers of patients on diet only: LCD 6/48, VLCD 9/45 Numbers on oral medications: LCD 26/48 vs. VLCD 26/45 Numbers in insulin: LCD 13/48 vs. VLCD 10/45	**Medication after treatment:** Change over 2 years: % on diet only: LCD (n total=37): 31%, VLCD (n total=36): 55% Participants requiring medication: 69% LCD, 45% VLCD
VLED vs. Bariatric surgery			
Steven 2016	S. Steven, K. G. Hollingsworth, P. K. Small et al., "Calorie restriction and not glucagon-like peptide-1 explains the acute improvement in glucose control after gastric bypass in type 2 diabetes," Diabetic Medicine, vol. 33, no. 12, pp. 1723–1731, 2016. - Study treatment nur 7 Tage, nicht passend für unserer Fragestellung		
VLED vs. MER			
Li 2017 http://www.ncbi.nlm.nih.gov/pubmed/28407662 #31832	Explorative randomized pilot study, one-week fasting period compared to usual care in T2DM, n=46, 32 completed trial (16 each), follow-up 4 months, Patients with manifest T2DM medically treated with oral hypoglycemic agents and/or insulin **Intervention**: initial 7-day modified fasting program (2 pre-fasting days) followed by advice about a Mediterranean diet, **Control:** advice to a Mediterranean diet with an additional offer to participate in a 7-day modified fasting program (wait list offer) In both groups: standard medical care as determined by individual requirements. All participants instructed to keep usual treatment unless required and changed by their treating physician. **ÄZQ: Change in Medication wird nicht berichtet.**		

Zitat	Studiencharakteristika	Baseline Medication	Medication change
	Anmerkungen: explorative Pilot-Study, nicht gepowert, per-protocol analyse, Baseline differences between groups		
Williams 1998 **#31833**	- n=54, 20-week intervention Intervention: 1500-1800kcal/d, 20 days 400-600 kcal/d VLCD (1 group 1day/week, 1 group 4x 5-days) Control: Standard behavioral therapy (SBT): 1500-1800kcal/d throughout 20 weeks	- oral diabetes medication stopped 2 weeks before participation in study, participants with FPG levels > 16,7mmol/L when medication discontinued were excluded. Change in medication throuout study: If FPG values >13,9mmol/l, oral diabetes medication restarted on half dose presented before study.	Number of subjects restarting oral diabetes medication based on FPG >13,9mmol/l did not differ between three groups (p>0,6) SBT: 3 subjects 1-day group: 1 subject 5-day group: 3 subjects
Laakso 1998	M. Laakso, M. Uusitupa, J. Takala, H. Majander, T. Reijonen, and I. Penttila, “Effects of hypocaloric diet and insulin therapy on metabolic control and mechanisms of hyperglycemia in obese non-insulin-dependent diabetic subjects,” Metabolism, vol. 37, no. 11, pp. 1092–1100, 1988 Nicht passend zur Fragestellung.		
SEM: Standard Error of Mean, MES: Medication effect score			

Ebenfalls in Recherche zu Gewichtsmanagement identifiziert:

- Stegenga H. Identification, assessment, and management of overweight and obesity: Summary of updated NICE guidance. BMJ 2014; 349:g6608. https://www.ncbi.nlm.nih.gov/pubmed/25430558. #26005, und Obesity: Identification, Assessment and Management of Overweight and Obesity in Children, Young People and Adults: Partial Update of CG43 2014. https://www.ncbi.nlm.nih.gov/pubmed/25535639. #31666
  - ausgeschlossen, da Suchzeitraum (bis Februar 2014) bei diesem Thema zu alt. Für weitere Informationen siehe Stegenga 2014 (NICE CG).

3.3.2 Ausgewählte ausgeschlossene Artikel

Aus der systematischen Recherche zu Gewichtsmanagement.

Stegenga 2014 (NICE CG): very low calorie diets

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Obesity: Identification, Assessment and Management of Overweight and Obesity in Children, Young People and Adults: Partial Update of CG43 2014.	partial update of NICE clinical guideline 43 (2006). Focus on use of bariatric surgery in people with recent onset T2DM, follow-up care after bariatric surgery, and **use of very low calorie diets.** - Hier nur Betrachtung der Daten zu very low calorie diets.	7 Studies included, - 3 studies reported on people with T2DM (Simonen 2000, Wing 1991, Wing 1994).	Low (Publication bias nicht angegeben)	- Keine Subgruppenanalyse für Menschen mit Diabetes (keine Daten identifiziert)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
https://www.ncbi.nlm.nih.gov/pubmed/25535639. #31666 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/Ref-Man/Volltexte/31666.pdf Stegenga H. Identification, assessment, and management of overweight and obesity: Summary of updated NICE guidance. BMJ 2014; 349:g6608. https://www.ncbi.nlm.nih.gov/pubmed/25430558. #26005 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/Ref-Man/Volltexte/26005.pdf	**Suchzeitraum:** Medline: 1946- 05/02/14, Embase: 1980- 05/02/14, Cochrane: Inception-05/02/14, PsycINFO: Inception to 05/02/14 **Fragestellung:** Review-question 6.2: In people who are overweight or obese, what is the clinical and cost effectiveness of very low calorie diets (VLCD) in reducing weight? **Population:** Adults (≥18 years), Children (> 2 years) **Intervention:** Very-low-calorie diet (≤800 calories per day) –nutritionally complete. Includes intermittent diets (for example VLCD meal replacements just 2 days a week – which may follow a period of daily VLCD (usually 8 weeks and then intermittent)). **Vergleich:** Standard dietary advice defined as: low-calorie (regular) diet (LCD) 800-1600 calories per day or 500/800 deficit diet. **Endpunkte:** - % weight in kg change - **Health related quality of life** - And others **Studien:** RCT or SR of RCTs **Subgroup analyses:** **laut Protokoll geplant:** - T2DM (T2DM; Non-diabetic people); Expect VLCD to have different outcomes in people with T2DM **Qualitätsbewertung:** Risk of bias Bewertung siehe Seite 24/154.	No evidence found to inform recommendations in the pre-specified subgroups from the protocol: type 2 diabetes, …. - Seite 54/154: „None of the included studies reported on the following outcomes from the protocol: health - related quality of life and improvement in physical activity.“	Suche: > 2 Datenbanken, Search strategy angegeben	- Lebensqualität als betrachteter Endpunkt des Reviews, aber keine Studie berichtete Lebensqualität. - Für diese Fragestellung (very low calorie diet) Suchzeitraum zu alt. Ggf. Update-Recherche.

3.4 Low carbohydrate diets

3.4.1 Evidenz aus der systematischen Recherche zu Mediterraner Diät

Per Alert und über die systematische Recherche zur mediterranen Diät identifiziert.

In der Recherche zu Gewichtsmanagement (2021) wahrscheinlich nicht gefunden, da nicht explizit nur auf adipöse bzw. übergewichtige Personen beschränkt.

Goldenberg 2021 (low or very low carbohydrate diets)

Zitat	Studiencharakteristka	Ergebnisse	AMSTAR 2	Kommentar
Goldenberg JZ, Day A, Brinkworth GD, et al. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: Systematic review and meta-analysis of published and unpublished randomized trial data. BMJ 2021; 372:m4743. DOI: 10.1136/bmj.m4743. http://www.ncbi.nlm.nih.gov/pubmed/33441384. *Laufnummer: 31840*	**Zeitpunkt der Suche:** 25 August 2020 **Objective:** To determine the efficacy and safety of low carbohydrate diets (LCDs) and very low carbohydrate diets (VLCDs) for people with type 2 diabetes. **Population:** adults with T2DM **Intervention:** LCDs (<130 g/ day or <26% of a 2000 kcal/day diet), or VLCDs (<10% calories from carbohydrates) **Vergleich:** any wait-list control, any active control including competing dietary programs higher in carbohydrates (≥26%) with or without exercise, lifestyle and behavior recommendations **Studien:** RCTs at least 12 weeks **Outcome:** Primary: - remission of diabetes (HbA1c <6.5% or fasting glucose <7.0 mmol/L, with or without the use of diabetes medication), - weight loss, HbA1c, - fasting glucose, and - adverse events Secondary: - health related quality of life - reduction of medication - and biochemical laboratory data **Qualitätsbewertung der Studien:** Cochrane risk of bias tool. **Definition:** Low carbohydrate diet: < 130 g/day or < 26% of calories from carbohydrates based on 2000 kcal/day. **Eingeschlossene Studien (RoB-Bewertung aus dem Review):** Low risk of bias:	23 trials (1357 participants) - primarily used low fat diets as control comparators (18/23; 78%). - 7/23 (30%) of eligible trials permitted reduction of medication and reported usable medication data. **6 months:** **Remission of diabetes (HbA1c <6,5%):** LCD 59/100 vs. Control 31/100, Risk ratio (RR) 1,87 (95% CI 1,18; 2,97), 8 studies, n=264, I^2=58%, **GRADE moderate** (Imprecision: optimal information size not met) **Remission diabetes (HbA1c <6,5% without medication):** LCD 16/100 vs. Control 13/100, RR 1,24 (95% CI 0,65; 2,38), 5 studies, n=199, **GRADE low** (Imprecision: optimal information size not met, wide confidence interval) **12 months:** **Remission of diabetes (HbA1c <6,5%):** LCD 49/100 vs. Control 38/100, RR 1,27 (95% CI 0,99; 1,64), 3 studies, n=171, **GRADE moderate** (Imprecision: optimal information seize not met) **Remission of diabetes (HbA1c <6,5% without medication):** LCD 13/100 vs. Control 16/100, RR 0,79 (0,36; 1,73), 2 studies, n=126, **GRADE low** (Imprecision: optimal information size not met, wide confidence interval) **Reduction in diabetes medication: Number of participants who reduced diabetes medication) LCD vs. Control** **6 months: Risk difference:** 0,24 (0,12; 0,35), 7 studies, n=240, GRADE moderate, **12 months: Risk difference:** 0,33 (-0,00; 0,66), 3 studies, n=148, GRADE low **Quality of life - diabetes specific overall score (DDS and PAID)** 6 months: SMD -0,63 (-1,41; 0,16), 4 studies, n=169, **GRADE Low** 12 months: MD 3,10 (-2,03; 8,23), 1 study, n=116, clinically important: Yes (harm) (minimal clinically important difference =1), GRADE low **Quality of life—diabetes specific overall score (PAID, converted)** 6 months: MD -0,97 (-2,68; 0,73), 4 studies, n=169, clinically important: no, GRADE low 12 months: MD 3,10 (-2,03; 8,23), 1 study, n=116, clinically important: Yes (harm) (minimal clinically important difference =1), **GRADE low** LCDs had clinically important harms on quality of life	Low y-y-n-y-y-y-n-n-y-n-y-y-y-y-y-y Nicht erfüllte kritische Domänen: Ausgeschlossene Studien nicht angegeben. (Suche in >2 Datenbanken, Experten kontaktiert, (unpublished Data), graue Literatur und Datenbanken für klinische Studien durchsucht, Recherchestrategie angegeben). Recherche scheint verlässlich.	Übergewicht/Adipositas war nicht als Einschlusskriterium definiert, aber: „trials primarily included overweight and obese patients with type 2 diabetes,“ - Identifiziert über Alert und Umbrella-Reviews aus der systematischen Recherche zu mediterraner Diät (Umbrella-Review von Szczerba 2023). Die Bewertung der Aussagesicherheit der Evidenz wurde aus dem Originalreview (Goldenberg) und die AMSTAR 2 Bewertung des Reviews durch das

Zitat	Studiencharakteristka	Ergebnisse	AMSTAR 2	Kommentar
	- Dyson 2010 - Guldbrand 2012 - Jönnson 2009 - Morris 2019 - Saslow 2014 - Saslow 2017 High risk/some concern: - Daly 2006 - Davis 2009 - Goldstein 2011 - Iqbal 2010 - Nishimori 2018 - Perna 2019 - Sato 2017 - Tay 2014 - Vlachos 2011 - Westman 2008 - Yamada 2014 - Zadeh 2018	Es erfolgte ein Vergleich zwischen GRADE- und NutriGRADE-Bewertung. Die NutriGRADE-Bewertung fällt tendenziell besser aus. **(Weight loss at 6 months:** LCD versus control: mean difference -3,46kg (95% CI -5,25; -1,67), n=882,18 trials, GRADE moderate (reasons for grading, siehe review). **Weight loss at 12 months:** LCD vs. Control: mean difference: 0,29kg (95% CI -1,02; 1,6), n=499, 7 trials, GRADE moderate (suggestive publication bias). **HbA1c at 6 months:** mean difference LCD vs. Control: -0,47% (95% CI -0,60; -0,34), n=474, 17 trials, GRADE high. **HbA1c at 12 months:** mean difference -0,23% (95% CI -0,46; 0,00), n=489, 8 trials, GRADE moderate (imprecision)) Risk of bias - 40.6% of outcomes judged to be at low risk of bias. - 59.4% of outcomes were rated as having some concern or high risk of bias - 18/23 (78%) reported missing participant outcome data, 10 studies reporting ≥20% missing data Subgroup-Analysis: Adherence - among VLCDs to which the patients were highly adherent, a larger clinically important weight loss occurred (mean difference –4.47, –8.21 to –0.73) compared with patients less adherent to VLCDs (mean difference –0.55, –1.76 to 0.66) (test for subgroup difference P=0.05) Missing data for participants is particularly important in nutrition research in general given the often dramatic losses to follow-up in diet based clinical trials (>20% among 10/23 (43%) of trials included in this analysis) and the corresponding risk of bias due to losses to follow-up		ÄZQ übernommen, wenn sie von der Bewertung durch Szczerba abwich (z. B. AMSTAR 2-Bewertung bei Szczerba high, da das Kritierum zu den ausgeschlossenen Studien anders ausgelegt wurde).

Silverii 2020 (low-carbohydrate diets)

Zitat	Studiencharakteristka	Ergebnisse	AMSTAR 2	Kommentar
Silverii, G. A.; Botarelli, L.; Dicembrini, I.; Girolamo, V.; Santagiuliana, F.;	**Zeitpunkt der Suche:** 03/2020 **Objective:** To assess whether LC diets are associated with long-term improvement in glycemic control and	**Quality of life:** SF36 physical: low carbohydrate versus balanced carbohydrate: mean difference: -0,1 (95% KI -1,59; 1,4), 3 RCTs, n=552; I2=0%, GRADE: moderate (RoB)	low	Identifiziert über Szczerba

Zitat	Studiencharakteristka	Ergebnisse	AMSTAR 2	Kommentar
Monami, M.; Mannucci, E. (2020): Low-carbohydrate diets and type 2 diabetes treatment. A meta-analysis of randomized controlled trials. In: Acta Diabetol 57 (11), S. 1375–1382. DOI: 10.1016/S0939-4753(04)80052-8	weight loss in people with T2DM, and their cardiovascular and renal safety. **Population:** patients with type 2 diabetes **Intervention:** low-carbohydrate diet **Vergleich:** balanced carbohydrate diets **Studien:** RCTs >3 months **Outcome:** **Principal endpoints:** - HbA1c, - BMI, - mean creatinine level and - mean estimated glomerular filtration rate Secondary endpoints: - adherence to described diet - **quality of life** **Qualitätsbewertung der Studien:** RoB Cochrane, GRADE	SF36 mental: low carbohydrate versus balanced carbohdrate: mean difference 1,09 (95% KI -1,09; 3,28), 4 RCTs, n=577, I2=14%, GRADE moderate Adherence: In a majority of trials, adherence was assessed by calculating nutrient intake from self-reported questionnaires; hohe Schwankungsbreite zwischen den Studien. Mean values: Prescribed Carbohydrate (E%): Low carbohydrate: 31,8 Balanced carbohydrate: 53 Actual carbohydrate (E%): Low carbohydrate (LC): 36 Balanced carbohydrate (BC): 48,6 Differerence: LC: 5,87 BC: -3,75 Aus der Discussion: “In trials assessing self-reported food intake, the differences in carbohydrate intake between treatment arms, which were evident in the first few months, disappeared afterwards. It can be speculated that a prescribed diet which is very different from usual (pre-morbid) eating habits is more difficult to follow [8], even in the controlled setting of a clinical trial. Notably, the assessment of adherence to dietary prescriptions in clinical trials poses relevant methodological issues [8]). It is possible that per-protocol analyses, excluding patients with low adherence to prescribed regimes, would have provided more favorable results; at the same time, the prescription of a therapy should be based on intention-totreat, rather than per-protocol, results [31].”	y-py-n-py-y-y-n-py-y-n-y-n-y-y-y-y (nicht erfüllte kritische Domänen: ausgeschlossene Studien nicht aufgeführt)	2023 (Umbrella Review aus der Recherche zu mediteraner Diät), in der NVL-Recherche zum Gewichtsmanagement wahrscheinlich nicht identifiziert, da Schlagwörter zu Adipositas nicht im Abstrakt auftauchen. study quality laut Szczerba 2023: moderate Quality of life als secondary endpoint

3.4.2 Evidenz aus systematischer Recherche zu Gewichtsmanagement

Naude 2014 und 2022 (low carbohydrate diet)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Naude CE. Low carbohydrate versus isoenergetic balanced diets for reduc-	**Zeitpunkt der Suche:** March 2014 **Fragestellung:** effects of low CHO and isoenergetic balanced weight loss diets in overweight and obese adults.	19 RCTs included (n = 3209)	Low	Update wurde mittlerweile als Cochrane-Re-

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
ing weight and cardiovascular risk: A systematic review and meta-analysis. PloS One 2014; 9(7):e100652. https://www.ncbi.nlm.nih.gov/pubmed/25007189. #31662	**Population: o**verweight or obese adults, who have diabetes, glucose intolerance or insulin resistance, cardiovascular conditions or risk factors such as hypertension and dyslipidaemia, as defined by trial authors. - participants with diabetes were analysed separately **Intervention:** Treatment diets: low CHO weight loss diet plans, including a) low CHO, high fat, high protein diet (high fat variant) or b) low CHO, recommended fat, high protein diet (high protein variant) **Vergleich:** Control diets: balanced weight loss diet plans (Table 3) with same or similar prescribed energy content as treatment diet. **Endpunkte:** Weight, markers of cardiovascular disease risk, markers of DM risk or glycaemic control. Mortality, myocardial infarction and stroke were not explicitly excluded as outcomes **Studien:** RCTs (≥10 participants randomised in each group), duration of intervention ≥12 weeks **Qualitätsbewertung:** Cochrane Collaboration risk of bias tool	**No included trials reported mortality, myocardial infarction or stroke as outcomes.**	y-n-y-py-y-y-y-y-y-y-y-y-y-y-y-y-y-y (Protokoll nicht aufgefunden, ansonsten gute Berichtsqualität) Suche: in mind. 2 Datenbanken, Suchstrategie für EMBASE angegeben, Referenzen von SRs durchsucht.	view veröffentlicht, siehe unten
Naude CE, Brand A, Schoonees A, et al. Low-carbohydrate versus balanced-carbohydrate diets for reducing weight and cardiovascular risk. Cochrane Database of Systematic Reviews 2022(1):CD013334. DOI: 10.1002/14651858.CD013334.pub2. http://dx.doi.org/10.1002/14651858.CD013334.pub2.				Über die themenübergreifende systematische Recherche bei Cochrane identifiziert, siehe dort

Ross 2021 (very low carbohydrate high fat diets)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Ross LJ. Exploring the highs and lows of very low carbohydrate high fat diets on weight loss and diabetes- and cardiovascular disease-related risk markers: A systematic review. Nutr	**Suchzeitraum:** beginning 2009 to 08/ 2018 **Fragestellung:** compare well-defined VLCHF diets (≤25% CHO; ≥35%E fat) with traditional low fat (LF) diets (≥45%E CHO; ≤30% fat) **Population:** overweight or obesity	8 studies (participants n=1157 analysed) - overweight or obese **adults with T2DM** (3 studies: Davis 2009, Guldbrand 2012, Tay 2015) or no history of significant disease (5 studies: Brinkworth 2009, Gardner 2016, Gardner 2018, Lim 2014, Ruth 2013)	Critically low (ausgeschlossene Studien nicht benannt, Publication bias	Im Supplement wird cardiovascular disease als ein Endpunkt angegeben, im Review aber nicht erwähnt oder berichtet.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Diet 2021; 78(1):41–56. https://www.ncbi.nlm.nih.gov/pubmed/33283417. #31702 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/Ref-Man/Volltexte/31702.pdf	**Intervention:** Very low carbohydrate high fat diet (VLCHF): ≤25% of total energy intake (%E) or <130 g from CHO and >35%E from fat **Vergleich:** Low fat (LF): <30%E from fat and ≥ 45%E from CHO **Endpunkte:** - weight loss - changes to diabetes- and CVD-related risk markers. (aus Supplement: auch Cardiovascular disease or CVD) **Studien:** RCTs, ≥ 3months duration **Qualitätsbewertung der Studien:** Cochrane collaboration tool.	No Meta-analysis: heterogeneity related to intervention duration and outcome measures. **Change in medication:** Seite 11/16: Nur narrative Darstellung im Hintergrundtext, daher Betrachtung der Einzelstudien Davis 2009, Guldbrand 2012, Tay 2015 (siehe unten). **RoB-Bewertung** der 3 Studien (durch die Review-Autoren): Tay 2015: low RoB, Davis 2009: Selection bias unclear, sonst low RoB, Guldbrand 2012: Reporting bias und performance bias (high), sonst alle Kategorien low.	nicht untersucht). Suchstrategie angegeben, ≥2 Datenbanken durchsucht	An zwei Stellen wird die Reduktion der Diabetes-Medikation angesprochen, aber es werden keine weiteren Daten genannt.

Kurzübersicht Einzelstudien (RCTs, T2DM) aus Ross et al., 2021 (Change in Medication)

Link zu den ausführlichen Evidenztabellen der Einzelstudien im Anhang: auf Autorennamen klicken.

Zitat	Intervention / Vergleich	Baseline medication	Change in Medication	Zusammenfassung
Davis 2009 **#31766**	N=105, Intervention 1 year **Intervention:** low carbohydrate diet (LC) (n=55) **Control:** low-fat diet (LF) (n=50) ITT-Analyse, - prerandomization: adjusted diabetes medication to minimize side effects	**Baseline Medications:** Metformin: LC 43/55 (78%), LF 43/50 (86%) Sulfonylurea: LC 29/55 (44%9, LF 26/50 (52%) Insulin LC 19/55 (35%), LF 12/50 (24%) Cholesterol lowering medication: LC 34/55 (62%), LF 28/50 (56%).	Participants using insulin: dose reduced by mean ±SD of 10 ±14 units in LC arm and increased by 4 ±19 units in the LF arm (P = 0.12) at 12 months. Participants using sulfonylurea: 26% had reduction in dose at 12 months. Dose reduction: 1.6 ± 3,6mg in both arms.	- tendenziell Reduktion der Insulindosis (12 Monate) in der LC Gruppe im Vergleich zur LF-Gruppe (n.s.)
Guldbrand 2012 #31769	N= 61, 2-year intervention **Intervention:** Low fat diet (LFD) **Control:** Low carbohydrate diet (LCD)	**Medication at baseline** - Diet only: LFD 2/31 patients, LCD 2/30 - oral glucose-lowering medication only: LFD 13/31, LCD: 15/30 - combination of insulin and oral medication LFD 11/31, LCD: 10/30	**Insulin dose baseline:** LFD: 39±51 E vs. LCD 42±65 E, p=0,86 (between groups) **Insulin dose 6 m:** LFD: 38±48 E (p for change from baseline 0,12) vs. LCD 30 ±47 (p=0,020), p for between group change 0,046 **Insulin dose 24 m:** LFD 36 ±44 (p=0,5), vs. LCD 35 ±56 (p=0,14) P value for change over all time points between groups 0,83 P value for change over all time points: LFD group 0,81, LCD group 0,007 **Metformin dose baseline (mg):**	- Reduktion der Insulindosis in der LCD-Gruppe (6 Monate). Dosis in LCD-Gruppe niedriger als in LFD-Gruppe. - nach 12 Monaten kein statistisch signifikanter Unterschied zwischen den Gruppen.

Zitat	Intervention / Vergleich	Baseline medication	Change in Medication	Zusammenfassung
			LFD 1,435 ±946 vs. LCD 1,375 ±950, p=0,8 (between groups) **Metformin dose 24 m:** LFD 1,306±901 (p=0,28) vs. LCD 1,292±911 (p=0,38), P value for change over all time points between groups 0,93 P-Werte in Klammern: Vergleich zu baseline **Glibenclamid:** LFD vs. LCD, P value for change over all time points between groups 0,56 Für weitere Details siehe Beschreibung Einzelstudien.	Keine statistisch signifikanten Unterschiede in der Dosis für Metformin und Glibenclamid.
Tay 2014 http://www.ncbi.nlm.nih.gov/pubmed/26224300. #31777	n=115, 24 weeks intervention **Intervention:** Low carbohydrate diet (LC) **Control:** High carbohydrate, low fat diet (HC)	**Medication at baseline** (%): LC: n=58, HC: n=57 Insulin: LC 10%, HC 11% Metformin: LC 79%, HC 72% Sulfonylureas: LC 34%, HC 28% Thiazolidinediones: LC 5%, HC 5% GLP-1-RA: LC 2%, HC 2% DPP-4-I: LC 2%, HC 4% Antiglycemic MES* (Medication effect score): LC: 1,3 ±1,0; HC: 1,1 ±1,1	**Week 52: (Changes) Antiglycemic MES***: LC: -0,5 (-0,7; -0,4) versus HC: -0,2 (-0,4; -0,06) Difference in change between groups: -0,3 (-0,6; -0,05), p=0,02 MES* reduction ≥ 20%, n (%): LC: 30 (52%) versus HC: 12 (21%), p=0,001 MES* reduction ≥ 50%, n (%): LC: 17 (29%) versus HC: 10 (18%), p=0,14 *Changes in diabetes medication requirements quantified by the antiglycemic medication effect score (MES). A higher MES corresponded to a higher diabetes medication requirement.	Stärkere Reduktion des Medication effect scores nach 52 Wochen in LC-Gruppe als in HC-Gruppe

3.4.3 Evidenz aus der themenübergreifenden systematischen Recherche

Naude 2022 (low carbohydrate diet)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Naude CE, Brand A, Schoonees A, et al. Low-carbohydrate versus balanced-carbohydrate diets for reducing weight and cardiovascular risk. Cochrane Database of Systematic Reviews 2022(1):CD013334. DOI: 10.1002/14651858.CD013334.pub2.	**Search:** up to 25 June 2021 **Fragestellung:** effects of low-carbohydrate weight-reducing diets to weight-reducing diets with balanced ranges of carbohydrates, in relation to changes in weight and cardiovascular risk, in overweight and obese adults ± type 2 diabetes mellitus (T2DM). **Population:** adults (18 years+) who were overweight or living with obesity, without or with T2DM, and without or with cardiovascular conditions or risk factors.	None of the included trials reported on the following outcomes for any of the four (siehe Subgruppen) comparisons: all-cause mortality, cardiovascular mortality, non-fatal myocardial infarction, non-fatal stroke and diagnosis of T2DM **In overweight and obese participants with T2DM:** low-carbohydrate weight-reducing diets versus balanced-carbohydrate weightreducing diets (weight-reducing phases only):	**High** y-y-(y)-py-y-y-y-y-y-y-y-y-y-y-y-y	Die in der NVL-Recherche priorisierten Endpunkte wurden nicht in den Studien berichtet. Eine Vorgängerversion des Artikels vom gleichen Autor

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
http://dx.doi.org/10.1002/14651858.CD013334.pub2.	**Intervention/Coparison:** trials had to compare low-carbohydrate weight-reducing diets to balanced carbohydrate (45% to 65% of total energy (TE)) weight-reducing diets, have a weight-reducing phase of 2 weeks or longer and be explicitly implemented for the primary purpose of reducing weight, with or without advice to restrict energy intake. **Endpoints:** Primary outcomes - change in body weight (kg) - number of participants per group with weight loss of at least 5%, assessed at short- (three months to < 12 months) and long-term (≥ 12 months) follow-up. Secondary endpoints (Auswahl der für die NVL-Recherche wichtigen Endpunkte): - All-cause mortality - Cardiovascular mortality, non fatal myocardial infarction or stroke - Adverse events **Subgruppenauswertungen** nach: - participants with or without diabetes - diets with weight-reducing phases only and those with weight-reducing phases followed by weightmaintenance phases **Studies:** RCTs **Qualitätsbewertung der Studien:** RoB 2	**change in body weight over 3 to 6 months:** MD −1.26 kg (95% CI −2.44 to −0.09), I^2 = 47%, 1114 participants, 14 RCTs, moderate-certainty evidence **change in body weight over 1 to 2 years:** MD −0.33 kg (95% CI −2.13 to 1.46), I^2 = 10%, 813 participants, 7 RCTs, moderate-certainty evidence); **number of participants per group with weight loss ≥ 5% at 1 to 2 years:** RR 0.90 (95% CI 0.68 to 1.20), I^2 = 0%, 106 participants, 2 RCTs, very low-certainty evidence. Evidence on participant-reported adverse effects was limited, and we could not draw any conclusions about these.		(2014) wurde in der systematischen Recherche zu Gewichtsmanagement gefunden. Siehe oben)

Korsmo-Haugen 2019 (low carbohydrate diet versus higher carbohydrate diets)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Korsmo-Haugen H-K, Brurberg KG, Mann J, et al. Carbohydrate quantity in the dietary management of type 2 diabetes: A systematic review and meta-analysis. Diabetes Obes Metab 2019; 21(1):15–27.	**Suchzeitraum:** 1983 – January 2016. **Fragestellung:** Compare effects of low carbohydrate diets (LCDs) with effects of higher carbohydrate diets (HCDs) in adults with T2DM. **Population:** adults with T2DM **Intervention:** diet below 40% total energy (%E) from carbohydrate.	23 studies, n= 2178 (1061 low-carbohydrate, 1194 control), follow-up: 3 months to over 3 years. - 12 studies included individuals either overweight or obese. - LCD was compared to variety of diets (low-fat diets (8 trials), diets typical of standard diabetes care (4 trials), high-carbohydrate diets (3 trials), low-protein diets (2 trials), standard protein diet (1 trial), Mediterranean diets (2 trials), high-carbohydrate, low-fat diets (2 trials), a high wheat-fibre diet (1 trial), low-glycaemic index diets (2 trials), high glycaemic index diet (1 trial) - 6 LCD and 10 of comparator diets: energy-restricted diets (≈1200 to 1800 kcal/day). - In 15 studies: weight reduction was a goal of dietary intervention.	Moderate (Funding in den Studien und Begründung der Studienauswahl nicht angegeben)	- LCD meist mit anderen Diäten verglichen, nicht mit neutraler Kontrolle. - übergewichtige und adipöse, als auch normgewichtige Menschen mit

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
DOI: 10.1111/dom.13499 . http://www.ncbi.nlm.nih.gov/pubmed/30098129. *Laufnummer: 31654* Identifiziert über NICE NG28	**Vergleich:** diet above 40% total energy from carbohydrate. **Ausschluss:** - No restriction regarding co-morbiditiy - Complex interventions with potential to interfere with effect of dietary intervention, such as parenteral administration or promotion of physical activity **Endpunkte:** weight, HbA1c, lipids, blood pressure and compliance with dietary intervention. **Studien:** RCTs (duration ≥3 months) **Subgroup analyses:** - duration of intervention, - extent of carbohydrate restriction and - risk of bias. **Qualitätsbewertung:** Cochrane RoB Bewertung.	**Use of diabetes medication:** *„The limited information given in the included studies suggests that, particularly in the VLCD groups, there was a greater reduction in the use of diabetes medication (mainly insulin) that may have masked a more positive impact on glycaemic control than what we have shown. On the other hand, only four studies showed a significant difference in change in diabetes medication between the diets; some of the studies repeated their analyses, adjusting for difference in medication and found that it did not alter the conclusions.“* Keine weiteren Angaben im Review, daher **Betrachtung der Einzelstudien** **Eingeschlossene Studien (RCTs) und Risk of bias-Bewertung durch Review-Autoren:** 1. Facchini 2003 (high risk of bias) 2. Samaha 2003 (high risk of bias) 3. Daly 2006 (high risk of bias) 4. Shai 2008 (unclear risk of bias) 5. Westman 2008 (high risk of bias) 6. Davis 2009 (unclear risk of bias) 7. Jönnson 2009 (unclear risk of bias) 8. Goldstein 2011 (unclear risk of bias) 9. Larsen 2011 (Low risk of bias) 10. Guldbrand 2012 (unclear risk of bias) 11. Krebs 2012 (low risk of bias) 12. Luger 2013 (high risk of bias) 13. Jenkins 2014 (unclear risk of bias) 14. Yamada 2014 (high risk of bias) 15. Wolever 2008 (unclear risk of bias) 16. McLaughlin 2007 (unclear risk of bias) 17. Jonasson 2014 (high risk of bias) 18. Pedersen 2014 (low risk of bias) 19. Brinkworth 2004 (unclear risk of bias) 20. Elhayany 2010 (unclear risk of bias) 21. Garg 1994 (high risk of bias) 22. Walker 1995 (high risk of bias) 23. Walker 1999 (high risk of bias)	Suche in > 2 elektronischen Datenbanken, Schlagworte angegeben, Referenzlisten durchsucht.	T2DM betrachtet. Keine Subgruppenanalyse nach Gewicht. - fast gleiche Fragestellung wie Huntriss 2018 (#31655) und Meng 2017 (#31657) Identifiziert über die themenübergreifende systematische Recherche

Kurzübersicht Einzelstudien (RCTs) aus Korsmo-Haugen et al., 2019 (Change in Medication)

Link zu den ausführlichen Evidenztabellen der Einzelstudien im Anhang: auf Autorennamen klicken.

- Die eingeschränkte Datenlage ist bei der zusammenfassenden Burteilung zu berücksichtigen. „Change in Medication“ war in keiner der Studien primärer Endpunkt. Alle Studien haben relevante Mängel (siehe auch RoB-Bewertung der Studien).

Nr	Zitat	Intervention / Vergleich	Baseline medication	Change in Medication		Zusammenfassung
1	**Facchini 2003** http://www.ncbi.nlm.nih.gov/pubmed/12716753 #31789	N=191, mean follow-up interval of 3.9 ± 1.8 years, **Intervention:** low-iron available, polyphenol-enriched (CR-LIPE) diet **Control:** standrad protein restricted diet **Population:** T2DM with various degrees of renal failure and proteinuria (attributed to diabetes)	**Baseline Use of Medication** Insulin, n (%) CR-LIPE: 49 (49%), Control: 46 (51%) Metformin: CR-LIPE: 6 (6%), Control: 5 (5%) Sulfonylurea: CR-LIPE 23 (23%), Control 24 (26%)	**Use of Medication**		- Soweit beurteilbar: kein relevanter Unterschied zwischen den Gruppen und im Zeitverlauf
				2 years Insulin, n (%) CR-LIPE: 41 (47%), Control: 38 (51%) Metformin (at 2 years): CR-LIPE: 5 (6%), Control: 5 (7%) Sulfonylurea (at 2 years): CR-LIPE 18 (20%), Control 19 (25%)	**4 years Insulin, n (%)** CR-LIPE: 23 (47%), Control: 26 (54%) Metformin (at 4 years): CR-LIPE: 5 (7%), Control: 4 (8%) Sulfonylurea (at 4 years): CR-LIPE 14 (19%), Control 10 (21%) (p-Werte nicht angegeben)	
2	**Samaha 2003** http://www.ncbi.nlm.nih.gov/pubmed/12761364. #31790	n=132, 6 months **Intervention:** Low-carbohydrate diet (LC) **Control:** calorie and fat restricted diet (LF) Population: ≥18y, BMI, ≥35kg/m^2	Diabetes (39%) LC-diet n=26 T2DM, LF-diet n=26 T2DM Für Informationen zu Baselinedaten „treatment for diabetes“ siehe table 1 der Studie.	**Change in medication by 6 months:** - LC-diet: 7 subjects had dose reductions in oral hypoglycemic agents or insulin. - LF diet: 1 subject had a dose reduction in insulin and one subject began oral therapy		- Tendenz: mehr Proband*innen mit Dosisreduktion in der LC-Gruppe als in der LF-Gruppe
3	**Daly 2006** http://www.ncbi.nlm.nih.gov/pubmed/16409560. #31791	N=102, 3 months **Intervention:** Low carbohydrate diet (LC) **Control:** healthy eating group (HE)	Baseline Medication (approximately post study evaluation) Pro Gruppe jeweils 40% oral hypoglycaemic agents (OHAs), 20% insulin 40% combination of the two	post-study analysis of medication changes from baseline, date available for 75% (not in the original study design, limited analysis) - Insulin use reduced in insulin using subjects: LC: 85%, LF: 22% - Increased insulin use (in insulin using subjects): LC: 5%, LF: 16% - Oral antihyperglycemic agents: LC: unchanged, LF: unchanged		- soweit aus post-hoc erhobenen Daten ableitbar: Mehr Patient*innen in der LC-Gruppe haben die Insulindosis senken können, weniger mussten sie steigern.
4	**Shai 2008** http://www.ncbi.nlm.nih.gov/pubmed/18635428. #31792	N=322, 2-years trial **Interventions:** 1.) Low fat diet 2.) Mediterranean diet 3.) Low carbohydrate diet **Population:** moderately obese subjects (nicht nur Menschen mit T2DM eingeschlossen)	Keine Subgruppenanalyse (T2DM: 46/322) mit Baselinedaten für Gewicht, HbA1c, Diabetes duration), keine Angaben zur Baseline medication.	Change in medication: „Twenty participants initiated blood-pressure treatment, five initiated medications for glycemic control, and one reduced the dosage of medications for glycemic control.“ (Keine weiteren Angaben.)		Angaben für Beurteilung nicht ausreichend

Nr	Zitat	Intervention / Vergleich	Baseline medication	Change in Medication	Zusammenfassung
	#31793				
5	**Westman 2008** http://www.ncbi.nlm.nih.gov/pubmed/19099589. # 31794	N=84, 24-week **Intervention:** Low-carbohydrate, Ketogenic Diet Group Intervention (LCKD) **Control:** Low-glycemic index diet group intervention (LGID)	**Baseline:** LCKD (n=21) 20 (95,2%) taking hypoglycemic medications - Insulin + oral agents, n=4 - Insulin only, n=4 - Oral agents, n=12 LGID (n=29) 22 (75,9%) taking hypoglycemic medication - Insulin, n=3 - Oral agents, n=19	**Week 24** Diabetes medications were reduced or eliminated in 95.2% of LCKD vs. 62% of LGID participants (p < 0.01). (zu Einzelauswertung der Patienten mit Insulintherapie zu Beginn der Studie, siehe Beschreibung der Einzelstudie)	- Mehr Patient*innen in der LCKD-Gruppe konnten die Diabetesmedikation reduzieren als in der LGID-gruppe.
6	**Davis 2009** **#31766**	N=105, Intervention 1 year **Intervention:** low carbohydrate diet (LC) (n=55) **Control:** low-fat diet (LF) (n=50) ITT-Analyse, - prerandomization: adjusted diabetes medication to minimize side effects	**Baseline Medications:** Metformin: LC 43/55 (78%), LF 43/50 (86%) Sulfonylurea: LC 29/55 (44%), LF 26/50 (52%) Insulin LC 19/55 (35%), LF 12/50 (24%)	Participants using insulin: dose reduced by mean ±SD of 10 ±14 units in LC arm and increased by 4 ±19 units in the LF arm (P = 0.12) at 12 months. Participants using sulfonylurea: 26% had reduction in dose at 12 months. Dose reduction: 1.6 ± 3,6mg in both arms.	- tendenziell Reduktion der Insulindosis (12 Monate) in der LC Gruppe und leichte Steigerung in der LF-Gruppe, im Vergleich nich signifikant.
7	**Jönnson 2009** http://www.ncbi.nlm.nih.gov/pubmed/19604407. #31795	randomized cross-over study, 2 consecutives 3 months periods, 13 patients Paleolithic (‚Old Stone Age') diet and a diabetes diet as generally recommended	**Baseline (n=13):** Antidiabetic drugs per day: 1,2 ± 0,9 Metformin (yes/no): 9/4 Sulfonylurea (yes/no): 3/10 Thiazolidinedione (yes/no): 3/10	**Medication:** „All medication remained unchanged during the whole study…" Eine Aussage zu unserer Fragestellung ist nicht möglich.	- Aussage nicht möglich.
8	**Goldstein 2011** #31797	N=52, 1 year **Intervention:** Modified Atkins diet (ATK) **Control:** Standard ADA calorie-restricted diet	Keine Analyse der Baseline-Medication. By 3-month: use of hypoglycemic medication reduced in 17/26 ATK and 11/26 ADA (p=0,16)		- Angaben zur Beurteilung nicht ausreichend. Tendenziell konnte in ATK-

Nr	Zitat	Intervention / Vergleich	Baseline medication	Change in Medication	Zusammenfassung
					Gruppe mehr Proband*innen hypoglykämische Therapie reduzieren (n.s.).
9	**Larsen 2011** #31768	N= 108, 12 months intervention **Intervention:** High-protein diet (HP) **Control:** High carbohydrate diet (HC) ITT Analyse	Diabetes treatment, n (%) (at baseline) None: HP: 5 (9%), HC: 5 (11%) Insulin: HP: 10 (10%), HC: 7 (15%) Tablets: HP: 38 (72%), HC: 34 (74%)	**Change in diabetes medication** (Weighted %change in diabetes medication), HP n=48, HC n=41 3 months: HP -8,71 vs. HC 0,68, Difference between groups: -9,38 (95% CI -17,85; -0,92) 12 months: HP -8,17 vs. HC 4,56, Difference between groups: -12,72 (95% CI -28,18; 2,73) trend for improved glycaemic control in HP, statistical adjustment of the change in medications did not modify the outcome of the change in HbA1c.	Change in diabetes medication nach 3 monaten in der HP-Gruppe höher (stärkere Reduktion), nach 12 Monaten Unterschied nicht mehr statistisch signifikant.
10	**Guldbrand 2012** #31769	N= 61, intervention 2 years **Intervention:** Low fat diet (LFD) **Control:** Low carbohydrate diet (LCD)	**Medication at baseline** - Diet only: LFD 2/31 patients, LCD 2/30 - oral glucose-lowering medication only: LFD 13/31, LCD: 15/30 - combination of insulin and oral medication LFD 11/31, LCD: 10/30	**Insulin dose baseline**: LFD: 39±51 E vs. LCD 42±65 E, p=0,86 (between groups) **Insulin dose 6 m:** LFD: 38±48 E (p for change from baseline 0,12) vs. LCD 30 ±47 (p=0,020), p for between group change 0,046 **Insulin dose 24 m:** LFD 36 ±44 (p=0,5), vs. LCD 35 ±56 (p=0,14) P value for change over all time points between groups 0,83 **Metformin dose baseline (mg):** LFD 1,435 ±946 vs. LCD 1,375 ±950, p=0,8 (between groups) Metformin dose 24 m: LFD 1,306±901 (p=0,28) vs. LCD 1,292±911 (p=0,38), P value for change over all time points between groups 0,93 P-Werte in Klammern: Vergleich zu baseline Glibenclamid: LFD vs. LCD, P value for change over all time points between groups 0,56 Für weitere Details siehe Beschreibung Einzelstudien.	- Reduktion der Insulindosis in der LCD-Gruppe (6 Monate). Dosis in LCD-Gruppe niedriger als in LFD-Gruppe. - nach 12 Monaten kein statistisch signifikanter Unterschied zwischen den Gruppen. Keine statisisch signifikanten Unterschiede in der Dosis für Metformin und Glibenclamid.
11	**Krebs 2012** http://www.ncbi.nlm.nih.gov/pubmed/22286528.	N=419, 12-month intervention, 12-month follow-up **Intervention:** Low fat high protein (HP) **Control:** low fat high carbohydrate (HC)	Diabetes medication nur als Baseline-Daten genannt. HbA1c-Outcomes: Differences are estimated controlling for changes in glucose-lowering medication over time (change in glucose medication aber nicht angegeben).		Keine Angaben

Nr	Zitat	Intervention / Vergleich	Baseline medication	Change in Medication	Zusammenfassung
	# 31800				
12	**Luger 2013** http://www.ncbi.nlm.nih.gov/pubmed/23674159. #31802	N=44, 12 weeks **Intervention:** High protein diet (HP) **Control:** Standard diet (ST)	**Baseline** Insulin dose (IU) HP (n=22): 57,3 ±26,3 ST, n=22): 52,7 ±28,8 31/44 subjects recieved an additional oral antidiabetic medication.	Insulin requirement (IU) **Baseline:** HP 57,7 ±27,2 versus ST 52,7 ±28,8 Difference between groups (ST vs. HP): -4,9 (-22,2; 12,3), p: n.s. **4 weeks:** HP 52,1 ±27,3 versus ST 53,1 ±28,3 Difference between groups (ST vs. HP): 1,0 (-16,2; 18,1) **12 weeks:** HP 48,2 ±30,8 versus ST 53,6 ±28,6 Difference between groups (ST vs. HP): 0,6 (-13,0; 23,6) Group x time interaction: p=0,07	Tendenziell in HP-Gruppe leichte Reduktion der Insulindosis, während diese in der ST-Gruppe nahezu konstant bleibt.
13	**Jenkins 2014** http://www.ncbi.nlm.nih.gov/pubmed/24929428. #31803	N=141, 3-month trial **Intervention:** Test group: low-glycemic-load (low-GL) diet with alpha-linolenic acid (ALA) and monounsaturated fatty acid (MUFA) given as a canola oil–enriched bread supplement **Control group:** whole-grain diet with a whole-wheat bread supplement	Control-diet (CD), n=71; Test-diet (TD), n=70 **Baseline antihyperglycemic medication:** Metformin: CD 94%, TD 93% Sulfonylurea: CD 25%, TD 31% Thiazolidinedione: CD 6%, TD 11% DPP-4-I: CD 17%, TD 17% Meglitinides: CS 3%, TD 1% Alpha-Glucosidase-I.: CD 0%, TD 1% Injectable GLP-1-RA: CD 0%, TD1% Combinatino (Janumet): CD 3%, TD 3%	**Ergebnisse Medication change:** Oral antihyperglycemic medication dosages: Test diet: increase: 1 participant, reduced: 5 participants Control diet: decreased: 4 participants no significant treatment differences.	- Wenige Angaben, kurze Studiendauer
14	**Yamada 2014** http://www.ncbi.nlm.nih.gov/pubmed/24390522. #31805	N=24, 6-month trial **Intervention:** conventional calorie-restricted diet (CR) **Control:** low-carbohydrate diet (LC)	**Glucose lowering drugs, no (%)** **Baseline** None: LC 0%, CR 0% Metfomrin: LC 41,7%, CR 8,3% Sulfonylurea: LC 41,7%, CR 66,7% Glinide: LC 8,3%, CR 0% Insulin LC 25%, CR 33,3% Thiazolidinedione LC 33,3%, CR 50% Alpha-Glucosidase I.: LC 16,7%, CR 0% DPP-4-I: LC 16,7%, 25%	- During study period: did not change the medications, unless hypoglycaemia occurred. - Three patients treated with a sulfonylurea or insulin in the low-carbohydrate group experienced symptomatic hypoglycaemia, although the events did not recur after adjusting the medications. Keine weiteren Angaben im Paper.	Nur wenige Angaben

Nr	Zitat	Intervention / Vergleich	Baseline medication	Change in Medication	Zusammenfassung
			GLP-1-RA: LC 0%, CR 0%		
15	**Wolever 2008** http://www.ncbi.nlm.nih.gov/pubmed/18175744. #22168	Anmerkung ÄZQ: Die für unsere Fragestellung relevanten Endpunkte werden nicht berichetet. Antihyperglykämische Medikation war zu Studienbeginn ein Ausschlusskriterium und die Indikation zur medikamentösen Therapie während der Studie wurde als treatment failure gesehen und Patienten wurden von der Studie ausgeschlossen.			-
16	**McLaughlin 2007**	Anmerkung ÄZQ: Die von uns betrachteten Endpunkte (z. B. Change in medication, QoL, harte patientenrelevante Endpunkte) wurden nicht berichtet.			-
17	**Jonasson 2014,** #31783	Siehe Guldbrand 2012 (gleiche Studie NCT01005498)			Siehe oben
18	**Pedersen 2014** #31804	Population: Adult, overweight participants with type 2 diabetes, with albuminuria (30- 600 mg/24 h or an albumin-to-creatinine ratio of 3.0-60 mg/mmol), and estimated GFR of >40 ml/min/1.73 m2 were enrolled. -> Zurückstellen für Kapitel Folgeerkrankungen (diabetische Nephropathie)			-
19	**Brinkworth 2004** #31801	Berichtet nicht über change in Medication			-
20	**Elhayany 2010**	Berichtet nicht über change in Medication			-
21	**Garg 1994**	Berichtet nicht über change in Medication			-
22	**Walker 1995**	Berichtet nicht über change in Medication			-
23	**Walker 1999**	Berichtet nicht über change in Medication			-

Huntriss 2018 (low carbohydrate diet)

Zitat	Studiencharakteristika	Ergebnisse	AMSTA 2	Kommentar

Huntriss R, Campbell M, Bedwell C (2018) The interpretation and effect of a low carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. European Journal of Clinical Nutrition 72(3):311–25 12.
 	
https://pubmed.ncbi.nlm.nih.gov/29269890/
 	
Identifiziert über NICE NG28
 	
#31655
	Zeitpunkt der Suche: June 2016
	
	Fragestellung: Is a low-carbohydrate diet effective in the management of type 2 diabetes in adults?
	
	Population: adults with T2DM aged ≥18 years.
	
	Intervention: low-carbohydrate diet as defined by the author (lower carbohydrate intake than control group).
	
	Vergleich: usual care, which included a variety of diets that could be offered to patients as part of their diabetes care.
	
	Endpunkte:
	primary outcome: change in HbA1c (%).
	Secondary outcomes: change in
	- diabetes medications,
	- weight (kg),
	- total, LDL- and HDL-cholesterol (mmol/L),
	- triglycerides (mmol/L),
	- systolic and diastolic blood pressure (mmHg), and
	- dietary adherence
	- quality of life (laut prospero).
	
	Studien: RCTs.
	Results analysed descriptively and meta-analyses at 1 year (to decrease study design heterogeneity and to allow for adherence issues that may occur in longer-term studies which is more likely to reflect long-term behaviour of patients.).
	
	Qualitätsbewertung: Cochrane risk of bias tool.
	
	Risk of bias in included studies:
	15/18 were considered high risk of bias. 15/18 with high risk of performance bias (due to nature of intervention, no blinding). High risk of detection bias in
		18 studies (n=2204 randomized, date analysed n=1937)
		- definition of a low-carbohydrate diet varied
		
		Diabetes medication changes:
		16/18 trials included participants on diabetes medication at trial start.
		- 2 trials did not report on medication changes (Yamada 2013, Elhayany 2010).
		- remaining 14 trials reported reduced requirement for diabetes medication in LCIA compared to control group.
		- 11 trials discussed statistical significance of the difference in medication reduction between groups. 9 of these trials (82%): significant reduction in diabetes medication in the LCIA ($p \leq 0.05$): Statistically significant reduction in
		  ○ Insulin (Pohl 2005, Pohl 2009)
		  ○ Oral hypoglycemic agents (Shirai 2013, Guldbrand 2012)
		  ○ Combined diabetes medication score (Tay 2014, Westman 2008, Larsen 2011, Rock 2014, Tay 2015)
		Two trials did not include participants on diabetes medication at trial start:
		- 1 study: no difference in commencement of medications at trial end (1 year) (Wolever 2008).
		- 1 study: no difference in commencement of medications at 1 year, however at 4 years 44% of participants in the LCIA in comparison to 70% of participants in the control group required treatment. (Esposito 2009)
		
		- Beschreibung der Studien (siehe unten)
		
		Kommentar: „Dietary adherence was an issue in most studies. A very low-carbohydrate diet (<50g/day) seems unrealistic in this population however a low-carbohydrate diet (<130g/day) appears achievable. Improved clinical outcomes were observed in some studies as a result of a achieving a low- or moderate-carbohydrate diet“
		
		Eingeschlossene Studien:
		1. Esposito 2009
		2. Guldbrand 2012
		3. Wolever 2008
		4. Tay 2015
		5. Rock 2014
		6. Larsen 2011
		7. Goldstein 2011
		8. Elhayany 2010
		9. Davis 2009
		10. Mayer 2014
			Critically low
			
			(viele Kriterien nicht erfüllt: Selektion, Extraktion, Publication bias, ausgeschlossene Studien, Funding in den Studien, Studien nicht ausführlich beschrieben).
				Methodik des Reviews nicht gut beschrieben, daher Betrachtung der Einzelstudien
				
				Identifiziert über die themenübergreifende systematische Recherche

Zitat	Studiencharakteristika	Ergebnisse	AMSTA 2	Kommentar
	some studies (blinding of outcome accessment). Insufficient detail of study processes often resulted in unclear risk of bias.	11. Yamada 2013 12. Jonasson 2014 13. Westman 2008 14. Tay 2014 15. Shirai 2013 16. Daly 2006 17. Pohl 2009 18. Pohl 2005		

Kurzübersicht Einzelstudien (RCTs) aus Huntriss R et al., 2018 (Change in Medication)

Link zu den ausführlichen Evidenztabellen der Einzelstudien im Anhang: auf Autorennamen klicken.

Zitat	Studiencharakteristika	Medication baseline	Medication change
Risk of bias in included studies: 15/18 were considered high risk of bias. 15/18 with high risk of performance bias (due to nature of intervention, no blinding). High risk of detection bias in some studies (blinding of outcome accessment). Insufficient detail of study processes often resulted in unclear risk of bias.			
2 trials not reporting on medication change			
Yamada 2014 (Yamada 2013) http://www.ncbi.nlm.nih.gov/pubmed/24390522. #31805	N=24, 6-month trial **Intervention:** conventional calorie-restricted diet (CR) **Control:** low-carbohydrate diet (LC)	**Glucose lowering drugs, no (%) Baseline** None: LC 0%, CR 0% Metfomrin: LC 41,7%, CR 8,3% Sulfonylurea: LC 41,7%, CR 66,7% Glinide: LC 8,3%, CR 0% Insulin LC 25%, CR 33,3% Thiazolidinedione LC 33,3%, CR 50% Alpha-Glucosidase I.: LC 16,7%, CR 0% DPP-4-I: LC 16,7%, 25% GLP-1-RA: LC 0%, CR 0%	- During study period: did not change the medications, unless hypoglycaemia occurred. - Three patients treated with a sulfonylurea or insulin in the low-carbohydrate group experienced symptomatic hypoglycaemia, although the events did not recur after adjusting the medications. Keine weiteren Angaben im Paper.
Elhayany 2010	Not reporting on medication changes		
Statistically significant reduction in Insulin			
Pohl 2005	Pohl M, Mayr P, Mertl-Roetzer M, Lauster F, Lerch M, Eriksen J *et al.* Glycaemic control in type II diabetic tube-fed patients with a new enteral formula low in carbohydrates and high in monounsaturated fatty acids: a randomised controlled trial. Eur J Clin Nutr 2005; 59: 1221-1232. - Relevant für NVL (Sondenernährung?), Proof of principle		

Zitat	Studiencharakteristika	Medication baseline	Medication change
Pohl 2009	Pohl M, Mayr P, Mertl-Roetzer M, Lauster F, Haslbeck M, Hipper B *et al.* Glycemic control in patients with type 2 diabetes mellitus with a disease-specific enteral formula: stage II of a randomized, controlled multicenter trial. JPEN J Pareneter Enteral Nutr 2009; 33: 37-865 49. - Relevant für NVL (Sondenernährung?), proof of principle		
Statistically significant reduction in oral hypoglycemic agents			
Shirai 2013 http://www.ncbi.nlm.nih.gov/pubmed/24331681. #31808	N=240, 24-weeks intervention **Intervention:** FD-group: low-caloric diet with partial use of formula diet **Control:** CD group: conventional low-caloric diet group Medication algorithm to reduce insulin, sulfonylurea, Thiazolidinedione before taking formula diets	Conventional diet group (n=110), formula diet group (n=119)	Changes of admistered drugs after intervention of diets Insulin therapy: - insulin dose reduced in 9/26 patients in CD vs. 17/20 patients in FD, not significant. Sulfonylureas: - discontinued 3/51 in CD vs. 20/57 in FD ($p < 0.02$), - reduced 3/51 in CD vs. 11/51 in FD ($p < 0.05$). thiazolizine: - discontinued 4/24 in CD vs. 12/27 in FD ($p < 0.01$).
Guldbrand 2012 #31769	N= 61, intervention 2 years **Intervention:** Low fat diet (LFD) **Control:** Low carbohydrate diet (LCD)	**Medication at baseline** - Diet only: LFD 2/31 patients, LCD 2/30 - oral glucose-lowering medication only: LFD 13/31, LCD: 15/30 - combination of insulin and oral medication LFD 11/31, LCD: 10/30	**Insulin dose baseline**: LFD: 39±51 E vs. LCD 42±65 E, p=0,86 (between groups) **Insulin dose 6 m:** LFD: 38±48 E (p for change from baseline 0,12) vs. LCD 30 ±47 (p=0,020), p for between group change 0,046 **Insulin dose 24 m:** LFD 36 ±44 (p=0,5), vs. LCD 35 ±56 (p=0,14) P value for change over all time points between groups 0,83 **Metformin dose baseline (mg):** LFD 1,435 ±946 vs. LCD 1,375 ±950, p=0,8 (between groups) Metformin dose 24 m: LFD 1,306±901 (p=0,28) vs. LCD 1,292±911 (p=0,38), P value for change over all time points between groups 0,93 P-Werte in Klammern: Vergleich zu baseline Glibenclamid: LFD vs. LCD, P value for change over all time points between groups 0,56 Für weitere Details siehe Beschreibung Einzelstudien. Anmerkung ÄZQ: Signifikantes Ergebnis für Insulintherapie nach 6 Monaten, nach 12 Monaten nicht..

Zitat	Studiencharakteristika	Medication baseline	Medication change
Statistically significant reduction in combined diabetes medication score			
Tay 2014	Tay 2014: Ergebnisse nach 24 Wochen, Tay 2015 (Ergebnisse nach 52 Wochen)		
Tay 2014 http://www.ncbi.nlm.nih.gov/pubmed/26224300. #31777	n=115, 52 weeks intervention **Intervention:** Low carbohydrate diet (LC) **Control:** High carbohydrate, low fat diet (HC)	**Medication at baseline** (%): LC: n=58, HC: n=57 Insulin: LC 10%, HC 11% Metformin: LC 79%, HC 72% Sulfonylureas: LC 34%, HC 28% Thiazolidinediones: LC 5%, HC 5% GLP-1-RA: LC 2%, HC 2% DPP-4-I: LC 2%, HC 4% Antiglycemic MES* (Medication effect score): LC: 1,3 ±1,0; HC: 1,1 ±1,1	Week 52: (Changes) Antiglycemic MES*: LC: -0,5 (-0,7; -0,4) versus HC: -0,2 (-0,4; -0,06) Difference in change between groups: -0,3 (-0,6; -0,05), p=0,02 MES* reduction ≥ 20%, n (%): LC: 30 (52%) versus HC: 12 (21%), p=0,001 MES* reduction ≥ 50%, n (%): LC: 17 (29%) versus HC: 10 (18%), p=0,14 *Changes in diabetes medication requirements quantified by the antiglycemic medication effect score (MES). A higher MES corresponded to a higher diabetes medication requirement.
Westman 2008 http://www.ncbi.nlm.nih.gov/pubmed/19099589. # 31794	N=84, 24-week **Intervention:** Low-carbohydrate, Ketogenic Diet Group Intervention (LCKD) **Control:** Low-glycemic index diet group intervention (LGID)	**Baseline:** LCKD (n=21) 20 (95,2%) taking hypoglycemic medications - Insulin + oral agents, n=4 - Insulin only, n=4 - Oral agents, n=12 LGID (n=29) 22 (75,9%) taking hypoglycemic medication - Insulin, n=3 - Oral agents, n=19	**Week 24** Diabetes medications were reduced or eliminated in 95.2% of LCKD vs. 62% of LGID participants (p < 0.01). (zu Einzelauswertung der Patienten mit Insulintherapie zu Beginn der Studie, siehe Beschreibung der Einzelstudie)
Rock 2014 http://www.ncbi.nlm.nih.gov/pubmed/24760261. #31809	N=227, 1-year intervention Intervention: Commercial weight loss programm arms - Higher carbohydrate, lower fat (LF) - lower carbohydrate, higher fat (LC) Control: usual care (UC)	**Insulin:** Baseline: LF 19, LC 10, UC 12 Stopped/decreased: LF 12(63%), LC 9/90%), UC 1 (8%) Started/increased: LF 2 (10%), LC 0, UC 3 (25%) P value for difference between UC and aggregated weight-loss programm participants: <0,001 **Oral hypoglycemic agents:** Baseline: LF 62, LC 69, UC 62 Stopped/decreased: LF 24 (39%), LC 22 (31%), UC 10 (16%) Started increased: LF 6 (0%), LC 6 (9%), UC 8 (13%) P value for difference between UC and aggregated weight-loss programm participants: 0,007	
Larsen 2011 #31768	N= 108, 12 months intervention	Diabetes treatment, n (%) (at baseline) None:	**Change in diabetes medication** (Weighted %change in diabetes medication), HP n=48, HC n=41

Zitat	Studiencharakteristika	Medication baseline	Medication change
	Intervention: High-protein diet (HP) Control: High carbohydrate diet (HC) ITT Analyse	HP: 5 (9%), HC: 5 (11%) Insulin: HP: 10 (10%), HC: 7 (15%) Tablets: HP: 38 (72%), HC: 34 (74%)	3 months: HP -8,71 vs. HC 0,68, Difference between groups: -9,38 (95% CI -17,85; -0,92) 12 months: HP -8,17 vs. HC 4,56, Difference between groups: -12,72 (95% CI -28,18; 2,73) trend for improved glycaemic control in HP, statistical adjustment of the change in medications did not modify the outcome of the change in HbA1c.
Oher trials reporting on change in medication			
Daly 2006 http://www.ncbi.nlm.nih.gov/pubmed/16409560. #31791	N=102, 3 months **Intervention:** Low carbohydrate diet (LC) **Control:** healthy eating group (HE)	Baseline Medication (approximately post study evaluation) Pro Gruppe jeweils 40% oral hypoglycaemic agents (OHAs), 20% insulin 40% combination of the two	post-study analysis of medication changes from baseline, date available for 75% (not in the original study design, limited analysis) - Insulin use reduced in insulin using subjects: LC: 85%, LF: 22% - Increased insulin use (in insulin using subjects): LC: 5%, LF: 16% - Oral antihyperglycemic agents: LC: unchanged, LF: unchanged
Jonasson 2014 http://www.ncbi.nlm.nih.gov/pubmed/24779961 #31783	Siehe Guldbrand 2012 (gleiche Studie NCT01005498)		
Goldstein 2011 #31797	N=52, 1 year **Intervention:** Modified Atkins diet (ATK) **Control:** Standard ADA calorie-restricted diet	Keine Analyse der Baseline-Medication. By 3-month: use of hypoglycemic medication reduced in 17/26 ATK and 11/26 ADA (p=0,16)	
Davis 2009 **#31766**	N=105, Intervention 1 year **Intervention:** low carbohydrate diet (LC) (n=55) **Control:** low-fat diet (LF) (n=50) ITT-Analyse, - prerandomization: adjusted diabetes medication to minimize side effects	**Baseline Medications:** Metformin: LC 43/55 (78%), LF 43/50 (86%) Sulfonylurea: LC 29/55 (44%9, LF 26/50 (52%) Insulin LC 19/55 (35%), LF 12/50 (24%) Cholesterol lowering medication: LC 34/55 (62%), LF 28/50 (56%).	Participants using insulin: dose reduced by mean ±SD of 10 ±14 units in LC arm and increased by 4 ±19 units in the LF arm (P = 0.12) at 12 months. Participants using sulfonylurea: 26% had reduction in dose at 12 months. Dose reduction: 1.6 ± 3,6mg in both arms.
Mayer 2014 http://www.ncbi.nlm.nih.gov/pubmed/23911112.	N=46, within al larger weight-loss trial (n=146), intervention 48 weeks Intervention: low-carbohydrate diet (LCD)	Insulin +/- oral agents (n (%)): LCD: 7 (31,8%); LFD+O: 8 (33,3%) Oral agents only (n (%)): LCD:12 (54,6%), LFD+O: 14 (58,3%) No agents (n (%)):	Estimated MES: LCD week 0: 1,78 (1,07; 2,47), week 48 0,53 (0,06; 1,00) LFD+O: w 0: 2,13 (1,46; 2,80), week 48: 1,31 (0,89; 1,74) LCD –LFD+O difference of change 48 weeks: -0,42 (-1,18; 0,33), p=0,27

Zitat	Studiencharakteristika	Medication baseline	Medication change
#31810	Control: Low fat diet + Olistat (LFD+O)	LCD: 3 (13,6%), LFD+O: 2 (8,3%)	% Achieving 20% decrease in MES (week 48): LCD 76,5%, LFD+O 56,5%, p=0,19 % Achieving 50% decrease in MES (week 48): LCD 70,6%, LFD+O 30,4%, p=0,01
trials not including participants on diabetes medication at trial start			
Wolever 2008 http://www.ncbi.nlm.nih.gov/pubmed/18175744. #22168	Anmerkung ÄZQ: Die für unsere Fragestellung relevanten Endpunkte werden nicht berichetet. Antihyperglykämische Medikation war zu Studienbeginn ein Ausschlusskriterium und die Indikation zur medikamentösen Therapie während der Studie wurde als treatment failure gesehen und Patienten wurden von der Studie ausgeschlossen.		
Esposito 2009 #31767	n=215, 4-year intervention and follow-up **Intervention:** Mediterranean-style diet, n=108 **Control:** low fat diet, n=107 **Population:** newly diagnosed T2DM, never treated with antihyperglycemic drugs **Primary outcome:** Start of antihyperglycemic drug therapy, defined by protocol as indicated for follow-up HbA1c level > 7%.	Baseline HbA1c (%): MED: 7,75 (0,9), LF: 7,71 (0,9)	Anahl der Patienten in den Gruppen: Year 1: MED: n=102, LF: n=97 Year 4: MED: n=50, LF: n=29 Patients requiring treatment: Year 1: MED: 5,5%, LF 9,4% (Difference -3,9 (95% CI -7,8; 1,2) Year 4: MED 44%, LF 70% (Difference -26 (95% CI -31; -20,1) HR (unadjusted): HR 0,63 (0,51; 0,86) HR (adjusted for weight change): HR 0,70 (0,59; 0,9) HR (adjusted for using HbA1c >7% as outcome): HR 0,64 (0,5; 0,82)

Meng 2017 (low carbohydrate diet)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Meng Y, Bai H, Wang S, Li Z, Wang Q, Chen L (2017) Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes research	**Suchzeitraum:** from inception through January 2017 **Fragestellung:** to assess the efficacy of Low Carbohydrate Diet (LCD) compared with a normal or high carbohydrate diet in patients with T2DM. **Population:** patients with T2DM **Intervention:** low carbohydrate diet (less than130 g carbohydrate /day or 26% of daily energy from carbohydrates)	**Egebnisse:** 9 trials, n= 734 length of follow-up: 3 to 24 months Aus dem HGT: „The low carbohydrate diet also produced a greater reduction in insulin dose, and that the reduction of insulin might promote weight loss.“ (Seite 7/8) Keine weiteren Informationen im Review. Siehe Betrachtung der Einzelstudien. Eingeschlossene Studien (aktive Links zu den Evidenztabellen): - Tay 2014 - Davis 2009 (Davis 2011)	Critically low (kein Protokoll, ausgeschlossene Studien, funding der Studien nicht angegeben)	- Keine „harten“ patientenrelevanten Endpunkte betrachtet. Reduktion der Medikation nicht als Endpunkt betrachtet und nicht im Text diskutiert (nur ohne Referenz in einem Satz erwähnt).

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
and clinical practice 131:124–31 11. https://pubmed.ncbi.nlm.nih.gov/28750216/ idnetifiziert über NICE NG28 *#31657*	**Vergleich:** normal or high carbohydrate diet; **Endpunkte:** change in body weight, fasting plasma glucose (FPG), HbA1c, total cholesterol (TC), triglycerides (TG), HDL cholesterol (HDL-c) and LDL cholesterol (LDL-c). **Studien:** RCTs **Qualitätsbewertung:** modified Jadad scale	- Guldbrand 2012 - Iqbal 2010 - Daly 2006 - Saslow 2014 - Goldstein 2011 - Westman 2008 - Yamada 2014		- Patienten mit T2DM betrachtet und nicht übergewichtige oder adipöse Patienten mit T2DM. Identifiziert über die themenübergreifende systematische Recherche

3.5 Formula-Diäten

Lean 2018

Siehe auch weitere Informationen in der Beschreibung der Einzelstudie im Anhang (Link durch Anklicken des Autorennamens)

Lean 2018, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645. Laufnummer: 27789

Weitere Zitate:

Lean ME, Leslie WS, Barnes AC, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet Diabetes Endocrinol 2019; 7(5):344–55. DOI: 10.1016/S2213-8587(19)30068-3. http://www.ncbi.nlm.nih.gov/pubmed/30852132. Laufnummer: 31846

Lean ME, Leslie WS, Barnes AC, et al. 5-year follow-up of the randomised Diabetes Remission Clinical Trial (DiRECT) of continued support for weight loss maintenance in the UK: an extension study. Lancet Diabetes Endocrinol 2024; 12(4):233–46. DOI: 10.1016/S2213-8587(23)00385-6. http://www.ncbi.nlm.nih.gov/pubmed/38423026. # 34562 (Daten nach 5 Jahren werden im Anhang dargestellt)

Studiencharakteristika: open label cluster randomized trial (DiRECT), n=306, duration 12 months, weiteres follow-up nach 24 Monaten

Intervention: weight management program: Withdrawel of of antidiabetic and antihypertensive drugs, total diet replacement (825–853 kcal/day formula diet for 3–5 months), stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance.

Control: best-practice care by guidelines (control)

Primary outcomes: Weight loss of 15kg or more, remission of T2DM (HbA1c <6,5% after at least 2m off all antidiabetic medications)
Attrition: 128 (86%) Intervention group, 147 (99%) control group attending 12-month assessment, weitere Informationen, siehe Studienbeschreibung.

Lean 2018, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645. Laufnummer: 27789	
Baseline Medication: Intervention group n=149, Control group n=149 Number of oral antidiabetic medication: 0: intervention 26%, Control 23% 1: Intervention 44%, control 53% ≥2: Intervention 31%, Control 24%	**Ergebnisse** **Diabetes remission 12 months, n (%):** Intervention 46% vs. Control 4%, odds ratio 19,7 (95% CI 7,8; 49,8), p<0,0001 **Weight loss of at least 15kg at 12 ms, n (%)** Intervention 24% vs. Control 0%, p<0,0001 **Diabetes remission 24 months (ITT Analyse), n (%)** Intervention: 53 (36%) versus Control 5 (3%), adjusted odds ratio: 25,82 (95% CI 8,25; 80,84), p<0,0001 **Weight loss of at least 15kg at 24 ms, n (%):** Intervention 17 (11%), vs. Control 3 (2%), adjusted odds ratio 7,49 (95% CI 2,05; 27,32), p=0,0023 **Remission in Diabetes in relation to weight loss at 12 months:** 0kg: 0%, <5 kg: 7%, 5-10kg: 34%, 10-15kg: 57%, ≥15 kg: 86% **Remission in Diabetes with weight loss >15kg (24 months):** 70%. Adherence: In the intervention group, six (4%) participants consented, but thereafter never engaged with the intervention, and 26 (17%) participants withdrew from treatment during the first 12 months (n=15 during total diet replacement, n=6 during stepped food reintroduction, and n=5 during weight loss maintenance).
Risk of bias Bewertung (ÄZQ): Selektion (Randomization: low, Allocation concealment: high), Performance: high, Detection: high / unclear, Attrition: unclear, Reporting: unclear Other biases: formula diet was donated by Cambridge Weight Plan.	
Anmerkung: identifiziert über Churuangsuk	

3.6 Intervallfasten

3.6.1 Evidenz aus der themenübergreifenden systematischen Recherche

Allaf 2021

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Allaf M. Intermittent fasting for the prevention of cardiovascular disease.	**Zeitpunkt der Suche:** 12 December 2019 **Fragestellung:** role of IF in preventing and reducing the risk of CVD in people with or without prior documented CVD.	26 studies met criteria, 18 (1125 participants) were included in pooled analysis; observed outcomes ranging from 4 weeks to 6 months. - 7 studies: IF versus ad libitum feeding, - 8 studies: IF versus CER	high	- Breite Suche (nur Suchbegriffe für die Intervention), die auch Studien an Menschen

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Cochrane Database Syst Rev 2021; 1(1):CD013496. https://www.ncbi.nlm.nih.gov/pubmed/33512717. #30986	**Population:** > 18 years, with and without cardiometabolic risk factors (for example diabetes). **Intervention:** Intermittend Fasting (IF) - categorised into alternate-day fasting, modified alternate-day fasting, periodic fasting and time-restricted feeding. Definitionen siehe Volltext. **Vergleich:** ad libitum feeding (eating at any time with no specific caloric restriction) or continuous energy restriction (CER), defined as a minimum of 25% reduction in caloric intake, **Endpunkte:** Primary outcomes: - all-cause mortality, - cardiovascular mortality, - stroke, - myocardial infarction, and heart failure. Secondary outcomes: - absolute change in body weight, BMI, waist circumference, FPG, HbA1c (etc.) - side effects such as headaches and changes in quality of life (validated quality of life scales) **Subgruppenanalyse:** - Male and female patients - Overweight and obese (BMI ≥25) and non-overweight patients (BMI < 25). - **Patients with and without diabetes.** - Intermittent fasting type **Studien:** RCTs **Qualitätsbewertung:** RoB	- 3 studies: IF versus both ad libitum feeding and CER Outcomes reported at short term (≤3 months) and medium term (> 3 months to 12 months) follow-up. 12 studies: recruited participants overweight or obese. 2 studies: recruited only participants with diabetes mellitus. Carter 2018, Griffiths 2016 **None of the included studies reported on all-cause mortality, cardiovascular mortality, stroke, myocardial infarction or heart failure.** **Side effects and quality of life** 4 studies reported data on side effects, with some participants complaining of mild headaches (13/187, 7%). In 3 der 4 Studien DM als Ausschlusskriterium. Quality of life in Studie berichtet, in der DM ein Ausschlusskriterium war. **Betrachtung der Einzelstudien (Typ-2-DM):** (Link zu Evidenztabellen: auf Autorennamen klicken) Carter 2018 - Betrachtet Change in Medication - Ris of bias: high: allocation concealment, Performance and Attrition bias; low: Random sequence generation and other bias; unclear: Detection bias and reporting bias. Griffiths 2016: - Risk of bias: high: Performance and Attrition bias, ansonsten unclear risk of bias.		mit Typ-2-Diabetes erfasst hätte. Subgruppenanalysen sind, wo möglich, erfolgt. Zwei Studien identifiziert, die nur Pat. mit Diabetes eingeschlossen haben. Griffiths 2016 nur als Kongressbeitrag (Pilot-Studie, n=10), Studie von Carter et al., 2018 an anderer Stelle dargestellt (siehe Link). Auch über die strukturierte Recherche identifiziert.

3.7 Mediterrane Diät

In der systematischen Recherche (weight loss interventions) wurde kein SR mit ausreichender methodischer Qualität identifiziert. Daher erfolgte eine gezielte systematische Recherche.

3.7.1 Evidenz aus der systematischen Recherche zur Mediterranen Diät

Becerra-Tomas et al., 2020

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR-2	Kommentar
Becerra-Tomás N, Blanco Mejía S, Viguiliouk E, et al. Mediterranean diet, cardiovascular disease and mortality in diabetes: A systematic review and meta-analysis of prospective cohort studies and randomized clinical trials. Critical reviews in food science and nutrition 2020; 60(7):1207–27. DOI: 10.1080/10408398.2019.1565281. http://www.ncbi.nlm.nih.gov/pubmed/30676058. *Laufnummer: 31924*	**Zeitpunkt der Suche:** 01 and 02/2017, update: 04 and 05/2018 **Fragestellung:** effect of Mediterranean diet (MedDiet) on the prevention of cardiovascular disease (CVD) incidence and mortality. **Population:** Population that included adults with type 1 diabetes or T2D **Intervention:** MedDiet, MetDiet as exposure (assessed by indexes or scores in the case of prospective cohort studies) **Endpunkte:** mortality from CVD, CHD, MI and stroke **Study:** Prospective cohort studies, RCTs, ≥1 year follow-up PREDIMED trial: original article (Estruch et al.	41 reports included: 3 RCTs, 38 cohorts 3 RCTs: - Estruch 2018 (PREDIMED), n - Lorgeril 1999 (Lyon diet heart study) - Singh 2002 (IndoMediterranean diet heart study) **Risk of bias assessment (RCTs):** Estruch 2018: allocation concealment (selection bias) high, others low. De Lorgeril 1999 und Singh 2002: random sequence generation and allocation concealment unclear, others low. - Furthermore, the study published by Singh et al., appears to have unreliable data, as stated by the editor of the Lancet journal in a letter of expression of concern (Horton 2005). **Ergebnisse RCTs:** ▪ Total CVD-incidence: RR: 0.62 (95% CI: 0.50, 0.78), 2 trials (Estruch 2018, Lorgeril 1999), n=8052, I^2= 86%, p<0,01, **GRADE moderate** (inconsistency). ▪ Total CVD mortality: RR 0,67 (95% CI 0,45; 1,00), 2 trials (Estruch 2018, Lorgeril 1999), n=8052, I^2=64%, p=0,05, **GRADE: low** (inconsistnency, imprecision) ▪ CHD incidence: 0,48 (95% CI 0,33; 0,71), 1 trial (Singh 2002), n= 1000, p<0,01, **GRADE: low** (risk of bias, indirectness) ▪ CHD mortality: RR 0,33 (95% CI 0,13; 0,85), 1 trial (Singh 2002), n= 1000, p=0,02, **GRADE: low** (risk of bias, indirectness) ▪ Stroke incidence: RR 0,58 (95% CI 0,42; 0,81), 1 trial (Estruch 2018), n=7447, p<0,01, **GRADE: moderate** (indirectness) ▪ Stroke mortality: no study ▪ total myocardial infarction (MI) incidence: RR: 0.65 (95% CI: 0.49, 0.88), 2 trials (Singh 2002, Estruch 2918), n=8447, I2=50%, p<0,01, **GRADE moderate** (risk of bias) ▪ Myocardial infarction mortality: RR 0,67 (95% CI 0,31; 1,43), 1 trial (Singh 2002), n= 1000, p-value: 0,30, **GRADE: very low** (risk of bias, indirectness, imprecision) **Meta-analyses of prospective cohort studies:** highest versus lowest categories of MedDiet adherence:	**Low** y-py-y-py-n-y-n-y-py-y-y-y-y-y-y (nicht erfüllte kritische Domänen: ausgeschlossene Studien nicht angegeben, unkritische Domänen: Selektion nicht ausreichend beschrieben)	- Recherche relativ alt - Daten überwiegend aus Studien mit hohem Verzerrungsrisiko (PREDIMED und Singh 2002). Dieses wurde bei der Bewertung der Aussagesicherheit der Evidenz (GRADE) nach Einschätzung des ÄZQ nicht ausreichend berücksichtigt. - Umgang mit PREDIMED Daten adäquat? Siehe Studiencharakteristika. - Studies **inclusive** of individuals with diabetes, (bei Estruch 2018 ca. 50% mit Diabetes, Lorgeril 1999: keine Angaben in dem angeführten Zitat)

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR-2	Kommentar
	2013) withdrawn and re-published in June 2018 (Estruch et al. 2018) because some deviations from the protocol randomization procedure were detected. - included results of the new report in the meta-analysis, which were similar to the findings originally reported (although search strategy did not identify this new publication)	**Total CVD incidence:** RR 0,88 (95% CI 0,74; 1,03), 8 trials, n= 53,508, I2=53%, p-value 0,12, GRADE: very low (imprecision) **total CVD mortality:** RR: 0.79 (95% CI: 0.77, 0.82), 21 trials, n=883,878, I2=0%, p-value <0,01, GRADE moderate (dose response) **CHD incidence:** RR 0,73 (0,62; 0,86), 7 trials, n=88,632, I2= 26%, p-value: <0,01, GRADE moderate (dose-response) **CHD mortality:** RR: 0.83 (95% CI: 0.75, 0.92) Abstract, Figure 2: RR 0,73 (95% CI 0,59; 0,89), 6 trials, n=270,565, I^2=63%, p-value <0,01), GRADE: loe (risk of bias, dose response) **stroke incidence**: RR: 0.80 (95% CI: 0.71, 0.90), 5 trials, n=79,287, I2=0%, GRADE: low (indirectness, dose, response) **stroke mortality**: RR: 0.87 (95% CI: 0.80, 0.96), 4 trials, n=195,644, I2=0% ▪ MI incidence (RR: 0.73; 95% CI: 0.61, 0.88).		- keine Subgruppenauswertung, keine Angabe, wie viele Studienteilnehmer*innen wirklich Typ-2-Diabetes hatten. - Zur Studie von Singh 2002: Expression of concerns (siehe Horton 2005)[2] (https://www.sciencedirect.com/science/article/pii/S0140673605670067?via%3Dihub)

Bloomfield et al., 2015

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentare
Bloomfield HE. Benefits and Harms of the Mediterranean Diet Compared to Other Diets. 2015. https://pubmed.ncbi.nlm.nih.gov/27559560 Department of Veterans Affairs, Evidence-based Synthesis Program (ESP)	**Suchzeitraum:** 1990 through August 2015. **Fragestellung:** to test the hypothesis that adopting a Mediterranean diet in adulthood reduces chronic disease burden (eg, incidence of and/ or mortality from cardiovascular disease, cancer, diabetes, hypertension, cognitive impairment, and kidney disease) and/or all-cause mortality **Key Question 1:** Is the Mediterranean diet more effective than other diets in preventing death or the development of type 2 diabetes mellitus, cardiovascular disease, cancer, hypertension,	93 papers reporting on 55 studies included **Key Question 1: Primary Prevention** ▪ 42 studies (3 RCTs and 39 cohort studies) that reported the association between conformity to a Mediterranean diet and the occurrence of outcomes in over 2 million people **Cardiovascular disease, all-cause mortality, and diabetes (RCTs only).** 2 trials (n= 56,282) evaluated the effect of the Mediterranean diet on major cardiovascular (CV) outcomes (myocardial infarction [MI], stroke, CV death) and diabetes. **3 RCTs** (n =56,711) reported all-cause mortality. **PREvención con Dieta MEDiterránea (PREDIMED):** Spanish trial of 7,447 people randomized to either a Mediterranean diet with supplemental extra virgin olive oil, a Mediterranean diet supplemented with nuts, or a low-fat control diet. Average follow-up of 4.8 years. Mediterranean diets versus control diet: ▪ major cardiovascular events (HR 0.71, 95% CI 0.56; 0.90). ▪ All-cause mortality: HR 0,89 (95% CI 0,71; 1,12)	**Critically low** (nicht-erfüllte kritische Domänen: kein Protokoll, keine Auflistung der ausgeschlossenen Studien, Publikationsbias nicht untersucht.)	- keine Subgruppenanalyse für Personen mit Typ-2-Diabetes Von der Fragestellung her wären für KQ 2 auch Personen mit Typ-2-Diabetes betrachtet und als Subgruppe untersucht worden.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentare
	cognitive impairment, or kidney disease? **Key Question 1a:** Do the effects vary by gender, age, or BMI? **Key Question 2:** Compared to other diets, is the Mediterranean diet associated with fewer adverse outcomes (including death) or less disease progression **in people who already have diabetes**, cardiovascular disease, cancer, hypertension, cognitive impairment, rheumatoid arthritis, or kidney disease? **Key Question 2a:** Do the effects vary by gender, age, or BMI? **Key Question 3:** What is the observed adherence to the Mediterranean diet in studies conducted in the United States or Canada? **Population:** Adults (age 18 or older), not pregnant or lactating, and not hospitalized or institutionalized. Subgroups of interest: people with type II diabetes, cardiovascular disease, rheumatoid arthritis, cancer, hypertension, cognitive impairment, or kidney disease; different genders, ages, and BMIs **Intervention:** A Mediterranean-style diet (ie, labelled as a Mediterranean diet or consisting of at least 2 of the following: 1. High monounsaturated: saturated fat ratio (use of olive oil as main cooking ingredient); 2. High consumption of fruits and vegetables; 3. High consumption of legumes; 4. High	▪ incidence of type 2 diabetes mellitus (T2DM) (n= 3,541): ○ Mediterranean diet supplemented with extra virgin olive oil (HR 0.60, 95% CI 0.43; 0.85) ○ Mediterranean diet supplemented with nuts (HR 0.82, 95% CI 0.61, 1.10) **The Women's Health Initiative – Dietary Modification (WHI-DM):** US trial of 48,835 women, aged 50-79, assigned to either a low-fat diet (which included 2 of the 7 components of the Mediterranean diet) or a usual diet control, average follow-up of 8.1 years, Mediterranean diet versus control diet: ▪ no significant reduction in major cardiovascular events, all-cause mortality, or incidence of T2DM in the group assigned to the intervention diet. **Third RCT** reporting mortality followed 429 residents of 14 old-age hostels in Hong Kong for 33 months. Intervention: diet containing 2 of the 7 Mediterranean diet components: fruit/vegetables and fish. Intervention versus control: mortality rate: 13% (27/204) vs. 11% (25/225). **Zusammenfassende Beurteilung (primary prevention):** All-cause Mortality: direction: similar, Strength of evidence: low; 3 RCTs, n=56,711 Für kardiovaskuläre Endpunkte wird keine Strength of evidence angegeben. Für Endpunkte cancer, cognitive impairment, rheumatoid arthritis, siehe Originalpublikation. **KQ2: Secondary Prevention** 15 studies (8 RCTs and 7 cohort studies, N = 19,972), 6 studies conducted in patients with cancer, 6 in patients with cardiovascular disease, 1 in patients with cognitive impairment, and 2 in patients with rheumatoid arthritis. Of note, there is credible although not definitive evidence that 3 of the RCTs may contain fraudulent data. Therefore we have not included those data in our summary, below. **Participants with cardiovascular disease** ▪ 6 RCTs (n=5,684) reported outcomes in participants with preexisting cardiovascular disease. ▪ 3 of the RCTs may contain fraudulent data (Singh 2002, 1992, 1991) -> analyses both including and excluding these studies. ▪ The other 3 RCTs had substantial limitations. The Lyon Heart Study was the strongest methodologically but it included only 605 people. The Welsh trial (n=3,114) was interrupted by funding problems, leading to convoluted analyses. The Spokane Washington trial enrolled only 101 patients. **All-cause mortality:** ▪ Pooled results from all 6 RCTs reporting on all-cause mortality: Mediterranean diet vs. Control diet groups (RR 0.85, 95% CI 0.59, 1.21; I^2 = 57%).	Evidence-Report der VA (VA's Evidence-based Synthesis Program)	In der PREDIMED-Studie waren 50% der Teilnehmenden von einem Typ-2-Diabetes betroffen. Diese Subgruppe wird für Key question 2 nicht betrachtet.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentare
	consumption of grains/cereals; 5. Moderate red wine consumption; 6. Moderate consumption dairy products; and 7. Low consumption of meat and meat products (replaced by increased consumption of fish) **Comparator:** Any other type of diet (eg, Western, low fat, vegetarian) **Outcome:** - Mortality - Quality of life - Progression of disease, ie: Development of retinopathy, neuropathy, end-stage renal disease, or congestive heart failure, new amputation, new myocardial infarction, stroke, or revascularization procedure - Adverse events **Study selection:** Key Questions 1 and 2 (other than cancer, RA, or cognitive impairment): RCTs or controlled clinical trials (CCTs) with at least 100 subjects followed for at least 1 year.	▪ analysis conducted without the questionable data: RR 0.95 (95% CI 0.53, 1.69; I^2 = 51%), 3 trials. **Cardiovascular mortality:** ▪ pooled results from all 5 RCTs reporting on cardiovascular mortality: Mediterranean diet vs. Control diet: RR 0.69 (95% CI 0.44, 1.08; I^2 = 67%). ▪ result essentially unchanged when analysis was conducted without the questionable data (RR 0.68, 95% CI 0.18, 2.47; I2 = 87%). **Myocardial infarction (MI)** ▪ reported in 5 RCTs, ▪ data from 4 of the RCTs could be pooled. Mediterranean diet vs. Control: RR 0.56 (95% CI 0.44, 0.72; I^2 = 0%). Finding remained essentially the same when analysis was conducted without the questionable data (RR 0.32, 95% CI 0.15, 0.67; I^2 = 0%). 4 studies reported adverse events related to the diet. ▪ 1found no side effects ▪ 3 reported minor digestive problems such as diarrhea, dyspepsia, and mild belching in a couple of patients assigned to the intervention diet. **Zusammenfassende Beurteilung (secondary prevention):** All-cause mortality: direction similar, strength of evidence: insufficient, 3 RCTs, n=2,277 **KEY QUESTION 2A:** Do the effects vary by gender, age, or BMI? The reported data did not allow for subgroup analysis by age, gender, or BMI.		

3.7.1.1 Betrachtung der PREDIMED-Studie

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]	
Weitere ergänzende Zitate	Von der Leitliniengruppe eingebrachte Literatur ▪ Salas-Salvadó J, Bulló M, Estruch R, et al. Prevention of diabetes with Mediterranean diets: A subgroup analysis of a randomized trial. Ann Intern Med 2014; 160(1):1–10. DOI: 10.7326/M13-1725. http://www.ncbi.nlm.nih.gov/pubmed/24573661. Laufnummer: 34120 ▪ Basterra-Gortari FJ, Ruiz-Canela M, Martínez-González MA, et al. Effects of a Mediterranean Eating Plan on the Need for Glucose-Lowering Medications in Participants With Type 2 Diabetes: A Subgroup Analysis of the PREDIMED Trial. Diabetes Care 2019; 42(8):1390–7. DOI: 10.2337/dc18-2475. http://www.ncbi.nlm.nih.gov/pubmed/31182491. Laufnummer: 34119 ▪ Siehe auch Darstellung der PREDIMED-Studie in: Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2022): Nationale VersorgungsLeitlinie Chroni-sche KHK – Langfassung. Version 6.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000491, zuletzt geprüft am 15.09.2022.

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]	
Studientyp	Parallel-group, multicenter, randomized trial, n=7447 ▪ After median follow-up of 4.8 years, trial was stopped on the basis of a prespecified interim analysis. ▪ In 2013 results were reported for the primary end point; Authors have withdrawn previously published report and report revised effect estimates based on analyses that do not rely exclusively on the assumption that all the participants were randomly assigned (2018).
Fragestellung	Mediterranean diet and cardiovascular risk
Population	7447 participants (55 to 80 years of age, 57% women) at high cardiovascular risk, but with no cardiovascular disease Cardiovascular risk: either type 2 diabetes mellitus or at least 3 of the of the following major risk factors: ▪ smoking, ▪ hypertension, ▪ elevated low-density lipoprotein cholesterol levels, ▪ low high-density lipoprotein cholesterol levels, ▪ overweight or obesity, ▪ family history of premature coronary heart disease.
Intervention/Control	▪ Mediterranean diet supplemented with extra-virgin olive oil, ▪ Mediterranean diet supplemented with mixed nuts, ▪ control diet (advice to reduce dietary fat). Participants received quarterly educational sessions and, depending on group assignment, free provision of extra-virgin olive oil, mixed nuts, or small nonfood gifts. No total calorie restriction was advised, nor was physical activity promoted
	Mediterranean diet with extra-virgin olive oil: goal was to consume 50 g (approximately 4 tbsp) or more per day of the polyphenol-rich olive oil supplied, instead of the ordinary refined variety, which is poor in polyphenols. Participants received a free supply (15 liters every 3 months) to include the oil used for cooking and family needs. Mediterranean diet with nuts: recommended consumption was one daily serving (30 g, composed of 15 g of walnuts, 7.5 g of almonds, and 7.5 g of hazelnuts). Participants received for free the needed allotments of tree nuts in packages of 2 kg of walnuts, 1 kg of almonds, and 1 kg of hazelnuts every 3 months, with the extra amounts to be shared with family members.
Endpoint	Primary endpoint - composite of myocardial infarction, stroke, and death from cardiovascular causes. Secondary end points - stroke, - myocardial infarction, - death from cardiovascular causes, and - death from any cause.
Studienablauf	- For participants in the two Mediterranean diet groups, dietitians held individual and group dietary-training sessions at the baseline visit and quarterly thereafter. - In each session, participants completed a 14-item dietary questionnaire to assess adherence to the Mediterranean diet, Questionnaire scores ranged from 0 to 14 (<10: low adherence to the Mediterranean diet.)

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]

- Participants in control group also received dietary training at the baseline visit and completed the 14-item questionnaire at baseline to assess their adherence to the Mediterranean diet. During the first 3 years of the study, they received a leaflet explaining the low-fat diet on any early basis.

→ realization: more infrequent visit schedule and less intense support for the control group might be limitations of the study → protocol amendment in October 2006. Thereafter, participants in the control diet received personalized advice and were invited to group sessions with the same frequency and intensity as those in the Mediterranean-diet groups, with the use of a separate 9-item dietary questionnaire. Scores ranged from 0 to 9, with higher scores indicating greater adherence to a low-fat diet.

A general medical questionnaire, a 137-item validated food-frequency questionnaire,17 and the Minnesota Leisure-Time Physical Activity Questionnaire were administered on a yearly basis.

Food	Goal
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day (tbsp: tablespoons)
Tree nuts and peanuts	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito (sauce made with tomato and onion, often including garlic and aromatic herbs, and slowly simmered with olive oil.)	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<2 servings/wk

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Spread fats	<1 serving/day
Red and processed meats	<1 serving/day
Low-fat diet (control)	
Recommended	
Low-fat dairy products	≥3 servings/day
Bread, potatoes, pasta, rice	≥3 servings/day
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Lean fish and seafood	≥3 servings/wk
Discouraged	
Vegetable oils (including olive oil)	≤2 tbsp/day
Commercial bakery goods, sweets, and pastries	≤1 serving/wk
Nuts and fried snacks	≤1 serving/wk
Red and processed fatty meats	≤1 serving/wk
Visible fat in meats and soups	Always remove
Fatty fish, seafood canned in oil	≤1 serving/wk
Spread fats	≤1 serving/wk
Sofrito	≤2 servings/wk

Protocol deviations	▪ including enrollment of household members without randomization, assignment to a study group without randomization of some participants at 1 of 11 study sites, and apparent inconsistent use of randomization tables at another site. ▪ N= 1588 participants: study-group assignments were known or suspected to have departed from the protocol: all 652 participants from Site D (35 were second members of a household), 593 participants from Site B (47 were second members of a household), and another 343 second household members from other sites.
Attrition	▪ After baseline visit, 210 participants (2.8%) chose not to attend subsequent visits: o 1.2% of the participants assigned to a Mediterranean diet with extra-virgin olive oil,

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	○ 2.7% of those assigned to a Mediterranean diet with nuts, and ○ 4.7% of those in the control group). ▪ Rate of study discontinuation (>2 years since last contact) was 11.3% in the control group and 4.9% in the Mediterranean-diet groups; subsequent follow-up was based on reviews of medical records
Adherence	▪ The main nutrient changes in the Mediterranean-diet groups reflected the fat content and composition of the supplemental foods

Results

	MedD + extra-virgin olive oil	**MedD + nuts**	**control**
No of particpants	2543	2454	2450
Primary endpoint (composite of myocardial infarction, stroke, and death from cardiovascular causes)	96 (3,8%)	83 (3,4%)	109 (4,4%)
ITT analysis (adjusting for baseline characteristics and propensity score)	HR 0,69 (95% CI 0,53; 0,91)	0,72 (95% CI 0,54; 0,95)	1,00 ref.
5-year absolute risk - % (95% CI)	3,6 (2,8; 4,5)	4,0 (3,1; 5,0)	5,7 (4,6; 6,9)
ITT-analysis: HR for mediterranean diets combined vs. control: Primary end point (95% CI)	0,70 (0,55; 0,89)		1,00 ref.
Primary end point, excluding Site D and second household members			
No of participants	2158	2109	2138
HR (95% CI)	0,66 (0,49; 0,89)	0,64 (0,47; 0,88)	1,00 ref.
5-year absolute risk - % (95% CI)	3,4 (2,6; 4,3)	3,9 (3,0; 5,0)	5,9 (4,8; 7,2)

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]			
Primary end point: Adjusted analysis after excluding 1588 subjects (non-randomized members of households, site D and site B)			
	MedDiet+EVOO versus control	**MedDiet+Nuts versus control**	**MedDiet (both) versus control**
Adjusted analysis after excluding 1588 subjects (non-randomized members of households, site D and site B)	0,71 (95% CI 0,51; 0,97)	0,68 (95% CI 0,49; 0,95)	0,69 (95% CI 0,53; 0,92)
Secondary end points			
	MedDiet+EVOO (n=2543)	**MedDiet+Nuts (n=2454)**	**Control diet (n=2450)**
Stroke			
No. of events	49	32	58
Incidence rate per 1000 person-years (95% CI)	4.1 (3.1–5.5)	3.1 (2.1–4.4)	5.9 (4.5–7.7)
5-yr absolute risk — % (95% CI)	1.7 (1.3–2.4)	1.5 (1.1–2.3)	3.0 (2.3–3.9)
Myocardial infarction			
No. of events	37	31	38
Incidence rate per 1000 person-years (95% CI)	3.1 (2.2–4.3)	3.0 (2.0–4.2)	3.9 (2.8–5.3)
5-yr absolute risk — % (95% CI)	1.4 (1.0–2.1)	1.6 (1.1–2.3)	2.1 (1.5–2.9)
Death from cardiovascular causes			
No. of events	26	31	30
Incidence rate per 1000 person-yr (95% CI)	2.2 (1.4–3.2)	3.0 (2.0–4.2)	3.1 (2.1–4.4)
5-yr absolute risk — % (95% CI)	1.0 (0.6–1.5)	1.4 (0.9–2.1)	1.6 (1.1–2.3)

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]			
Death from any cause			
No. of events	118	116	114
Incidence rate per 1000 person-yr (95% CI)	10.0 (8.2–11.9)	11.2 (9.3–13.4)	11.7 (9.6–14.0)
5-yr absolute risk — % (95% CI)	4.4 (3.6–5.4)	5.4 (4.4–6.6)	5.4 (4.4–6.7)
ITT analysis: hazard ratio for each Mediterranean diet vs. control (95% CI) – secondary end points			
	MedDiet+EVOO (n=2543)	**MedDiet+Nuts (n=2454)**	**Control diet (n=2450)**
Stroke	0.65 (0.44–0.95)	0.54 (0.35–0.82)	1.00 (ref)
Myocardial infarction	0.82 (0.52–1.30)	0.76 (0.47–1.25)	1.00 (ref)
Death from cardiovascular causes	0.62 (0.36–1.06)	1.02 (0.63–1.67)	1.00 (ref)
Death from any cause	0.90 (0.69–1.18)	1.12 (0.86–1.47)	1.00 (ref)
Post-hoc exploratory subgroup-analysis: Need for glucose lowering medication in people with diabetes: 1) introduction of the first glucose-lowering medication (oral or injectable) among participants on lifestyle management at enrollment (after median follow-up of 3.2 years) and 2) insulin initiation (after median follow-up of 5,1 years). - aus: Basterra-Gortari FJ, Ruiz-Canela M, Martínez-González MA, et al. Effects of a Mediterranean Eating Plan on the Need for Glucose-Lowering Medications in Participants With Type 2 Diabetes: A Subgroup Analysis of the PREDIMED Trial. Diabetes Care 2019; 42(8):1390–7. DOI: 10.2337/dc18-2475. http://www.ncbi.nlm.nih.gov/pubmed/31182491. Laufnummer: 34119 - von der Leitliniengruppe eingebrachte Literatur			
	MedD + extra-virgin olive oil	MedD + nuts	control
No.of participants in subgroup (insulin initiation analyses)	1158	1017	1055
Unadjusted HR for staying free of insulin	0,90 (95% CI 0,72; 1,14)	0,91 (95% CI 0,71; 1,16)	reference
Multivariate adjusted HR of starting long-term insulin treatment	0,87 (95% CI 0,68; 1,11)	0,89 (95% CI 0,69; 1,14)	reference

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]			
Asssessing both groups together	0,88 (95% CI 0,71; 1,09)		reference
No. of participants in the glucose lowering medication initiation analyses	447	394	369
Unadjusted HR of starting glucose lowering medication	0,83 (95% CI 0,69; 0,99)	0,92 (95% CI 0,76; 1,11)	reference
Assessing both groups together	HR 0,87 (95% CI 0,74; 1,02)		reference
Multivariable adjusted HR	0,78 (95% CI 0,62; 0,98)	0,89 (95% CI 0,71; 1,12)	reference
Assessing both groups together	0,83 (95% CI 0,68; 1,02)		
Incidence of new-onset type 2 diabetes mellitus (prespecified secondary outcome) - Subgroup: Men and women without diabetes (3541 patients aged 55 to 80 years) at high cardiovascular risk. - median follow-up, 4.1 years - aus: Salas-Salvadó J, Bulló M, Estruch R, et al. Prevention of diabetes with Mediterranean diets: A subgroup analysis of a randomized trial. Ann Intern Med 2014; 160(1):1–10. DOI: 10.7326/M13-1725. http://www.ncbi.nlm.nih.gov/pubmed/24573661. Laufnummer: 34120 - von der Leitliniengruppe eingebrachte Literatur			
	MedD + extra-virgin olive oil	MedD + nuts	control
No. of patients in subgroup	1154	1240	1147
Person-years, n	4990	4876	4271
New cases of diabetes, n	80	92	101
Incidence rate per 1000 person-years (95% CI)	16,0 (12,7; 19,9)	18,7 (15.1-22.9)	23,6 (19,3; 28,7)
Cumulative incidence (95% CI)	6,93 (5,53; 8,55)	7,42 (6,02; 9,02)	8,81 (7,23; 10,60)

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]

HR of Diabetes

	MeD + extra-virgin olive oil versus contol diet	MedD + nuts versus control diet	Both MedD versus control diets
crude	0,69 (0,51; 0,92)	0,81 (0,61; 1,08)	0,75 (0,58; 0,96)
Age- and sex-adjusted	0,68 (0,51; 0,92)	0,80 (0,60; 1,06)	0,74 (0,58; 0,95)
Multivariate-adjusted (age, sex, BMI)	0,68 (0,51; 0,92)	0,82 (0,61; 1,09)	0,75 (0,58; 0,96)
Multivariate adjusted (age, sex, BMI, smoking, fasting glucose level, dyslipidemia, hypertension, total energy intake level, adherence to MedD, physical activity level, education level, alcohol intake level)	0,60 (0,43; 0,85)	0,82 (0,61; 1,10)	0,70 (0,54; 0,92)

Incidence of diabetic retinopathy and diabetic nephropathy according to intervention group in the PREDIMED trial after a median 6.0 years of follow-up

- **Post hoc analysis:** Outcome of interest: Incidence of DR, Case definition: nonmydriaic fundus camera, subset of n=3 614 with type-2-Diabetes without DR at baseline, male n=1 707; age: male (55-80years), femal (60-80 years), median follow-up 6 years
- **Results (aus https://diabetesjournals.org/care/article/38/11/2134/37621/Mediterranean-Diet-Retinopathy-Nephropathy-and, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6150426/):**

	MedDiet+EVOO group	MedDiet+Nuts	Control
Anzahl der Personen je Gruppe (Diabetic retinopathy, n)	1,282	1,142	1,190
new-onset retinopathy during follow-up	22	20	32
cases, n/person-years of follow-up	22/7 830	20/6 622	32/6 856
Diabetic retinopathy by intervention group, HR (95% CI)			
Crude model	0.57 (0.32–0.98)	0.62 (0.35–1.07)	1 (Ref.)

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]

Age- and sex-adjusted model	0.56 (0.33–0.98)	0.64 (0.36–1.12)	1 (Ref.)
Multivariable-adjusted model 1	0.56 (0.32–0.97)	0.63 (0.35–1.11)	1 (Ref.)

Model 1 was additionally adjusted for baseline BMI (continuous variable), waist circumference (continuous variable), smoking (never, current, or former smoker), physical activity in MET min/day (continuous variable), educational level (primary/secondary education or academic/graduate), hypertension (yes or no), dyslipidemia (yes or no), family history of premature coronary heart disease (yes or no), and baseline adherence to the MedDiet (low, <10 points; high, ≥10 points). All models were stratified by recruitment center.

Risk of bias assessment

Selection bias	**Generierung der Randomisierungssequenz: high risk** ▪ „computer-generated random-number sequence provided randomization tables for the 11 participating sites, which encompassed 169 clinics.“ ▪ „We did not use blocks for randomization.“ ▪ „We included 425 participants who shared a household with a previously enrolled participant. These 425 participants were not randomly assigned but were assigned to the same intervention as the member of the household who was already enrolled“ ▪ „at 1 of the 11 study sites (Site D), 467 participants were not randomly assigned as individual participants but instead were assigned according to clinic — that is, all the participants in each clinic received the same intervention (2 clinics assigned a Mediterranean diet with extra-virgin olive oil, 5 assigned a Mediterranean diet with nuts, and 4 assigned a control diet)“ ▪ „review of the documentation about randomization procedures and of the actual assignments to the three groups suggested that the randomization tables were inconsistently used in another study site (Site B, 593 participants)“
	Generierung der Randomisierungssequenz: high risk ▪ Randomization was concealed with the use of closed envelopes during part of the pilot phase of the study, but envelopes were not used for the remainder of the study. ▪ Siehe oben (randomization tables inconsistently used, not randomly assigned as individual participants, participants in the same household were not randomly assigned)
Performance bias	**Verblindung von Studienpersonal/-teilnehmern während der Behandlung: high Risk of bias** - Studienteilnehmerinnen nicht verblindet, aber bei Ernährung auch schlecht möglich.
Detection bias	**Verblindung bei der Endpunkterhebung/- bewertung (primärer EP): low** All medical records that were related to end points were examined by the end-point adjudication committee, whose members were unaware of the intervention-group assignments.
Attrition bias	**Fehlende Daten bei Endpunkterhebung (primärer EP): unklares RoB** - Unterschiedliche Abbruchraten in den verschiedenen Gruppen (1,2 bis 4,7%). Die zunächst engmaschige Betreuung der Personen in den MedD-Gruppen (Protokoll wurde im Verlauf geändert), sowie die kostenfreie Bereitstellung von Nahrungsmitteln in den Interventionsgruppen können als Gründe erwogen werden. - Rate of study discontinuation (>2 years since last contact) was 11.3% in the control group and 4.9% in the Mediterranean-diet groups
Reporting bias	**selektive Ergebnisdarstellung (primärer EP): low**

Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: *N Engl J Med* 378 (25), e34. DOI: 10.1056/NEJMoa1800389 [3]	
Andere Ursachen für Bias	- Protokolländerungen im Verlauf (Behandlung in der Kontroll-Gruppe) - In wie weit unterschieden sich die Diäten tatsächlich.
Diskussion in der Leitliniengruppe	Zur mediterranen Diät diskutiert die Gruppe insbesondere Verzerrungsrisiken und Bedeutung der PREDIMED-Studie und geht dabei unter anderem auf folgende Punkte ein: ▪ Verzerrungsrisiken der Studie (Randomisierung aufgehoben, selbstberichtete Interventionen, Ungleichgewicht in den Gruppen bezogen auf begleitende Schulung), ▪ Übertragbarkeit der Studienergebnisse auf den deutschen Versorgungskontext ist schwierig (Indirektheit),“nur” ca. 50% hatten einen T2DM (dennoch n=3614), ▪ Inkonsistente Ergebnisse in den zwei Med-Diät-Gruppen, ▪ Personen mit Typ-2-Diabetes wurden nach Kenntnis der Gruppe bezogen auf den primären Endpunkt nicht getrennt betrachtet, ▪ Worauf die positiven Effekte in der PREDIMED-Studie zurückzuführen sind, ist nicht eindeutig klar. Hauptunterschied der Ernährungsmuster war die Aufnahme von Kohlenhydraten und pflanzlichen Fetten. Die Effekte waren unabhängig von einer Gewichtsreduktion. ▪ Mitglieder der Leitliniengruppe machen deutlich, dass die Studie trotz der oben genannten Einschränkungen aktuell von der Anzahl der Teilnehmenden und der Betrachtung kardiovaskulärer Endpunkte ihrer Einschätzung nach die beste vorliegende Evidenz ist.

3.7.1.2 Endpunkt: Diabetische Retinopathie

Vier systematische Übersichtsarbeiten (AMSTAR 2 critically low) befassen sich mit dem Einfluss von Ernährung auf Augenerkrankungen und identifizieren für die Intervention mediterrane Diät und den Endpunkt diabetische Retinopathie eine post hoc-Auswertung der PREDIMED-Studie. Die Suche scheint in mindestens einem der SR verlässlich. Da Reviews unterschiedlich ausführlich über die Studie berichten, erfolgt hier eine zusammenfassende Darstellung. Zur Beurteilung der Einzelstudie PREDIMED-Studie;

GRADE-Bewertung (NVL) zur Aussagesicherheit der Evidenz für die Diabetische Retinppathie: very low
Der Endpunkt wurde in verschiedenen SR untersucht, aber es wurde jeweils nur Daten der PREDIMED-Studie identifiziert.
RoB: -2 (serious concerns, Randomisierung aufgehoben, selbstberichtete Interventionen, Ungleichgewicht in den Gruppen bezogen auf begleitende Schulungen)
Inkonsistenz: -1 (nur eine Studie; Unterschied in den Effekten der beiden Behandlungsarme)
Indirectness: 0 -1? (für die Studie kein Herabstufen, aber für NVL-Fragestellung: Vergleich zweier Diäten, “nur” ca. 50% hatten einen Diabetes)
Präzision: 0 bis -1 (geringe Ereignisrate)
Publication bias: 0-1 (nicht erhoben, nur eine Studie identifiziert)

Wu et al., 2023

Zitat	**Studien-charakteristika**	**Ergebnisse**	**AMSTAR 2**	**Kommentar**
Wu Y. The Mediterranean Diet and Age-Related Eye Diseases: A	**Suchzeitraum:** inception up to 02/2023 **Fragestellung:** associations between adherence to the Mediterranean Diet (MD) and cataract, glaucoma, age-related macular degeneration (AMD), diabetic retinopathy (DR) and dry eye syndrome (DES).	18 studies included: cataract (1 study), glaucoma (2 studies), AMD (9 studies), **DR (2 studies, davon 1 RCT)**, and DES (4 studies), respectively.	**Critically low** y-py-n-py-y-y-n-py-y-n-	- nur ein RCT (Diaz-Lopez 2015, PREDIMED) zum

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
Systematic Review. Nutrients 2023; 15(9). https://www.ncbi.nlm.nih.gov/pubmed/37432187.	**Population:** Individuals without eye diseases such as cataract, age-related macular disease, diabetic retinopathy and dry eye syndrome **Intervention:** good compliance with Mediterranean Diet **Control:** poor compliance with Mediterranean Diet **Outcome:** onset or development of above-mentioned eye diseases **Studies:** RCT, prospective and retrospective observational studies (cohort, cross-sectional, case-control studies) **Risk of bias (quality) assessment:** - Newcastle-Ottawa Quality Assessment Scale (NOS): case-control and cohort studies. - Agency for Healthcare Research and Quality (AHRQ) methodological checklist: cross-sectional studies. - Cochrane risk of bias tool: RCTs	1 RCT, in dem die Assoziation zwischen mediterraner Diät und diabetischer Retinopathie untersucht wurde: Diaz-Lopez 2015 (PREDIMED), n=3614, male n=1707; age: m (55-80years), F (60-80 years), follow-up 6 years, Outcome of interest: Incidence of DR, Case definition: nonmydriaic fundus camera, Risk factor: Mediteranean diet intervention versus low-fat diet RoB: Sequence generation: low; allocation concealment: low; blinding: low; incomplete outcome data: some concerns; selective outcome reporting: low, Other bias: low. ▪ post hoc analysis of PREDIMED study: participants with T2DM achieved a 40% reduction in DR incidence in the MD group (either added mixed nuts or extra virgin olive oil, EVOO) as compared with the control group. (aus Wong et al (siehe unten): any Med diet vs. control diet, HR 0.60 (95% CI 0.37–0.96). ▪ DR for MedDiet + EVOO: HR 0,56 (95% CI 0,32; 0,97). The MD with added EVOO manifested greater protection on DR incidence than the MD with added nuts (−44% vs. −37%, p < 0.001)).	noMa-noMa-y-y-n-y nicht-erfüllte kritische Domänen: - ausgeschlossene Studien nicht aufgeführt -Publication bias	Endpunkt DR identifiziert; - RoB-Bewertung der Studie wohlwollend. - Darstellung der Ergebnisse nicht ausführtlich (Angabe der HR aus anderem SR angegeben).

Dow et al., 2018

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Dow C. Diet and risk of diabetic retinopathy: A systematic review. Eur J Epidemiol 2018; 33(2):141–56. https://www.ncbi.nlm.nih.gov/pubmed/29204902.	**Zeitpunkt der Suche:** in 11/2015, last updated 10/2017 **Fragestellung:** association between diet and dietary intakes of specific foods, nutrients, and food groups, and the risk of diabetic retinopathy. **Population:** nicht eindeutig benannt **Intervention:** dietary intakes of foods (individual food items or broader food groups), macronutrients (carbohydrates, protein, fat, fibre), micronutrients (minerals, vitamins), dietary supplements (as	27 relevant studies. ▪ prospective (n = 13), of which 6 were RCTs or nested case–control studies within RCTs. ▪ 1 study, though prospective, collected some information cross-sectionally. The remainder of the studies were cross-sectional (n = 10) or case–control studies (n = 4). Im folgenden nur Ergebnisse zur mediterranen Diät extrahiert: 1 prospective Study nested in RCT (Diaz-Lopez et al. 2015, PREDIMED) investigated the **Mediterranean diet,** enriched with either extra virgin olive oil or nuts and compared it with a low-fat diet in a prospective study (6 years, > 3600 participants). ▪ Mediterranean diet enriched with olive oil: more than 40% decreased risk of retinopathy. ▪ those in the highest quintile of adherence to the diet had more than a 60% decreased risk of retinopathy compared to those with the lowest adherence.	**Critically low** y-n-n-py-n-y-n-y-y-n-noMa-NoMa-n-y-n-y	Nur eine Studie zu mediterraner Diät identifiziert, HR nur graphisch im Forrest Plot, aber nicht als Zahlen angegeben. Wenig Informationen (Intervention in der Vergleichsgruppe) über die Studien.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
	vitamins or minerals) or dietary patterns (a posteriori or a priori). **Comparator:** nicht benannt **Outcome:** development of diabetic retinopathy or macular edema **Studies:** Eligible study designs included randomized controlled trials (RCTs), and cohort, case–control, cross-sectional, and ecological studies	▪ The Mediterranean diet enriched with nuts was associated with a 37% decreased, though non-statistically significant reduction in the risk of retinopathy. Studies suggest that adherence to the Mediterranean diet and high fruit, vegetable and fish intake may protect against the development of diabetic retinopathy, although the evidence is limited. Studies concerning other aspects of the diet are not in agreement. The role of the diet in the development of diabetic retinopathy is an area that warrants more attention. RoB der Studien nicht eindeutig angegeben. Studie von Diaz-Lopez herabgestuft, da Diabetsdauer als confoundingfactor nicht berücksichtigt. Weitere Bewertung bleibt unklar.		The search strategy employed for the Pubmed search was based on the protocol developed in a systematic review by Schwingshackl et al

Wong et al., 2018

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Wong MY. Dietary intake and diabetic retinopathy: A systematic review. PLoS One 2018; 13(1):e0186582. https://www.ncbi.nlm.nih.gov/pubmed/29324740.	**Suchzeitraum:** 01/1967 to 01/2017 **Fragestellung:** association between dietary intake and diabetic retinopathy (DR) **Population:** participants with type 1 diabetes, type 2 diabetes or both **Intervention:** micro- and macro-nutrient intakes; food and beverage consumptions; and dietary patterns **Comparator:** nicht angegeben **Outome:** prevalence, incidence or progression of DR or diabetic macula oedema (DME) **Studies:** Interventional and observational studies **Methodical quality assessment:** modified Newcastle-Ottawa scale for observational studies, and the Cochrane collaboration tool for interventional studies.	RESULTS 31 studies (3 RCTs, 28 observational studies: 9 prospective, 4 case-control, and 15 cross-sectional) **Ergebnisse zu Mediterraner Diät (RCTs):** 1 RCT (Diaz-Lopez and associates, PREDIMED; quality: moderate bias) suggests a protective association of a Med diet on incident DR. 3614 patients with type 2 diabetes from the PREDIMED trial were split between a control (low-fat) diet, and two types of Med diets (oil, nuts). Incident DR (multivariable cox regression model): any Med diet vs. control diet, HR 0.60 (95% CI 0.37–0.96). ▪ Low incident cases of DR (n=74) Methodological quality: medium risk of bias	**Critically low** y-n-n-py-y-y-n-py-y-n-noMa-noMa-y-y-n-y	

Shah et al., 2022

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Shah J. Dietary Intake and Diabetic Retinopathy: A Systematic Review of the Literature. Nutrients 2022; 14(23). https://www.ncbi.nlm.nih.gov/pubmed/36501054.	**Suchzeitraum:** between 01/1967 to 05/2022 **Fragestellung:** effect of dietary consumption on DR and diabetic macular edema (DME). **Population:** human subjects with type-1, type-2 diabetes or both **Interventions or exposure:** dietary intake including specific food, beverages, micronutrients, macronutrients, and dietary patterns **Outcomes:** prevalence, incidence or progression of DR with or without DME **Studies:** prospective, case-control, cross-sctional, and randomized controlled trials (RCTs)	54 relevant articles were retained: 3 interventional, 17 prospective, 29 cross-sectional, 5 case-control Von den 3 identifizierten Interventionsstudien, betrachtete nur eine Mediterrane Diät als dietary factor (Diaz-Lopez 2015, PREDIMED,Quality Score: moderate bias) An interventional study showed the benefit of consumption of the Mediterranean diet on reducing the incident DR (any Mediterranean diet vs. control diet, HR: 0.60, 95%CI: 0.37–0.96) in type 2 diabetics, when using a multivariable cox regression model.	**Critically low** (nicht alle Kriterien durchgeführt, aber folgende kritische Domänen bereits nicht erfüllt: - kein Protokoll auffindbar - Ausgeschlossene Studienicht aufgeführt, - publication bias nicht angegeben Weitere Bewertung be Bedarf möglich	Wie bereits in den SR von Dow et al., und Wong et al., wurde nur der RCT von Diaz-Lopez (PREDIMED) identifiziert. Daher hier nicht weiter betrachtet.

3.7.2 Ausgewählte zurückgestellte Artikel

Aus der systematischen Recherche zu mediterraner Diät

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
Hallberg SJ. Improving the scientific rigour of nutritional recommendations for adults with type 2 diabetes: A comprehensive review of the American Diabetes Association guideline-recommended eating patterns. Diabetes Obes Metab 2019; 21(8):1769–79. https://www.ncbi.nlm.nih.gov/pubmed/30941880.	**Suchzeitraum:** - Betrachtung der in den ADA-Dokumenten zitierten Evidenz - eigene Recherche: 01/2000-05/2018 **Fragestellung:** appropriateness of sources cited in the American Diabetes Association's (ADA) guidelines on eating patterns for T2D management, identify additional relevant sources, and evaluate the evidence. **Population:** people with T2DM	**Results for mediterranean diet:** **ADA documents** cite 6 studien, including 3 RCTs of longer duration Two RCTs found that the Mediterranean diet was superior to comparison diets [25,28]: one found that a low-carbohydrate Mediterranean diet resulted in a significantly greater HbA1c reduction compared to the control diet, [28] and the other found at 4-year follow-up that the Mediterranean diet resulted in significant HbA1c reduction, sustained improvements in triglyceride and HDL cholesterol levels, and less medication initiation in people with newly diagnosed T2D.[25] A third RCT, [26] for which data were reanalysed with essentially the same results in 2018, [27] reported a significant reduction of major cardiovascular events in both versions of the Mediterranean diet studied, compared with the control. Two systematic reviews [29,30] found limited evidence that the Mediterranean diet is effective for glycaemic control, but more robust support for CVD risk reduction. Also cited was a commentary favouring the Mediterranean diet that was based on a non-systematic selection of articles. [31] **Additional evidence (neue Recherche)** We identified 12 other studies on the Mediterranean diet worthy of consideration: 4 RCTs, 2 RCT follow-up studies, and 6 systematic reviews with meta-analysis (Table S3).[32-43]	Für den eigenen Review: Critically low y-y-n-y-n-n-y-n-n-noMa-noMa-n-y-n-y Wichtig: formell nur eine Datenbank durchsucht (Medline)	- zurückstellen, primärer-Endpunkt war glycaemic control (insbesondere HbA1c), über methodische Qualität ausgeschlossen. Der Review gibt aber Hinweis zur Qualität der zugrundeliegenden Evidenzrecherche

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
#31970	**Intervention:** one study arm that followed one of the three eating patterns, recommended by the 2018 standards (DASH-diet, mediterranean diet, plant-based diet), or a low carbohydrate-diet (new in 2019). **Vergleich:** nicht eindeutig benannt. **Outcomes:** outcomes including glycaemic control (HbA1c primary biomarker) **Studientypen:** clinical trial, a systematic review, or a systematic review with meta-analysis of clinical trials	▪ 1 RCT found that this diet significantly improved HbA1c and body mass index in post-menopausal women with T2D, but the diet was not superior to usual care for improving blood pressure and lipids.[32] ▪ A 2-year RCT [36] comparing low-fat, low-carbohydrate and Mediterranean diets in obese people with T2D, with data available for 36 persons with T2D, found that the Mediterranean diet improved FBG, but not HbA1c levels,compared to a low-fat and low-carbohydrate diet. ▪ 2 studies [33,34] followed up Esposito 2009, [25] which was included in the ADA-cited evidence (Table 1). Both studies found longer times to medication requirement in the Mediterranean diet arm versus the low-fat diet arm, as well as increased partial remission and improved FBG and CVD risk markers. ▪ 1 of 2 smaller 12-week RCTs found a statistically significant HbA1c reduction favouring a Mediterranean diet over a typical diet; the other did not find a difference between the Mediterranean diet and a low-fat diet. [35,37] Neither of these trials resulted in between-group statistical significance for CVD risk factor markers including body mass index, blood pressure and lipids, but one found improvement in inflammation markers and flow-mediated dilation in the Mediterranean diet arm only. [35] ▪ 4 systematic reviews with meta-analysis [38-41] and 2 with network meta-analysis [42,43] concluded that the Mediterranean diet is superior to other eating patterns for glycaemic control, weight loss, lipid profile, and reduced need for diabetes medication. **Summary of evidence** The ADA-cited sources combined with additional ones identified through our search resulted in a total of seven RCTs, two follow-up RCT studies, and seven systematic reviews (including five with meta-analysis) that are appropriate for consideration in developing nutrition guidelines for T2D. Among the included trials are several large-scale studies, one with 3614 participants [26,27] and one with more than 200 participants. [25,33,34] Longer-term studies include one lasting 12 months, [28] one lasting 24 months, [36] and two lasting longer than 4 years. [25-27,33,34] As recommended by the ADA guidelines, we found that the Mediterranean eating pattern has demonstrated effectiveness in improving glycaemic control [25,28,32-34,38-43] as well as CVD risk factors and even in reducing CVD events. [22,23,26,27,29,30,33,34,38-43] This diet appears to be appropriately considered helpful for T2D management; its inclusion in the recommended eating patterns is warranted. However, questions remain about which components of the Mediterranean diet contribute to its effectiveness on all of these outcomes. Some studies suggest that it is the diet's more moderate carbohydrate content (<50% total energy intake) that accounts for reductions in weight and CVD risk, [44] while others suggest that the high monounsaturated fat content in the diet plays an important role in improving insulin sensitivity, glycaemic control, and inflammation. [45,46] Research in these areas will strengthen future nutritional recommendations and provide more in-depth guidance on how the Mediterranean diet can be used for T2D management. RESULTS: We found a wide variation in the evidence for each eating pattern. Issues that have hampered the guideline process include: lack of a rigorous literature review, resulting in the omission of pertinent studies; an overreliance on prospective cohort studies; inconsistent standards for evidence; inclusion of studies not		des ADA Standards. - Ziel des Reviews war es, die Evidenzgrundlage der ADA-Empfehlungen (2018 and 2019 ADA Standards of Care and the 2014 ADA Nutrition Therapy Recommendations for Adults with Diabetes) zu Ernährungsmustern zu bewerten. Zusätzlich wurde eine eigene Recherche durchgeführt. Diese erfolgte allerdings nur in PubMed and Medline Ovid, was streng genommen einer Datenbank entspricht.

Zitat	Studien-charakteristika	Ergebnisse	AMSTAR 2	Kommentar
		on persons with T2D; and bias. CONCLUSIONS: The ADA Guidelines recommended eating patterns fall short of rigorous standards of scientific review according to state-of-the-art systematic review and guideline creation practices.		
Schwingshackl L. A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. Eur J Epidemiol 2018; 33(2):157–70. https://www.ncbi.nlm.nih.gov/pubmed/29302846.	**Suchzeitraum:** until July 2017 **Fragestellung:** comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus **Population:** adults with type 2 diabetes mellitus **Intervention:** dietary approach **Outcome:** HbA1c (%) and/or fasting glucose (mmol/l); **Studies:** RCTs with minimum intervention period of 12 weeks	total of 56 trials (n=4937), comparing nine dietary approaches ▪ low-fat, ▪ Vegetarian, ▪ Mediterranean, ▪ high-protein, ▪ moderatecarbohydrate, ▪ low-carbohydrate, ▪ control, ▪ low GI/GL, ▪ Palaeolithic For reducing HbA1c, the low-carbohydrate diet was ranked as the best dietary approach (SUCRA: 84%), followed by the Mediterranean diet (80%) and Palaeolithic diet (76%) compared to a control diet. For reducing fasting glucose, the Mediterranean diet (88%) was ranked as the best approach, followed by Palaeolithic diet (71%) and Vegetarian diet (63%). The network analysis also revealed that all dietary approaches significantly reduce HbA1c (- 0.82 to - 0.47% reduction) and fasting glucose (- 1.61 to - 1.00 mmol/l reduction) compared to a control diet. According to the network meta-analysis the Mediterranean diet is the most effective and efficacious dietary approach to improve glycaemic control in type 2 diabetes patients.		Von den Endpunkten nicht passend, aber Überblick für intermediäre Endpunkte

Aus der sytematischen Recherche zu Gewichtsmanagement

Franquesa 2019 (Mediterrane Diät)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Franquesa M. Mediterranean Diet and Cardiodiabesity: A Systematic Review through Evidence-Based Answers to Key Clinical Questions. Nutrients 2019; 11(3). https://www.ncbi.nl	**Suchzeitraum:** between September 2013 and July 2016 (update eines früheren Reviews (Garcia-Fernandez et al.) **Fragestellung:** 5 Critical Questions, von Population und Endpunkten für unsere Fragestellung interessant: **CQ 2:** What effect does the MedDiet have on the incidence and prevention of T2DM?	**CQ 2:** What Effect Does the MedDiet have on the Incidence and Prevention of T2DM? **The MedDiet reduces the symptoms of T2DM and modulates disease course** Level of evidence: Moderate Rationale: MedDiet adherence has been found to reduce glycated hemoglobin (HbA1c) [43,44], CRP (C-reactive protein), and adiponectin [46] levels in diabetic patients. - Esposito et al.,2015 [43], Systematic review and meta-analysis, n= 1266, initial disease: Overweight or obesity with T2DM	Critically low (kaum Kriterien erfüllt, keine doppelte Selektion, Extraktion, keine ausreichende RoB-Bewertung der Studien (nur nach Studientyp),	- Ausschließen, da kaum methodische Kriterien erfüllt. - Systematische Übersichtsarbeiten und RCT zusammen betrachtet; Ergebnisse der SRs oder der Einzelstudie aus dem Review numerisch nicht ersichtlich.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
m.nih.gov/pubmed/30889891. #31694 file://kbvnetapp-aezq/azq$/ÄZQ-Berlin/7000%20IVS/RefMan/Volltexte/31694.pdf	**CQ 4:** What effect does the MedDiet have on the prevention of CVD and the modulation of disease course? **Population:** CQ 2 Men and women with or at risk of T2DM CQ: 4: Men and women **Intervention:** Application of MedDiet and/or monitoring of MedDiet adherence **Vergleich:** Epidemiologically similar control group that does not follow the MedDiet **Endpunkte:** CQ2**:** all-cause mortality, mortality due to CVD, heart attack, or T2DM CQ4: CVD incidence or mortality **Studien:** prospective cohort, cross-sectional, and clinical trial studies, Systematic reviews **Publication types:** Systematic reviews and meta-analyses **Qualitätsbewertung:** Levels of scientific evidence anhand der Studiencharakteristika vergeben. Grundlage für Bewertung nicht ausreichend beschrieben.	- Sleiman et al. 2015[44], Systematic review and meta-analysis, n= 1266, initial disease: Obesity with T2DM and non-high-risk diabetes - Maiorino et al., 2016 [46]: parallel group RCT (MEDITA), n=215, initial disease: recent diagnoses of T2DM. **CQ 4:** What Effect Does the MedDiet have on the Prevention of CVD and the Modulation of Disease Course? Level of evidence: High **- MedDiet adherence reduces the incidence of CVD in individuals with high cardiovascular risk** Rationale: The protective role of the MedDiet on the incidence of cardiovascular events has been widely demonstrated in large clinical trials [28,30,35,37,39,53–55]. Furthermore, Estruch et al. [26] showed that, compared against the low-fat diet recommended by the American Heart Association, the MedDiet supplemented with nuts or extra-virgin olive oil protected high-risk individuals from CVD. A meta-analysis of 20 studies containing data from 888,257 individuals by Grosso et al. [56] showed that increased MedDiet adherence was associated with a relative risk reduction of 40% for CVD incidence. Literatur Martínez-González et al., 2011 [28]; Cohort Gullar-Castillón et al., 2012 [30]; EPIC-Cohort Kastorini et al.,2016 [35]; ATTICA-Study Stewart et al., 2016 [37]; RCT Stefler et al., 2015 [39]; Panagiotakos et al.,2007 [53]; Eguaras et al., 2015 [54]; Casas et al., 2014 [55]; Estruch et al., 2013 [26]; Grosso et al., 2015 [56], systematic review and metaanalysis. **- MedDiet adherence reduces CVD mortality in individuals without CVD but with high cardiovascular risk** Rationale: Several studies have reported an association between the MedDiet and a reduction in CVD mortality in individuals with risk factors for CVD [37–39]. Bonaccio et al. [38], in turn, showed that high MedDiet adherence was associated with a relative risk reduction of 34% for CVD mortality in patients with T2DM. **- MedDiet adherence reduces CVD incidence and mortality in the general population**	kein Protokoll, k, keine Meta-analysen, ausgeschlossene Studien nicht benannt, Publication bias nicht erhoben…),	Die Evidenz wird von den Reviewautoren zusammengefasst (und interpretiert). Eine eigenständige Beurteilung ist nicht möglich, Review daher ungeeignet.

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Rationale: MedDiet intervention studies in the general population without baseline data on health status have concluded that adherence to the diet has a protective effect on CVD incidence and mortality [31–33,36,37,57,58]. A study by Fung et al. [32] of women with T2DM without a history of CVD also showed that high MedDiet adherence protected against CVD risk and associated mortality. Similarly, Knoop et al. [59] showed that higher MedDiet adherence was associated with reduced CVD-specific and all-cause mortality in the elderly population (70–90 years).		

3.8 Themenverwandte AWMF-Leitlinien und vorherige NVL zum Themenbereich Diabetes

Zitat	Kommentar
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2014): Nationale VersorgungsLeitlinie Therapie des Typ-2-Diabetes - Langfassung, 1. Auflage. Version 4. Online verfügbar unter http://doi.org/10.6101/AZQ/000213, zuletzt geprüft am 12.01.2017.	NVL Therapie des Typ-2-Diabetes (2014)
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2022): Nationale VersorgungsLeitlinie Chronische KHK – Langfassung. Version 6.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000491, zuletzt geprüft am 15.09.2022.	NVL Chronische KHK
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): Nationale VersorgungsLeitlinie Chronische Herzinsuffizienz – Langfassung, Version 4.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000510, zuletzt geprüft am 12.12.2023.	NVL Chronische Herzinsuffizienz
Bundesärztekammer (BÄK); Kassenärztliche Bundesvereinigung (KBV); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): Nationale VersorgungsLeitlinie Hypertonie - Langfassung. Version 1.0. Online verfügbar unter http://doi.org/10.6101/AZQ/000502, zuletzt geprüft am 29.06.2023.	NVL Hypertonie
Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie (DGPM); Deutsches Kollegium für Psychosomatische Medizin (DKPM) (2020): S3-Leitlinie Screening, Diagnose und Behandlung alkoholbezogener Störungen. Registernummer 076-001. Version 2021-02. Online verfügbar unter https://www.awmf.org/leitlinien/detail/ll/076-001.html, zuletzt geprüft am 20.06.2022.	Alkoholbezogene Störungen
S3-Leitlinie Adipositas - Prävention und Therapie, AWMF-Register-Nummer 050/001, Version 5.0, Oktober 2024. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/050-001, zuletzt geprüft am 19.11.2024	Adipositas-LL

3.9 Von der Leitliniengruppe eingebrachte Evidenz

Zitat	Kommentar
Nationale Diabetes-Surveillance am Robert Koch-Institut (2019): Diabetes in Deutschland – Bericht der Nationalen Diabetes-Surveillance 2019. Online verfügbar unter https://diabsurv.rki.de/SharedDocs/downloads/DE/DiabSurv/diabetesbericht2019.html, zuletzt geprüft am 24.01.2024.	RKI Diabetes-Surveillance
Gut essen und trinken – die DGE-Empfehlungen https://www.dge.de/gesunde-ernaehrung/gut-essen-und-trinken/dge-empfehlungen/	DGE-Empfehlungen
Deutsche Gesellschaft für Ernährung (DGE). DGE-Ernährungskreis: Der DGE-Ernährungskreis zeigt auf einen Blick wie eine gesunde und ökologisch nachhaltige Ernährung aussieht. 2024 [cited: 2024-10-15]. https://www.dge.de/gesunde-ernaehrung/gut-essenund-trinken/dge-ernaehrungskreis/. #34569	DGE-Ernährungskreis
Schäfer AC, Boeing H, Conrad J, et al. Wissenschaftliche Grundlagen der lebensmittelbezogenen Ernährungsempfehlungen für Deutschland: Methodik und Ableitungskonzepte. Ernahrungs Umschau 2024; 71(3):M158–66. e5–7. DOI: 10.4455/eu.2024.009. # 34566	DGE Wissenschaftliche Grundlage
Deutsche Gesellschaft für Ernährung (DGE). Am besten null Promille – neues DGE-Positionspapier zu Alkohol. 2024 [cited: 2024-09-27]. https://www.dge.de/presse/meldungen/2024/dge-positionspapier-zu-alkohol/. Darüber identifiziert: Canadian Centre on Substance Use and Addiction (CCSA). Canada's guidance on alcohol and health: Final report. Ottawa, Ont.: Canadian Centre on Substance Use and Addiction; 2023. https://www.ccsa.ca/canadas-guidance-alcohol-and-health.	DGE-Positionspapier Alkohol
Skurk, Thomas; Bosy-Westphal, Anja; Grünerbel, Arthur; Kabisch, Stefan; Keuthage, Winfried; Kronsbein, Peter et al. (2023): Empfehlungen zur Ernährung von Personen mit Typ-2-Diabetes mellitus. In: *Diabet Stoffw* 18 (S 02), S270-S304. DOI: 10.1055/a-1997-7924.	DDG Praxisempfehlungen
Salas-Salvadó, Jordi; Bulló, Mònica; Estruch, Ramón; Ros, Emilio; Covas, Maria-Isabel; Ibarrola-Jurado, Núria et al. (2014): Prevention of diabetes with Mediterranean diets. A subgroup analysis of a randomized trial. In: Ann Intern Med 160 (1), S. 1–10. DOI: 10.7326/M13-1725.	Ergänzende Auswertungen PREDIMED
Estruch, Ramón; Ros, Emilio; Salas-Salvadó, Jordi; Covas, Maria-Isabel; Corella, Dolores; Arós, Fernando et al. (2018): Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. In: N Engl J Med 378 (25), e34. DOI: 10.1056/NEJMoa1800389.	Ergänzende Auswertungen PREDIMED
Basterra-Gortari, F. Javier; Ruiz-Canela, Miguel; Martínez-González, Miguel A.; Babio, Nancy; Sorlí, José V.; Fito, Montserrat et al. (2019): Effects of a Mediterranean Eating Plan on the Need for Glucose-Lowering Medications in Participants With Type 2 Diabetes. A Subgroup Analysis of the PREDIMED Trial. In: Diabe-tes Care 42 (8), S. 1390–1397. DOI: 10.2337/dc18-2475.	Ergänzende Auswertungen PREDIMED

3.10 Ausgewählte zurückgestellte Artikel (Gewichtsmanagement / Ernährung)

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Lohner S, Kuellenberg dG, Toews I, et al. Non-nutritive sweeteners for diabetes mellitus. Cochrane Database of Systematic Reviews 2020(5):CD012885. DOI: 10.1002/14651858.CD012885.pub2. http://dx.doi.org/10.1002/14651858.CD012885.pub2.	**Zeitpunkt der Suche:** last search of all databases (except for Scopus) May 2019. Scopus: January 2019. **Fragestellung:** effects of non-nutritive sweeteners (NNS) in people with diabetes mellitus. **Population:** individuals with type 1 or type 2 diabetes **Intervention:** any type of NNS Trials with concomitant behaviour-changing interventions, such as diet, exercise, or both, were eligible for inclusion, given that the concomitant interventions were the same in the intervention and comparator groups. **Control:** usual diet, no intervention, placebo, water, a different NNS, or a nutritive sweetener **Studies:** RCTs with duration ≥ 4 weeks **Subgroup-analysis:** Type 1 diabetes or Type 2 diabetes	9 RCTs included (total of 979 people with type 1 or type 2 diabetes). - intervention duration ranged from 4 to 10 months. - we judged none of these trials as at low risk of bias for all 'Risk of bias' domains; most of the included trials did not report the method of randomisation. **Vergleich: dietary supplement containing NNS versus sugar:** - 3 trials - HbA1c was 0.4% higher in the NNS group (95% CI −0.5 to 1.2; P = 0.44; 3 trials; 72 participants; very low-certainty evidence). - weight change: MD −0.1 kg (95% CI −2.7 to 2.6; P = 0.96; 3 trials; 72 participants; very low-certainty evidence). - None of the trials with sugar as comparator reported on adverse events. **Vergleich: NNS versus placebo:** - 5 trials - HbA1c: MD 0%, 95% CI −0.1 to 0.1; P = 0.99; 4 trials; 360 participants; very low-certainty evidence. The 95% prediction interval ranged between −0.3% and 0.3%. - body weight: MD −0.2 kg, 95% CI −1 to 0.6; P = 0.64; 2 trials; 184 participants; very low-certainty evidence. - 3 trials reported the numbers of participants experiencing at least one non-serious adverse event: 36/113 participants (31.9%) in the NNS group versus 42/118 participants (35.6%) in the placebo group (RR 0.78, 95% CI 0.39 to 1.56; P = 0.48; 3 trials; 231 participants; very low-certainty evidence). **Vergleich: NNS versus nutritive low-calorie sweetener (tagatose):** - 1 trial - HbA1c was 0.3% higher in the NNS group (95% CI 0.1 to 0.4; P = 0.01; 1 trial; 354 participants; very low-certainty evidence). - This trial did not report body weight data and adverse events. **The included trials did not report data on health-related quality of life, diabetes complications, all-cause mortality, or socioeconomic effects.**	High y-y-n(?)-y-y-y-y-y-y-y-y-y-y-y-y-y	The included trials did not report data on health-related quality of life, diabetes complications, all-cause mortality, or socioeconomic effects. Für HbA1c keine statistisch signifikanten positiven Effekte. Thema des Reviews war nicht Fragestellung in der Überarbeitung des Kapitels. Für Informationen hinsichtlich kalorienfreier oder kalorienarmer Süßungsmittel verweist die Leitliniengruppe auf die S3 Leitlinie „Prävention

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		No subgroups: there were not enough trials to estimate effects in various subgroups. (1 trial: only individuals with type 1 diabetes; two trials included both individuals with type 1 and 2 diabetes, whilst all other trials (6) included participants with type 2 diabetes only. **Authors' conclusions:** There is inconclusive evidence of very low certainty regarding the effects of NNS consumption compared with either sugar, placebo, or nutritive low-calorie sweetener consumption on clinically relevant benefit or harm for HbA1c, body weight, and adverse events in people with type 1 or type 2 diabetes. Data on health-related quality of life, diabetes complications, all-cause mortality, and socioeconomic effects are lacking.		und Therapie der Adipositas“ {Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) 2024: 34568}.

3.11 Anhang: Evidenztabellen Einzelstudien

Look AHEAD (intensive lifestyle interventions)

Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: One-year results of the look AHEAD trial. Diabetes Care 2007; 30(6):1374–83. http://www.ncbi.nlm.nih.gov/pubmed/17363746. #20826

Weitere Zitate:
- Protokoll: Ryan DH, et al. Look AHEAD (Action for Health in Diabetes): Design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes. Control Clin Trials 2003; 24(5):610–28. DOI: 10.1016/s0197-2456(03)00064-3. http://www.ncbi.nlm.nih.gov/pubmed/14500058. #31781
- Daten nach 4 Jahren: Wing RR, Wing RR. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: Four-year results of the Look AHEAD trial. Arch. Intern. Med 2010; 170(17):1566–75. DOI: 10.1001/archinternmed.2010.334. http://www.ncbi.nlm.nih.gov/pubmed/20876408. *Laufnummer: 20925*
- Daten nach Ende der Studie: Wing RR, Bolin P, Brancati FL, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med 2013; 369(2):145–54. DOI: 10.1056/NEJMoa1212914. http://www.ncbi.nlm.nih.gov/pubmed/23796131. *Laufnummer: 22980*

Studiencharakteristika: multi-centered RCT, n= 5,145, intervention 4 years, follow up planned 11.5 years (gesamt), stopped early due to lack of cardiovascular benefit (futility), follow-up 9,6years, (hier 1-Jahres Daten), recruitment from clinical centers

Objective	- effectiveness of intentional weight loss in reducing cardiovascular disease (CVD) events in overweight or obese adults with T2DM.
Population	overweight or obese adults with T2DM
Pre-randomization (all participants)	2-week run-in period: - pre-randomization diabetes education session - self-monitoring of diet and physical activity required - exercise tests to assess fitness
Intervention	Intensive Lifestyle Intervention (ILI): group and individual meetings to achieve and maintain weight loss (minimum 7% in year 1) through decreased caloric intake and increased physical activity. - Months 1-6: weekly (3 group meetings, 1 individual session), months 7-12: group sessions every other week + monthly individual session - Caloric restriction; % of total calories: ≤30% from fat (≤10% from saturated fat) and a ≥15% from protein, portion-controlled diets, including use of liquid meal replacements (provided free of charge) and frozen food entrées, as well as structured meal plans (comprised of conventional foods), monthly reviews (individual sessions) - Physical activity (PA) program: gradual progression toward a goal of 175 min of moderate intensity PA/ week - „toolbox“: pre set algorithm included use of a weight loss medicine (orlistat) and/ or advanced behavioral strategies for individuals who had difficulty in meeting goals.
Control	Diabetes Support and Education (DSE) condition - initial pre-randomization diabetes education session and invited to 3 additional group sessions during year 1 (information and opportunities for discussing topics related to diet, physical activity, and social support). - not weighted at these sessions and no counseling in behavioral strategies for changing diet and activity
Primary Outcome	Time to incidence of major CVD events (cardiovascular death, non-fatal myocardial infarction, nonfatal stroke)
Statistic	- intention to treat approach - interims analyses of efficacy an futility
Einschlusskriterien:	aged 45–74 years (changed to 55-74 years during 2nd year to increase anticipated CV-event rate), body mass index ≥25 kg/m^2 (≥27 kg/m^2 if taking insulin), HbA1c ≤11%
Change in medication during	by own physicians, except temporary reductions in hyperglycemia medicines during periods of intensive weight loss intervention (made by intervention sites following a standardized treatment protocol)

Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: One-year results of the look AHEAD trial. Diabetes Care 2007; 30(6):1374–83. http://www.ncbi.nlm.nih.gov/pubmed/17363746. #20826

study	
Attrition	Randomized: ILI: 2,570, DSE: 2,575, attended Year 1 examination: ILI 2,496 (97,1%), DSE 2,463 (95,7%) - basline insulin use varied significantly between non-attendees (21.0%) versus attendees (15.1%), p=0.04.
Baseline:	Age ca. 58,7y (±6,8), BMI females ca. 36,5kg/m2 (±6,1), male ca. 35,2kg/m2 (±5,5), 14.0% history of CV disease, 15.3% taking insulin, 87.5% diabetes medicines (including insulin), 75.3% using anti-hypertensive medicines, 51.0% using lipid-lowering medicines

Ergebnisse			
	Intensive lifestyle intervention n=2496	**Diabetes support Education n=2463**	
Average weight loss of initial weight (%) 1 year	8,6% (SD 6,9%)	0,7% (SD 4,8%)	P<0,001
weight loss goal (≥10% of initial weight) 1 year	37,8%	3,2%	
Weight loss ≥7% 1 year	55,2%	7,0%	
Average weight loss of initial weight (%) study end	6,0%	3,5%	
Patients on insulin loosing less weight than others (ILI 7,6 ± 7,0% insulin users vs. Non users 8,7 ± 6,9% p=0,002); DSE: insulin users 0,3 ± 5,1% vs. Non-users 0,8 ± 4,7%)			
HbA1c (SD)			
Mean HbA1c at baseline	7,25% (0,02)	7,29% (0,02)	0,26
Mean HbA1c at 1 year	6,61% (0,02)	7,15% (0,02)	P<0,001
Difference (1 year)	-0,64% (0,02)	-0,14 % (0,02)	P<0,001
HbA1c <7,0% (%) Baseline	46,3 (1,0)	45,4 (1,0)	0,50
HbA1c <7,0% (%) Year 1	72,7 (0,9)	50,8 (1,0)	<0,001
Difference (1 year)	26,4% (1,0)	5,4% (1,0)	<0,001
Metabolic syndrome			
Metabolic syndrome (%) baseline	93,6 (.05)	94,4 (0,5)	0,23
MetS Year 1	78,9 (0,8=	87,3 (0,7)	<0,001
Change (1 year)	-14,7 (0,8)	−7,1 (0,7)	<0,001
Use of Diabetes medicines (%)			
Baseline	86,5% (0,7)	86,5% (0,7),	p= 0,93
Year 1	78,6% (0,8)	88,7% (0,6)	p=<0,001
Change (1 Year)	-7,8 (0,6)	2,2 (0,5)	p<0,001
Use of antihypertensive medicines (%)			
Baseline	75,3% (0,9)	73,7% (0,9)	p=0,23
Year 1	75,2% (0,9)	75,9% (0,9)	p=0,54
Change (1 year)	-0,1 (0,6)	2,2 (0,6)	p=0,02
Use of lipid lowering medicines (%)			

Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: One-year results of the look AHEAD trial. Diabetes Care 2007; 30(6):1374–83. http://www.ncbi.nlm.nih.gov/pubmed/17363746. #20826

Baseline	49,4% (1,0)	48,4% (1,0)	p=0,52
Year 1	53,0% (1,0)	57,8% (1,0)	p<0,001
Change (1 Year)	3,7 (0,8)	9,4 (0,8)	p<0,001

Daten nach 4 Jahren: aus Wing RR, et al 2010 (Handsuche)
Mean changes and difference between groups averaged over 4 years

Measure	Mean Change ILI	Mean Chaneg DSE	Mean Difference ILI -DSE	pvalue
Weight (%initial weight)	−6.15 (−6.39, −5.91)	−0.88 (−1.12, −0.64)	−5.27	<0,0001
HbA1c (averaged effects unadjusted for medication use.	−0.36 (−0.40, −0.33)	−0.09 (−0.13, −0.06)	−0.27	<0,0001

Proportion of DSE and and ILI participants who initiate or terminate medication for diabetes

	Among those not using at baseline			Among those using at baseline		
	DSE	ILI	P value	DSE	ILI	P value
Diabetes medication						
Baseline	N=348	N=354		N=2208	N=2202	
Year 1	33%	10%	<0,0001	97%	89%	<0,0001
Year 2	46%	17%	<0,0001	96%	88%	<0,0001
Year 3	59%	27%	<0,0001	95%	89%	<0,0001
Year 4	67%	42%	<0,0001	96%	91%	<0,0001
Insulin						
Baseline	N=2167	N=2190		N=408	N=380	
Year 1	4%	2%	<0,0001	92%	81%	<0,0001
Year 2	7%	3%	<0,0001	86%	76%	<0,0001
Year 3	9%	4%	<0,0001	86%	78%	<0,0001
Year 4	12%	7%	<0,0001	88%	77%	<0,0001

End of trial: Primary and secondary outcomes

	N	DSE N, events/100pyears	ILI n, evnets/100 pyears	HR, 95% CI, p-value
Primary: MI, stroke, hospitalized angina and CVD death	821	418 (1,92/100person years)	403 (1,83/100person years)	0,95 (0,83; 1,09), p=0,505
Secondary 1: MI, Stroke and CVD Death	550	283, 1,25	267, 1,17	0,93 (0,79; 1,10), p=0,417
Secondary 2: primary + total mortality	1025	529, 2,43	496, 2,25	0,93 (0,82; 1,05), p=0,229
Other outcomes: death	376	202, 0,86	174, 0,73	0,85 (0,69; 1,04), p=1,112

End of trial

	DSE	ILI
Mean weight loss from baseline	3,5%	6,0%

Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: One-year results of the look AHEAD trial. Diabetes Care 2007; 30(6):1374–83. http://www.ncbi.nlm.nih.gov/pubmed/17363746. #20826

Anmerkungen:
- liquid meal replacement, provided free of charge,
- annually a $100 honorarium was provided
- Adhärenz zur Diät nicht bewertet und berichtet (dietary records)
- Weitere: Participants completed maximal graded exercise tests to assess fitness prior to randomization. (Voraussetzungen für Patient*innen realistisch oder relevante Vorauswahl?)

Qualitätsbewertung der Studie (aus Martenstyn 2020): moderate to high quality evidence (2010 CONSORT checklist)

Risk of bias assessment (ÄZQ): Selektion: Randomization: low (unclear), Allocation concealment: unclear, Performance: high, Detection: low (unclear), Attrition: unclear, Reporting: unclear, Other biases: siehe oben
Sponsor: None of the corporate sponsors had any role in the trial design, data analysis, or reporting of results

Wolf 2004 (Improving Control with Activity and Nutrition (ICAN))

Wolf an colleagues 2004 (Wolf AM, Conaway MR, Crowther JQ, et al. Translating lifestyle intervention to practice in obese patients with type 2 diabetes. Diabetes Care. 2004;27(7):1570-1576.), #31764

Studiencharakteristika: 12-month randomized controlled trial, n=147 health plan members

Objective	compare efficacy of lifestyle case management to usual care given in the primary care setting, as measured by clinical, healthrelated quality of life (HRQOL), and economic outcomes (Improving Control with Activity and Nutrition (ICAN))
Population	obese patients with T2DM (BMI ≥27 kg/m^2) Setting: US
Intervention	lifestyle case management: individual and group education, support, and referral by registered dietitians - Individual sessions six times throughout the year (total 4h) - six 1-h small-group sessions. - Brief monthly phone contacts provided support.
Control	usual care: rechieved educational material and were free to join other weight management or diabetes care programs.
Einschlusskriterien	T2-DM, use of diabetes medications, BMI ≥27 kg/m^2, age ≥20 years, membership in the Southern Health Services (SHS) health plan
Primary outcome	Weight and waist circumference, Secondary: included HbA1c, lipid levels, use of prescription medications, and HRQOL (Medical Outcomes Study Short Form-36 [SF-36])
Statistic:	randomized (total 147): CM=74, UC=73, n=3 withdrew before baseline assessment ITT: CM=73, UC=71, withdrawn (n=29 (20%)): CM 19/73, UC 10/71 Gründe für Studienabbruch nur für beide Gruppen zusammen berichtet. 118 individuals (80%) completed 12-month intervention
Baseline	HbA1c 7,7% (SD 1,6), weight ca. 106,9kg ±≈25kg, BMI ca.

Baseline/Ergebnisse

	Case management group (CM), n=73	**usual care group (UC), n=71**	
Baselinecharacteristics (SD or 95%CI)			
Age (years)	53.3 ± 8.6	53.4 ± 8.0	

Wolf an colleagues 2004 (Wolf AM, Conaway MR, Crowther JQ, et al. Translating lifestyle intervention to practice in obese patients with type 2 diabetes. Diabetes Care. 2004;27(7):1570-1576.), #31764			
Weight (kg)	107.1 ± 25.5	106.7 ± 24.3	
BMI (kg/m^2)	37.6 ± 7.7	37.5 ± 6.4	
Weight and HbA1c			
Weight change (average at 12months)	-2.4 kg (4.1 to 0.6kg),	+ 0.6 kg (1.0 to 2.2kg)	net group difference: 3.0 kg (5.4 to 0.6kg)
Weight loss up to 5% of initial weight	53%	32%	
Weight loss ≥5% of initial weight	20%	14%	
HbA1c* difference between groups at 4 months			-0.57% (95% CI 1.0 to 0.2) P=0.008
HbA1c* difference between groups at 12 months			-0,2% (95% CI 0.7 to 0.3) P=0.45
Subsequent analyses were adjusted for additional baseline characteristics. For HbA1c, models were adjusted for age, sex, duration of diabetes, and change in diabetes medications.			
Medication “Total” included various doses of the same medication (assessed changes in dose). “Unique” counted individual medications once (changes in type).			
	CM group, n=73	**UC group, n=71**	
Number of prescription medications/day Baseline	6,3 ±2,9	5,8 ±2,6	
Number of diabetes medications/day Baseline	1,8 ±0,92	1,8 ±0,85	
At 6 months	**CM group, n=58**	**UC group, n=65**	
Individuals **decreasing** total medications	45%	28%	
Individuals **increasing** total medications	19%	35%	P=0,03
12 months	**CM group, n=54**	**UC group, n=64**	
Individuals **decreasing** total medications	57%	39%	
Individuals **increasing** total medications	17%	32%	P=0,13
Difference in medications/day after 12m (CM vs. UC): difference between groups (Absolute Zahlen aus Figure 2B nicht extrahierbar).			-0.8 (95% CI 0.05–1.1), p=0,03
CM group reduced diabetes medications 0.46 medications/day more than those in the UC group (P 0.001), 12 months.			
Health related quality of life	Change in SF-36 scores in CM group was significantly different from UC in 7/9 domains. Domains with greatest improvement in CM group were emotional role (15.1, 3.4–26.8) and physical role (10, 1.2–24.7). (ÄZQ: nur Abbildung, absolute Zahlen können nur geschätzt werden).		
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear Performance bias: high, Detection: high oder unclear, Attrition: high, Reporting: unclear, Other biases: Vorauswahl bei Recrutierung? Sponsor: Any opinions, results, or conclusions set forth in this article are those of the authors and do not necessarily reflect the policies or opinions of SHS or any subsidiaries or affiliate companies			

Li 2005 (Meal replacement)

Li and colleagues, 2005 (Li Z, Hong K, Saltsman P, DeShields S, et al. Long-term efficacy of soy-based meal replacement vs an individualized diet plan in obese type II DM patients: Relative effects on weight loss, metabolic parameters, and C-reactive protein. Eur J Clin Nutr. 2005;59(3): 411-418.), #31765	
Studiencharakteristika: 104 subjects, 52-week 2-arm randomized clinical trial	
Objective	effects of soy-based meal replacement (MR) plan vs an individualized diet plan (IDP); as recommended by the American Diabetes Association) on weight loss and metabolic profile.
Population:	≥30 years, patients with T2-DM treated with oral hypoglycaemic agents, 27–40 kg/m^2, HbA1c 7–12%
Intervention in both groups:	- individual consultation with dietitian at baseline, weeks 2, 4, 6, 8, then monthly for the duration of 1-y study. - Individualized caloric target to achieve a daily caloric deficit of 500 calories per day
Intervention:	- first 5 days, subjects replaced 3 meals/day per day with a soy MR (Slim Fast Food Company), instruction to add fruits and vegetables - next 3 months: replace 2 meals/d, 1 sensible meal, fruits, vegetables - rest of study: replace 1 meal/d, 1-2 sensible meals
Control:	macronutrient recommendations of the American Diabetes Association (ADA): consumption of ≤ 30% calories from fat, 10–20% from protein, 55–65% from carbohydrates (Clinical Practice Recommendation, 1997).
Primary outcome:	difference from baseline in body weight (nach power-calculation zu urteilen)
Einschlusskriterien	≥30years, NIDDM with oral hypoglycaemic agents, BMI of 27–40 kg/m2, HbA1c of 7–12%
Attrition	77/104 subjects completed study, 26% dropout rate over study 104 randomized, - 11 dropped out during screening and baseline visits ((MR 3, IDP 8) Most of the subjects who dropped out at this time did so because they were not randomized into the MR group, or they realized the time commitment of the study was not manageable. - 11 lost within first 6 months (MR 3, IDP 8) These 22 were xcluded from analysis, ITT on al 104 subjects: same statistical results - Second 6 months: 5 droppouts (MR4, IPD 19
Adjustment medication	Adjustments in medication levels and use were made by research physicians and subjects' primary care physicians.
Statistic:	Intention to treat (including participants returning for initial follow-up)

Baseline:

	MR (n=46)	IDP (n=36)	
Age mean ±se	54,4 ±9,3	56,6 ± 10,4	
Baseline BMI (kg/m2)	32.8 ± 3.7	33.7 ± 3.6	P=0.279
Baseline HbA1c (%)	7,6 ± 1,4	7,5 ± 1,7	P=0,774

Ergebnisse

	Meal replacement (MR)		**individualized diet plan (IDP)**		
Weight					
Changes in weight (kg)		p-value comparison to baseline		p-value comparison to baseline	p-value comparison between groups
1 month	-2,88 ± 0,32	<0,0001	-1,42 ± 0,32	<0,0001	0,0002
3 month	-5,58 ± 0,46	<0,0001	- 2,89 ± 0,56	<0,0001	<0,0002

Li and colleagues, 2005 (Li Z, Hong K, Saltsman P, DeShields S, et al. Long-term efficacy of soy-based meal replacement vs an individualized diet plan in obese type II DM patients: Relative effects on weight loss, metabolic parameters, and C-reactive protein. Eur J Clin Nutr. 2005;59(3): 411-418.), #31765					
12 month	-4,35 ±0,81	<0,0001	-2,36 ± 0,76	0,0038	0,0670
Percentage of weight loss (end of 12 months)	4.57 ± 0.81%		2.25 ± 0.72%		P<0,05
HbA1c					
HbA1c (%)		p-value comparison to baseline		p-value comparison to baseline	p-value comparison between groups
6 months	-0,95	<0,0001	-0,44	0,08	0,110
12 months	-0,3	0,291	-0,15	0,563	0,594
Medication					
- All study subjects ≥1 oral hypoglycaemic agent at study entry, medication profiles campatible between groups - At 12 months: MR group: significant number of subjects hat reduction in Sulfonylurea (p<0,0002) and metformin (p<0,05) use - Nur Darstellung in Figure 2 ohne Angabe absoluter oder prozentualer Zahlen (Sulfonylharnstoffe: MR Med. decrease ca. 35% (?), no increase, IDP: ca. 12,5% increase, decrease ca. 20% (???); Metformin: MR 5.					
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear Performance bias: high, Detection: high oder unclear, Attrition: low (unclear), Reporting: unclear, Other biases: einige Zahlen nicht in absoluten Werten angegeben (Medikation), Erhebung nicht ausführlich beschrieben, Meal replacement wurde Probanden umsonst zur Verfügung gestellt. Sponsor: Meal replacements provided by SlimFast Foods Co. Inc. (West Palm Beach, FL). All serology studies processed by Quest Diagnostics (Van Nuys, CA). Keine weiteren Angaben zum Einfluss des Sponsors.					

Shirai 2013 (formula diets)

Shirai K, Saiki A, Oikawa S, et al. The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients-multicenter trial. Obes Res Clin Pract 2013; 7(1):e43-54. DOI: 10.1016/j.orcp.2012.03.002. http://www.ncbi.nlm.nih.gov/pubmed/24331681. Laufnummer: 31808	
Studiencharakteristika: multi-center, randomized controlled trial, intervention: 24 weeks, n=240	
Objective	Clarify usefulness of a 24-week dietary regimen using formula diet once a day in combination with conventional low-caloric diet in obese patients with type 2 diabetes mellitus.
Population	Obese patients [BMI >25 kg/m2] with diabetic mellitus (HbA1c ≥6,0%)
Interventionen in beiden Gruppen	Visits every 4 weeks (guidance on lifestyle improvement conducted by dieticians and/or nurses)
Intervention	FD-Group: low-caloric diet with partial use of formula diet - 1 pack formula diet (MicroDiet®, 240 kcal/pack) in place of one of three daily low-caloric meals for 24 weeks. - protein:fat:carbohydrate ratio prescribed 18:30:52 in FD. - Total daily calorie same in both groups (20 kcal/kg times standard body weight (kg)
Vergleich	CD group: conventional low-caloric diet group - protein: fat:carbohydrate ratio prescribed 15:25:60
Medical change	- Dose of insulin -50% just before taking formula diet. - Sulfonylurea stopped just before taking formula diet. - Thiazolidinedione changed depending on the levels of blood glucose and HbA1c. - Sulfonylurea discontinued or dose decreased if fasting plasma glucose (FPG) < 90 mg/dl (12 in FD and 6 in CD).
Attrition	11 participants withdrew from study before completion (10 CD an 1 FD), reason for drop-out was mainly inconvenience of the patients.

Shirai K, Saiki A, Oikawa S, et al. The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients-multicenter trial. Obes Res Clin Pract 2013; 7(1):e43-54. DOI: 10.1016/j.orcp.2012.03.002. http://www.ncbi.nlm.nih.gov/pubmed/24331681. Laufnummer: 31808

Ergebnisse

	Conventional diet, n=110	**Formula diet, n=119**	p-Value
Baseline weight	77.9 ± 14.9	79.9 ± 17.8	0,793
Change of weight 24 weeks	−1.4±3.4, p compared with baseline <0,005	−3.5 ± 4.0, p compared with baseline <0,005	<0,001
BMI (kg/m2)	30.0 ± 4.6	30.8 ± 5.8	0,514
Change of BMI 24 weeks	−0.6 ± 1.3, p compared with baseline <0,005	−1.4 ± 1.5 p compared with baseline <0,005	<0,001
HbA1c (%) baseline	7.7 ± 1.3	7.7 ± 1.4	0,994
HbA1c change 24 weeks	−0.2 ± 0.8, p compared with baseline <0,005	−0.6± 1.1, p compared with baseline <0,005	0,002

changes of administered drugs after intervention of diets.

	Conventional diet group (*n* = 110)			**Formula diet group (*n* = 119)**		
	Admistered case	Reduced case	Discontinued case	Admistered case	Reduced case	Discontinued case
Insulin	19	9	0	20	17	0
Sulfonylureas	51	3	3	57	11, p<0,05	20, p<0,02
Thiazolizine	24	0	4	27	0	12, p<0,02
Biganides	31	0	0	33	4	4
Glinides	9	0	0	9	0	4
Alpha-Glucosidase inhibitors	15	0	0	13	0	0

Dietary adherence (Comparison of dietary compositions between conventional diet group and formula diet group at 16 weeks.)

composition	Conventinoal group at 16 weeks, n=22	Formula diet group at 16 w, n=22	p-values
Total energy (kcal)	1574±299	1386±210	0,037
Protein (g)	62.3±14 (15.8±4.1%)	73.4±8.6 (21±3.2%)	0.019
Fat (g)	53.1±8.3 (32.9±4.1%)	48.5±12.9 (31±6.4%)	0,132
Carbohydrate (g)	212±46.7 (54±12%)	164±26.8 (47±8.2%)	0,032

Mean protein:fat:carbohydrate ratio (PFC ratio):
FD:21±3.2 : 31±6.4 : 47±8.2
CD:16±4.1 : 33±4.1 : 54±12

Anmerkungen
- Studie aus Japan: Übertragbarkeit auf Deutschland
- HbA1c-Grenzwert für Diagnose des Diabetes in der Studie ≥6,0%) (Setting Japan)
- Analysis of dietary composition during the period of intervention was done using the food records at one point in one institute.
- MicroDiet® was provided by Sunny Health Co. Ltd (Tokyo, Japan), free of charge (?)
- Study duration too short to see long term results

Shirai K, Saiki A, Oikawa S, et al. The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients-multicenter trial. Obes Res Clin Pract 2013; 7(1):e43-54. DOI: 10.1016/j.orcp.2012.03.002. http://www.ncbi.nlm.nih.gov/pubmed/24331681. Laufnummer: 31808

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: high, Detection: unclear oder high, Attrition: high (Ungleichgewicht zwischen den Gruppen), Reporting: unclear, Other biases: siehe bei Anmerkungen
Sponsor: The funding source had no role in the design, conduction of reporting of the study or in the decision to submit the manuscript for publication.

Davis 2009 (Low carbohydrate versus low fat)

Davis and colleagues, 2009 (Davis NJ, Tomuta N, Schechter C, et al. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. Diabetes Care. 2009;32(7):1147-1152.) [19], #31766

Studiencharakteristika: nonblinded, two-arm randomized clinical trial (N=105), Intervention: 1 year

Objective	effects of a 1-year intervention with low-carbohydrate and low-fat diet on weight loss and glycemic control in patients with T2DM
Population	>18 years, diagnosis of T2DM for at least 6 months, BMI ≥25kg/m^2, HbA1c between 6 and 11%
Ablauf der Studie (all participants)	**Prerandomization** (3- to 4-weeks): participants received instructions, were asked to complete dietary and blood glucose self-monitoring activities. **At randomization**, 45 min individual dietary instruction by dietitian and specific gram allowance of carbohydrates or fat to achieve 1-pound weight loss each week. Structured menus for the first 2 weeks. During 12-month study: total of 6 scheduled, 30-min visits with dietitian (1st month individual visit once or twice weekly, after 1st month every six weeks)
Intervention	**low-carbohydrate diet:** modeled after the Atkins diet, initiated with a 2-week phase of carbohydrate restriction of 20–25 g daily depending on baseline weight. As participants lost weight, able to increase carbohydrate intake at 5-g increments each week. - general recommendations to achieve 150 min of physical activity each week, but PA was not an emphasis of the study.
Vergleich	Low fat diet: fat gram goal, which was 25% of energy needs, based on baseline weight. - general recommendations to achieve 150 min of physical activity each week, but PA was not an emphasis of the study.
Primäre Endpunkte	Weight and HbA1c
Statistics	ITT-Analyse, 154 entered prerandomization, 49 discontinued during prerandomization, 105 patients randomized: low carbohydrate (n=55) versus low-fat (n=50) diet,
Baseline-Daten	
Medication change	- prerandomization: adjusted diabetes medication to minimize side effects - randomization: low carbohydrate-arm: insulin dose -50%, sulfonylurea discontinued low fat-arm: indulin dose -25%, sulfonylurea dose -50% Subsequently, the algorithm for medication adjustment was the same in both groups. Metformin war not adjusted during study.
Attrition	Data collection (weight and A1C): 91% of participants at 3 months (*n*=95), 80% at 6 months (*n*=84), and 81% at 12 months (*n* = 85). No difference in attrition between dietary arms.

	Low carbohydrate n=55	**Low-fat N=50**	
Baseline Age mean ±sd	**54** ±6 years	**53** ±7 years	
Baseline weight mean ±sd	**93,6** ±18 kg	**101** ±19 kg	
Baselline HbA1c mean ±sd	**7,5** ±1,5 %	**7,4** ±1,4 %	
Ergebnisse			

Davis and colleagues, 2009 (Davis NJ, Tomuta N, Schechter C, et al. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. Diabetes Care. 2009;32(7):1147-1152.) [19], #31766			
Mean HbA1c change (SD)	3 month: -0,64 (±1,4) 6 month: -0,29 (±0,92) 12month: -0,02 (±0,89)	3 month: -0,26 (±1,1) 6 month: -0,15 (±1,1) 12 month: 0,24 (±1,4	P=0,71
Mean Weight change (SD)	3 month: -5,2 (±2,8) 6 month: -4,8 (±3,5) 12month: -3,1 (±4,8)	3 month: -3,2 (±3,7) 6 month: -4,4 (±5,3) 12month: -3,1 (±5,8)	P=0,005 *P* values for diet difference over all time points
Baseline Medications			
Metformin	43 (78%),	43 (86%)	
Sulfonylurea	29 (44%)	26 (52%)	
Insulin	19 (35%)	12 (24%)	
Cholesterol lowering medication	34 (62%),	28 (56%).	
Change in Diabetes Medication			
Participants using insulin at 12 months (mean reduction ±SD)	Decrease of 10 ±14 units	Increase of 4 ±19 units	(P = 0.12)
Participants using Sulfonylurea (change in sulfonylurea dose at 12 months)	Reduction 1.6 ±3,5 mg	Reduction 1.6 ±3,5 mg	
Participants using Sulfonylurea	26% had reduction in dose at 12 months		
Dieatry adherence			
Baseline	≈43% of calories from carbohydrates, 36% from fat, 23% from proteins.		
3 months	24% calories from carbohydrate (equivalent to 77±44 g of carbohydrates daily), 49% from fat.	53% calories from carbohydrate (equivalent to 199 ± 69 g of carbohydrates) 25% from fat.	
12 months (Table 3) (% total energy: %E)	Carbohydrate (%E): 33,4 ±13,2 Fat (%E): 43,9 ±10,8	Carbohydrate (% total energy): 50,1 ±10,0 Fat (% total energy) 30,8 ±10,2	
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: high, Detection: unclear / high, Attrition: low, Reporting: unclear, Other biases: Baseline differences (differences wee adjusted for in the statistical model). Sponsor: The funding sources did not have any role in the design, implementation, or analysis of the study. The funding sources did not review the manuscript before publication.			
RoB-Bewertung: Goldenberg 2021**:** high risk/some concerns, Ross 2021: selection bias unclear, ansonsten low, Korsmo-Haugen 2019: unclear risk of bias.			

Samaha 2003 (low carbohydrate versus low fat)

Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003; 348(21):2074–81. DOI: 10.1056/NEJMoa022637. http://www.ncbi.nlm.nih.gov/pubmed/12761364. Laufnummer: 31790	
Studiencharakteristika: n=132, 6 months	
Objective	test the hypothesis that severely obese subjects with a high prevalence of diabetes or the metabolic syndrome would have a greater weight loss, without detrimental effects on risk factors for atherosclerosis, while on a carbohydrate-restricted (low-carbohydrate) diet than on a calorie- and fat-restricted (low-fat) diet.

Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003; 348(21):2074–81. DOI: 10.1056/NEJMoa022637. http://www.ncbi.nlm.nih.gov/pubmed/12761364. Laufnummer: 31790	
Population	≥18y, BMI, ≥35kg/m2
Studienablauf	2h-teaching session each week for 4 weeks, followed by monthly 1-h sessions for 5 additional months - diet overview handout, additional material - no specific exercise programm was recomended
Intervention	carbohydrate-restricted (low-carbohydrate) diet: ≤30g/d
Vergleich	calorie- and fat-restricted (low-fat) diet: -500calories/d, ≤30% derived from fat
Primary endpoint	Weight loss at 6 months
Statistic	- last observation carried forward
Attrition	Primary analysis n=132 (68LF, 64 LC), - 79 completed 6-month study (36 LF, 43 LC), - 29 dropped out but had six-month data available (routine office visits), - 24 subjects: weight recorded at the last follow-up visit was carried forward Second analysis: last follow-up visit carried forward for all 53 subjects who dropped out Differences in attrition between groups: 3 month (P=0.03), not significant at six months (P=0.10).
Baseline	Diabetes (39%), metabolic syndrome (43%)

Berichtete Ergebnisse für Subgruppe: Change from baseline at 6 months

	Baseline	p-value between group	6 months	Absolute change	p-value between group
HbA1c in diabetic subjects (%)	LF diet 7,4 ±1,5 LC diet: 7,8±1,2	0,42	LF diet 7,4 ±1,8 LC diet: 7,2±1,7	0,0 ±1,0 -0,6 ±1,2	0,06

analysis includes all 1subjects, with base-line values carried forward for subjects who had dropped out 95ft he study by six months (LC-diet n=26 T2DM, LF-diet n=26 T2DM, siehe Table 1)

Change in medication by 6 months:
- LC-diet: 7 subjects had dose reductions in oral hypoglycemic agents or insulin.
- LF diet: 1 subject had a dose reduction in insulin and one subject began oral therapy

Für Informationen zu Baselinedaten „treatment for diabetes“ siehe table 1.

Keine Subgruppenauswertung für Menschen mit Diabetes in Bezug auf Gewichtsreduktion. Baselinedaten werden nicht für die Gruppe der Menschen mit Diabetes angegeben (Alter, BMI, Diabetes duration)

Risk of bias Bewertung (aus Korsmo-Haugen 2019): high risk of bias.

Guldbrand 2012 (Low fat versus low carbohydrate)

Guldbrand and colleagues, 2012 (Guldbrand H, Dizdar B, Bunjaku B, et al. In type 2 diabetes, randomization to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing similar weight loss. Diabetologia. 2012;55(8): 2118-2127.), #31769	

Andere Publikation zur gleichen Studie (aus Review #31702)
Jonasson L, Guldbrand H, Lundberg AK, et al. Advice to follow a low-carbohydrate diet has a favourable impact on low-grade inflammation in type 2 diabetes compared with advice to follow a low-fat diet. Ann Med 2014; 46(3):182–7. DOI: 10.3109/07853890.2014.894286. http://www.ncbi.nlm.nih.gov/pubmed/24779961.
Laufnummer: 31783
- Betrachteter Endpunkt: effects of diets on inflammation

Study charcteristics: prospective randomised parallel non-blinded trial, n= 61, 2 primary healthcare centers Sweden, intervention 2 years

Objective	compare effects of a 2 year intervention with a low-fat diet (LFD) or a low carbohydrate diet (LCD)
Population	Adults with T2DM treated with diet with or without additional oral glucose-lowering medication, incretin-based therapy or insulin. - no weight or age exclusion criteria

Guldbrand and colleagues, 2012 (Guldbrand H, Dizdar B, Bunjaku B, et al. In type 2 diabetes, randomization to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing similar weight loss. Diabetologia. 2012;55(8): 2118-2127.), #31769	
Intervention	Low fat diet (LFD): 55–60 energy per cent (%E) from carbohydrate, 30 %E fat (<10 %E saturated fat), 10-15%E protein - energy content 1,600 kcal/day women, 1,800 kcal/day men - 4 group meetings to achieve compliance, at baseline, 2, 6 and 12 months - No information was given to change the level of physical activity.
Vergleich	Low carbohydrate diet (LCD) 20 %E from carbohydrate, 50 %E fat, 30 %E protein - energy content 1,600 kcal/day women, 1,800 kcal/day men - 4 group meetings to achieve compliance, at baseline, 2, 6 and 12 months - No information was given to change the level of physical activity.
Primary outcomes	Weight and HbA1c.
Adjustment of medication	physician responsible for each patient at the primary healthcare centre was allowed to adjust hypolipidaemic and antihypertensive medications consecutively in the trial. - Patients were recommended to check plasma glucose to allow proper adjustment
Baseline	BMI 32.7±5.4 kg/m2, HbA1c 57.0±9.2 mmol/mol
Attrition	61 patients randomized 3 in LFD group, 4 in the LCD group had severe difficulty following prescribed diets and were not willing to participate in group meetings (nicht ausgeschlossen). ITT-Analysis No patients were lost to follow-up. Lack of data on food registration at 24months: LFD n=4, LCD: n=10

Ergebnisse

	Low fat diet (LFD), n=31	**Low carbohydrate diet (LCD), n=30**	p-value (for change compared with baseline)
Weight baseline (kg)	98,8 ± 21	91,4 ±19	P=0,15 between groups at baseline
Weight 12 months	94,9 ±21	89,5 ±19	P=<0,001 (for each group)
Weight 24 months	95,9 ±21	89,4 ±22	P=0,002 (LFD) P=0,020 (LCD)
Weight loss at 6 months	−3.99±4.1 kg (n=31)	−4.31±3.6 kg (n=30)	P=0,75: difference in change between groups p<0,001 within groups
Weight loss at 12 months	−2.97±4.9 kg	−2.34±5.1 kg	
Weight loss at 24 months	−2.97±4.9 kg	−2.34±5.1 kg	Compared with baseline P=0,002 LFD P=0,02 within groups
HbA1c			
HbA1c Baseline (%)	7,2 ±2,9	7,5 ±3,1	P=0,23 (between groups)
HbA1c at 6 months (%)	7,2 ±3,0, p=0,56 (change from baseline)	7,1 ±3,1, p=0,004 (change from baseline)	
HbA1c at 12 months (%)	7,3 ±3,2, p=0,66	7,3 ±3,3, p=0,12	
HbA1c at 24 months (%)	7,4 ±3,1, p=0,29	7,5 ±3,1, p=0,98	
P value for change over all time points between groups 0,76			

Medication	**LFD (n=31)**	**LCD (n=30)**	
Medication at baseline - Diet only - oral glucose-lowering medication only - combination of insulin and oral medication	 2 patients 13 patients 11 patients	 2 patients 15 patients 10 patients	

Guldbrand and colleagues, 2012 (Guldbrand H, Dizdar B, Bunjaku B, et al. In type 2 diabetes, randomization to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing similar weight loss. Diabetologia. 2012;55(8): 2118-2127.), #31769			
Insulin dose Baseline	39±51 E	42±65 E,	p=0,86 (between groups)
Insulin Dose 6 months	38±48 E, p=0,12 (for change compared with baseline)	30±47 E, p=0,02 (for change compared with baseline)	P=0,046 for between grou change
Insulin dose 12 months	38±48 E, p=0,29	33 ±54, p=0,041	
Insulin dose 24 months	36 ±44, p=0,5	35 ±56, p=0,14	
P-value for change over all time points: LFD 0,81, LCD 0,007 P value for change over all time points between groups 0,83			
Metformin baseline (mg)	1,435 ±946	1,375 ±950	P=0,8 (between groups)
Metformin at 12 months	1,371±875, p=0,40 (for change compared with baseline)	1,358±915, p=0,86 (for change compared with baseline)	
Metformin at 24 months	1,306±901, p=0,28	1,292±911, p=0,38	
P value for change over all time points between groups 0,93			
Glibenclamid (mg) at baseline	0.4±1.9	1.1±2.6	P=0,26 (between groups)
Glibenclamid (mg) at 12 months	0.3±1.3, p=0,66 (for change compared with baseline)	0.5±2.0, p=0,24 (for change compared with baseline)	
Glibenclamid (mg) at 24 months	0.3±1.3, p=0,66	0.1±0.7, p=0,055	
P value for change over all time points between groups 0,56			

Adherence to diet	**LFD**	**LCD**	Baseline: n=61 12 months: n=42 24 months: n=47
Energy intake (kj)	0 months: 7569 ±2063, 12 months: 6619 ±2075, p=0,075 24 months: 6104 ±1891, p=0,002	0 months: 7071 ±1782 12 months: 6017 ±2075, p=0,037 24 months: 5234 ±1799, p<0,001	For change over all time points (between groups), p=0,065
Carbohydrate energy (%)	0 months: 48±6 12 months: 47 ±6, p=0,38 24 months: 47 ±7, p=0,31	0 months: 41 ±11 12 months: 27 ±8, p<0,001 24 months: 31 ±6, p<0,001	For change over all time points (between groups), p<0,001
Protein energy (%)	0 months: 19 ±3 12 months: 20 ±3, p=0,044 24 months:20 ±2, p=0,045	0 months: 19 ±3 12 months: 23 ±5, p=0,002 24 months: 24 ±4, p<0,001	For change over all time points (between groups), p=0,009
Fat energy (%)	0 months: 32 ±5 12 months: 31 ±6, p=0,96 24 months: 31 ±7, p=0,87	0 months:39 ±7 12 months: 47 ±6, p<0,001 24 months: 44 ±5, p<0,001	For change over all time points (between groups), p<0,001

Reductions in oral medication and insulin dose were made consecutively to avoid hypoglycaemia, and the reduction in insulin was statistically significant only in the low-carbohydrate group at 6 months (Table 1). This change in the average insulin dose was statistically significant between the two groups at 6 months (p=0.046).

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: high, Detection: high, Attrition: low, Reporting: unclear (laut Bericht in Naude et al Systematic review 2014: high risk: protocol available prespecified outcomes vague.); Other biases: Baseline differences (weight, BMI), Vorauswahl durch betreuende study nurse.
Sponsor: k.A: zum Einfluss des Sponsors.

RoB-Bewertung: Goldenberg 2021**:** low risk, Ross 2021: Reporting bias und performance bias high, sonst alle Kategorien low, Korsmo-Haugen 2019: unclear risk of bias.

Iqbal 2010 (low carbohydrate versus low fat)

Iqbal N, Vetter ML, Moore RH, et al. Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. A low-fat diet in obese, diabetic participants. Obesity (Silver Spring, Md.) 2010; 18(9):1733–8. DOI: 10.1038/oby.2009.460. http://www.ncbi.nlm.nih.gov/pubmed/20019677. Laufnummer: 31811	
Studiencharakteristika: 24-month randomized–controlled trial, n=144	
Intervention	low-carbohydrate diet of 30 g/day (without restrictions total fat or caloric intake)
Vergleich	low-fat diet (≤30% calories from fat and a deficit of 500 kcal/day).
Participants provided a self-reported medical history and a list of medications at each assessment visit; however, this information was not verified from the electronic medical record. As many participants were unable to provide adequate information about changes in their medications or new medical diagnoses, we were unable to account for these potential influences on study outcomes. - Medikation wird als Baselinedaten berichtet, aber nicht im Verlauf angegeben.	
Risk of Bias Bewertung (aus Goldenberg 2021): high risk/some concerns	

Esposito 2009 (Mediterranean diet)

Esposito and colleagues, 2009 (Esposito K, Maiorino MI, Ciotola M, et al. Effects of a Mediterraneanstyle diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: A randomized trial. Ann Intern Med. 2009;151(5):306-314.) [20], #31767	
Studycharacteristics: Single-center, randomized trial, n=215, 4 year intervention and follow-up, setting: italy	
Objective	compare effects of a low-carbohydrate Mediterranean-style or low-fat diet on need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes.
Population	Overweight (BMI >25kg/m^2), newly diagnosed T2DM who were never treated with antihyperglycemic drugs and had HbA1c levels < 11%.
Run-in period	2 weeks, required to successfully self-monitor diet and ohysical activity - dietary education, emphasized importance of eating a healthy diet and being physically active for both weight loss and improvement of glycemic control.
Intervention	Mediterranean-style diet (<50% of daily calories from carbohydrates) - diet rich in vegetables and whole grains, low in red meat, which was replaced with poultry and fish. Energy intake restricted (1500 kcal/d women, 1800 kcal/d men), - no less than 30% calories from fat (main source of added fat 30 to 50 g of olive oil). - Dietary advice: monthly sessions in the first year and bimonthly sessions thereafter. - Advice on Physical activity: gradual progression toward a goal of 175 minutes of moderate-intensity physical activity per week.
Vergleich	low-fat diet (<30% of daily calories from fat) - rich in whole grains and restricted additional fats, sweets, and high-fat snacks - energy intake restricted (1500 kcal/d women, 1800 kcal/d men), - no more than 10% of calories from saturated fat. - Dietary advice: monthly sessions in the first year and bimonthly sessions thereafter. - Advice onPhysical activity: gradual progression toward a goal of 175 minutes of moderate-intensity physical activity per week.
Endpunkte	Primary outcome: Start of antihyperglycemic drug therapy, defined by protocol as indicated for follow-up HbA1c level > 7% Secondary outcomes: changes in weight, glycemic control, and coronary risk factors.
Attrition	Equal numbers of patients withdrew from groups during trial - patient preference (3 MED diet participants, 4 low-fat diet participants), - loss to follow-up (6 MED diet participants, 5 low-fat diet participants) - other reasons (1 MED diet participant, 1 low-fat diet participant).
Statistics	ITT-Analyse; Results of the analysis omitting patients lost during follow-up did not differ from that including these patients' last available records; however, because few participants were lost during follow-up, we used a complete case analysis with respect to secondary end points.
Baseline (SD)	

	MD (*n* =108)	**Low fat (*n* = 107).**	

Esposito and colleagues, 2009 (Esposito K, Maiorino MI, Ciotola M, et al. Effects of a Mediterraneanstyle diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: A randomized trial. Ann Intern Med. 2009;151(5):306-314.) [20], #31767			
Age (years)	52,4 (11,2)	51,9 (10,7)	
Body weight (kg)	86,0 (10,4)	85,7 (9,9)	
HbA1c (%)	7,75 (0,9)	7,71 (0,9)	
Ergebnisse			
	MED Year 1: n=102 Yea 4:n=50	**Low-fat Diet Year 1: n=97, Year 4: n=29**	Difference 95% CI
Patients requiring treatment (%)			
Year 1	5,5%	9,4%	-3,9 (-7,8 to 1,2)
End of trial (4 Years)	44,0%	70,0%	-26,0 (-31; -20,1)
Hazard Ratio unadjusted			HR 0,63 (0,51; 0,86)
HR adjusted for weight change:			HR 0,70 (0,59; 0,9)
HR adjusted for using HbA1c >7% as outcome:			HR 0,64 (0,5; 0,82)
Glycemic control			
HbA1c level, (%)* Year 1 Year 4	 -1,2 (1,0) -0,9 (0,6)	 -0,6 (0,6) -0,5 (0,4)	Difference (95% CI) -0,6 (-0,9; -0,3) -0,4 (-0,9; -0,1)
Patients HbA1c ≤ 7% Year 1 Year 4	 72 % 37%	 53% 24%	Difference (95% CI) % points 19 (14; 23) 13 (8; 17)
Weight			
Weight (kg) Year 1 Year 4	 -6,2 (3,2) -3,8 (2,0)	 -4,2 (3,5) -3,2 (1,9)	 -2,0 (-3,0; -0,9) -0,6 (-1,6; 1,2)
*wahrscheinlich als Differenz zu Baseline. In Abbildung nicht angegeben.			

Adherence to diet and recommendations
- composition of diets consumed did not statistically significantly differ between groups at baseline.
- Daily energy intake decreased in both groups during the study without statistically significant between-group differences in any trial year
- percentage of carbohydrate intake decreased in MED group compared with low fat group, and the percentage of monounsaturated and polyunsaturated fatty acid intake increased. Between-group differences in these variables statistically significant throughout the trial.
- Physical activity time increased (from 45 min/wk [SD, 12] to 125 min/wk [SD, 41] MED diet group and from 43 min/wk [SD, 13] to 119 min/wk [SD, 48] low-fat diet group), no statistically significant between-group difference in the amount of increase.

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: low, Performance bias: high, Detection: unclear, Attrition: low, Reporting: unclear; Other biases: -
Sponsor: The funding source had no role in the design, conduct, and analysis of the study or in the decision to submit the article for publication.

Larsen 2011 (High protein versus high carbohydrate)

Larsen and colleagues, 2011 (Larsen RN, Mann NJ, Maclean E, Shaw JE. The effect of a high-protein, low-carbohydrate diets in the treatment of type 2 diabetes: A 12 month randomized controlled trial. Diabetologia. 2011;54(4): 731-740.), #31768			
Studiencharakteristika: 12 months, parallel design, single-centre, randomised controlled trial, n=108, Setting: Australia			
Objective	to determine whether high-protein diets are superior to high-carbohydrate diets for improving glycaemic control in individuals with type 2 diabetes.		
Population	Overweight/obese individuals (BMI 27–40 kg/m2) with T2DM (HbA1c 6.5–10%)		
Ablauf der Studie	- dietitian administered the dietspecific advice to each study participant. study consisted of two dietary periods: - 3 months energy restrictive period (~6,400 kJ/day or 30% energy restriction), - 9 months of energy balance. Visits every 3 months regular faceto-face dietary counselling appointments, written materials were supplied - Individual appointments (behavioural therapy): 4 visits during 3 months energy restrictive period (total 2,5h), 5 visits during 9 months of energy balance - Group meetings every 3 months (total 3,3h) Physical activity was encouraged as a strategy to increase energy expenditure		
Intervention	High-protein diet (HP): low-fat (30% total energy) diet high in protein (30% total energy), 40% energy intake from carbohydrate.		
Vergleich	High carbohydrate diet (HC): low-fat (30% total energy) diet high in carbohydrate (55% total energy), 15% energy intake from protein - (7% saturated fat, 10% polyunsaturated at, 13% monounsaturated fat)		
primary end-point	Change in HbA1c Secondary endpoints: unter anderem change in weight - (7% saturated fat, 10% polyunsaturated at, 13% monounsaturated fat)		
statistics	intention-to-treat model for all participants who received dietary advice. Follow-up visits were encouraged regardless of dietary adherence and last measurements were carried forward for study non-completers. This study used the single imputation method of last measurement carried forward for missing data for primary and secondary outcomes.		
Attrition	intention-to-treat model, 18.9% (10/53) of HP participants and 19.6% (9/46) of HC participants discontinued the diet, but returned for followup assessments lost to follow-up HP group 9.2% vs 4.2% HC - study followed up 94% of all participants who received dietary advice and relied on the last measurement carried forward for the small number of individuals who discontinued the study.		
Medication change	All medication changes were made independently of the study personnel by the treating physician		
Baseline			
	High protein (HP), n=53	High carbohydrate (HC), n=46	
Age	59,6 (57,5; 61,8)	58,8 (55,8; 61,7)	
Weight (kg)	94,6 (90,5; 98,8)	95,5 (91,5; 99,6)	
HbA1c (%)	7,89 (7,63; 8,15)	7,78 (7,50; 8,05)	
Diabetes duration (years)	8,7 (6,8; 10,5)	8,6 (6,6; 10,6)	
Diab. treatment n (%)			
none	5 (9%)	5 (11%)	
Insulin	10 (19%)	7 (15%9	
Tablets	38 (72%)	34 (74%)	
Ergebnisse			
	High protein (HP), n=53	**High carbohydrate (HC), n=46**	Difference between groups

Larsen and colleagues, 2011 (Larsen RN, Mann NJ, Maclean E, Shaw JE. The effect of a high-protein, low-carbohydrate diets in the treatment of type 2 diabetes: A 12 month randomized controlled trial. Diabetologia. 2011;54(4): 731-740.), #31768			
HbA1c (%) 3 months 12 months	 -0,52% -0,23%	 -0,49 -0,28	 -0,03 (-0,28; 0,23) 0,04 (-0,37; 0,46)
Weight (kg) 3 mopnths 12 months	 -2,79 -2,23	 -3,08 -2,17	 0,29 (-1,03; 1,61) -0,07 (-1,67; 1,54)
Change in diabetes medication (Weighted per cent change in diabetes medication)			
	High protein (HP), n=48	**High carbohydrate (HC), n=41**	Difference between groups
3 months 12 months	-8,71 -8,17	0,68 4,56	-9,38 (-17,85; -0,92) -12,72 (-28,18; 2,73)
trend for improved glycaemic control in HP, statistical adjustment for the change in medications did not modify the outcome for the change in HbA1c.			
Physical activity	This study also found no significant group difference in self-reported time spent in physical activity.		
Dietary adherence			
% of total energy= %E	**High protein (HP), n=30**	**High carbohydrate (HC), n=**	P (repeated measures incorporationg data from all time points) group and time interaction
Energy (kJ) 12 months	**6,664**	**6,628**	0,22
Carbohydrate (%E) 12months	41,8	48,2	<0,001
Protein %E 12 months	26,5	18,9	<0,001
Fat (%E) 12 months	30,7	32,0	0,47
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: low, Performance bias: high, Detection: low (unclear), Attrition: unclear, Reporting: low (laut Naude et al 2014: Prespecified and important outcomes addressed, protocol available); Other biases: Verzerrung durch recruitment? Sponsor: k.A. zum Einfluss des Sponsors.			

Krebs 2012 (high protein low fat versus high carbohydrate low fat)

Krebs JD, Elley CR, Parry-Strong A, et al. The Diabetes Excess Weight Loss (DEWL) Trial: A randomised controlled trial of high-protein versus high-carbohydrate diets over 2 years in type 2 diabetes. Diabetologia 2012; 55(4):905–14. DOI: 10.1007/s00125-012-2461-0. http://www.ncbi.nlm.nih.gov/pubmed/22286528. Laufnummer: 31800	
Studiencharakteristika: Multicentre parallel (1:1) design, blinded randomised controlled trial, n=419, 12 months intervention, 12 months follow-up, New Zealand, recruitment: mail-out invitations through primary and secondary care, communit and media advertisement.	
Objective	effectiveness of low-fat high-protein and low-fat high-carbohydrate dietary advice on weight loss, using group-based interventions, among overweight people with type 2 diabetes.
Population	T2DM aged 30–75 years, BMI >27 kg/m2
Studienablauf	- group sessions every 2 weeks for first 6 months, then every month for 6 months (18 sessions) - Weekly text or email reminders and motivational messages were also offered to participants to enhance adherence 101ft he diets. - reduce total energy intake by 2,000 kJ/day (approximately 500 kcal/day)
Intervention	low-fat high-protein (30% of energy as protein, 40% as carbohydrate, 30% as fat)
Vergleich	low-fat high carbohydrate (15% of energy as protein, 55%as carbohydrate, 30% as fat)

Krebs JD, Elley CR, Parry-Strong A, et al. The Diabetes Excess Weight Loss (DEWL) Trial: A randomised controlled trial of high-protein versus high-carbohydrate diets over 2 years in type 2 diabetes. Diabetologia 2012; 55(4):905–14. DOI: 10.1007/s00125-012-2461-0. http://www.ncbi.nlm.nih.gov/pubmed/22286528. Laufnummer: 31800

Primärer Endpunkt	change in weight and waist circumference assessed at baseline, 6 and 12 months. Secondary outcomes: body fatness, glycaemic control, lipid profile, blood pressure and renal function
Statistics	ITT
Baseline	mean±SD age 58±9.5 years, BMI 36.6±6.5 kg/m2 and HbA1c 8.1±1.2% (65 mmol/mol) Glycaemic control: Diet only (16,6%), oral agents only (56,7%), Insulin ±oral agents (26,7%)
Attrition	completed by 70%(294/419).

Ergebnisse

Outcome	Baseline		12 months		24 months		Difference in change over time	p-value
	HP, n=207	HC, n=212	HP, n=152	HC, n=158	HP, n=144	HC, n=150		
Weight (kg)	103.4±19.7	101.9±20.1	100.2±17.8	99.5±19.1	99.5±17.2	95.9±17.1	0.00 (−1.20, 1.21)	0,73
HbA1c (%)	8.1±1.2	8.0±1.2	8.0±1.3	7.8±1.3	8.2±1.5	8.1±1.4	0.00 (−0.18, 0.18)	
SF36 physical	44.8±9.6	44.7±9.1	46.1±9.0	45.5±9.4	43.9±9.9	45.8±9.3	−0.20 (−1.44, 1.04)	0,59
SF36 mental	52.0±10.0	52.4±9.3	53.4±9.2	52.3±9.2	52.7±9.2	52.1±11.0	1.67 (0.25, 3.09)	0,65
Dietary intake								
Energy	7,860.2±2 3,35.3	7,850.2± 2,298.1	7,258.0± 2,098.0	6,784.4± 1,792.0	7,170.1± 1,973.6	7,093.2± 1,851.2	508.2 (110.3, 906.1)	0,012
Protein (% TE)	19.1±3.6	19.2±4.0	21.2±4.5	20.6±4.4	20.6±3.9	20.3±4.4	1.1 (0.5, 1.8)	0,001
CHO (% TE)	47.1±7.6	46.0±7.9	44.7±8.2	48.1±7.4	45.5±6.9	48.1±6.6	−3.7 (−5, −2.4)	<0.001
Fat (% TE)	32.0±6.6	33.0±6.9	32.4±7.3	30.1±6.0	32.8±6.3	30.4±6.8	2.3 (1.2, 3.4)	<0.001

Anmerkungen:
- high dropout rate (Study not powered)
- failure of individuals to achieve and maintain target diet macronutrient compositions
- Self-reported food diaries
- Diabetes medication nur als Baseline-Daten genannt. HbA1c-Outcomes: Differences are estimated controlling for changes in glucose-lowering medication over time (change in glucose medication aber nicht angegeben)

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: low, Performance bias: high, Detection: low (unclear), Attrition: high (unclear), Reporting: unclear; Other biases: siehe Anmerkungen oben
Sponsor: k.A. zum Einfluss des Sponsors.

Risk of Bias-Bewertung: Korsmo-Haugen 2019: low risk of bias.

Wing 1991 (very low calorie diet)

Wing RR, Marcus MD, Salata R, et al. Effects of a very-low-calorie diet on long-term glycemic control in obese type 2 diabetic subjects. Arch Intern Med 1991; 151(7):1334–40. http://www.ncbi.nlm.nih.gov/pubmed/2064484. Laufnummer: 31831

Studiencharakteristika: n=36, 20-week program, 1-year follow-up

Population	35-70 years, 30% above ideal body weight, T2DM
Ablauf der Studie	20 week program

Wing RR, Marcus MD, Salata R, et al. Effects of a very-low-calorie diet on long-term glycemic control in obese type 2 diabetic subjects. Arch Intern Med 1991; 151(7):1334–40. http://www.ncbi.nlm.nih.gov/pubmed/2064484. Laufnummer: 31831

	Weekly meetings for 20 weeks, mainenance meetings at week 24, 28, 46, 72 with 1-year follow-up at week 72.
Intervention	Behavior therapy program including 8-week period of very low calorie diet (VLCD) - Week 1-4: 4200-6300 J/d - Weeks 5-12: 1680J/d of lean meat, fish and fowl, option of using optifast 70 (liquid meal replacement) - Week 13-16: Reintroduction of other foods - Week 17-20: balanced diet (4200-6300J/d)
Vergleich	Standard behavior therapy program (BT) - 4200-6300 J/d
Attrition	33 (92%) /36 completed both, the post-treatment (week 20) and 1-year assessment (16/19 BT group, 17/17 VLCD group). All analysis based onthese 33 subjects.
Medication change	- Changes made by project physichian during first 20 weeks of program, then by patient`s own phy-sichian - Subjects recieving insulin started the VLCD in the hospital, where insulin was either withdrawn or sharply reduced

Baseline

	BT	**VLCD**	
Age	51,9 ± 9,9	50,6 ±7,7	
N (M/F)	16 (4/12)	17 (4/13)	
Weight (kg)	104,5 ±21,5	102,1 ±11,7	
HbA1c (%)	10,4 ±2,0	10,4 ±2,2	
Diabetes duration (years)	7,8 ± 7,5	5,7 ±4,3	
Diab. treatment n			
diet	3	3	
oral	10	10	
Insulin	3	4	

Ergebnisse: Glycemic control in BT and VLCD conditions

	BT (n=16)	**VLCD (n=17)**	p	
			Time x group	time
HbA1c (%) before after 1 year	 10,4 ± 2,0 8,6 ±1,0 11,8 ±2,7	 10,4 ±2,2 7,3 ±1,0 9,2 ±2,1	 … 0,083 0,001	 … 0,001 >0,10
Weight, kg Before After 1y	 104,5±21,5 94,4 ±19,8 97,7 ±17,4	 102,1 ±11,7 83,5 ±9,5 93,5 ±10,4	 … 0,003 >0,1	 … 0,001 0,001
Dietary adherence (self reported intake and Exercise)				
Calorie intake, kj/wk 1 8 20	 4829 ±510 4654 ±820 4859 ±870	 4976 ±707 1795 ±230 3854 ±837	 … 0,001 0,001	 …. 0,001 0,002
Exercise, kJ/wk Before After 1 y	 3122 3750 3281	 1640 6143 3398	 … 0,03 >0,1	 … … …

Wing RR, Marcus MD, Salata R, et al. Effects of a very-low-calorie diet on long-term glycemic control in obese type 2 diabetic subjects. Arch Intern Med 1991; 151(7):1334–40. http://www.ncbi.nlm.nih.gov/pubmed/2064484. Laufnummer: 31831

Comparison of subject **in the VLCD group** who could bei maintained on diet only with those required oral hypoglycemic medications

	Treated with diet only	Required medication	
n	11	6	
Medication at baseline, diet/oral/insulin	3/5/3	0/5/1	>0,1
Years diabetic	5,9 ±4,1	5,5 ±4,7	>0,1
Weight loss, kg Before to after Vefore to 1 y	 -21,6 ±9,9 -11,8 ±9,3	 -12,9 ±5,9 -2,7 ±5,9	 0,039 0,028

Subjects being treated with diet only
Posttreatment: BT group: 8/16, VLCD group: 16/17, p<0,01
1-year follow-up: BT 8/16 vs. VLCD 11/17, n=n.s.

Anmerkungen ÄZQ:
- Geschlechterverhältnis nicht ausgeglichen
- Deposit of 150$ at start, earned back for meeting goals
- Relativ alte Studie (diagnostiche Grenzwerte von heutigen abweichend).

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: high, Detection: unclear, Attrition: high, Reporting: unclear; Other biases: siehe Anmerkungen oben
Sponsor: k.A. zum Einfluss des Sponsors.

Anderson 1994

Anderson JW, Brinkman-Kaplan V, Hamilton CC, et al. Food-containing hypocaloric diets are as effective as liquid-supplement diets for obese individuals with NIDDM. Diabetes Care 1994; 17(6):602–4. DOI: 10.2337/diacare.17.6.602. http://www.ncbi.nlm.nih.gov/pubmed/8082533.
Laufnummer: 31829

Studiencharakteristika: n=40, randomized controlled trial, 12-week intervention, follow-up 1 year

Population	NIDDM, BMI 30-40kg/m2, 40-70years	
Interven-tion/Control	800-kcal diet Group A: liquid supplements only Group B: supplement plus evening meal - Both groups received intensive behavioral education program - Weekly group classes - Emphasis on increase in physical activity	
Attrition	1 subject in group B discontinued (Coronary bypass surgery)	
Treatment	**Baseline (n=39)** Insulin: 5 subjects Insulin and oral hypoglycemic agents: 3 subjects Oral hypoglycemic agents: 24 subjects Diet alone 7 subjects	**At 12 weeks (n=39)** Insulin 2 subjects Oral hypoglycemic agents 7 subjects Diet alone: 30 subjects

Ergebnisse

	Supplement onla group (A)			**Supplement plus food (B)**		
	0 months	3 months	%Change	0 months	3 months	%Change
Body weight, kg	105,1 ±3,4	88,6±2,8	-15,3,	104,3 ±3,2	89,4 ±2,7	-14,1
HbA1c, %	8,2 ±0,5	6,2 ±0,2	-21,8	8,6±0,5	6,8±0,3	-19,7

One-year follow-up: n=37 (beide gruppen):
Baseline: 104,7±2,3kg, 12-week-follow-up 89,0 ±1,9kg, 1-year follow-up 95,9 ±2,3 (p<0,0001 vs. Initial weight)

Anmerkungen ÄZQ:
- Liquid supplements provided free of charge.
- Keine Auflistung der Diabetesmedikation nach Gruppen

Wing 1994 (intermittent very low calorie diet)

R. R. Wing, E. Blair, M. Marcus, L. H. Epstein, and J. Harvey, "Year-long weight loss treatment for obese patients with type II diabetes: does including an intermittent very-low-calorie diet improve outcome?," American Journal of Medicine, vol. 97, no. 4, pp. 354–362, 1994. #31773

Studiencharakteristika: n=93, 50-week treatment, 2-year follow-up

Population	30-70 years, 30% or 18kg above ideal body weight, T2DM
Ablauf der Studie (both groups)	50 week behavior weight control program Weekly meetings fo1 year, follow up after 2 years (from start).
Intervention	VLCD: Balanced low calorie diet (1000-1500kcal)/d plus 2x 12-week period of VLCD (400-500kcal/d) - Weeks 1-12 and 24-36: VLCD, option of liquid formulas - - weekly exercise goals
Vergleich	LCD: Balanced low calorie diet (1000-1500kcal)/d throuout 50 weeks, less than 30% calories from fat - Weekly exercise goals
Attrition	LCD 41 (86%), VLCD 38 (84%) completed 1-year assessment LCD 34 (70%), VLCD 33 (73%) completed assessments at 0, 3, 6 and 12 months Average attendance (meetings): week 1-12: 10 out of 12 Final quarter: 5 out of 12. Apparent in both treatment groups. Follow up (recontact 2 years after study entry): 38/48 LCD, 36/45 VLCD
Medication change	- Diabetes medication were discontinued at start of treatment - Subjects recieving insulin in VLCD group: insulin administration was discontinued in hospital - Algorithm to restart medication (if mean of 2 weekly fasting blood sugars averaged ≥240mg/dL for 2 weeks)

Baseline

	LCD, n=48	**VLCD, n=45**	p-value
Age	51,3 ± 8,7	52,3 ± 10,3	0,62
N (M/F)	48 (18/30)	45 (15/30)	
Weight (kg)	107,7 ±18,7	105,8 ±19,4	0,63
BMI (kg/m2)	38,31 ±6,52	37,42 ±6,13	0,5
HbA1c (%)	10,5 ±2,0	10,3 ±2,0	0,61
Years since diagnosis	7,6 ± 7,1	5,9 ±5,1	0,18
Diab. treatment n			
Diet only	6	9	0,59
Oral medications	26	26	
Insulin	13	10	

Ergebnisse: Glycemic control in LCD and VLCD conditions

	LCD	**VLCD**	p	
			Time	Group x time
HbA1c (%) prestudy 6 months	10,5 ±2,0 8,8 ±1,8	10,4 ±2,0 8,4 ±2,2	… 0,000	… ns

R. R. Wing, E. Blair, M. Marcus, L. H. Epstein, and J. Harvey, "Year-long weight loss treatment for obese patients with type II diabetes: does including an intermittent very-low-calorie diet improve outcome?," American Journal of Medicine, vol. 97, no. 4, pp. 354–362, 1994. #31773				
1 year	9,2 ±2,0	8,9 ±2,5	0,000	ns
Psychologic changes				
	LCD	VLCD	p-value	
Becks Depression Inventory	Baseline 11,4 At 6 months: 7,8 (p<0,001) At 1 year: 7,8 (p<0,001)	Baseline 10,5 At 6 ms: 6,2, (p<0,001) At 1 year: 5,7, p<0,001	No significant between group difference	
Changes over two-year results				
	LCD (n=37)	**VLCD (n=36)**	**p-value**	
Weight, kg	-5,7 ±7,9, p<0,001 (change from baseline)	-7,2 ±8,0, p<0,001	0,37	
HbA1c, %	+0,24 ±2,4	+0,07 ±2,22	0,74	
% on diet only	31% (n=12)	55% (n=20)	0,01	
Commonly reported side effects (cold intolerance, constipation, hair loss) resolved when VLCD termindated.				
Anmerkungen ÄZQ: - Geschlechterverhältnis nicht ausgeglichen - Deposit of 150$ at start, earned back for meeting goals - Relativ alte Studie (diagnostiche Grenzwerte von heutigen abweichend).				
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: high, Detection: unclear, Attrition: high (unclear), Reporting: unclear; Other biases: siehe Anmerkungen oben Sponsor: k.A. zum Einfluss des Sponsors.				

Williams 1998 (intermittent verly low calorie diet)

K. V. Williams, M. L. Mullen, D. E. Kelley, and R. R. Wing, "The effect of short periods of caloric restriction on weight loss and glycemic control in type 2 diabetes," Diabetes Care, vol. 21, no. 1, pp. 2–8, 1998. http://www.ncbi.nlm.nih.gov/pubmed/9538962. #31833	
Studiencharakteristika: n=54, 20-week intervention	
Population:	T2DM, 30-70years, 20% above ideal body weight, not currently receiving insulin, oral diabetes medication stopped 2 weeks before participation in study, participants with FPG levels > 16,7mmol/L when medicatoin discontinued were excluded.
Interventions in all study arms	20-week behavioral trialment program: weekly group meetings - Subjects instructed to increase alking, weekly exercise goals.
Intervention	1500-1800kcal/d, 20 days 400-600kcal/d very low calorie diet (VLCD) - One group (1-day) followed VLCD 5 consecutive days during week 2 of the study and then 1d/week for 15 weeks - One group (5-day) followed VLCD 5 consecutive days during week 2, 7, 12 and 17 - VLCD diets foods were provided - Identical caloric intake for interventions groups, but 18000-28000 lower than SBT
Control	Standard behavioral therapy (SBT): 1500-1800kcal/d throughout 20 weeks
Change in medication	oral diabetes medication was stopped 2 weeks before participation in the study. If FPG values (twice weekly measured) were >13,9mmol/l, oral diabetes medication restarted on half dose presented before study.
Number of subjects restarting oral diabetes medication based on FPG >13,9mmol/l did not differ between three groups (p>0,6)	

K. V. Williams, M. L. Mullen, D. E. Kelley, and R. R. Wing, "The effect of short periods of caloric restriction on weight loss and glycemic control in type 2 diabetes," Diabetes Care, vol. 21, no. 1, pp. 2–8, 1998. http://www.ncbi.nlm.nih.gov/pubmed/9538962. #31833

SBT: 3 subjects, 1-day group: 1 subject, 5-day group: 3 subjects
Anmerkung: ÄZQ: Keine weiteren Angaben im Artikel (keine Baselinedaten)

Li 2017

Li C, Sadraie B, Steckhan N, et al. Effects of A One-week Fasting Therapy in Patients with Type-2 Diabetes Mellitus and Metabolic Syndrome - A Randomized Controlled Explorative Study. Exp Clin Endocrinol Diabetes 2017; 125(9):618–24. DOI: 10.1055/s-0043-101700. http://www.ncbi.nlm.nih.gov/pubmed/28407662. #31832

Studiencharakteristika: Explorative randomized pilot study, follow-up 4 months, n=46	
Population	Patients with manifest T2DM medically treated with oral hypoglycemic agents and/or insulin
Intervention	initial 7-day modified fasting program (2 pre-fasting days) followed by advice about a Mediterranean diet
Control	advice to a Mediterranean diet with an additional offer to participate in a 7-day modified fasting program (wait list offer)
Attrition	32 completed trial (16 each)
Change in medication	In both groups: standard medical care as determined by individual requirements. All participants instructed to keep usual treatment unless required and changed by their treating physician.
Ergebnisse	
Ergebnisse: 4 months mean weight: FG: -3.5 kg vs. CG -2kg, (p = 0.03) Fasting increased quality-of-life: WHO-5 Fasting group: baseline 16,4 ±4,1, follow-up 18,2± 4,0, mean change 1,8 ±2,2, p-value 0,003 Control group: baseline 14,8 ±6,5, follow-up 15,7 ±5,1, mean change 0,9 ±2,7; p-value 0,61 Median of difference 1 (95% CI 0,0; 2,0), p-value 0.04	
ÄZQ: Change in Medication wird nicht berichtet. Anmerkungen: explorative Pilot-Study, nicht gepowert, per-protocol analyse, Baseline differences between groups	

Tay 2014/2015 (low carbohydrate versus high carbohydrate diet)

Tay J, Luscombe-Marsh ND, Thompson CH, et al. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: A randomized trial. Am J Clin Nutr 2015; 102(4):780–90. DOI: 10.3945/ajcn.115.112581. http://www.ncbi.nlm.nih.gov/pubmed/26224300.
Laufnummer: 31777, Ergebnisse 52 weeks

Weiteres Zitat: Tay J, Luscombe-Marsh ND, Thompson CH, et al. A very low-carbohydrate, low-saturated fat diet for type 2 diabetes management: A randomized trial. Diabetes Care 2014; 37(11):2909–18. DOI: 10.2337/dc14-0845. http://www.ncbi.nlm.nih.gov/pubmed/25071075.
Laufnummer: 31778, Ergebnisse 24 weeks

Study characteristics: single-center, parallel group randomized, controlled study, n=115, recruited via public advertisement, 52 weeks (Zwischenerhebung 24 weeks in #31778), Australia

Objective	compare effects of very low-carbohydrate, high–unsaturated/low–saturated fat diet (LC) with high–unrefined carbohydrate, low-fat diet (HC) on glycemic control and cardiovascular disease (CVD) risk factors in T2DM.
Population	Overweight/obese (BMI 26–45 kg/m^2) adults with T2DM, HbA1c ≥7% and/or taking antiglycaemic medication
Intervention in both groups	- Individual meeting with dietitian biweekly for 12 weeks, then monthly. - Free of charge key foods (≈30% total energy) representative of allocated diet profile for 12weeks and key foods or AU $50 food voucher on alternate months thereafter. - free of charge, 60-min structured exercise classes on 3 nonconsecutive days/week, incorporating moderate-intensity aerobic/resistance exercises, under supervision of exercise professionals
Intervention	Low Carbohydrate (LC) diet: - carbohydrate 14% of total energy (%E), restrict intake <50 g/day,

Tay J, Luscombe-Marsh ND, Thompson CH, et al. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: A randomized trial. Am J Clin Nutr 2015; 102(4):780–90. DOI: 10.3945/ajcn.115.112581. http://www.ncbi.nlm.nih.gov/pubmed/26224300.
Laufnummer: 31777, Ergebnisse 52 weeks

	- protein 28%E, - total fat 58%E (35% monounsaturated fat, 13% polyunsaturated fat) Saturated fat <10%E in both diets. Energy levels: moderate restriction (500–1,000 kcal/day deficient), 1357–2143-kcal/d energy prescription
Vergleich	High Carbohydrate (HC) diet: - carbohydrate 53%, emphasis on low–glycemic index foods, - protein 17%, - total fat 30% (15% monounsaturated fat and 9% polyunsaturated fat). Saturated fat <10% in both diets. Energy levels: moderate restriction (500–1,000 kcal/day deficient), 1357–2143-kcal/d energy prescription
Outcomes	Primary: HbA1c; others included antiglycemic medication changes (antiglycemic medication effects score [MES]), and blood lipids and pressure, weight
Baseline	BMI 34.4 ± 4.2 kg/m^2, age 58 ± 7 years, duration of diabetes: 8 ± 6 y
Attrition	Commenced: 11593 participants completed 24 weeks, (LC 79%, HC 82%) completion rates 52 weeks (LC diet:71%; HC diet: 65%)

Baseline

	LC-diet (n=58)	**HC-diet (57)**	
Age (years)	58 ± 7	58 ± 7	
Females (%)	36%	49%	
Weight (kg)	101.7 ± 14.4	101.6 ± 15.8	
BMI (kg/m2)	34.2 ± 4.5	35.1 ± 4.1	
HbA1c	7,3 ± 1,1	7,4 ±1,1	
Diabetes medications [n (%)]	Insulin [n (%)]: 6 (10) Metformin: 46 (79) Sulfonylureas: 20 (34) Thiazolidinediones: 3 (5) GLP-1-RA: 1 (2) DPP-4-I: 1 (2)	Insulin [n (%)]: 6 (11) Metformin: 41 (72) Sulfonylureas: 16 (28) Thiazolidinediones: 3 (5) GLP-1-RA: 1 (2) DPP-4-I: 2 (4)	
MES (Medication effect score)	Antiglycemic MES: 1,3 ±1,0	Antiglycemic MES: 1,1 ±1,1	

Ergebnisse 24 weeks

	LC diet (n=46)		**HC diet (n=47)**		**p-value**
	Week 24	change	**Week 24**	change	
HbA1c					
Body weight (kg)	88.1 (13.7)	-12.0 (6.3)	89.9 (14.9)	-11.5 (5.5)	0,57
BMI (kg/m2)	30.0 (4.4)	-4.0 (2.0)	30.9 (4.2)	-4.0 (1.8)	0.74
Medications (24 weeks)					
Antiglycemic MES*	0.8 (0.7)	-0.5 (0.5)	1.0 (1.1)	-0.2 (0.5)	0.003
Proportion of cohort that achieved decrease in MES* (24 weeks)					
≥20% decrease, n (%)	31 (67.4)		13 (27.7)		<0.005
≥50% decrease, n (%)	16 (34.8)		8 (17.0)		0,05

Tay J, Luscombe-Marsh ND, Thompson CH, et al. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: A randomized trial. Am J Clin Nutr 2015; 102(4):780–90. DOI: 10.3945/ajcn.115.112581. http://www.ncbi.nlm.nih.gov/pubmed/26224300.
Laufnummer: 31777, Ergebnisse 52 weeks

Physical activity Mean activity counts (counts/min)	232.7 (88.5)	44.3 (57.9)	232.5 (78)	51.7 (45.3)	0.51

HbA1c	- significant interaction of group and baseline HbA1c (P = 0.02), indicating the diet effects depended on initial HbA1c levels. The LC diet reduced HbA1c to a greater extent among participants with baseline HbA1c >7.8% (62 mmol/mol), with no diet effect in participants with baseline HbA1c ≤7.8%. Percentage weight loss was not different between the groups for participants with baseline HbA1c >7.8% (LC -11.9±5.6%, HC -11.2 ± 5.4%; P = 0.77).

Ergebnisse 52 weeks (changes from baseline)

	LC diet	**HC diet**	**Difference in change between groups / p- value (time+diet interaction)**
BMI, kg/m2	-3.2 (95% CI -3.9, –2.6)	-3.5 (-4.2, -2.9)	0,3 (-0,6; 1,2) P 0,31
Reduktion in weight	-9,8kg (-11,7; -7,9)	-10,1kg (-12,0; -8,2)	
HbA1c (%)	-1,0% (-1,2; -0,7)	-1,0% (-1,3; -0,8)	0,1 (-0,3; 0,5)
Medication Antiglycemic MES*	-0,5 (-0,7; -0,4)	-0,2 (-0,4; -0,06)	-0,3 (-0,6; -0,05) P 0,02
MES* reduction ≥ 20%, n (%)	30 (52)	12 (21)	- P 0,001
MES* reduction ≥ 50%, n (%)	17 (29)	10 (18)	- 0,14

Energy Intake, dietary adherence

	LC, n=41			**HC, n=37**		
	Week 0-12	Week 13-24	Week 37-52	Week 0-12	Week 13-24	Week 37-52
Total energy, kcal	1552 ± 236	1599 ± 249	1700 ± 335	1555 ± 171	1627 ± 183	1737 ± 309
Carbohydrate, %E	13.4 ± 1.4	14.4 ± 2.3	16.6 ± 2.5	50.5 ± 2.4	49.9 ± 2.4	49.0 ± 3.2
Protein %E	27.0 ± 1.5	26.3 ± 1.7	25.6 ± 2.1	18.9 ± 1.0	18.9 ± 1.2	18.4 ± 1.4
Total fat, %E	54.4 ± 2.5	54.1 ± 3.2	52.5 ± 3.0	24.1 ± 2.7	24.6 ± 2.5	26.1 ± 3.5

Anmerkungen:
- free of charge food,
- free of charge exercise

*Changes in diabetes medication requirements were quantified by the antiglycemic medication effect score (MES), which was computed on the basis of potency and dosage of diabetes medications including insulin. A higher MES corresponded to a higher diabetes medication requirement.

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: high, Detection: unclear, Attrition: unclear, Reporting: unclear; Other biases: siehe Anmerkungen oben
Sponsor: No sponsor or funding source had a role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

Risk of bias Bewertung: in Goldenberg 2021: high risk/ some concern; in Ross 2012: (Tay 2015) low risk of bias.

Walker 1995

Walker KZ, O'Dea K, Nicholson GC, et al. Dietary composition, body weight, and NIDDM. Comparison of high-fiber, high-carbohydrate, and modified-fat diets. Diabetes Care 1995; 18(3):401–3. DOI: 10.2337/diacare.18.3.401. http://www.ncbi.nlm.nih.gov/pubmed/7555486. Laufnummer: 31787	
Studiencharakteristika: n=24 (9 men, 15 women), random crossover design for 3 months each, with a 1-month washout.	
Objective	To examine the effects of a high-carbohydrate low-fat (HCLF) and a modified-fat (MF) diet on body weight and metabolic control in subjects with noninsulin- dependent diabetes mellitus (NIDDM) living at home.
Studienablauf	- 1 month on patients usual diet, - subjects followed HCLF or MF diets in a random crossover design for 3 months each with a 1-month washout. - Usual alcohol intake and physical activity were maintained. - At beginning and end of each dietary period: 2 appointments, 4 days apart, after an overnight fast
Intervention	High-carbohydrate low-fat diet (HCLF): 21% of energy from fat (with polyunsaturatcd: monounsaturated:saturated ratio [PMS] of 1:1:1) and 59% of energy from fiber rich carbohydrate (2 g fiber/420 kj).
Vergleich	Modified fat diet (MF): 40% of energy from fat (PMS 1:2:1) and 40% of energy from carbohydrate.
Baseline	age 58.3 ±2.1 years, body mass index 29.2 ± 0.7 kg/m^2, controlled their diabetes by low-dose oral hypoglycemic agents or by diet alone
Ergebnisse	
Subjects lost weight on both HCLF and MF diets (mean loss 0.7 and 1.3 kg, respectively). Although the MF diet resulted in a small decrease in fasting glucose levels, there was no significant change in HbA1c. Similarly, there was no significant difference between the diets in changes in blood pressure or fasting blood lipids. Most subjects (65%) preferred the MF diet. Questionnaire scores indicated a significantly higher acceptance 110ft he MF diet than the HCLF diet (response scores 1.8 ± 0.1 and 2.4 ± 0.2, respectively; P < 0.05).	
➔ Kein Bericht über Change in Medication.	
Risk of bias Bewertung (aus Korsmo-Haugen 2019): high risk of bias.	

Walker 1999

Walker KZ, O'Dea K, Nicholson GC. Dietary composition affects regional body fat distribution and levels of dehydroepiandrosterone sulphate (DHEAS) in post-menopausal women with Type 2 diabetes. Eur J Clin Nutr 1999; 53(9):700–5. DOI: 10.1038/sj.ejcn.1600835. http://www.ncbi.nlm.nih.gov/pubmed/10509765. Laufnummer: 31788
➔ Change in Medication nicht als betrachteter Endpunkt. Auch die anderen Endpunkte aus unserer Recherche nicht untersucht (mortalität, CVD etc.)
high risk of bias in der Cochrnae-Risk of bias-Bewertung (Korsmo-Haugen, 2019)

Brinkworth 2004

Brinkworth GD, Noakes M, Parker B, et al. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: One-year follow-up of a randomised trial. Diabetologia 2004; 47(10):1677–86. DOI: 10.1007/s00125-004-1511-7. http://www.ncbi.nlm.nih.gov/pubmed/15480538. #31801	
Studiencharakteristika: n=66, intervention 12 weeks, follow-up 12 months	
Objective	compared the long-term weight loss and health outcomes at 1-year follow-up, after a 12-week intensive intervention consisting of the low-fat, weight-loss diets, which differed in protein content.
Population	Patients (BMI: 27–40 kg/m2) with Type 2 diabetes
Intervention	low-protein (15% protein, 55% carbohydrate) or for 8 weeks of energy restriction (~6.7 MJ/day) and 4 weeks of energy balance. Subjects were asked to maintain the same dietary pattern for a further 12 months of follow-up.

Brinkworth GD, Noakes M, Parker B, et al. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: One-year follow-up of a randomised trial. Diabetologia 2004; 47(10):1677–86. DOI: 10.1007/s00125-004-1511-7. http://www.ncbi.nlm.nih.gov/pubmed/15480538. #31801			
Vergleich	high-protein diet (30% protein, 40% carbohydrate) for 8 weeks of energy restriction (~6.7 MJ/day) and 4 weeks of energy balance. Subjects were asked to maintain the same dietary pattern for a further 12 months of follow-up.		
Attrition	N=66 assigned, study completed=38, with equal dropouts in each group		
Baseline			
	LP n=19 Men 7, women 12	HP, n=19 Men 8, women 11	
Age	62.7±1.8	60.9±1.8	
Weight (kg)	91.2±4.3	96.2±4.0	
BMI (kg/m2)	33.3±1.3	33.6±1.2	
HbA1c	6.2±0.2	6.5±0.2	
Ergebnisse			
	LP	HP	
weight reductions against baseline at week 64	−2.2±1.1 kg	−3.7±1.0 kg	p<0.01, with no diet effect
Of the 38 subjects who completed the study, 17 required oral hypoglycaemic medications and 3 required insulin.			
Keine für unsere Analyse relevanten Endpunkte erhoben. Change in medication nicht berichtet.			
Risk of bias Bewertung (Korsmo-Haugen 2019): unlear risk of bias.			

Daly 2006

Daly ME, Paisey R, Millward BA, et al. Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes-a randomized controlled trial. Diabet Med 2006; 23(1):15–20. DOI: 10.1111/j.1464-5491.2005.01760.x. http://www.ncbi.nlm.nih.gov/pubmed/16409560. Laufnummer: 31791	
Studiencharakteristika: randomized, controlled multicentre study involving three UK centres (Exeter, Plymouth and Torbay). N=102, 3-month trial	
Objective	effects of a 3-month programme of dietary advice to restrict carbohydrate intake compared with reduced-portion, low-fat advice in obese subjects with poorly controlled T2DM.
Population	Obese (BMI ≥30 kg/m2), poorly controlled T2DM (HbA1c 8–12%) with a serum creatinine < 150 µmol / l, under the care of a hospital-based diabetes consultant
Studienablauf	3-month intervention: dietary education and support delivered via 3 monthly group sessions (education: medical issues, energy balance, physical activity), 1 individual consultation and final assessment consultation.
Intervention	Low carbohydrate diet (LC) group: up to 70 g of carbohydrate/day, ≥half a pint of milk and 1 piece of fruit into the daily carbohydrate allowance to improve vitamin/mineral intake. Advice: lower saturated fat and salt intake, oily fish 2x/week, ≥ 5 portions of vegetables/fruit daily.
Vergleich	healthy eating group (LF): standard healthy eating advice, focusing on reducing fat intake. This was combined with instruction to reduce portion sizes Advice: lower saturated fat and salt intake, oily fish 2x/week, ≥ 5 portions of vegetables/fruit daily.
Primärer Endpunkt	Change in weight, HbA1c, total cholesterol : HDL ratio and triacylglycerol concentrations.
Attrition	22.5% attrition rate at 3 months. No difference in attrition between groups.

Daly ME, Paisey R, Millward BA, et al. Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes-a randomized controlled trial. Diabet Med 2006; 23(1):15–20. DOI: 10.1111/j.1464-5491.2005.01760.x. http://www.ncbi.nlm.nih.gov/pubmed/16409560.
Laufnummer: 31791

Baseline			
Mean (Standard Error of Mean)	**LC, n=51**	**LF, n=51**	
Age (years)	58.2 (1.55)	59.1 (1.48)	
Weight (kg)	101.6 (1.84)	102.3 (2.49)	
BMI (kg/m2)	35.4 (0.70)	36.7 (1.26)	
HbA1c (%)	9.00 (0.20)	9.11 (0.17)	

Ergebnisse (Data were analysed as absolute change from baseline in subjects who completed the final assessment.)			
	LC	LF	Confidence intervals for between-group differences p-value
Weight (kg) Changes from baseline	-3.55 (0.63)	-0.92 (0.40)	1.16–4.09, p=0,001
HbA1c (%)	-0.55 (0.17)	-0.23 (0.13)	-0.10–0.75, p=0.132
Dietary adherence			
	LC, n=37	**LF, n=37**	**p-value**
Engergy (kcals/day)	1290 (70.6)	1434 (78.6)	0,179
Carbohydrate (% energy)	33.5 (1.55)	45.2 (1.31)	<0,001
Protein (% Energy)	26.4 (0.96)	20.9 (0.58)	<0,001
Fat (% Energy)	40.1 (1.60)	32.9 (1.07)	< 0.001
Medication			
Baseline Medication (approximately) post study evaluation (?)	40% oral hypoglycaemic agents (OHAs), 20% insulin 40% combination 112ft he two.	40% oral hypoglycaemic agents (OHAs), 20% insulin 40% combination 112ft he two.	
Post-study analysis of medication changes from baseline, date available for 75% (not in the original study design, limited analysis)			
	LC	**LF**	
Inuslin use reduced in insulin using subjects	85%	22%	
Increased insulin (insulin using subjects)	5%	16%	
OHA	unchanged	unchanged	

Daly ME, Paisey R, Millward BA, et al. Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes-a randomized controlled trial. Diabet Med 2006; 23(1):15–20. DOI: 10.1111/j.1464-5491.2005.01760.x. http://www.ncbi.nlm.nih.gov/pubmed/16409560.
Laufnummer: 31791

Anmerkung:
- Wahrscheinlich längere Diabetes-Dauer als in anderen Studien (HBA1c, 2nd care patients)
- Analyse (Change in medication) post-study erhobene Daten, unvollständig.

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: high, Detection: unclear, Attrition: high, Reporting: high; Other biases: siehe Anmerkungen oben
Sponsor: k.A. zum Einfluss des Sponsors.

Risk of bias Bewertung: aus Goldenberg 2021: high risk of bias / some concerns; in Korsmo-Haugen 2019: high risk of bias

Westman 2008

Westman EC, Yancy WS, Mavropoulos JC, et al. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutr Metab (Lond) 2008; 5:36. DOI: 10.1186/1743-7075-5-36. http://www.ncbi.nlm.nih.gov/pubmed/19099589.
Laufnummer: 31794

Studiencharakteristika: randomized controlled trial, N=84 community volunteers (newspaper advertisements.)

Objective	tested the hypothesis that a diet lower in carbohydrate would lead to greater improvement in glycemic control over a 24-week period in patients with obesity and T2DM.
Population	diagnosis T2DM > 1 year (confirmed HbA1c > 6.0%), onset of diabetes after age 15 years, no history of diabetic ketoacidosis, age 18– 65 years, BMI 27–50 kg/m2, and desire to lose weight.
Interventionen in beiden Gruppen	- group sessions (every week for 3 months, then every other week for 3 months), diet instruction, nutritional supplements, exercise recommendation (exercise for 30min ≥3 times/week, no formal exercise program provided). - nutritional supplements (mild glucose-lowering effect (vanadyl sulfate 200 mcg/day, chromium dicotinate glycinate 600 mcg/day, alpha-lipoic acid 200 mg/day))
Intervention	*Low-carbohydrate, Ketogenic Diet Group Intervention (LCKD):* - < 20 gr carbohydrate/day, without explicitly restricting caloric intake. - Allowed foods: unlimited amounts of animal foods and eggs; limited amounts of hard cheese, fresh cheese, salad vegetables, and non-starchy vegetables. - encouraged to drink at least 6 glasses of permitted fluids daily. Drinking bouillon dissolved in water recommended 2–3x/day
Vergleich	*Low-glycemic index diet group intervention (LGID):* - low glycemic index, reduced-calorie diet with ≈55% caloric intake from carbohydrate. - Energy intake individualized 113ft h 2.1 MJ (500 kcal) less than participant‘s calculated intake
Statistics	Fort he primary outcome variable: completer‘s analysis and last observation carried forward (LOCF)
Attrition	N=97 randomized. - N=48 LCKD, 10 discontinued prior to week 0 - N=49 LGID, 3 discontinued prior to week 0 Analyses: - LCKD: n=38 analysed, 21 (55.3%) completed study, reasons for discontinuation: 3 refused assigned diet, 2 unsatisfied with diet, 2 lost to follow-up, 2 were too busy, 1 relocated, and 7 cited no reason. - LGID: n=46 analysed, 29 (63.0%) completed study; reasons for discontinuation: 1 refused assigned diet, 1 unsatisfied with diet, 2 lost to follow-up, 3 were too busy, 1 relocated, 1 had difficulty adhering to the diet and 9 cited no reason. In order to detect a clinically meaningful change in hemoglobin A1c (absolute change of 1%, SD = 1.5) with 80% power (two-sided alpha of .05) in a completers analysis, a total of 60 participants was required.
Change in medication	Medications were adjusted using a pre-specified algorithm based upon home and return visit blood capillary glucose measurements

Baseline

	LCKD (Low-carbohydrate, ketogenic diet)			LGID (Low –glycemic, reduced-calorie diet)		
Means ± SD	Enrollees n=38	Completers, n=21	Non-completers, n=17	Enrollees, n=46	Completers, n=29	Non-completers, n=17

Westman EC, Yancy WS, Mavropoulos JC, et al. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutr Metab (Lond) 2008; 5:36. DOI: 10.1186/1743-7075-5-36. http://www.ncbi.nlm.nih.gov/pubmed/19099589. Laufnummer: 31794						
Female gender, %	76.3	66.7	88.2	80.4	79.3	82.3
Age, years	51.8 ± 7.3	51.2 ± 6.1	52.4 ± 8.7	51.8 ± 7.8	50.0 ± 8.4	54.9 ± 5.7
Body weight, kg	105.5 ± 19.5	108.4 ± 20.5	101.9 ± 18.1	106.3 ± 20.1	105.2 ± 19.8	108.1 ± 20.9
Body mass index, kg/m2	37.7 ± 6.1	37.8 ± 6.7	37.6 ± 5.3	38.5 ± 5.6	37.9 ± 6.0	39.4 ± 5.0

Ergebnisse

	LCKD (Low-carbohydrate, ketogenic diet), n=21			**LGID (Low –glycemic, reduced-calorie diet), n=29**			Between groups p-value	Between groups adjusted for baseline values
	Week 0	Week 24	Mean change	Week 0	Week 24	Mean change		
HbA1c, %	8.8 ± 1.8	7.3 ± 1.5	-1,5	8.3 ± 1.9	7.8 ± 2.1	-0,5	0,03	0,06
BMI, kg/m2	37.8 ± 6.7	33.9 ± 5.8	-3,9	37.9 ± 6.0	35.2 ± 6.1	-2,7	0,05	0,1
Body weight, kg	108.4 ± 20.5	97.3 ± 17.6	-11,1	105.2 ± 19.8	98.3 ± 20.3	-6,9	0,008	0,01

Medication baseline

Hypoglycemic medications	20 (95,2%) taking hypoglycemic medications - Insulin + oral agents, n=4 - Insulin only, n=4 - Oral agents, n=12	22 (75,9%) taking hypoglycemic medication - Insulin, n=3 - Oral agents, n=19	

Dietary adherence

	Baseline both groups	**LCKD 24 months**	**LGID 24 months**
Energy intake	2128 ± 993 kcal,	1550 ± 440 kcal/day	1335 ± 372 kcal/day
Carbohydrate (%E: daily energy intake))	245 ± 136 g, 46%E	49 ± 33g, 13%E	149 ± 46 g, 44%E
Protein (%E)	86 ± 33 g, 18%E	108 ± 33 g, 28%E	67 ± 20 g, 20%E
Fat (%E)	88 ± 57 g, 36%E	101 ± 35 g, 59%E	55 ± 23 g, 36%E

There was no difference in self-reported exercise between the groups: the mean number of exercise sessions per week increased from 2.0 ± 2.0 to 3.0 ± 2.0 for the LCKD group and from 2.2 ± 2.2 to 3.8 ± 2.9 for the LGID group (p = 0.39 for comparison).

Ergebnisse: Diabetes medication

Diabetes medications were reduced or eliminated in 95.2% of LCKD vs. 62% of LGID participants (p < 0.01).

Change in medication among patients taking insulin at baseline

Participant	**Week 0: total daily dose**	**Week 24: total daily dose**
Low-glycaemic, reduced calorie diet group (total n=29)		
1	Insulin 24 units, insulin sliding scale three times a day	None none

Westman EC, Yancy WS, Mavropoulos JC, et al. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutr Metab (Lond) 2008; 5:36. DOI: 10.1186/1743-7075-5-36. http://www.ncbi.nlm.nih.gov/pubmed/19099589. Laufnummer: 31794		
2	insulin 85 units	Insulin 13 units
3	insulin 160 units	insulin 120 units
Low-carbohydrate, ketogenic diet group (total n = 21)		
1	Insulin 50 units	Nonr
2	Insulin 90 units	nonr
3	Insulin 32 units Rosiglitazone 4mg/metformin 2000mg	None Metformin 2000mg
4	Insulin 40 units Metfomrin 2000mg	None Metformin 2000mg
5	Insulin 40 units Insulin sliding scale trhee times a day	Insulin 35 units none
6	Insulin 120 units Metformin 2000mg	Insulin 90 units Metformin 2000mg
7	Insulin 135 units	Insulin 60 units
8	Insulin 80 units Pioglitazone 45mg Glimiperide 8mg	Insulin 8 units Pioglitazone 45mg Glimiperide 8mg
No monetary incentives were given.		
Anmerkungen ÄZQ: ,- limitation is the baseline imbalance in the primary outcome, HbA1c, ,- The equation used to calculate energy requirements for the LGID participants may underestimate requirements, particularly in obese people. This would result in more severe energy restriction than the 500 kcal deficit as stated, which might bias the weight loss effects in favor of the LGID. ,- high attrition ,- power calculation n=60 wären benötigt worden ,- predominantly women		
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear / high, Performance bias: high, Detection: high, Attrition: unclear / high, Reporting: unclear; Other biases: siehe Anmerkungen oben Sponsor: the investigators conducted the study independently of the funding source. The funding source had no involvement in conduct of the study.		
Risk of bias Bewertung: in Goldenberg 2021: high risk / some concerns,; in Korsmo-Haugen: high risk.		

Pedersen 2014

Pedersen E, Jesudason DR, Clifton PM. High protein weight loss diets in obese subjects with type 2 diabetes mellitus. Nutr Metab Cardiovasc Dis 2014; 24(5):554–62. DOI: 10.1016/j.numecd.2013.11.003. http://www.ncbi.nlm.nih.gov/pubmed/24374004. Laufnummer: 31804	
Studiencharakteristika: parallel, randomized, 12-month dietary intervention Study, recruited via advertisement in local papers, radio and television	
Population	Adult, overweight participants with type 2 diabetes, with albuminuria (30 -600 mg/24 h or an albumin-to-creatinine ratio of 3.0e60 mg/mmol), and estimated GFR of >40 ml/min/1.73 m2 were enrolled.
Intervention	high protein diet (HPD): protein:fat:carbohydrate ratio 30:30:40% total energy - protein intake was 90-120 g/day - Both diet regimes aimed at reducing body weight with energy content reduced to 6000 kJ.
Vergleich	Standard protein diet (SPD): protein:fat:carbohydrate ratio 20:30:50 %TE - protein intake 55-70 g/day - Both diet regimes aimed at reducing body weight with energy content reduced to 6000 kJ

Pedersen E, Jesudason DR, Clifton PM. High protein weight loss diets in obese subjects with type 2 diabetes mellitus. Nutr Metab Cardiovasc Dis 2014; 24(5):554–62. DOI: 10.1016/j.numecd.2013.11.003. http://www.ncbi.nlm.nih.gov/pubmed/24374004. Laufnummer: 31804	
Medical change	Before start of study: medication was optimized by endocrinologist to achieve good metabolic control The volunteers own doctors also monitored them and made medication changes.
Attrition	76 volunteers commenced the study. 45 participants (35 men and 10 women) completed the one year dietary intervention (21 HPD and 24 SPD), and were included in the analysis.
- Zurückstellen für das Kapitel Folgeerkrankungen (diabetische Nephropathie).	

Luger 2013

Luger M, Holstein B, Schindler K, et al. Feasibility and efficacy of an isocaloric high-protein vs. Standard diet on insulin requirement, body weight and metabolic parameters in patients with type 2 diabetes on insulin therapy. Exp Clin Endocrinol Diabetes 2013; 121(5):286–94. DOI: 10.1055/s-0033-1341472. http://www.ncbi.nlm.nih.gov/pubmed/23674159. Laufnummer: 31802	
Studiencharakteristika: randomized controlled trial, n=44, 12 weeks, recruitment via outpatient clinic, Vienna	
Objective	efficacy of high-protein diet compared with a standard diet
Studienablauf	- Diet caunselling (recipes), assessment at weeks 0, 4, 8 and 12 - No food provided - 5-day food records at week 4 and 12
Population	type-2 diabetic patients on insulin therapy
Intervention	High protein diet (HP), energy-balanced, 30% protein, 40% carbohydrate, 30% fat
Vergleich	Standard diet (ST), energy balanced, 15% protein,, 55% Carbohydrate, 30% fat.
Attrition	N=44, 2 withdrew in HP diet before 12 weeks
Medication change	Insulin dose adjusted by blinded physician

Baseline

	HP (n=22)	ST (n=22)	Total (n=44)	p-value
Age (years)	61,0 ± 5,7	63,7 ± 5,2	62,4 ±5,6	n.s.
Sex (female/male)	8/14	16/6	24/20	0,015
Diabetes duration (years)	17,6 ±9,4	16,2 ±9,2	16,9 ±9,2	n.s.
Insulin dose (IU)	57,3 ±26,3	52,7 ±28,8	55,0 ±27,5	n.s.
HbA1c (%)	7,8 ±1,4	7,6 ±0,9	7,7 ±1,2	n.s.
Weight (kg)	94,1 ±15,6	91,5 ±20,2	92,8 ±17,9	n.s.

31/44 subjects recieved an additional oral antidiabetic medication. („We could not find change in concomitant medications)

	HP (n=21)		**ST (n=22)**		Diff. Between groups ST vs. HP	p-value*		
		p-value		p-value		group	time	Group x time interaction
Insulin require. Baseline 4 weeks 12 weeks	 57,7 ±27,2 52,1 ±27,3 48,2 ±30,8	0,01	 52,7 ±28,8 53,1 ±28,3 53,6 ±28,6	n.s.	 -4,9 (-22,2; 12,3) 1,0 (-16,2; 18,1) 0,6 (-13,0; 23,6)	n.s.	0,02	P=0,007

Luger M, Holstein B, Schindler K, et al. Feasibility and efficacy of an isocaloric high-protein vs. Standard diet on insulin requirement, body weight and metabolic parameters in patients with type 2 diabetes on insulin therapy. Exp Clin Endocrinol Diabetes 2013; 121(5):286–94. DOI: 10.1055/s-0033-1341472. http://www.ncbi.nlm.nih.gov/pubmed/23674159. Laufnummer: 31802								
HbA1c (%) Baseline 4 weeks 12 weeks	7,8 ±1,4 7,6 ±1,3 7,5±1,4	0,05	(n=21) 7,7 ±1,0 7,5 ±1,0 7,5 ±0,9	n.s.	-0,1 (-0,9; 0,6) -0,1 (-0,9; 0,6) -0,04 (-0,8; 0,7)	n.s.	0,03	n.s.
Weight (kg) Baseline 4 weeks 12 weeks	94,1 ±16,0 92,7 ±16,1 91,0± 15,7	0,000	91,5 ±20,2 90,5 ±20,0 90,5 ±19,4	n.s.	-2,5 (-13,8; 8,7) -2,1 (-13,3; 9,1) -0,4 (-11,3; 10,5)	n.s.	0,00	0,004
*repeated measures ANOVA incorporating data from all time points (0, 4, 12 weeks)								
Dietary adherence								
Protein (Energy-%d^{-1})								
Baseline 4 weeks 12 weeks	22,9 ±6,3 26,5 ±4,1 25,6 ±4,7	n.s.	19,8 ±6,7 17,0 ±2,8 16,6 ±3,2	0,02	-3,1 (-7,3; 1,2)	0,000	n.s.	0,004
Carbohydrate (Energy-%d^{-1})								
Baseline 4 weeks 12 weeks	43 ±11,2 37,3 ±8,3 37,5 ±6,6	n.s.	43,1 ±8,5 48,5 ±8,9 50,4 ±7,6	0,003	0,5 (-6,4 ; 6,5) 11,1 (5,5 ; 16,8) 12,9 (8,3; 17,5)	0,001	n.s.	0,001
Fat (Energy-%d^{-1})								
Baseline 4 weeks 12 weeks	32,4 ±11,9 34,2 ±7,8 34,8 ±6,1	n.s.	33,7 ±9,6 29,7 ±7,0 29,4 ±5,0	n.s.	1,3 (-5,7; 8,3) -4,5 (-9,1; 0,3) -5,4 (-9,0; -1,8)	n.s.	n.s.	n.s.
Energy intake (kcal d^{-1})								
Baseline 4 weeks 12 weeks	1318,8±486,9 1219,1±302,8 1272,7±337,8	n.s.	1326,0±361,0 1332,4±254,3 1235,6±325,4	n.s.	-7,1 (-270; 284,2) 113,3 (-67,9; 294,5) -37,1 (-252,3; 178,1)	n.s.	n.s.	n.s.
Physical activity: st 28%, HP 42% practiced sport or were physically acive (p=0,045) Hypoglycemia: no increase in self-reported hypoglycemia in either group								
Anmerkungen: Inhomogenous distribution of sex Relativ kurze Studie, geringe Zahl an Proband*innen								
RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: high, Detection: unclear /high, Attrition: unclear, Reporting: unclear; Other biases: Baseline imbalance, siehe Anmerkungen oben Sponsor: k. A. zum Einfluss eines Sponsors.								
Risk of bias Bewertung: in Korsmo-Haugen 2021 high risk of bias.								

Jenkins 2014

Jenkins DJ, Kendall CW, Vuksan V, et al. Effect of lowering the glycemic load with canola oil on glycemic control and cardiovascular risk factors: A randomized controlled trial. Diabetes Care 2014; 37(7):1806–14. DOI: 10.2337/dc13-2990. http://www.ncbi.nlm.nih.gov/pubmed/24929428. Laufnummer: 31803	
Studiencharakteristika: parallel design, randomized trial, 3-month treatment, Kanada, n=141	
Objective	the combined effect of ALA, MUFA, and low GL on glycemic control and CVD risk factors in type 2 diabetes
Population	type 2 diabetes (HbA1c 6.5%–8.5% [48–69mmol/mol]) treated with oral antihyperglycemic agents Canola oil: Rapsöl

Jenkins DJ, Kendall CW, Vuksan V, et al. Effect of lowering the glycemic load with canola oil on glycemic control and cardiovascular risk factors: A randomized controlled trial. Diabetes Care 2014; 37(7):1806–14. DOI: 10.2337/dc13-2990. http://www.ncbi.nlm.nih.gov/pubmed/24929428. Laufnummer: 31803

Studienablauf	Visits: week -1, 0, 2, 4, 8, 10, 12; - Food records (7-day record) discussed with dietitian - No specific exercise advice was given
Intervention	Test group: low-glycemic-load (low-GL) diet with alpha-linolenic acid (ALA) and monounsaturated fatty acid (MUFA) given as a canola oil–enriched bread supplement (4.5 slices of canola oil–enriched whole-wheat bread (500 kcal/day), 31 g canola oil per 2,000 kcal) Dietary advice: low-GI foods, including legumes, barley, pasta, parboiled rice, and temperate-climate fruit
Vergleich	Control group: whole-grain diet with a whole-wheat bread supplement (7.5 slices of whole-wheat bread without canola oil per day (500 kcal)) Dietary advice: avoid white-flour products and replace them with whole-wheat breakfast cereals, study breads, brown rice
Primary outcome	HbA1c change
Attrition	79% (55/70) of test group, 90% (64/71) of control group completed the trial. Completers (n=119, data in last month): 3 on test diet and 7 on control missing 1 or 2 of 3 final values. Attrition rates not significantly different between treatments compliance with the test bread was 89% (95% CI 86%–93%) versus the control bread 77% (95% CI 74%–80%) (P < 0.0001).

Baseline

	Control diet, n=71	**Test diet, n=70**
Antihyperglycemic medication (n in %)	71 (100%)	70 (100%)
Metformin	67 (94%)	65 (93%)
Sulfonylurea	18 (25)	22 (31)
Thiazolidinedione	4 (6)	8 (11)
Dipeptidyl peptidase-4 inhibitors	12 (17)	12 (17)
Meglitinides (nonsulfonylurea	2 (3)	1 (1)
alpha-Glucosidase inhibitors	0 (0)	1 (1)
Injectable GLP-1 analog (Victoza)	0 (0)	1 (1)
Combination (Janumet)	2 (3)	2 (3)

Ergebnisse Medication change:
Oral antihyperglycemic medication dosages:
Test diet: increase: 1 participant, reduced: 5 participants
Control diet: decreased: 4 participants
- no significant treatment differences.

Ergebnisse
Changes from baseline in study measurements on the basis of raw data and significance of treatment differences for raw and multiple imputation

	Control diet		Test diet		Between diets		
	Week 0 (n=71)	Change within diet	Week 0 (n=70)	Change within diet	change	p-value (raw)	P value (Multiple imputations)
Weight (kg)	84.4 (79.9, 88.9)	-1.6 (-2.0, -1.3), p<0,05	84.5 (79.7, 89.4)	-2.1 (-2.5, -1.7), p<0,05	-0.5 (-1.0, 0.0)	0.070	0.458

Jenkins DJ, Kendall CW, Vuksan V, et al. Effect of lowering the glycemic load with canola oil on glycemic control and cardiovascular risk factors: A randomized controlled trial. Diabetes Care 2014; 37(7):1806–14. DOI: 10.2337/dc13-2990. http://www.ncbi.nlm.nih.gov/pubmed/24929428. Laufnummer: 31803

HbA1c (%)	7.2 (7.1, 7.4)	-0.31 (-0.38, -0.25), p<0,05	7.4 (7.2, 7.5)	-0.47 (-0.54, -0.40), p<0,05	-0.16 (-0.25, -0.06)	0.002	0.016
Dietary adherence							
Erergy (kcal)	1817 (1703, 1930)	-187 (-236, -138), p<0,05	1758 (1658, 1857)	-219 (-272, -167), p<0,05	-32 (-104, 40)	0.374	0.619
ALA (%kcal)	0.7 (0.6, 0.8)	-0.1 (-0.2, 0.0), p<0,05	0.7 (0.6, 0.8)	1.3 (1.2, 1.4), p<0,05	1.4 (1.3, 1.5)	0,000	0,000
Total fat (% kcal)	32.6 (30.9, 34.3)	-5.2 (-6.4, -4.0), p<0,05	31.8 (30.2, 33.3)	5.4 (4.2, 6.7), p<0,05	10.6 (8.9, 12.3)	0,000	0,000
MUFA (% kcal)	12.7 (11.9, 13.5)	-2.8 (-3.5, -2.2), p<0,05	12.3 (11.6, 13.1)	5.1 (4.5, 5.8), p<0,05	8.0 (7.1, 8.9)	0,000	0,000
Glycaemic load	109 (100, 117)	16 (11, 20), p<0,05	111 (103, 120)	-36 (-41, -31), p<0,05	-52 (-59, -45)	0,000	0,000

Anmerkungen
- study breads provided

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: unclear / high, Detection: unclear / high, Attrition: unclear / high, Reporting: unclear; Other biases: Bread free of charge, Sponsor: k. A. zum Einfluss des Sponsors.

Risk of bias Bewertung: in Korsmo-Haugen 2019: unclear risk of bias.

Goldstein 2011

Goldstein T, Kark JD, Berry EM, et al. The effect of a low carbohydrate energy-unrestricted diet on weight loss in obese type 2 diabetes patients – A randomized controlled trial. E-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 2011; 6(4):e178-e186. DOI: 10.1016/j.eclnm.2011.04.003. Laufnummer: 31797

Studiencharakteristika: 1 year, n=52, randomized controlled trial, Israel

Population	Age 35-75y, T2DM, BMI 30-39,9kg/m2, HbA1c >7% not recieving insulin
Studienablauf	Stage 1 (4 weeks before randomization) DASH-diet: 80% of caloric requirements, advice to engage physical aerobic activities 3x/w for at least 30min Stage 2 (3 months following randomization) - Modified Atkins diet (ATK): very low carbohydrate diet (up to 25g Carbohydrate (CHO)/d for 6 weeks after randomization, then increasing to 40gr CHO/d; no restrictions placed on intake of energy, proteins or fats. Fats rich in MUFA. - Standard ADA calorie-restricted diet, calorie-restriction (men 1500kcal/d, women 1200 kcal/d), 10-20% protein, 80% fats and carbohydrates Weekly nutrition counselling (12 weeks), then monthly Stage 3 (4-12 months following randomization): - Continue diet with monthly monitoring
Intervention	Atkins diet with unrestricted energy intake
Vergleich	ADA recommended diet
Attrition	56 began DASH-diet, 4 dropped out during stage 1, 52 patients randomized, 22/26 of each group completed stage 2, 20/26 in each group persisted on diet for 6 months, 14/26 Atkins and 16/26 ADA completed 1 year follow up (7 ATK and 4 ADA returned for final measurement).

Goldstein T, Kark JD, Berry EM, et al. The effect of a low carbohydrate energy-unrestricted diet on weight loss in obese type 2 diabetes patients – A randomized controlled trial. E-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 2011; 6(4):e178-e186. DOI: 10.1016/j.eclnm.2011.04.003.
Laufnummer: 31797

Both diet groups increased exercise activity by 1h/week.

Keine Analyse der Baseline-Medication.
- By 3-month: use of hypoglycemic medication reduced in 17/26 ATK and 11/26 ADA (p=0,16)

Anmerkungen
- Low adherence
- High attrition rate
- Baseline inequalitiy in dietary intake (lower energy intake in atkins group)

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: unclear / high, Detection: unclear, Attrition: high (unclear), Reporting: unclear; Other biases: siehe Anmerkungen, Sponsor: k. A. zum Einfluss des Sponsors (there was no study sponsors for this manuscript).

Ris of bias Bewertung: in Goldenberg 2021: high risk / some concern; in Korsmo-Haugen 2019: unclear risk.

Jönnson 2009 (Paleolithic diet)

Jönsson T, Granfeldt Y, Ahrén B, et al. Beneficial effects of a Paleolithic diet on cardiovascular risk factors in type 2 diabetes: A randomized cross-over pilot study. Cardiovasc Diabetol 2009; 8:35. DOI: 10.1186/1475-2840-8-35. http://www.ncbi.nlm.nih.gov/pubmed/19604407. Laufnummer: 31795

Studiencharakteristika: randomized cross-over study, 13 patients

Objective	compare effects of a Paleolithic (‚Old Stone Age') diet and a diabetes diet as generally recommended on risk factors for cardiovascular disease in patients with type 2 diabetes not treated with insulin.

Anmerkung ÄZQ:
Results/Medication: „All medication remained unchanged during the whole study…"
- Es wird diskutiert, ob ein Ausschluss eines Patietnen, der eine Medikation reduziert hat, eine Änderung ergeben hätte.
- Baselinedaten (Medication) werden genannt.

Risk of bias Bewertung: in Goldenberg 2021: low risk of bias, in Korsmo-Haugen 2019: unclear risk of bias.

Shai 2008

Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med 2008; 359(3):229–41. DOI: 10.1056/NEJMoa0708681. http://www.ncbi.nlm.nih.gov/pubmed/18635428. Laufnummer: 31793

Studiencharakteristika: randomized controlled trial, 2 years, n=322, Israel (workplace at a research center)

Population	40 – 65 years, BMI ≥ 27kg/m2, or T2DM or coronary heart disease, regardless of age and BMI
Interventionen	1.) Low fat diet 2.) Mediterranean diet 3.) Low carbohydrate diet

Anmerkug ÄZQ: Studie hat nicht nur Menschen mit T2DM eingeschlossen.
- n=46/322 (Table 1) mit Typ-2-DM at baseline. Keine Subgruppenanalyse mit Baselinedaten für Gewicht, HbA1c, Diabetes duration), keine Angabe zur Baseline medication.
- Change in medication: „Twenty participants initiated blood-pressure treatment, five initiated medications for glycemic control, and one reduced the dosage of medications for glycemic control." Keine weiteren Angaben.
- no financial compensation or gifts.

Risk of bias Bewertung: in Korsmo-Haugen: unclear risk of bias.

McLaughlin 2007

McLaughlin T, Carter S, Lamendola C, et al. Clinical efficacy 121ft he hypocaloric diets that vary in overweight patients with type 2 diabetes: Comparison of moderate fat versus carbohydrate reductions. Diabetes Care 2007; 30(7):1877–9. DOI: 10.2337/dc07-0301. http://www.ncbi.nlm.nih.gov/pubmed/17475941. Laufnummer: 31792	
Studiencharakteristika: dietary intervention lasted 16 weeks	
Objective	we randomized diet treated patients with type 2 diabetes to hypocaloric diets, moderately restricted in either carbohydrate or fat, to determine whether weight loss or metabolic improvement differed as a function of macronutrient composition.
Population	T2DM, BMI 27–36 kg/m2, fasting plasma glucose concentration 7.2– 8.3 mmol/l, no use of antihyperglycemic medications, stable weight
Anmerkung ÄZQ: Die von uns betrachteten Endpunkte (z. B. Change in medication, QoL, harte patientenrelevante Endpunkte) wurden nicht erhoben und betrachtet.	
Risk of bias Bewertung: in Korsmo-Haugen: unclear risk of bias.	

Wolever 2008

Wolever TM, Gibbs AL, Mehling C, et al. The Canadian Trial of Carbohydrates in Diabetes (CCD), a 1-y controlled trial of low-glycemic-index dietary carbohydrate in type 2 diabetes: No effect on glycated hemoglobin but reduction in C-reactive protein. Am J Clin Nutr 2008; 87(1):114–25. http://www.ncbi.nlm.nih.gov/pubmed/18175744. Laufnummer: 22168	
Studiencharakteristika: long-term, multicenter, randomized controlled trial, n=162	
Objective	to compare the effects of altering the glycemic index or the amount of carbohydrate on glycated hemoglobin (HbA1c), plasma glucose, lipids, and C-reactive protein (CRP) in T2DM patients.
Population	T2DM managed by diet alone, 35–75 y old and had HbA1c ≤130%, BMI 24-40kg/m^2.
Die für unsere Fragestellung relevanten Endpunkte werden nicht untersucht und nicht berichetet. Antihyperglykämische Medikation war zu Studienbeginn ein Ausschlusskriterium und die Indikation zur medikamentösen Therapie während der Studie wurde als treatment failure gesehen und Patienten wurden von der Studie ausgeschlossen.	
Risk of bias Bewertung: in Korsmo-Haugen: unclear risk of bias.	

Facchini 2003

Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes 2003; 52(5):1204–9. DOI: 10.2337/diabetes.52.5.1204. http://www.ncbi.nlm.nih.gov/pubmed/12716753. Laufnummer: 31789	
Studiencharakteristika: randomized controlled trial, n=191, mean follow-up interval of 3.9 ± 1.8 years,	
Objective	To evaluate whether a carbohydrate-restricted, low-iron available, polyphenol-enriched (CR-LIPE) diet may delay and improve the outcome of diabetic nephropathy to a greater extent than standard protein restriction.
Population	T2DM with various degrees of renal failure and proteinuria (attributed to diabetes)
Intervention	**low-iron available, polyphenol-enriched (CR-LIPE) diet:** - 50% reduction of CHO - substitution of iron-enriched red meats (beef and pork) with iron-poor white meats (poultry and fish) and with protein-enriched food items known to inhibit iron absorption, e.g., dairy, eggs, and soy - elimination of all beverages other than tea, water, and red wine. Milk was recommended for breakfast. - exclusive use of polyphenol-enriched extra-virgin olive oil for both dressing and frying - - no other reductions then in CHO
Vergleich	**standard protein restriction diet:** (0.8 g/kg)
Outcomes	**outcomes monitored: doubling of serum creatinine, cumulative incidence of endstage renal disease, and all cause mortality.**

Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes 2003; 52(5):1204–9. DOI: 10.2337/diabetes.52.5.1204. http://www.ncbi.nlm.nih.gov/pubmed/12716753. Laufnummer: 31789	
Attrition	N=191, 21 patients lost to follow-up (CR-LIPE 9, Control 12), reasons: loss of insurance ot moving out of town
Statistics	Intention to treat

Baseline

	CR-LIPE (n=100)	**Control (n=91)**	**p-value**
Age (years	59 ±10	60 ± 12	ns
Sex (m/f)	53/47	48/43	ns
Diabetes duration (years)	9 ± 4	10 ± 5	ns
BMI (kg/m2)	28 ±5	28 ±5	ns
Hba1c (%)	7,6 ± 1,6	7,7 ±1,6	ns
GFR (ml/min)	64 ± 28	62 ± 32	ns
Proteinuria (mg/day)	2411 ± 2371	2533 ± 2488	ns

Ergebnisse: Use of medications in the two study groups

	Baseline	**2 years**	**4 years**
Insulin, n (%) CR-LIPE Control	 49 (49%) 46 (51%)	 41 (47%) 38 (51%)	 34 (47%) 26 (54%)
Metformin CR-LIPE Control	 6 (6%) 5 (5%)	 5 (6%) 5 (7%)	 5 (7%) 4 (8%)
Sulfonylurea	 23 (23%) 24 (26%)	 18 (20% 19 (25%)	 14 (19%) 10 (21%)

Ergebnisse (over follow-up intervall of 3,9 ± 1,8 years

	CR-LIPE	**Control**	
Doubling of serum creatinin concentration	19 (21%)	31 (39%)	P<0,01
Renal replacement therapy (RRT) or death	18 (20%)	31 (39%)	P <0,01
RRT and death	10 and 8	17 and 14	
Weight (kg)	Baseline 78 ± 15 Follow-up 76 ±14	Baseline 79 ± 16 Follow-up 78 ± 14	

Cox regression analysis between predictor and outcome variables:

	End Stage renal disease		**Death**	
	Hazard risk ratio	(95% CI)	Hazard risk ratio	(95% CI)
Not on CR-LIPE	1,32	(1,11-1,44)	1,44	(1,13-1,68)

Facchini FS, Saylor KL. A low-iron-available, polyphenol-enriched, carbohydrate-restricted diet to slow progression of diabetic nephropathy. Diabetes 2003; 52(5):1204–9. DOI: 10.2337/diabetes.52.5.1204. http://www.ncbi.nlm.nih.gov/pubmed/12716753. Laufnummer: 31789

Anmerkungen:
- Compliance and nutrient and energy intake were not estimated

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: high, Detection: unclear, Attrition: unclear/low, Reporting: unclear; Other biases: siehe Anmerkungen,
Sponsor: k. A. zum Einfluss eines Sponsors.

Risk of bias Bewertung: in Korsmo-Haugen: high risk of bias.

Yamada 2014

Yamada Y, Uchida J, Izumi H, et al. A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. Intern Med 2014; 53(1):13–9. DOI: 10.2169/internalmedicine.53.0861. http://www.ncbi.nlm.nih.gov/pubmed/24390522. Laufnummer: 31805

Studiencharakteristika: single centre, 6-month, comparative, two-arm, randomised, open-label trial, outpatient Clinic, Japan

Objective	to examine the effects of a non-calorie-restricted, low-carbohydrate diet in Japanese patients unable to adhere to a calorie-restricted diet		
Population	T2DM from outpatient clinic, who had recieved guidance regarding calorie restriction at least once, HbA1c level at enrolment 6.9-8.4%		
Studienablauf	consultations every 2 months from a registered dietician for six months - received diet instructions at every medical consultation		
Intervention	conventional calorie-restricted diet: - target calorie intake was defined based on the Japan Diabetes Society: total calorie intake (kcal) = ideal body weight (kg; =height (m) ×height (m) ×22) ×25 - recommendationscarbohydrates=50-60%, protein=1.0-1.2 g/kg (<20%), fat=<25%		
Vergleich	low-carbohydrate diet: total carbohydrate intake <130 g/day lower limit of carbohydrate intake to 70 g/day		
primary outcomes	HbA1c and body weight, secondary: also included effects 123ft he diets on the quality of life, the patients completed the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (13) and the Problem Areas In Diabetes (PAID) scale (14) at enrolment and at the end 123ft he study; hypoglycemia		
Attrition	100% completers		
Baseline	123ft he123a, 63.3±11.7 years; 50% women		
Change medication	During the study period, we did not change the medications, unless hypoglycaemia occurred.		
	LC diet, n=12	**Calorie restricted diet, n=12**	
Glucose lowering drugs, no (%) Baseline			
none	0 (0%)	0 (0%)	
Metformin	5 (41,7%)	1 (8,3%)	
Sulfonylurea	5 (41,7%)	8 (66,7%)	
Glinide	1 (8,3%)	0 (0%)	
Insulin	3 (25%)	4 (33,3%)	
Thiazolidinedione	4 (33,3%)	6 (50%)	
α-Glucosidase inhibitor	2 (16,7)	0 (0%)	

Yamada Y, Uchida J, Izumi H, et al. A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. Intern Med 2014; 53(1):13–9. DOI: 10.2169/internalmedicine.53.0861. http://www.ncbi.nlm.nih.gov/pubmed/24390522. Laufnummer: 31805

DPP-4-I	2 (16,7)	3 (25%)	
GLP-1-RA	0 (0%)	0 (0%)	

Three patients treated with a sulfonylurea or insulin in the low-carbohydrate group experienced symptomatic hypoglycaemia, although the events did not recur after adjusting the medications.
- Keine weiteren Angaben im Paper.

Ergebnisse

	LC diet n=12			**Calorie restricted diet, n=12**			
	Baseline	**6 months**	**p-value**	**Baseline**	**6 months**	**p-value**	p-value between groups
HbA1c (%)	7.6 ± 0.4	7.0 ± 0.7	0,03	7.7 ± 0.6	7.5 ± 1.0	0,45	0,03
Weight (kg)	67.0 ± 15.9	64.4 ± 14.2	0,62	68.1 ± 7.7	66.7 ±7.0	0,56	0,8
BMI (kg/m2)	24.5 ± 4.3	23.6 ± 3.5	0,39	27.0 ± 3.0	26.4 ±	0,42	0,86
DTSQ total score	24.0 ± 6.6	27.6 ± 5.7	0,23	21.6 ± 3.3	24.7 ± 4.5	0,07	0,95
DTSQ item 2: High BS	3.50 ± 1.68	2.42 ± 1.83	0,13	3.83 ± 0.94	3.67 ± 1.37	0,77	0,21
DTSQ item 3: Low BS	1.17 ± 1.90	1.42 ± 1.98	0,95	1.83 ± 1.53	1.75 ± 1.14	0,98	0,31
PAID score	42.1 ± 13.5	37.8 ± 11.3	0,37	57.8 ± 12.6	57.2 ± 11.9	0,98	0,64

DTSQ: Diabetes Treatment Satisfaction Questionnaire, BS: blood sugar, PAID: Problem Areas In Diabetes scale

Dietary adherence (Nutrition intage at 6 months)

	LC diet n=12		**Calorie restricted diet, n=12**		p-value
	Intake	Energy ratio (%)	intake	Energy ratie (%)	
Calorie intake(kcal)	1,634 ± 531	100	1,610 ± 387	100	0,84
Protein (g)	100.4 ± 36.6	25.3 ± 7.3	67.6 ± 21.2	16.6 ± 2.8	0,021
Carbohydrate (g)	125.7 ± 71.9	29.8 ± 12.5	202.9 ± 42.0	51.0 ± 4.6	0,008
Fat (g)	82.1 ± 33.0	45.4 ± 8.9	58.5 ± 20.7	32.3 ± 5.2	0,028

Anmerkungen:
- Kleine und kurze Studie
- Population: Japaner mit anderen Ernährungsgewohnheiten. Übertragbar auf Patiente*innen in Deutschland?
- Wenig Angaben zur Reduktion der Medikation (eher indirekt über Hypoglykämien gesenkt). Wie viele Hypoglykämien auftraten wird nicht bereichtet.

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: unclear, Allocation concealment: unclear, Performance bias: high, Detection: high, Attrition: low, Reporting: unclear; Other biases: siehe Anmerkungen,
Sponsor: k. A. zum Einfluss eines Sponsors.

Risk of bias Bewertung: in Goldenberg 2021: high risk / some concern, in Korsmo-Haugen 2019: high risk.

Mayer 2014

Mayer SB, Jeffreys AS, Olsen MK, et al. Two diets with different haemoglobin A1c and antiglycaemic medication effects despite similar weight loss in type 2 diabetes. Diabetes Obes Metab 2014; 16(1):90–3. DOI: 10.1111/dom.12191. http://www.ncbi.nlm.nih.gov/pubmed/23911112. Laufnummer: 31810

Einige Daten au: Yancy WS Jr. Westman EC, McDuffie JR, Grambow SC, Jeffreys AS, Bolton J, Chalecki A, Oddone EZ. A randomized trial of a low-carbohydrate diet vs orlistat plus a low-fat diet for weight loss. Arch Intern Med. 2010; 170:136–45. [PubMed: 20101008]

Studiencharakteristika: analysis of participants with type 2 diabetes (n=46) within a larger weight loss trial (n=146), intervention 48 weeks, Veterans Affairs clinics in Durham

Objective	to determine the glycemic, weight, and pertinent adverse effects weight-loss diet plans in patients with type 2 diabetes, and to compare the intensity of antiglycemic agent use.
Population	Adults, ≤70 years, BMI 27-30 kg/m^2 plus an obesity-related disease, or BMI ≥30 kg/m^2
Interventionen in beiden Gruppen	Both interventions included small group meetings (6 to 12 participants) at an outpatient clinic every 2 weeks for 24 weeks, then every 4 weeks for 24 weeks. All participants advised to exercise on their own for 30 minutes at least 3 times per week, take a multivitamin daily, drink 6 to 8 glasses of fluids daily, and minimize consumption of caffeine and alcohol.
Intervention	low-carbohydrate diet (LCD): initially carbohydrate intake ≤20g/day but calories not restricted. CH intake slowly liberalized if approached goal weight or cravings threatened adherence.
Vergleich	Low fat diet + Orlistat (LFD+O): restricted daily intake of total fat (<30% energy), saturated fat (<10% energy), cholesterol (<300mg), and calories (500-1000 kcal deficit), plus orlistat 120mg 3x/d.
Change of medication	In both arms, antiglycemic medications individually adjusted following algorithm to prevent hypoglycemia and minimize medications that hinder weight loss.
Primary outcomes	HbA1c, MES.
Baseline	mean BMI 39.5 kg/m^2 (SD 6.5) and HbA1c 7.6% (SD 1.3).
Attrition	Nicht berichtet, laut Analyse: n=46 (baseline), 37 patients (N=16 LCD; N=21 LFD+O) had complete data at 48 weeks. Gründe für fehlende Daten nicht benannt.

Baseline

	Low Carbohydrate Diet (n=22)	**Low Fat Diet + Orlistat (n=24)**	P value
Age, y, mean (SD)	56.6 (7.3)	54.7 (8.4)	0.43
Sex, male (n (%))	19 (86.4%)	21 (87.5%)	1.00
Duration of diabetes years, mean (SD)	5.9 (4.4)	7.3 (8.9)	0.80
Antiglycemic medication regimen			
Insulin +/− oral agents (n (%))	7 (31.8%)	8 (33.3%)	
Oral agents only (n, (%))	12 (54.6%)	14 (58.3%)	
No agents (n (%))	3 (13.6%)	2 (8.3%)	

Ergebnisse

	LCD		**LFD + Orlistat**		LCD –LFD+O, difference of change48 weeks (95%CI)	p-value
	Week 0	Week 48 (n=16)	Week 0	Week 48 (n=21)		
BMI	38.7	36.3	40.0	37.3	0.3 (−1.5, 2.2)	0.7
Body weight (kg)	116.9	109.4	125.1	117.0	0.6 (−5.4, 6.7)	0.8

Mayer SB, Jeffreys AS, Olsen MK, et al. Two diets with different haemoglobin A1c and antiglycaemic medication effects despite similar weight loss in type 2 diabetes. Diabetes Obes Metab 2014; 16(1):90–3. DOI: 10.1111/dom.12191. http://www.ncbi.nlm.nih.gov/pubmed/23911112. Laufnummer: 31810

% change Body weight	0	-6,7	0	-7,3	7 (−5.1, 6.4)	0.8
Hemoglobin A1C %	7.6	6.9	7.6	7.7	−0.8 (−1.6, −0.02)	0.045
Antiglycemic medication analysis						
Estimated MES*	1.78 (1.07, 2.47)	0.53 (0.06, 1.00)	2.13 (1.46, 2.80)	1.31 (0.89, 1.74)	−0.42 (−1.18, 0.33)	0.27
% Achieving 20% decrease in MES*		76.5%		56.5%		0.19
% Achieving 50% decrease in MES*		70.6%		30.4%		0.01

37 patients (N=16 LCD; N=21 LFD+O) had complete data at 48 weeks.

For diabetes medication, 1 of 16 LCKD participants (6%) had an increase and 13 (81%) had a decrease, while 1 of 22 O + LFD participants (5%) had an increase and 15 (68%) had a decrease (Yancy et al).

Dietary adherence

	LCD, n=11	**LFD+O, n=11**		
mean daily carbohydrate intake	75.9 g (SD = 76.9),	155.8 g (SD = 78.5)		
Total fat	103.2 g (SD = 58.1)	55.5 g (SD = 41.7)		
energy	1707.9 kcal/day (SD = 741.1)	1419.6 kcal/day (SD = 634.1).		

Medication effect score (MES): assessed overall utilization of antiglycemic agents. First, percentage of each medication's maximum daily dose was determined. Maximum daily dose of insulin was defined as 1 unit per kilogram of baseline weight, delineating insulin resistance (4). All daily insulin was summed. Next, the percentage of maximum daily dose for each medication was multiplied by an adjustment factor, and these products were summed 126ft he126 final MES. Adjustment factors were the reported median absolute decrease in HbA1c for each medication (2), e.g., for metformin and the sulfonylureas, the adjustment factor is 1.5; for insulin: 2.5.

Anmerkungen:
Subgruppenanalyse (Patienten mit Typ-2-DM) eines größeren Trials
- loss of power and multiplicity of testing
- characteristics of our sample (87% men, 54% black) limits generalizibility

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: high, Detection: high, Attrition: unclear, Reporting: unclear; Other biases: siehe Anmerkungen,
Sponsor: k. A. zum Einfluss des Sponsors.

Rock 2014

Rock CL, Flatt SW, Pakiz B, et al. Weight loss, glycemic control, and cardiovascular disease risk factors in response to differential diet composition in a weight loss program in type 2 diabetes: A randomized controlled trial. Diabetes Care 2014; 37(6):1573–80. DOI: 10.2337/dc13-2900. http://www.ncbi.nlm.nih.gov/pubmed/24760261. Laufnummer: 31809

Studiencharakteristika: randomized controlled trial at two university medical centers (San Diego, Menneapolis), n= 227, 1 year intervention

Population	overweight or obese adults (≥18years) with type 2 diabetes; BMI 25–45 kg/m^2 - Ausschluss HbA1c >11%
Intervention	Commercial weight loss programm arms: - Inperson diet and exercise counseling, prepackaged foods in planned menu during initial phase. Weekly counseling visits during first 9 months, thereafter biweekly or monthly consultations - reduced in energy relative to expenditure (typically 1,200–2,000 kcal/day) - physical activity encouraged 30 min of physical activity on ≥5 days/week

Rock CL, Flatt SW, Pakiz B, et al. Weight loss, glycemic control, and cardiovascular disease risk factors in response to differential diet composition in a weight loss program in type 2 diabetes: A randomized controlled trial. Diabetes Care 2014; 37(6):1573–80. DOI: 10.2337/dc13-2900. http://www.ncbi.nlm.nih.gov/pubmed/24760261. Laufnummer: 31809

	Entweder: - Higher carbohydrate, lower fat (LF) diet (carbohydrate 60%E, fat 20%E, protei 20%E - lower carbohydrate,higher fat (LC) diet (carbohydrates 45%E, fat 30%E, protein 25%E)
Vergleich	to usual care (UC; two weight loss counseling sessions and monthly contacts). Deficit of 500–1,000 kcal/day to achieve a weight loss of 10% of initial weight. Recommended: (20–35% [average 30%] of energy from fat, 45– 65% [average 55%] from carbohydrates, and 10–35% [average 15%] from protein)
primary outcomes	Weight change
Statistics:	ITT with baseline substitution for missing data
Attrition	Primary outcome data were obtained at study end from 90%of the participants who were randomized. Attrition did not differ by study Group.

Ergebnisse

	LF		**LC**		**UC**	
Mean (SD)	Baseline	12month	Baseline	12 months	Baseline	12 months
Weight (kg)	105.4 (17.8)	97.7 (18.0)	106.4 (18.3)	96.7 (19.7)	104.6 (16.9)	101.9 (17.4) P=0,005
Weight change (%)		-7.4 (7.6)		-9.0 (8.4)		-2.5 (5.5) P<0,001
BMI (kg/m2)	36.2 (4.3)	33.5 (4.7)	36.2 (4.7)	33.0 (5.5)	36.3 (4.4)	35.4 (4.6) P=0,001
Beck Depression Inventory	7 (6)	4 (4)	6 (5)	5 (7)	7 (6) P=0,95	6 (7) P=0,28
SF-36 physical	78 (15)	82 (15)	80 (15)	80 (21)	80 (15) P=0,70	80 (16) P=0,52
SF-36 mental	80 (16)	82 (14)	79 (17)	74 (20)	82 (16) P=0,44	80 (18) P=0,72
HbA1c (%)	7.5 (1.2)	7.2 (1.5)	7.3 (1.4)	6.6 (1.0) P<0,05 compared to LF	7.4 (1.1)	7.5 (1.5) P<0,01

P values for differences between UC and aggregated weight loss program participants, Becks Depression inventory, SF-36, 36-item short form health survey quality-of-life questionnaire.

Medication use and change in medication use during study

	LF	**LC**	**UC**	P value
Insulin	Baseline: 19 Stopped/decreased: 12 (63%) Started/ increased: 2 (10%)	Baseline 10 Stopped/decreased: 9 (90%) Started increased: 0	Baseline: 12 Stopped/decreased: 1 (8%) Started increased: 3 (25%)	<0,001
Oral hypoglycemic	Baseline: 62 Stopped/decreased: 24 (39%) Started/increased: 6 (10%)	Baseline: 69 Stopped/decreased: 22 (31%) Started/increased: 6 (9%)	Baseline: 62 Stopped/decreased: 10 (16%) Started/increased: 8 (13%)	0,007

P values for differences between UC and aggregated weight loss program participants

Dietary adherence: self reported dietary data: Daten werden nicht gezeigt.

Rock CL, Flatt SW, Pakiz B, et al. Weight loss, glycemic control, and cardiovascular disease risk factors in response to differential diet composition in a weight loss program in type 2 diabetes: A randomized controlled trial. Diabetes Care 2014; 37(6):1573–80. DOI: 10.2337/dc13-2900. http://www.ncbi.nlm.nih.gov/pubmed/24760261. Laufnummer: 31809

Anmerkungen:
- Participants were reimbursed $25 for each data collection clinic visit, with incremental increases
- Participants in the commercial weight loss programms arms: free of charge programm and food
- Self-reported medication use
- Self reported dietary data, Daten werden nicht gezeigt, kein Rückschluss auf dietary adherence möglich.

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: unclear, Performance bias: high, Detection: high, Attrition: unclear / low, Reporting: unclear; Other biases: siehe Anmerkungen,
Sponsor: The sponsor contributed to the development of the design and protocol through discussions with the investigators during the development phase of the study. The funding sponsor had no role in the conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript (except for verifying the specific weight loss program activities that comprised the intervention); and decision to submit the manuscript for publication.

Pohl 2005

Pohl M, Mayr P, Mertl-Roetzer M, et al. Glycaemic control in type II diabetic tube-fed patients with a new enteral formula low in carbohydrates and high in monounsaturated fatty acids: A randomised controlled trial. Eur J Clin Nutr 2005; 59(11):1221–32. DOI: 10.1038/sj.ejcn.1602232. http://www.ncbi.nlm.nih.gov/pubmed/16077745. Laufnummer: 31806

Abstract:
Objectives: To investigate the effects of long-term treatment with a new enteral formula low in carbohydrates and high in monounsaturated fatty acids (MUFAs), in comparison with a standard formula, on glycaemic control in tube-fed type II diabetic patients.

Design: Randomised, double-blind, controlled, multi-centre trial.
Setting: Early rehabilitation centres, primary care and nursing facilities.

Subjects: A total of 78 patients with insulin-treated type II diabetes with HbA1C Z7.0% and/or fasting blood glucose 46.66 mmol/l, who required enteral tube feeding due to neurological dysphagia.

Interventions: Patients received 113 kJ (27 kcal)/kg of body weight of either test feed or an isoenergetic, isonitrogenous enteral formula (control) for 12 weeks. Glycaemic control (total daily insulin dosage (IU), fasting blood glucose, and HbA1C) and gastrointestinal tolerance were monitored daily.

Results: After 12 weeks, median values for changes from baseline were as follows (test group vs control group, 'data as available' analysis): total daily IU -6.0 vs 0.0 (P=0.0024), fasting blood glucose (mmol/l) -1.59 vs -0.08 (P=0.0068); HbA1C (%) -0.8 vs 0.0 (P=0.0016). Both formulas were tolerated comparably.

Conclusions: This study indicates that in tube-fed insulin-treated type II diabetic patients, the new low-carbohydrate, high MUFA formula results in a more effective glycaemic control than the standard diet, while being comparable in safety.

Stage 1 der Studie von Pohl et al 2009 (#31807)
Frage ÄZQ: Population und Interventino relevant für NVL? „Proof of concept"

SR zu diesem Thema, der die Arbeiten von Pohl et al einschließt: Ojo O. The Effect of Diabetes-Specific Enteral Nutrition Formula on Cardiometabolic Parameters in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. Nutrients 2019; 11(8):1905. https://www.ncbi.nlm.nih.gov/pubmed/31443185. (in der systematischen Recherche zu Formula-Diäten identifiziert)

Pohl 2009

Pohl M, Mayr P, Mertl-Roetzer M, et al. Glycemic control in patients with type 2 diabetes mellitus with a disease-specific enteral formula: Stage II of a randomized, controlled multicenter trial. JPEN J Parenter. Enteral Nutr 2009; 33(1):37–49. DOI: 10.1177/0148607108324582. http://www.ncbi.nlm.nih.gov/pubmed/19011146. Laufnummer: 31807

Abstract:
Background: Stage I of a preplanned 2-stage study has provided good evidence for improved glycemic control with a diseasespecific enteral formula low in carbohydrates and high in monounsaturated fatty acids (MUFAs), fish oil, chromium, and antioxidants in insulin-treated type 2 diabetes. The study was continued with stage II to give confirmatory proof of these beneficial effects.

***Methods*:** 105 patients with HbA1C ≥ 7.0% and/or fasting blood glucose (FG) > 6.7 mmol/L (>120 mg/dL) requiring enteral tube feeding due to neurological dysphagia received 113 kJ (27 kcal)/kg body weight of either test formula (Diben) or an isoenergetic, isonitrogenous standard formula (control) for up to 84 days. Total insulin (TI) requirements, FG, and afternoon blood glucose (AG) were assessed daily. HbA1C and safety criteria were evaluated on days 1, 28, 56, and 84.

Results: 55 patients completed the study; on day 84, median changes from baseline (data as available, test vs control) were the following: TI, −8.0 vs +2.0 IU; FG, −2.17 vs −0.67 mmol/L (−39.0 vs −12.1 mg/dL); HbA1C, −1.30% vs −1.20%; AG, −2.36 vs −0.49 mmol/L (−42.5 vs −8.9 mg/dL). The number of relevant hypoglycemic episodes (FG < 3.33 mmol/L < 60 mg/dL) was 1 vs 5. Feeding tolerance was comparable in both groups.

***Conclusions*:** Long-term tube feeding with a disease-specific enteral formula was safe and well tolerated in type 2 diabetic patients with neurological disorders. When compared with a standard diet, TI requirement decreased significantly with less hypoglycemia whereas FG and AG were significantly lowered, resulting in improved glycemic

Stage 2 der Studie von Pohl et al 2005 (#31806)
Frage ÄZQ: Population und Intervention relevant für NVL? „Proof of concept“

SR zu diesem Thema, der die Arbeiten von Pohl et al einschließt: Ojo O. The Effect of Diabetes-Specific Enteral Nutrition Formula on Cardiometabolic Parameters in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. Nutrients 2019; 11(8):1905. https://www.ncbi.nlm.nih.gov/pubmed/31443185.
(in der systematischen Recherche zu Formula-Diäten identifiziert)

Saslow 2014

Saslow LR, Kim S, Daubenmier JJ, et al. A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese individuals with type 2 diabetes mellitus or prediabetes. PloS one 2014; 9(4):e91027. DOI: 10.1371/journal.pone.0091027. http://www.ncbi.nlm.nih.gov/pubmed/24717684. Laufnummer: 31812

Studiencharakteristika: single site, parallel-group, balanced randomization (1:1) trial, n=34, 3 months, recruited from the community and from local health organizations through advertising and announcements, San Francisco, California (UCSF), Pilot study

Objective	trial was aimed in part at comparing the effects of each diet on glycemic control, an important goal was to test the feasibility of our research design for conducting a larger scale, longer-term trial to more definitively address the limitations of prior research studies.
Ablauf der Studie	Participants attended 13 2-hour classes that met weekly, including - instruction on their assigned diet, - discussing the importance of sleep and exercise. - a break during which snacks were provided appropriate 129ft he assigned diet. - focus on learning skills to support behavior change and diet maintenance. - participants were asked to practice a guided meditation 10 minutes per day at least three times a week using audio CDs recorded 129ft he129 intervention; - psychological skills training hour was led by psychologist with experience teaching mindfulness and health behavior change
Intervention	LCK (low carbohydrate, ketogenic) diet - classes taught by author experienced in using the low carbohydrate dietary approach. - carbohydrate intake between 20–50 grams of carbohydrates a day, not including fiber (referred to as net grams of carbohydrates), with goal of achieving nutritional ketosis (blood beta-hydroxybutyrate level between 0.5 and 3 mM, as measured twice a week) - keep protein levels as they were before, as long as meeting the minimum amount suggested - remaining calories from fat
Vergleich	MCCR (moderate carbohydrate, calorie-restricted) diet representative of conventional diabetic diet recommendations - classes taught by registered dietician - 45% to 50% of calories from carbohydrates - ≈165 grams of carbohydrates a day. - protein levels about the same as before

Saslow LR, Kim S, Daubenmier JJ, et al. A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese individuals with type 2 diabetes mellitus or prediabetes. PloS one 2014; 9(4):e91027. DOI: 10.1371/journal.pone.0091027. http://www.ncbi.nlm.nih.gov/pubmed/24717684. Laufnummer: 31812

	- lower fat consumption. - -500 kilocalories (kcal) per day than calculated maintenance needs	
Population	≥18 years, T2DM, HbA1c ≥6.5% or prediabetes (HbA1c > 6.0%), BMI ≥25kg/m2 - Exclusion: currenttly using insulin or taking >3 hypoglycemic medications	
primary outcomes	change in glycated hemoglobin (HbA1c) from baseline to 3 months	
Change in medication	Medication management algorithm when starting LCK diet: - metformin continued for duration of study unless participant or his/her doctor requested it be lowered, (reducing dose 50% or discontinue completely); - sulfonylurea: entry HbA1c <7.5%: doses -50% (or discontinued if minimum dose); sulfonylurea discontinued if predinner glucose levels < 110 mg/dL despite prior dose reduction; - thiazolidinediones: continued if starting HbA1c> 7% and discontinued if starting HbA1c > 7%.	
Statistics	ITT-Analyse	
Attrition	MCCR Allocated: n=18, recieved allocated treatment, n=17 Analysed: ITT n=18, participant who moved away did most follow-up tests	LCK Allocated: n=16 recieved allocated treatment, n=15 Analysed: ITT n=15, participant who moved away did not do follow-up tests

Baseline

4 participants had prediabetes (HbA1c.6.0% but ,6.5% and on no diabetes medications): MCCR group (3), LCK group (1).

Baseline Data

Means (SD)	**LCK, n=16, 15 with T2DM**	**MCCR, n=18, 15 with T2DM**	
Age (years)	64.8 (7.7)	55.1 (13.5)	
Female	9 (56.3%)	16 (88.9%)	
BMI >30	11 (69%)	15 (83%)	
No diabetes medication use	4 (25%)	5 (28%)	
Use of Metformin only	5 (31%)	8 (44%)	
Use of metformin and another oral antidiabetic agent	7 (44%)	5 (28%)	

Dietary adherence

Means and SD	**LCK**			**MCCR**			**MD (LCK-MCCR)**	**95% CI**
	0 months	**3 m**	**Mean difference**	**0 m**	**3m**	**MD**		
Kilocalories	2,390.6 (1,542.7)	1,693.7 (569.1)	-696.9	2,172.9 (784.1)	1,380.8 (527.6)	-792.1 P<0,01	95.2	[-749.2 to 939.6]
Net carbohydrates (carbs-fiber, g)	208.9 (100.6)	57.8 (41.5)	-151.0, P<0,01 within group	207.8 (77.3)	138.5 (54.7)	-69.3 P<0,05	-81.7, p<0,05	[-156.0 to -7.5]
Net CH (% of total kilocalories)	38.1 (11.8)	14.4 (11.9)	-23.7, P<0,01 within group	39.5 (12.0)	40.7 (9.3)	1.2	-24.9, p<0,01	[-35.7 to -14.1]

Saslow LR, Kim S, Daubenmier JJ, et al. A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese individuals with type 2 diabetes mellitus or prediabetes. PloS one 2014; 9(4):e91027. DOI: 10.1371/journal.pone.0091027. http://www.ncbi.nlm.nih.gov/pubmed/24717684. Laufnummer: 31812								
Proteil (% of total kilocalories)	19.9 (5.8)	24.2 (6.1)	4.3	18.8 (7.8)	20.5 (6.8)	1.6,	2.6	[-4.7 to 10.0]
Fat (% of total kilocalories)	37.6 (11.3)	58.0 (8.6)	20.4, P<0,01 within group	38.9 (11.2)	35.1 (8.7)	-3.9,	24.2, p<0,01	[15.1 to 33.4]
Ergebnisse								
	LCK			**MCCR**			**MD (LCK-MCCR)**	**95% CI**
	0 m	3 m	MD	0 m	3 m	MD		
HbA1c (%)	6.6 (0.3)	6.0 (0.3)	-0.6, p<0,01	6.9 (0.7)	6.9 (1.1)	0.0	-0.6, p<0,05	[-1.1 to -0.03]
Weight (kg)	100.1 (26.4)	94.6 (23.3)	-5,5, p<0,01	99.7 (24.2)	97.1 (23.3)	-2,6, p<0,05	-2,9	[-6.3 to 0.5]
BMI (kg/m2)	36.2 (8.2)	34.3 (7.4)	-1,9, p<0,01	37.4 (6.4)	36.4 (6.4)	-0,9, p<0,05	-1,0	[-2.2 to 0.2]
Diabetes Distress	1.8 (0.5)	1.3 (0.6)	-0,5, p<0,01	2.3 (0.9)	2.1 (0.8)	-0,2	-0,3	[-0.8 to 0.2]
For Information on CES-D Depression, CES-D Positive Affect and other outcomes, see original article								
no episodes of clinically evident hypoglycemia in study,								
Change in medication (participants taking diabetes medication at baseline)								

LCK, n=16, 15 with T2DM,			**MCCR, n=18, 15 with T2DM,**		
Participant	**0 month daily dose**	**3 months daily dose**	**participant**	**0 month daily dose**	**3 months daily dose**
1	Glimepiride 4 mg Actos 15 mg Exenatide 5 mg twice a day Metformin 1000 mg twice a day	Unknown (dropped out of study)	**1**	Metformin 500 mg	**No change**
2	Metformin 500 mg twice a day	**No change**	**2**	Metformin 500 mg twice a day	**No change**
3	Metformin 850 mg twice a day	**No change**	**3**	Metformin 500 mg twice a day	**No change**
4	Metformin 1000 mg twice a day	**No change**	**4**	Metformin 500 mg twice a day	**No change**
5	Metformin 2000 mg	**No change**	**5**	Metformin 500 mg twice a day	**No change**
6	Metformin 500 mg	**Metformin discontinued**	**6**	Metformin 1000 mg twice a day	**No change**
7	Glyburide 2.5 mg twice a day Metformin 1000 mg twice a day	Glyburide and Metformin discontinued	**7**	Metformin 1000 mg twice a day	**No change**
8	Glipizide 2.5 mg Metformin 1000 mg twice a day	Glipizide discontinued	**8**	Glipizide 10 mg Metformin 1000 mg twice a day	**No change**

Saslow LR, Kim S, Daubenmier JJ, et al. A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese individuals with type 2 diabetes mellitus or prediabetes. PloS one 2014; 9(4):e91027. DOI: 10.1371/journal.pone.0091027. http://www.ncbi.nlm.nih.gov/pubmed/24717684. Laufnummer: 31812

9	Glipizide 5 mg Metformin 1000 mg twice a day	Glipizide discontinued	**9**	Glimepiride 8 mg Januvia 1000 mg twice a day Metformin 50 mg twice a day	**No change**
10	Glyburide 2.5 mg twice a day Metformin 500 mg	Glyburide discontinued	**10**	Glipizide 2.5 mg twice a day Metformin 1000 mg twice a day	**No change**
12	Januvia 50 mg Metformin 1000 mg twice a day	Januvia discontinued	**11**	Glipizide 5 mg Metformin 2000 mg Januvia 50 mg	**No change**
13	Glyburide 2.5 mg Januvia 100 mg Metformin 1000 mg twice a day	Glyburide and Januvia discontinued	**12**	Metformin 850 mg 3 times a day	Metformin lowered to 500 mg twice a day
			13	Glipizide 5 mg Metformin 500 mg twice a day Acarbose 50 mg three times a day	Glipizide discontinued

Anmerkungen: Patients were paid $25 for completing
- Pilot-study, no power-calculation
- Patienten mit Diabetes und Prädiabetes gemeinsam betrachtet.

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: low, Performance bias: high, Detection: high, Attrition: unclear, Reporting: unclear; Other biases: siehe Anmerkungen,
Sponsor: The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Risk of bias Bewertung: in Goldenberg 2021: low.

Carter 2018

Carter S, Clifton PM, Keogh JB. Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial. JAMA Netw Open 2018; 1(3):e180756. DOI: 10.1001/jamanetworkopen.2018.0756. http://www.ncbi.nlm.nih.gov/pubmed/30646030. Laufnummer: 31771

Andere Zitate zu dieser Studie:
Carter et al, 2019; http://www.ncbi.nlm.nih.gov/pubmed/30902672; Laufnummer: 31772, 24-month follow up
Carter e al, 2016; http://www.ncbi.nlm.nih.gov/pubmed/27833048; Laufnummer: 31770 (Pilot-Study zu diesem RCT)

Studiencharakteristika: Randomized Noninferiority Trial, N = 137, south australia, 12 months intervention, Participants recruited using flyers posted in public places and via advertisements in print and broadcast media.

Objective	Compare effects of intermittent energy restriction (2 days per week) with continuous energy restriction on glycemic control and weight loss in patients with T2DM during a 12-month period
Population	≥18 years, T2DM, overweight or obese (BMI ≥27 kg/m^2)
Studienablauf	- written dietary information (portion advice, sample menus); no food or meal replacements provided. - Dietitian appointments every 2 weeks for first 3 months and every 2 to 3 m for final 9 m - Participants encouraged to increase their step count by 2000 from baseline - both groups: similar dietary energy restrictions (per week) recommended
Intervention	intermittent energy restriction (IRG) (500-600 kcal/d, ≥50g Protein/day) followed for 2 nonconsecutive days per week (usual diet for other 5 days)
Vergleich	continuous energy restriction (1200-1500 kcal/d, 30% protein, 45% carbohydrate, 25% fat)) followed for 7 days/week for 12 months.
Primärer Endpunkt	Noninferiority: Change in HbA1c (90% CI margin of ±0.5%) Secondary: weight loss (equivalence set at ±2.5 kg (±1.75 kg for fat mass loss and ±0.75 kg for fat-free mass loss) All other outcomes were tested for superiority.

Carter S, Clifton PM, Keogh JB. Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial. JAMA Netw Open 2018; 1(3):e180756. DOI: 10.1001/jamanetworkopen.2018.0756. http://www.ncbi.nlm.nih.gov/pubmed/30646030. Laufnummer: 31771

Baseline	77 women and 60 men; mean [SD] age, 61.0 [9.1] years; BMI 36.0 [5.8], HbA1c level, 7.3%[1.3%]),
Attrition	97 completed the trial.
Statistics	ITT analysis, effects did not differ using completers analysis Hierarchische Testung: Nicht-Unterlegenheit für Change in HbA1c und weight loss, alle anderen Endpunkte explorativ als test auf Überlegenheit
Change in Medication	Medications reduced at baseline according to medication management protocol, which was modified, after 38th patient commenced new protocol: - HbA1c < 7% (all patients) discontinuation sulfonylureas and insulin - HbA1c > 7% < 10%: sulfonylureas and insulin discontinued on intermittent energy restriction (IER) days only, long-acting insulin discontinued night before IER. - Medications could be reduced in the continuous energy restriction diet group depending on dose, at the endocrinologist's discretion. - HbA1c level >10%, sulfonylurea: unchanged, long-acting insulin decreased 10 units on IER days only.

Baseline (Mean (SD) value)

	Continuous energy restriction group (CRG), n=67	Intermittent energy restriction group (IRG), n=70	All participants (n=137)	Participants who completed study (n=97)	Participants Who Did Not Complete Study (n = 40)
Age, y	61.0 (9.2)	61.0 (9.0)	61.0 (9.1)	62.0 (8.8)	59.0 (9.6)
Female (%)	38 (56.7)	39 (55.7)	77 (56.2)	48 (49.5)	29 (72.5)
Duration of diabetes, y	8.1 (6.5)	7.9 (5.9)	8.0 (6.2)	7.9 (6.2)	8.3 (6.2)
Weight, kg	102 (17)	100 (19)	101 (18)	100 (17)	103 (19)
HbA1c	7.5 (1.4)	7.2 (1.2)	7.3 (1.3)	7.1 (1.2)	7.8 (1.4)
Medication effect score					
OHA	1.4 (0.8)	1.3 (0.8)	1.4 (0.8)	1.3 (0.8)	1.4 (0.7)
Insulin	1.5 (1.1)	1.8 (1.1)	1.6 (1.1)	1.5 (0.9)	2.1 (1.6)
total	1.8 (1.1)	1.7 (1.3)	1.8 (1.2)	1.7 (1.2)	1.8 (1.1)

Daten zu den einzelnen Wirkstoffgruppen (siehe Originalartikel)

Ergebnisse (Outcomes From Baseline to 12 ms for Intermittent vs Continuous Groups (Intention-to-Treat Analysis))

	Mean (SEM) [95%CI]	P value over time	CRG, mean (SEM) [95%CI]	IRG, mean (SEM) [95% CI]	P for diet by time
HbA1c, %	−0.4 (0.1) [−0.6; −0.2]	<0,001	−0.5 (0.2) [−0.8; −0.2]	−0.3 (0.1) [−0.6; −0.08]	0,65
Weight, kg	−5.9 (0.6) [−7.1; −4.8]	<0,001	−5.0 (0.8) [−6.6; −3.5]	−6.8 (0.8) [−8.5; −5.1]	0,25
Medication effect score					
Total mean (SEM) MES	(–0.5 [0.1])	*P* <.001	–0.3 [0.1]	–0.6 [0.1]	0,11

Carter S, Clifton PM, Keogh JB. Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial. JAMA Netw Open 2018; 1(3):e180756. DOI: 10.1001/jamanetworkopen.2018.0756. http://www.ncbi.nlm.nih.gov/pubmed/30646030. Laufnummer: 31771

Mean MES (SEM) for oral hypoglycemic agents	(–0.3 [0.1])	*P* < .001	(–0.2 [0.1])	–0.3 [0.1]	0,45
Mean MES (SEM) for insulin			(–0.3 [0.1])	–1.2 [0.2]	0,006

SEM: Standard Error of Mean, MES: medication effect score (calculated as (actual drug dose/maximum drug dose) × drug mean adjustment factor. Higher MES corresponded to higher dose of diabetes medication, and reduction in MES corresponded to reduction in diabetes medication.
- no significant differences between groups in total medication effect score at 12 months.

Overall compliance to both diets during the first 3 months of treatment (90% CER and 97% IER; *P* = .21), after which the compliance rates decreased in both groups (49% CER group and 44% in IER group; *P* = .62).

Glycemic events (Hypoglycaemia, hyperglycaemia):
- 35% (16/46) of participants using sulfonylureas and/or insulin experienced glycemic events (the mean [SEM] number of events was 3.2 [0.7] in the continuous energy restriction group and 4.9 [1.4] in the intermittent energy restriction group; *P* = .28) in the first 2 weeks of treatment.
- 8/46 (17%) hypoglycemia (2 CRG, 6 IRG): mean [SEM] number of events, 2.4 [0.6]) no differences between groups (2.0 [1.0] CRG vs 2.5 [0.8] IRG; *P* = .74), All participants who experienced hypoglycemic events either reported events before starting treatment or were unsure.
- 22% (10/46) hyperglycemia (3 in CRG and 7 in IRG) in the first 2 weeks (mean [SEM] number of events, 5.1 [1.4]), no difference between groups (the mean [SEM] number of events was 4.0 [0.6] in the CRG vs 5.6 [2.0] in the IRG; *P* = .47).

Anmerkungen:
- Participants received an A$25 (US $19) voucher at 3 and 12 months to thank them for their participation; participants were not aware that they would receive a voucher.
- Medication Algorithm wurde während der Studie angepasst (nach 38. Patient).

24 month follow-up (12 months after intervention):
- N=137 recruited (110%), 97 completed 12 months intervention (71%), 84 were followed up at 24 months (61%).
- Loss to follow up not different between groups (p=0,86)
- HbA1c increasing above baseline levels in both groups

Outcomes by timepoint and change from baseline to 24 months for intermittent vs. Continuous groups (ITT-Analysis)

	Mean (SEM)			P value for time	MEAN (SEM) [95% CI]		P value for diet by time
	Baseline	12m	24m		CER	IER	
HbA1c, %	7,3 (0,1)	6,9 (0,1)	7,6 (0,2)	<0,001	0,4 (0,3) [-0,2; 0,9]	0,1 (0,2) [-0,3; 0,5]	0,32
Weight, kg	101 (1,2)	95 (1,5)	97 (1,5)	<0,001	-3,9 (1,1) [-6; -1,7]	-3,9 (1,1) [-6,1; -1,7]	0,19
MES OHA	1,4 (0,1)	1,1 (1,0)	1,1 (0,1)	<0,001	-0,2 (0,1) [-0,4; 0,03]	-0,2 (0,1) [-0,5; -0,01	0,49
MES Insulin	1,7 (0,2)	0,9 (0,2)	1,2 (0,2)	<0,001	-0,2 (0,1) [-0,5; 0,02]	-0,6 (0,2) [-1,2; -0,1]	0,002
MES Total	1,8 (0,2)	1,3 (0,1)	1,4 (0,1)	<0,001	-0,2 (0,1) [-0,5; 0,1]	-0,4 (0,2) [-0,7; -0,1]	0,15

- increase in mean [SEM] HbA1c level at 24 months in both the continuous and intermittent groups (0.4% [0.3%] vs 0.1% [0.2%] respectively; P = 0.32) (4.4 [3.3 mmol/mol] vs 1.1 [2.2 mmol/mol]; P = 0.32), with a between-group difference of 0.3% (90% CI, -0.31 to 0.83%) (3.3 mmol/mol [90% CI, -3.2 to 9.1 mmol/mol]) outside the prespecified boundary of ± 0.5% (5.5 mmol/mol), so statistical equivalence was not shown.
Weight loss was maintained (P < 0.001) at -3.9 kg [1.1 kg] in both groups at 24 months, with a between-group difference of 0.07 kg (90% CI, -2.5 to 2.6 kg) outside the prespecified boundary of ±2.5 kg.
- no significant differences between groups in total medication effect score at 24 months. MES for Insulin change was significantly different between groups at 24 months.

Carter S, Clifton PM, Keogh JB. Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial. JAMA Netw Open 2018; 1(3):e180756. DOI: 10.1001/jamanetworkopen.2018.0756. http://www.ncbi.nlm.nih.gov/pubmed/30646030. Laufnummer: 31771

Weitere Zitate zu dieser Studie

Carter S, Clifton PM, Keogh JB. The effect of intermittent compared with continuous energy restriction on glycaemic control in patients with type 2 diabetes: 24-month follow-up of a randomised noninferiority trial. Diabetes Res Clin Pract 2019; 151:11–9. DOI: 10.1016/j.diabres.2019.03.022. http://www.ncbi.nlm.nih.gov/pubmed/30902672.
Laufnummer: 31772

Carter S, Clifton PM, Keogh JB. The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. Diabetes Res Clin Pract 2016; 122:106–12. DOI: 10.1016/j.diabres.2016.10.010. http://www.ncbi.nlm.nih.gov/pubmed/27833048.
Laufnummer: 31770 (Pilot-Study zu diesem RCT)

RoB-Bewertung der Studie (ÄZQ): Selektion: Randomization: low, Allocation concealment: high, Performance bias: high, Detection: unclear / high, Attrition: unclear, Reporting: unclear; Other biases: Incentives für Teilnehmende, Algorithmus zur Anpassung der Medikation während der laufenden Studie geändert,
Sponsor: The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Risk of bias Bewertung: in Allaf 2021: Ris of bias: high: allocation concealment, Performance and Attrition bias; low: Random sequence generation and other bias; unclear: Detection bias and reporting bias.

Carter 2016

Carter S, Clifton PM, Keogh JB. The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. Diabetes Res Clin Pract 2016; 122:106–12. DOI: 10.1016/j.diabres.2016.10.010. http://www.ncbi.nlm.nih.gov/pubmed/27833048. Laufnummer: 31770

Studiencharakteristika: Pilot study, parallel randomized controlled trial, N = 63, south australia, 12 weeks intervention, Participants recruited using flyers posted in public places and via advertisements in media.

Objective	Compare effects of intermittent energy restriction (2 days per week) with continuous energy restriction on glycemic control and weight loss in patients with T2DM
Population	≥18 years, T2DM, overweight or obese (BMI ≥27 kg/m^2)
Studienablauf	- written dietary information (portion advice, sample menus); no food or meal replacements provided. - Dietitian appointments every 2 weeks for 12 weeks
Intervention	intermittent energy restriction (IRG) 1670-2500kJ/d followed for 2 nonconsecutive days per week (usual diet for other 5 days)
Vergleich	continuous energy restriction (5000-6500kJ/d) followed for 7 days/week.
Primärer Endpunkt	Change in HbA1c (Secondary including: weight loss, change in body composition, daily step count, appetite markers
Baseline	*77 women and 60 men; mean [SD] age, 61.0 [9.1] years; BMI 36.0 [5.8], HbA1c level, 7.3%[1.3%]),*
Attrition	51/63 (81%) completed 12-week intervention, Allocated CER n=32, discontinue intervention n=7 Allocated IER n=31, discontinue intervention n=5
Statistics	ITT analysis
Change in Medication	HbA1c <8% discontinue any OHA, that may cause hypoglycemia Insulin: reduce dose -10units/day in CER-group, or -50% on ER-days in IER group. HbA1c >8%, oHA remained the same, Insulin dose decreased by 5-10 units on ER days (IER group) Medication protocol changed midway through study due to poorly controlled blood glucose levels (siehe auch Carter et al 2018)

Baseline (Mean (SD) value)

	Continuous energy restriction group (CRG), n=32	**Intermittent energy restriction group (IRG), n=31**

Carter S, Clifton PM, Keogh JB. The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. Diabetes Res Clin Pract 2016; 122:106–12. DOI: 10.1016/j.diabres.2016.10.010. http://www.ncbi.nlm.nih.gov/pubmed/27833048. Laufnummer: 31770		
Age, y	62 ±9.1	61 ±7,5
Male/Female	16/16	14/17
Diagnosis, y	9,2 ±6,6	8,3 ±5,8
Weight, kg	99 ±15	99 ±16
HbA1c	7.5 ±1,4	7.2 ±1,3
MES for OHA	1,5 ± 0,8	1,2 ±0,7
MES for Insulin	1,5 ±1,1	2,4 ± 1,2
Total MES for OHA & insulin	1,9 ±1,2	1,6 ±1,1

Change in MEedication effect score and other outcomes

MES	Time	CER (n=18)	IER (n=20)	P value by time	P value time by treatment
MES for OHA	-0,3 ± 0,5	-0,4 ±0,6	-0,2 ± 0,4	0,001	0,3
MES for Insulin	-0,5 ±0,5	-0,3 ±0,5	-0,9 ±0,4	0,006	0,06
Total MES	-0,4 ±0,5	-0,4 ±0,6	-0,4 ± 0,5	<0,001	0,7

Daten zu den einzelnen Wirkstoffgruppen (siehe Originalartikel)

	Time	**CER**	**IER**	**P value by time**	**P value by treatment**
HbA1c change	-0,7 ±0,9	-0,8 ±1	-0,6 ±0,8	<0,001	0,3
HbA1c change (ITT)	-0,5 ±0,9	-0,6±1,0	-0,5 ±0,8	<0,001	0,7
Weight change	-5,9 ±4%	-5,6 ±4,4	-6,2 ±3,6	<0,001	0,6

Anmerkungen:
- Pilot trial, low study numbers limit generalisability
- Change in medication protocol

Griffiths 2016

Griffiths C, Overland J, Sainsbury A, Little T, Franklin J, Gibson A, et al. Intermittent fasting: appears an eLective and safe strategy for weight loss and metabolic control in Type 2 Diabetes. In: ADS-ADEA. 2016. [http://ads-adea-2016.m.asnevents.com.au/schedule/session/9323/abstract/36569], #31813

Studiencharakteristika: Pilot study, 12-week intervention, n=10
Informationen aus einem Abstrakt-Beitrag!

Population	T2DM
Intervention	Intermittent fasting (IF): 3 very-low energy diet (VLED) shakes a day (ca. 2500kJ/d) on any 2 days a week and to eat to appetite on other days

Griffiths C, Overland J, Sainsbury A, Little T, Franklin J, Gibson A, et al. Intermittent fasting: appears an eLective and safe strategy for weight loss and metabolic control in Type 2 Diabetes. In: ADS-ADEA. 2016. [http://ads-adea-2016.m.asnevents.com.au/schedule/session/9323/abstract/36569], #31813	
Control	Continuous energy restriction (CER): reduce energy intake by 30% every day
Keine Informationen zu Change in medication oder andere Endpuntke, die in unserer Recherche betrachtet werden sollten.	
Risk of bias Bewertung: in Allaf 2021: Risk of bias: high: Performance and Attrition bias, ansonsten unclear risk of bias.	

Garg 1994

Garg A, Bantle JP, Henry RR, et al. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. JAMA 1994; 271(18):1421–8. DOI: 10.1001/jama.1994.03510420053034. http://www.ncbi.nlm.nih.gov/pubmed/7848401. *Laufnummer: 31786*	
Studiencharakteristika: four center randomized crossover trial, n=42, initially 6 weeks each, 21 patientes continued diet they recieved second for additional 8 weeks.	
Objective	To study effects of variation in carbohydrate content of diet on glycemia and plasma lipoproteins in patients with NIDDM.
Population	NIDDM on glipizide therapy
Intervention	High carbohydrate (55%E), 30% E fat
Control	High monounsaturated-fat diet containing 40% E carbohydrates and 45%E fats
Anmerkungen: - Study diets were provided as sole nutrients to subjects for 6 weeks each - Es wird nicht über change in medication berichtet.	

Lean 2018

Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645. ***Laufnummer: 27789***	
Weitere Zitate: Lean ME, Leslie WS, Barnes AC, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet Diabetes Endocrinol 2019; 7(5):344–55. DOI: 10.1016/S2213-8587(19)30068-3. http://www.ncbi.nlm.nih.gov/pubmed/30852132. Laufnummer: 31846 Lean ME, Leslie WS, Barnes AC, et al. 5-year follow-up of the randomised Diabetes Remission Clinical Trial (DiRECT) of continued support for weight loss maintenance in the UK: an extension study. Lancet Diabetes Endocrinol 2024; 12(4):233–46. DOI: 10.1016/S2213-8587(23)00385-6. http://www.ncbi.nlm.nih.gov/pubmed/38423026. # 34562	
Studiencharakteristika: open label cluster randomized trial (DiRECT), 49 primary care practices in Scotland and Tyneside region of England, n=306, duration 12 months, weiteres follow-up nach 24 monaten	
Objective	to assess whether intensive weight management within routine primary care would achieve remission of type 2 diabetes.
Population	20-65 years. Diagnosed with T2DM, within past 6 years, BMI 27-45kg/m2, not receiving insulin.
Intervention	weight management programme (intervention) Withdrawel of of antidiabetic and antihypertensive drugs, total diet replacement (825–853 kcal/day formula diet for 3–5 months), stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance.
Control	best-practice care by guidelines (control)
primary outcome	Weight loss of 15kg or more, remission of T2DM (HbA1c <6,5% after at least 2m off all antidiabetic medications)

Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645.
Laufnummer: 27789

statistics	ITT The co-primary outcomes were analysed in a hierarchical manner, the weight loss outcome first, with no adjustment of the p values for multiple comparisons. Prticipants not attending 12 month assessment. Assumption; primary outcome not met:
Medication change in trial	All oral antidiabetic and antihypertensive drugs were discontinued on day 1 of the weight management programme, with standard protocols for drug reintroduction under national clinical guidelines, if indicated by regular monitoring of blood glucose and blood pressure
Attrition	306 recruited, 23 (8%) lost to follow up; 128 (86%) Intervention group, 147 (99%) control group attending 12-month assessment, weitere Informationen, siehe Studienbeschreibung. Verschiedene Imputationsverfahren getestet (conservative, return to baseline; optimistic, last observation carried forward; realistic)

Baseline

	Intervention, n=149	**Control, n=149**
Sex (f/m) (%)	44/56	38/62
Age	52,9 (7,6)	55,9 (7,3)
Weight, kg	101,0 (16,7)	98,8 (16,1)
BMI, kg/m2	35,1 (4,5)	34,2 (4,3)
HbA1c (%)	7,7 (1,25)	7,5 % (1,05)
Mean Time since diagnosis (years)	3,0 (1,7)	3,0 (1,8)
Prescribed oral antidiabetic medication	111 (74,5)	115 (77,2)
Number of oral antidiabetic medications	0: 26% 1: 44% ≥2: 31%	0: 23% 1: 53% ≥2: 24%

Ergebnisse 12 months

	N*	**Mean (SD)**			**Intervention effect**		**Interclass correlation**
		Baseline	**12m**	**change**	**estimate**	**P value**	
Weight, kg		-	-	-	-8,8 (-10,3; -7,3)	<0,0001	<0,01
Intervention	137	100,4 (16,5)	90,4 (16,4)	-10,0 (8,0)	-	-	-
Control	148	98,7 (16,1)	97,7 (16,4)	-1,0 (3,7)	-	-	-
HbA1c (%)	-	-	-	-	-0,85 (-1,1; -0,59)	<0,0001	<0,01
Intervention	138	7,7 (1,2)	6,8 (1,2)	-0,9 (1,4)	-	-	-
Control	148	7,5 (1,1)	7,6 (1,1)	0,1 (1,1)	-	-	-
Number of prescribed oral antidiabetic medications	-	-	-	-	-0,97 (-1,11; -0,84)	<0,0001	<0,01
Intervention	148	1,1 (0,9)	0,4 (0,7)	-0,8 (0,8)	-	-	-
Control	148	1,0 (1,1)	1,0 (1,0)	0,1 (0,5)	-	-	-
Quality of life (EuroQol 5)	-	-	-	-	6,4 (2,5; 10,3)	0,0012	0,01
Intervention	125	66,4 (19,2)	73,7 (19,0)	7,2 (21,3)	-	-	-

Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645.
Laufnummer: 27789

Control	147	72,0 (16,9)	69,1 (15,6)	-2,9 (15,5)	-	-	-
Proportion achieving remission at 12 months (%)					Odds ratio: 19,7 (95% CI 7,8 vs. 49,8), p<0,0001		
Intervention			46% (n=68)				
Control			4% (n=6)				

Proportion achieving reduction in weight of ≥15kg	
Intervention (n=137)	36 (24%)
Control (n=148)	0 (0%)

N*= number of participants with data available at baseline and 12 months for each outcome; verschiedene Imputationsverfahren für fehlende Daten führten zu keiner wensentlichen Änderung der Ergebnisse (siehe Supplement)

Primary outcome in relation to weight loss

	Weight loss at 12 months (kg)					
	0	<5kg	5-10kg	10-15kg	≥15kg	
Proportion achieving remission (%)	0%	7%	34%	57%	86%	Odds ratio per kg weight loss 1,32 (95% CI 1,23; 1,41)

Number of participants prescribed antidiabetic medications at 12 months

	Intervention group	**Control group**
No oral antidiab. Medic. One oral antidiab. Medic. Two or more oral antidiabetic medications	109 (73%) 26 (18%) 13 (9%)	27 (18%) 70 (47%) 51 (34%)

Ergebnisse 24 months (ITT n=149 in each group)

	Intervention	**Control**	**Adjusted odds ratio**
Weight loss of at least 15kg (n (%))	17 (11%)	3 (2%)	7,49 (95% CI 2,05; 27,32), p=0,0023
Remission of diabetes	53 (36%)	5 (3%)	25,82 (95% CI 8,25; 80,84), p<0,0001
Adjusted mean difference in change in body weight (control and intervention group)	-5,4kg (95% CI -6,9; -4,0), p<0,001		
Adjusted mean difference in change in HbA1c (control and intervention group)	-0,44% (-0,76; -0,13), p=0,0063		

- 51 (40%) of 129 patients in the intervention group using anti-diabetes medication compared with 120 (84%) of 143 in the control group (24months).
- Serious adverse events were similar to those reported at 12 months, but were fewer in the intervention group than in the control group in the second year of the study (nine vs 22)

Risk of bias assessment:
Selektion:
- **Randomization: low** (computer generated, stratified)

Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645.
Laufnummer: 27789

- **Allocation concealment: high** (Praxis war Randomisation-Einheit, Zuteilung konnte nicht geheim sein, patients aware of planned allocation)

Performance: high (keine Verblindung der Teilnehmenden oder des Studienpersonals)
Detection: high oder unclear (keine Verblindung bei der Endpunkterhebung. Inwieweit dies bei teils objectiven Endpunkten (HbA1c einen Einfluss hat, ist unklar)
Attrition: unclear (dropout rate of 25% in the intervention group, Attrition in den Gruppen unterschiedlich, wahrscheinlich in Zusammenhang mit Intervention, es weden unterschiedliche Imputationsverfahren angewendet, bei denen sich keine Änderung der Ergebnisse zeigt).
Reporting: unclear (primären Endpunkte aus Protokoll berichtet, Einschlusskriterien im Verlauf angepasst, Ecological Momentary assessment berichtet?)
Other biases: The formula diet was donated by Cambridge Weight Plan.
Sponsor: Neither organisation had any input into the study design, data analysis or interpretation.

Extension study

Lean ME, Leslie WS, Barnes AC, et al. 5-year follow-up of the randomised Diabetes Remission Clinical Trial (DiRECT) of continued support for weight loss maintenance in the UK: an extension study. Lancet Diabetes Endocrinol 2024; 12(4):233–46. DOI: 10.1016/S2213-8587(23)00385-6. http://www.ncbi.nlm.nih.gov/pubmed/38423026. # 34562

Study characteristics	After the 2-year results, UK National Health Service data were collected annually until year 5 from remaining intervention participants who received low-intensity dietary support, intervention withdrawals, and the original randomly allocated groups. The primary outcome was remission of type 2 diabetes; having established in the DiRECT trial that sustained weight loss was the dominant driver of remission, this was assumed for the Extension study.
Population	all intervention participants still in the trial (101 [68%] of 149) were approached to receive low-intensity support for a further 3 years (once every 3 months, 15-30min with local nurse or dietitian). 95 (94%) of 101 were able to continue and consented and were allocated to the DiRECT extension group (6 withdrew). 54 participants were allocated to the non-extension group, where intervention was withdrawn.
Intervention	- Low-intensity dietary support for further 3 years (DiRECT extension group) - Intervention withdrawals
Primary outcomes	- Bodyweight - HbA1c - and other biochemistry - (remission of type 2 diabetes)

Ergebnisse (up to 5 years)

	Control vs. Intervention				Intervention: non-extension vs. Extension			
	Control		Intervention		Non-extention		extension	
	N	Summary	n	Summary	n	Summary	N	Summary
In remission								
Year 1	148	6 (4%)	138	68 (49%)	43	9 (21%)	95	59 (62%)
Year 2	142	5 (4%)	129	52 (40%)	34	4 (12%)	95	48 (51%)
Year 3	115	5 (4%)	126	25 (20%)	37	2 (5%)	89	23 (26%)
Year 4	100	1 (1%)	119	9 (8%)	32	0 (0%)	87	9 (10%)
Year 5	93	5 (5%)	118	12 (10%)	33	1 (3%)	85	11 (13%)
	Control vs. intervention				Intervention: non-extension vs. Extension			
	Control		Intervention		Non-extension		extension	

Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial. Lancet 2018; 391(10120):541-551. DOI: 10.1016/S0140-6736(17)33102-1. http://www.ncbi.nlm.nih.gov/pubmed/29221645.
Laufnummer: 27789

	n	summary	n	summary	n	summary	n	summary
Weight change (kg)								
Year 1	148	-1,0 (3,7)	137	-10,0 (8,0)	42	-5,3 (6,8)	95	-12,1 (7,6)
Year 2	143	-2,3 (5,2)	129	-7,6 (6,5)	34	-3,7 (5,0)	95	-9,1 (6,4)
Year 3	110	-3,8 (5,6)	120	-6,4 (6,5)	31	-5,4 (8,0)	89	-6,7 (5,9)
Year 4	85	-3,7 (6,8)	114	-5,4 (5,8)	28	-3,6 (6,9)	86	-5,9 (5,3)
Year 5	82	-4,6 (6,1)	116	-5,6 (5,8)	31	-4,4 (7,2)	85	-6,1 (5,2)

At 5 years, DiRECT extension participants (n=85) lost an average of 6·1 kg, with 11 (13%) of 85 in remission. Compared with the non-extension group, DiRECT extension participants had more visits with HbA1c <48 mmol/mol (<6·5%; 36% vs 17%, p=0·0004), without glucoselowering medication (62% vs 30%, p<0·0001), and in remission (34% vs 12%, p<0·0001). Original control participants (n=149) had mean weight loss 4·6 kg (n=82), and 5 (5%) of 93 were in remission. Compared with control participants, original intervention participants had more visits with weight more than 5% below baseline (61% vs 29%, p<0·0001), HbA 1c below 48 mmol/mol (29% vs 15%, p=0·0002), without antidiabetic medication (51% vs 16%, p<0·0001), and in remission (27% vs 4%, p<0·0001). Of those in remission at year 2, 26% remained in remission at 5 years. Serious adverse events in the original intervention group (4·8 events per 100 patient-years) were under half those in the control group (10·2 per 100 patient-years, p=0·0080).

Anmerkungen ÄZQ: von den initialen 149 Personen in der Interventionsgruppe wurden diejenigen für eine Fortführung selektioniert, die bis zur 2 Jahreserhebung dabeigeblieben sind und die dann fähig waren, weiterzumachen (95/149, ca. 63%, 5-Jahresergebnisse aus der Extension-Gruppe von n=85, 57%).
Aus dem Paper: „The DiRECT extension group was self-selected by remaining engaged with the intervention at 2 years. Furthermore, control group participants were strongly encouraged to control their weight after the end of the 2-year randomised trial, so their outcomes do not reflect usual care. Consequently, differences between groups beyond the 2-year point might not reflect intervention."

„We report observed data without assumptions about outcomes with missing data, thus numbers and remission rates differ slightly from previous publications from DiRECT."

Literaturverzeichnis

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2. Horton R. Expression of concern: Indo-Mediterranean Diet Heart Study. Lancet 2005; 366(9483):354–6. DOI: 10.1016/S0140-6736(05)67006-7. http://www.ncbi.nlm.nih.gov/pubmed/16054927.
3. Estruch R, Ros E, Salas-Salvadó J, et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. N Engl J Med 2018; 378(25):e34. DOI: 10.1056/NEJMoa1800389. http://www.ncbi.nlm.nih.gov/pubmed/29897866.

NATIONALE VERSORGUNGS LEITLINIEN

Nationale VersorgungsLeitlinie

Typ-2-Diabetes

Recherchedokumentation + Evidenztabellen
zum Kapitel Nicht-medikamentöse Therapie
Teil 3: körperliche Aktivität / strukturierte Bewegungsprogramme

Ergänzung zu Version 3

AWMF-Register-Nr. nvl-001

Träger:

Bundesärztekammer

Kassenärztliche Bundesvereinigung

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften

BUNDESÄRZTEKAMMER KBV AWMF

Inhaltverzeichnis

1 Aufbau der Recherche-/Evidenz-Dokumente

Zur leichteren Handhabung der umfangreichen Evidenzrecherchen werden die Recherchedokumentationen und Evidenztabellen in verschiedenen Teilen dargestellt:

- Teil 1
  - Evidenzbasis des Kapitels Nicht-medikamentöse Therapie
  - Themenübergreifende systematische Recherche
  - Themenverwandte AWMF-Leitlinien
  - Nationale und internationale Konsensuspapiere (von der Leitliniengruppe eingebrachte Literatur)
- Teil 2
  - Systematische Recherche zum Gewichtsmanagement
  - Systematische Recherche zu Formuladiäten
  - Systematische Recherche zu Mediterraner Diät
- Teil 3 (vorliegendes Dokument)
  - Systematische Recherche zu körperlicher Aktivität und strukturierten Bewegunsprogrammen
- Teil 4
  - Systematische Recherche Alkoholkonsum und Neuropathie
  - Systemtische Recherche Interventionen zur Stressbewältigung

2 Recherchedokumentation körperliche Aktivität und strukturierte Bewegungsprogramme

2.1 Systematische Recherche: körperliche Aktivität und strukturierte Bewegungsprogramme

Die initiale Recherche fand 2021 statt. Eine Update-Recherche erfolgte 2023.

2.1.1 PICO-Fragestellung

P: Erwachsene Patient*innen mit Typ-2-Diabetes

I: Bewegungsprogramme, körperliche Aktivität

C: primärere Vergleichsgruppe: keine geplante Erhöhung der körperlichen Aktivität/keine strukturierten Bewegungsprogramme

O: 1. Kardiovaskuläre Morbidität / Mortalität, Gesamtmortalität

2. Lebensqualität

3. ggf. HbA1c, wenn dadurch eine medikamentöse Therapie verhindert wird (Diabetesremission)

S: Systematische Übersichtsarbeiten von RCTs ab 2014, Update ab letzer Recherche vom 17.12.2021

Sprache: deutsch, englisch

2.1.2 Recherchestrategien

2.1.2.1 Recherche 2021

Medline via Pubmed (www.pubmed.gov) (17.12.2021)

Search	Suchfrage	Results
#15	**Search: #12 AND #13 Filters: from 2014/1/1 - 3000/12/12**	**1,096**
#14	Search: #12 AND #13	1,715
#13	Search: (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation study[pt] OR validation study[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	555,286
#12	Search: #3 AND #11	31,372
#11	Search: #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	614,470
#10	Search: "Physical Fitness"[Mesh]	33,965
#9	Search: "Physical Exertion"[Mesh]	57,119
#8	Search: Sports[Mesh]	200,588
#7	Search: „Exercise"[Mesh]	223,197
#6	Search: ((aerobic[tiab] OR program[tiab] OR physical[tiab] OR endurance[tiab] OR resistance[tiab] OR regular[tiab] OR treadmill[tiab]) AND exercis*[tiab])	152,240
#5	Search: (training*[tiab] AND (aerobic*[tiab] OR strength*[tiab] OR physical[tiab] OR endurance[tiab] OR resistance[tiab] OR exercis*[tiab]))	114,332
#4	Search: (exercise*[tiab] OR activit*[tiab] OR training*[tiab] OR fitness[tiab] OR sport*[tiab]) AND (physical*[tiab])	283,276
#3	Search: #1 OR #2	715,051
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	150,185
#1	Search: diabet*[tiab]	702,693

Epistemonikos (www.epistemonikos.org) (17.12.2021)

Advanced search

Search	Most Recent Queries	Result
#1	(advanced_title_en:((diabet*) AND (((aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill) AND (exercis*)) OR ((training*) AND (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)) OR ((exercise* OR activit* OR training* OR fitness OR sport*) AND (physical*)))) OR advanced_abstract_en:((diabet*) AND (((aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill) AND (exercis*)) OR ((training*) AND (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)) OR ((exercise* OR activit* OR training* OR fitness OR sport*) AND (physical*)))) [Filters: classification=systematic-review, protocol=no, min_year=2014, max_year=2021]	**763**

Cochrane Datenbank (www.cochranelibrary.com) 17.12.2021

Search	Most Recent Queries	Result
#14	**#12 AND #3 in Cochrane Protocols; Publication date: from 2014**	**1**
#13	**#12 AND #3 in Cochrane Reviews; Publication date: from 2014**	**41**
#12	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	114351
#11	(exercis* NEAR/3 (aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill)):ab	30470
#10	exercis*:ti	45382
#9	(training* NEAR/3 (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)):ti,ab	25195
#8	(physical activit*):ti,ab	44179
#7	MeSH descriptor: [Sports] explode all trees	16693
#6	MeSH descriptor: [Physical Education and Training] explode all trees	1630
#5	MeSH descriptor: [Exercise Therapy] explode all trees	15476
#4	MeSH descriptor: [Exercise] explode all trees	27223
#3	#1 OR #2	102259
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	19238
#1	(Diabet*):ti,ab,kw	102259

2.1.2.2 Update-Recherche 2023

Medline via Pubmed (www.pubmed.gov) (16.02.2023)

Nr.	Suchfrage	Anzahl
#15	**Search: #12 AND #13 Filters: from 2021/12/1 - 3000/12/12**	**263**
#14	Search: #12 AND #13	1,951

Nr.	Suchfrage	Anzahl
#13	Search: (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation study[pt] OR validation study[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	633,989
#12	Search: #3 AND #11	34,124
#11	Search: #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	666,449
#10	Search: "Physical Fitness"[Mesh]	35,858
#9	Search: "Physical Exertion"[Mesh]	57,420
#8	Search: Sports[Mesh]	212,817
#7	Search: „Exercise"[Mesh]	241,381
#6	Search: ((aerobic[tiab] OR program[tiab] OR physical[tiab] OR endurance[tiab] OR resistance[tiab] OR regular[tiab] OR treadmill[tiab]) AND exercis*[tiab])	166,399
#5	Search: (training*[tiab] AND (aerobic*[tiab] OR strength*[tiab] OR physical[tiab] OR endurance[tiab] OR resistance[tiab] OR exercis*[tiab]))	127,653
#4	Search: (exercise*[tiab] OR activit*[tiab] OR training*[tiab] OR fitness[tiab] OR sport*[tiab]) AND (physical*[tiab])	314,844
#3	Search: #1 OR #2	772,503
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	166,379
#1	Search: diabet*[tiab]	759,884

Epistemonikos (www.epistemonikos.org) (16.02.2023)

Advanced search

Search	Most Recent Queries	Result
#1	(title:((title:((((diabet*) AND (((aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill) AND (exercis*)) OR ((training*) AND (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)) OR ((exercise* OR activit* OR training* OR fitness OR sport*) AND (physical*))))) OR abstract:(((diabet*) AND (((aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill) AND (exercis*)) OR ((training*) AND (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)) OR ((exercise* OR activit* OR training* OR fitness OR sport*) AND (physical*))))))) OR abstract:((title:(((diabet*) AND (((aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill) AND (exercis*)) OR ((training*) AND (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)) OR ((exercise* OR activit* OR training* OR fitness OR sport*) AND (physical*))))) OR abstract:(((diabet*) AND (((aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill) AND (exercis*)) OR ((training*) AND (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)) OR ((exercise* OR activit* OR training* OR fitness OR sport*) AND (physical*))))))) [Filters: classification=systematic-review, min_year=2021, max_year=2023]	**309**

Cochrane Datenbank (www.cochranelibrary.com) 16.02.2023

Search	Most Recent Queries	Result
#14	**#12 AND #3 in Cochrane Protocols; Publication date: from 01/11/2021**	**1**
#13	**#12 AND #3 in Cochrane Reviews; Publication date: from 01/11/2021**	**6**
#12	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	128420
#11	((exercis* NEAR/3 (aerobic OR program OR physical OR endurance OR resistance OR regular OR treadmill))):ab	34337
#10	(exercis*):ti	50293
#9	(training* NEAR/3 (aerobic* OR strength* OR physical OR endurance OR resistance OR exercis*)):ti,ab	28238
#8	(physical activit*):ti,ab	49908
#7	MeSH descriptor: [Sports] explode all trees	19261
#6	MeSH descriptor: [Physical Education and Training] explode all trees	1746
#5	MeSH descriptor: [Exercise Therapy] explode all trees	18436
#4	MeSH descriptor: [Exercise] explode all trees	32772
#3	#1 OR #2	110657
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	22682
#1	(Diabet*):ti,ab,kw	110657

2.1.3 Übersicht der eingeschlossenen Treffer

2.1.3.1 Recherche 2021

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	**1096**	**763**	**42**	**1901**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 647

A2 (nicht englisch/deutsch): 43

A3 (Conference Abstract): 7

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 1204

2.1.3.2 Recherche 2023

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	263	309	7	**579**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund

A1 (Dubletten): 173

A2 (Dubletten mit alter Recherche): 142

A3 (nicht englisch/deutsch): 8

A4 (Conference Abstract): 5

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 251

2.1.4 TiAb-Screening

TiAb-Tabelle		
	Einschluss	**Ausschluss**
Population	Erwachsene mit Typ 2 Diabetes	- Studien, die nicht zwischen Typ-1- und Typ-2-Diabetes unterscheiden - Diabetes bei besonderen Patientengruppen (Cystische Fibrose, nach Transplantation); Alter < 18 Jahre, Diabetes in und um die Schwangerschaft
Intervention	Bewegungsprogramme, körperliche Aktivität	
Comparison	Jeglicher Vergleich	
Outcome	- Mortalität - Kardiovaskuläre und diabetische Morbidität - Lebensqualität - (Glykämische Kontrolle (HbA1c), wenn dadurch Medikamente eingespart werden können, Diabetesremission.)	- *Andere Laborwerte* - *Lipide* - *Andere Stoffwechselparameter (HOMA-Index)* - *Körpergewicht, Änderung Körpergewicht* - *RR*

2.1.5 Flowchart

Recherche 2021

Legende TiAb:

Aa: Fragestellung Population nicht passend

Ap: Protokoll

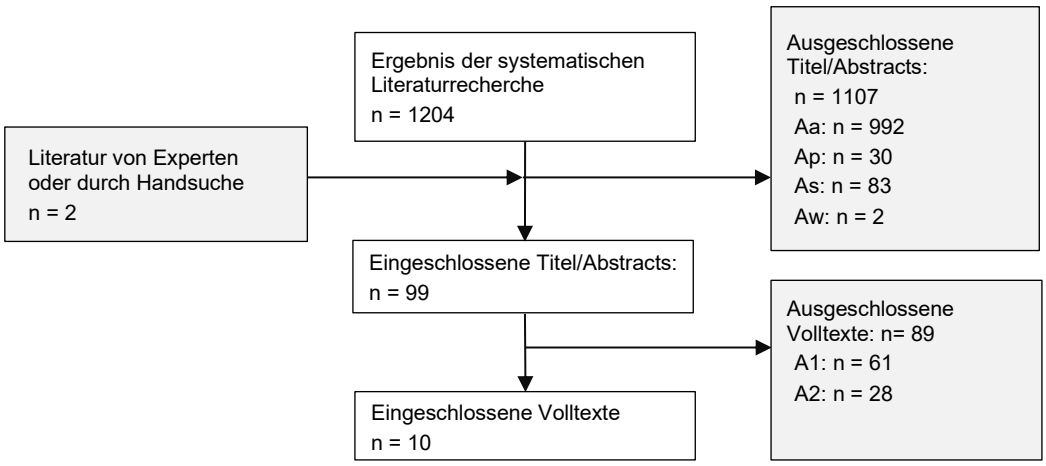
As: Methodik nicht ausreichend, kein SR

Aw: zurückgezogen

Legende Volltextscreening:

A1: Ausschluss, Thema nicht passend, Population nicht passend, Endpunkte nicht passend

A2: Methodisch nicht ausreichend



Eingeschlossene Studien:

- Acosta-Manzano 2020
- Matos 2018
- Cai 2017
- Miranda 2018
- Qin 2020
- Schlesinger 2020
- Yusufu 2019
- Mohammad Rahimi 2022
- Powell 2018
- World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 (Handsuche)

Recherche 2023

Legende TiAb:

Aa: Fragestellung, Population nicht passend

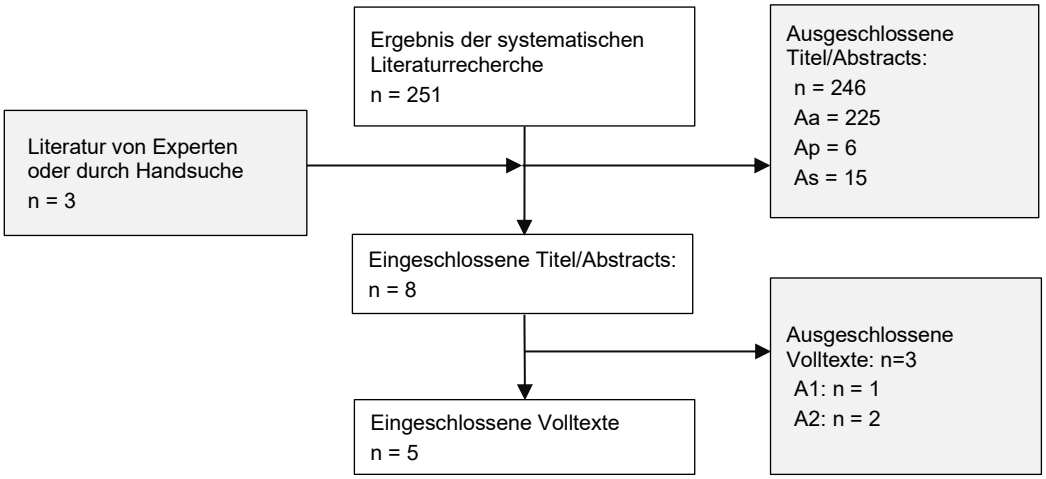
Ap: Protokoll

As: Methodik nicht ausreichend

Legende Volltextscreening:

A1: Ausschluss, Thema nicht passend, Population nicht passend

A2: Endpunkte nicht passend



Eingeschlossene Studien:

- Rijaal 2022
- Jayedi 2022
- Rietz 2022
- Zhang 2023
- Zucatti 2022 (Handsuche)

Außerdem betrachtet: Organization (WHO) (2024): Global level s of physical inactivity in adults. Off track 2030. (Handsuche)

2.1.6 Evidenzzusammenfassung

In der Recherche wurden wenige systematische Übersichtsarbeiten von RCTs identifiziert, die Effekte von Bewegungsprogrammen, Sport bzw. körperlicher Aktivität auf die priorisierten Endpunkte untersuchten. Diese hatten gemäß der AMSTAR-2-Bewertung überwiegend eine niedrige oder sehr niedrige Berichtsqualität. In den meisten Studien wurden komplexe Interventionen eingesetzt, bei denen weitere Maßnahmen wie zum Beispiel Ernährungsumstellung gleichzeitig implementiert wurden. Häufig kann daher der Effekt, der sich durch die Intervention Sport/körperliche Bewegung ergibt, nicht vom Effekt anderer Maßnahmen getrennt werden.

Zur Evidenzbeschreibung siehe Kapitel Nicht-medikamentöse Therapie (Ergänzung zu Version 3) [1].

3 Evidenztabellen: Körperliche Aktivität und strukturierte Bewegungsprogramme

3.1 Systematische Übersichtsarbeiten von RCTs

3.1.1 Kardiovaskuläre Endpunkte

Rijal et al., 2022

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Rijal A. Effects of adding exercise to usual care in patients with either hypertension, type 2 diabetes or cardiovascular disease: A systematic review with meta-analysis and trial sequential analysis. Br J Sports Med 2022. https://www.ncbi.nlm.nih.gov/pubmed/36450440. #33324	**Suchzeitraum:** inception to 07/2020. **Population:** participants with either hypertension, T2DM or CVD* **Intervention:** adding any form of trialist defined exercise to usual care **Control:** no exercise (primary comparison) or usual care (or similar terms defined by the trialists) **Outcomes:** Primary outcomes. - all-cause mortality - serious adverse events - quality of life Secondary outcomes: 1. Cardiovascular mortality 2. Blood pressure. 3. Microvascular complications (retinopathy, nephropathy, neuropathy, diabetic foot) 4. Myocardial infraction **Studies:** RCTs	248 trials reported predefined outcomes (n=21 633 participants), - All trials at **high risk of bias** (most trials failed to define process of randomization, allocation concealment, losses to follow-up, blinding was impossible). - **major types of exercise** reported: o dynamic aerobic exercise (126/248 trials), o dynamic resistance exercise (25/248 trials), and o combined aerobic and resistance exercise (58/248 trials). - **study participants**: o cardiovascular diseases (189/248 trials), o T2DM (41/248 trials, ca. 17%), o hypertension (16/248 trials). o CVD and T2DM: 2 (0,8%) - Median intervention period 3 months (IQR: 2-4 months), median follow-up period 6 months (IQR: 3-8 months) **Metaanalyse (total, all study participants: CVD, diabetes, hypertension)** **All-cause mortality** (median follow up 6 months): exercise 434/6649 (6,5%) vs.control 525/6327 (8,3%); RR 0.82 (95% CI 0.73; 0.93), p=0,0014; anticipated absolute effect: Risk with usual care: 83/1000, Risk difference with exercise: 15 fewer/1000 (range 22-6 fewer); 99 (or 98?) RCTs, n=12 976; I^2=0%, GRADE*: **moderate** certainty of evidence (downgraded one for risk of bias) **serious adverse events,** median follow-up 6 months: exercise 578/8473 (6,8%) vs, control 716/7768 (9,2%), p=0,0000; RR 0.79 (95% CI 0.71 to 0.88); anticipated absolute effect: risk with usual care 92/1000, Risk difference with exercise: 19 fewer/1000 (range 27-11 fewer); 151 RCTs, n=16 241, I^2=0%, GRADE*: **moderate** certainty of evidence (downgraded one for Risk of bias). **Quality of life (QoL):** 96 trials (7 676 participants) reported on health related QoL: seven different scales. Each scale was analyses separately; in 4 out of 7 scales exercise improved QoL, but in 3 effect size was below predetermined minimal important differences. The remaining scales did not show difference.	**Critically low** y-py-y-py-y-y-n-py-n (RoB nicht studienspezifisch dargestellt, endpunktspezifisch)-n-y-y-y-y-y-y Nicht erfüllte kritische Domänen: - Keine Auflistung/Begründung der Studienausschlüsse (Look-AHEAD? Wahrscheinlich, da multicomponent intervention) - keine studienspezifische RoB-Bewertung Ausführliche Suche/Recherche, aber Darstellung der Ergebnisse für „Diabetes-Subgruppe“	**Limitationen:** - Typ-2-Diabetes-Studien machen nur kleinen Teil der eingeschlossenen Studien aus (17%); - all trials at high risk of bias - Heterogenität der Studien (Population, type of diseases, types of exercises, definition of usual care) - Median follow-up was short (6 months), intervention volume was low

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar

	*CVD (Cardiovascular disease): including cerebrovascular disease, rheumatic heart disease, deep vein thrombosis, pulmonary thrombosis, coronary heart disease, heart failure	**Secondary outcomes:**
		Cardiovascular mortality, median follow-up 12 months: RR 0,75 (95% KI 0,64; 0,89);
		Anticipated absolute effect: Risk with usual care: 97/1 000, Risk difference with exercise: 24 fewer/1 000 (range 35-11 fewer); 23 RCTs, n=6 068,
		GRADE*: **moderate** certainty of evidence (downgraded one for Risk of bias).
		
		Myocardial infarction, follow-up median 12 months: RR 0,83 (95% KI 0,65; 1,06);
		Anticipated absolute effect: Risk with usual care 45/1000, Risk difference with exercise 8 fewer/1000 (range 16 fewer to 3 more); 33 RCTs, n=6 397,
		GRADE*: **Low** certainty of evidence (downgraded one for risk of bias, downgraded one for imprecision)
		
		Stroke, median follow-up 3,6 months: RR 0,93 (95% KI 0,64; 1,34),
		Anticipated absolute effect: Risk with usual care 28/1000, Risk difference with exercise 2 fewer/1000 (range 10 fewer to 9 more); 22 RCTs, n=3 934;
		GRADE*: **low** certainty of evidence (downgraded one for risk of bias, downgraded one for imprecision)
		
		Subgruppenanalyse Type-2-Diabetes:
		All-cause Mortality: RR 0,80 (95% KI 0,4; 1,59), 4 trials, n=? (siehe unten), p-value 0,524;
		GRADE*: **Low** (serious risk of bias, serious imprecision, publication bias: undetected (insufficient information))
		- Anmerkung ÄZQ: aus dem SR nicht direkt ersichtlich, welche Studien für die Metaanalyse herangezogen wurden und wie viele Teilnehmende eingeschlossen wurden (power?).
		- Studien, die laut Supplement Menschen mit Typ-2-eingeschlossen haben und all-cause-Mortality (ACM) berichteten ([ ]=Literaturstellen im Review).
		  ○ ISRCTN04252749, 2012 [81], n=606, 12 Monate (Mortalität nur als adverse event, High- versus Low-Intensity Supervised Aerobic and Resistance Training
		  ○ NCT00637546, 2010 [144], n=71, 12 weeks, physiotherapeutic group training including gait and balance exercises with function-orientated strengthening
		  ○ NCT00955201, 2019 a, b, c [149], n=45, 12 weeks structured program of aerobic, isokinetic strength, or the combination of aerobic-isokinetic strength exercise intervention in patients with advanced length-dependent distal symmetric polyneuropathy
		  ○ NCT01343602, 2015, [161], n=156 (nach clinical trial keine Studie an Personen mit Diabetes).
		
		Serious adverse events: 0,82 (95% KI 0,52; 1,28), p: 0,362;
		GRADE*: **Low** certainty of evidence (serious risk of bias, serious imprecision, publication bias: undetected)
		
		CONCLUSIONS: “A short duration of any type of exercise seems to reduce the risk of all-cause mortality and serious adverse events in patients with either hypertension, type 2 diabetes or cardiovascular diseases. Exercise seems to have statistically significant effects on quality of life, but the effect sizes seem minimal.”
		
		- Microvascular outcomes: did not find any data to report.
		
		GRADE*: GRADE-Bewertung durch die Autor*innen des Reviews
			nicht ausführlich beschrieben.	(135 mins/week)
				
				- Subgruppenanalyse wahrscheinlich nicht ausreichend gepowert: Im Review können nur eingeschränkt Rückschlüsse gezogen werden, welche Studien in die Subgruppenanalysen eingeschlossen wurden;
				
				Subgruppenanalyse zu T2DM mit kurzer Studiendauer und „unpassender“ vergleichsgruppe (low intensity versus high intensity training)
				
				- bei usual care als Vergleichsgruppe bleibt unklar, wie viel Sport in der Vergleichsgruppe

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
				getrieben wurde.

Zucatti et al., 2022

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Zucatti KP, Teixeira PP, Wayerbacher LF, et al. Long-term Effect of Lifestyle Interventions on the Cardiovascular and All-Cause Mortality of Subjects With Prediabetes and Type 2 Diabetes: A Systematic Review and Meta-analysis. Diabetes Care 2022; 45(11):2787–95. DOI: 10.2337/dc22-0642. http://www.ncbi.nlm.nih.gov/pubmed/36318674. Laufnummer: 33040	**Suchzeitraum:** until 15 May 2022 **Population:** adults with prediabetes and type 2 diabetes **Intervention:** intensive lifestyle interventions (dietary and physical exercise recommendations) (at least 2 years active intervention). **Comparison:** usual care or standard advice or placebo **Studies:** RCTs **Outcomes:** cardiovascular death or all-cause mortality **Assessment of study quality:** RoB 2.0, GRADE-approach **Intervention:** provision of a dietary prescription and/or group based structured program recommendations for lifestyle intervention with diet as the main treatment intervention **Planned subgroup analysis (Auszug):** - glycemic status (prediabetes, t2DM) - sex - age - mean duration of follow-up - type of dietary (advice or prescription), physical exercise (advice or prescription) intervention, and dietary and physical exercise advice or recommendation applied to control groups sensitivity analysis excluding studies without reporting of deaths as main outcomes	11 RCTs, n=16574 Seven studies (63,6%) subjects with prediabetes, 4 studies (36,3%) subjects with diabetes, all but one with BMI of overweight and/or obesity - mean duration of intervention 4,25 years, total follow-up ranges from 2 to 30 years. - All trials: lifestyle interventions combined diet and physical exercise recommendations - Pharmacological treatment (hypoglycaemic): 1 study metformin as one treatment arm **Cardiovascular mortality** (follow-up: median 15,8 years) Control 274/5213 (5,3%) vs intervention 353/5804 (6,1%), RR 0,99 (95% CI 0,79; 1,23), 5 RCTs, n=11017, from 11 fewer to 12 more per 1000, GRADE*: moderate certainty of evidence (downgraded: imprecision) Subgroup analyses: Prediabetes: RR 0,97 (95% CI 0,55; 1,72), 3 RCTs, n=2815, I^2=67% Diabetes: RR 1,04 (95% CI 0,86; 1,25), 2 RCTs, n=8202, I^2=0% **All-cause mortality** (follow-up: mean 11 years): Intervention 1205/8782 (13,7%) vs. Control 1085/7772 (14,0%), RR 0,93 (0,85; 1,03), I^2=15%, 11 RCTs, n=16554, 10 fewer events per 1000 to 4 more (95% CI -21 to 4) GRADE*: moderate certainty of evidence (imprecision: CI includes benefits and harms) **Subgroup-Analyses:** Prediabetes: RR, 0.91; 95% CI, 0.70 to 1.18, 7 RCTs, n=6013, I^2=35% Diabetes: RR, 0.94; 95% CI, 0.87 to 1.03, 4 RCTs, n=10541, I^2=0% *: according to the review authors	**low** y-y-n-y-y-y-n-py-py-n-y-y-y-y-y Nicht-erfüllte kritische Domänen: ausgeschlossene Studien nicht aufgeführt. nicht-erfüllte unkritische Domänen: Keine Begründung für Wahl des Studientyps, Funding in den Studien nicht genannt, Risk of bias assessment: allocation concealment nicht als rob-Kriterium benannt. Bei derartiger Intervention aber auch schlecht zu verblinden.)	Handsuche Prof. Müller (AkdÄ). Fragestellung wurde im Kapitel Erhöhtes Diabetesrisiko durch Cochrane Review von Hemmingsen abgedeckt. Hier nun auch neuere Literatur und Personen mit Typ-2-Diabetes. - “RCTs had to include provision of a dietary prescription and/or group-based structured program recommendations for lifestyle intervention with diet as the main treat-

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	Metaregression analysis: relationship between mean weight changes from baseline and RR of mortality (studies reporting only BMI excluded from analysis).			ment intervention“.

WHO-Guidelines on physical activity and sedentary behaviour 2020

World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 [cited: 2023-02-23]. https://apps.who.int/iris/rest/bitstreams/1315866/retrieve. Laufnummer: #33331	
Weitere Zitate	- Identifiziert über: Dempsey PC. Global Public Health Guidelines on Physical Activity and Sedentary Behavior for People Living With Chronic Conditions: A Call to Action. Journal of physical activity & health 2020; 18(1):76–85. https://www.ncbi.nlm.nih.gov/pubmed/33276323 - Dempsey PC. New global guidelines on sedentary behaviour and health for adults: Broadening the behavioural targets. Int J Behav Nutr Phys Act 2020; 17(1):151. https://www.ncbi.nlm.nih.gov/pubmed/33239026.
Fragestellungen	(mehrere Populationen in der guideline betrachtet, hier nur T2DM berichtet): - association between physical activity/sedentary behaviour and health-related outcomes? - dose-response association? - Does association vary by type or domain of physical activity/sedentary behaviour? - In adults only: Does physical activity modify the effect of sedentary behaviour on mortality?
Population:	adults and older adults with chronic conditions (u. a. Type-2-Diabetes)
Exposure:	greater volume, duration, frequency or intensity of physical activity than comparison
Comparison:	no physical activity or lesser volume, frequency, intensity or duration of physical activity.
Critical outcomes (Web Annex):	- All-cause and cause-specific mortality - Disease progression - Health related quality of life - Physical function
Studien	- Keine Einschränkung auf ein Studiendesign gefunden. Im Ergebnisteil werden sowohl Kohortenstudien, als auch RCTs beschrieben.
Vorgehen bei der Aktualisierung der Guideline	- identifiying and updating most recent, relevant umbrella reviews related to scope of the guideline - search for recent systematic reviews
Suchzeitraum	last search of identified umbrella review to September 2019

World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 [cited: 2023-02-23]. https://apps.who.int/iris/rest/bitstreams/1315866/retrieve. Laufnummer: #33331	
Ergebnisse Evidenzrecherche	
Evidenzbasis	Identified umbrella review: - The scientific report of the Physical Activity Guidelines Advisory Group (PAGAC) which provides a systematic update of evidence on physical activity and sedentary behaviours and health outcomes published 2008–2016 as part of the development of the 2018 Physical activity guidelines for Americans, 2nd Edition, (a total of 38 main research questions, 104 subquestions) o PAGAC Report: U.S. Department of Health and Human Services. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. 2018 [cited: 2023-03-13]. https://health.gov/sites/default/files/2019-09/PAG_Advisory_Committee_Report.pdf. Laufnummer: #33405 o Powell KE. The Scientific Foundation for the Physical Activity Guidelines for Americans, 2nd Edition. Journal of physical activity & health 2018:1–11. https://www.ncbi.nlm.nih.gov/pubmed/30558473 o U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. 2018 [cited: 2023-03-13]. https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf.[2] New evidence: - report of PAGAC was updated (searches were updated) with 16 new reviews identified from 2017 to 2019 for cancer (n= 1), hypertension (n= 2) and type-2 diabetes (n= 13).
Evidence from updated searches (T2DM)	13 Reviews included for update for diabetes (AMSTAR 2-Bewertung), berichtete Endpunkte: Risk of comorbid condition, Quality of life (QoL), disease progression (DP) 1. Chao 2018 (moderate): DP 2. De Nardi 2018 (moderate): DP 3. Jang 2019 (low): DP 4. Lauche 2018 (moderate): Risk of comorbid conditions, DP 5. Liu, Zhu 2019 (moderate): DP 6. Liu, Ye 2019 (moderate): DP 7. Qui 2017 (moderate): DP 8. Rees 2017 (low): QoL, DP 9. Song 2018 (moderate): DP 10. Thind 2017 (low): DP 11. Xia 2019 (low): DP 12. Yu 2018 (moderate): QoL, DP 13. Zhou (moderate): QoL, DP
Ergebnisse	
Risk of comorbid conditions	Recherche: - Update-Recherche: 1 Review: Lauche 2018: no trials identified. - PAGAC evidence (2018): 3 existing systematic reviews (ESRs): o Sluik 2012: prospektive Kohortenstudie und Metaanalyse, o Kodama 2013: Metaanalyse von Kohortenstudien, o Sadarangani 2014: Analyse von Kohortenstudien Anmerkung ÄZQ: Veröffentlichung der identifizierten Studien vor Suchzeitraum der NVL-Recherche und es sind keine Reviews von RCTs

World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 [cited: 2023-02-23]. https://apps.who.int/iris/rest/bitstreams/1315866/retrieve. Laufnummer: #33331	
	Gemäß PAGAC: - Large cohort studies in adults with CVD endpoints were included even though adults with type 1 diabetes were included as well as adults with type 2 diabetes (rationale see page 546/779 (#33405)). - Evidence on the Overall Relationship: sufficient evidence only for CVD mortality. Sources of evidence: 2 meta-analyses and 1 pooled analysis. - 1 meta-analysis of CVD mortality: 8 cohort studies (n nearly 20,000). [Sluik D, et al., 2012] CVD mortality: highest versus lowest amounts of physical activity (PA): total PA: HR=0.61 (95% CI: 0.47-0.80); leisure-time PA: HR=0.63 (95% CI: 0.48-0.83), walking: HR=0.58 (95% CI: 0.42-0.79) - 1 meta-analysis of CVD risk (composite outcome: CVD mortality and CVD events (e.g., stroke)): 11 cohort studies, total sample size of about 20,000. [Kodama et al., 2013] Combined outcome (CVD events or CVD mortality): high versus low amounts of PA: RR=0.71 (95% CI: 0.60-0.84). analysis limited to 6 studies (only adults with type 2 diabetes): RR=0.64 (95% CI: 0.56-0.71). Overall, the 2 meta-analyses [Kodama et al., 2013, Sluik et al., 2012] included 14 individual studies, with 5 studies included in both meta-analyses. - 1 pooled analyses, sample size > 3,000 adults. [Sadrangani et al., 2014)] used a single questionnaire assessing leisure-time moderate-to-vigorous physical activity. - CVD mortality: Some activity vs. no activity: adjusted HR= 0.68 [95% CI: 0.51 to 0.92]) [Sadarangani et al., 2014] - CVD mortality: amounts of activity meeting physical activity guidelines or above vs. no activity: adjusted HR= 0.60 (95% CI: 0.44 to 0.82) [Sadarangani et al., 2014]. PAGAC-Conclusion: Strong evidence demonstrates an inverse association between volume of PA and risk of cardiovascular mortality among adults with T2DM. PAGAC Grade: Strong. Siehe Laufnummer: #33405, Seite 542/779, 546/779. - Dose-Response Relationship: Moderate evidence indicates an inverse, curvilinear dose-response relationship between PA and CV mortality among adults with T2DM (1 Metaanalysis [Kodama et al., 2013], 1 pooled analysis [Sadarangani et al., 2014]). PAGAC Grade: Moderate - Evidence on specific factors: o Insufficient evidence available to determine whether the relationship between PA and CVD mortality among adults with T2DM varies with age, sex, race/ethnicity, socioeconomic status, or weight status. PAGAC Grade: Not assignable. o Insufficient evidence available to determine whether the relationship between PA and CVD mortality among adults with T2DM varies with frequency, duration, intensity, or type (mode) of PA or how PA is measured among people with T2DM. PAGAC Grade: Not assignable.
Health related quality of life	Recherche - Update Recherche: 3 systematische Übersichtsarbeiten (SR), - PAGAC evidence (2018): 6 existing SR Ergebnisse der Update Recherche (3SR): 1. Rees (2017): aquatic exercise, 2 pre-post studies, AMSTAR*: moderate (*nach Bewertung durch den Review) Studies evaluated effect of aquatic exercise vs. land-based exercises or no-exercise control groups. differences before and after aquatic exercise for [SF-36 or SF-12 forms]: o physical function domain (SMD = 0.08 [95% CI, -2.80 to 2.96], 2 studies, n=40) o mental health domain (SMD = -0.36 [95%CI, -2.85 to 2.12], 2 studies, n=40) Certainty of evidence*: low (Bewertung nicht nachvollziehbar, da laut Legende: Certainty of evidence upgraded given no major limitations (S. 365/535 und 370/535))

World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 [cited: 2023-02-23]. https://apps.who.int/iris/rest/bitstreams/1315866/retrieve. Laufnummer: #33331	
	Anmerkung AZQ: Auch in NVL-Recherche identifiziert Für NVL-Recherche zurückgestellt/ausgeschlossen, da keine umfasssende Darstellung des Endpunktes QoL. Aus dem Abstract des Reviews (Rees 2017): "Assessment of glycemic control was necessary for inclusion, while secondary outcomes such as quality of life and cardiometabolic risk factors (i.e., blood pressure, triglycerides and total cholesterol) were considered, but not required for inclusion.". Vergleichsgruppe teils nicht passend (aquatic versus land-based exercise). 2. Yu (2018): traditional Chinese exercises, 6 RCTs, AMSTAR*: Moderate Studies evaluated traditional Chinese exercises (Tai Chi, Ba duan jin, qigong) for patients with T2D, mean age range 49-70 years. Tai Chi associated with greater improvements in physical function domain (MD = 5.92 [95% CI 0.68 to 11.16], 5 RCTs), but not on mental health domain of SF-36 form. No effect of ba duan jin on QOL as reported by 2 studies. Certainty od evidence*: low (downgraded given serious risk of bias and imprecision in effect estimates (wide confidence intervals ranged from clinically significant to non-clinically significant) - Anmerkung ÄZQ: zunächst nicht in NVL-Recherche identifiziert, als Handsuche im TiAb eingeschlossen 3. Zhou (2019): Tai Chi, 5 RCTs, AMSTAR*: Moderate, Studies evaluated Tai Chi among adults with T2D, mean age range 36 to 70 years. Mean sessions of exercise ranged from 15 to 120 min with 2 to 14 sessions per week. Total intervention duration ranged from 4 to 24 weeks. Tai Chi was associated with significant improvement in physical function domain (MD = 7.07 [95% CI, -0.79 to 13.35], 5 RCTs), bodily pain domain (MD = 4.30 [95% CI, 0.83 to 7.77], 5 RCTs), and social function domain (MD = 13.84 [95% CI, 6.22 to 21.47], 5 RCTs) of the SF-36, but not the other 5 components of QOL. Certainty of evidence*: Low (downgraded given serious inconsistency and imprecision (very wide confidence intervals)) Anmerkung ÄZQ: Auch in der NVL-Recherche identifiziert, siehe unten Ergebnisse PAGAC evidence (2018): 6 ESRs, Insufficient evidence available to determine relationship between PA and health-related quality of life in adults with T2DM. PAGAC Grade: Not assignable.
Disease Progression	Recherche: - Update Recherche: Keine neuen SR identifiziert; - PAGAC-evidence (2018): 34 existing SRs Ergebnisse PAGAC evidence (2018): Insufficient evidence available to determine relationship between PA and indicators of progression of neuropathy, nephropathy, retinopathy, and foot disorders. PAGAC Grade: Not assignable.
Intermediate outcomes/Markers of disease progression	Anmerkung ÄZQ: War nicht priorisierter Endpunkt der NVL-Recherche, daher hier nicht ausführlich dargestellt. PAGAC: There is high certainty evidence that PA improves markers of disease progression (HbA1c, blood pressure, BMI, and lipids) in adults with T2DM. There is high certainty evidence that aerobic activity, muscle-strengthening activity, and aerobic plus musclestrengthening activity improve markers of disease progression (HbA1C, blood pressure, BMI, and lipids) in adults with T2DM. PAGAC Grade: Strong.
Sedentary behavior	Due to a lack of population-specific evidence, the primary evidence base for assessing the associations between sedentary behaviour and health outcomes in adults living with T2DM, was the scientific literature collated and reviewed for adult populations (Certainty of evidence downgraded due to indirectness). In adults (aged over 18 years), there is moderate certainty evidence of an association between greater time spent in sedentary behavior and higher all-cause mortality, cardiovascular disease mortality, cancer mortality and incidence of cardiovascular disease and type-2 diabetes. (Seite 50/104 der guideline) Extraktion siehe unten.

World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 [cited: 2023-02-23]. https://apps.who.int/iris/rest/bitstreams/1315866/retrieve. Laufnummer: #33331	
Methodische Bewertung	AMSTAR-2 nicht anwendbar (Betrachtung von Umbrella-Reviews und update dieser Reviews), Betrachtung der einzelnen Kriterien: - PICO-Fragestellung angegeben, - Protokoll nicht aufgefunden (wird es wahrscheinlich gegeben haben) - Suche nach Umbrella-Reviews wird nicht genauer beschrieben, nur Anforderungen an die Reviews - Update der PAGAC-Searches in drei Datenbanken - AMSTAR-2-Bewertung der eingeschlossenen Reviews durchgeführt - GRADE-Bewertung der Evidenz erfolgt
Kommentare	- Kein SR von RCTs, sondern Betrachtung von Umbrella-Reviews und ggf. SRs,
Sedentary behaviour	
Sedentary behaviour	- Population: Adults 18 years of age and older - Exposure: Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour - Comparison: Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour - Outcomes: o all-cause ande cause-specific mortality o incidence of cardiovascular disease o incidence of cancer o incidence of type-2-DM o Adiposity/Prevention of weight gain/Body cmoposition Ergebnisse: A total of 13 reviews were included in the Evidence Profiles (AMSTAR 2: 1x high, 9x moderate, 3x low). - sedentary behaviour (examined mostly via self-reporting or device-based assessments of sitting or television viewing time) Overall, there is evidence of an association between greater time spent in sedentary behaviour (examined mostly via self-reporting or device-based assessments of sitting or television viewing time) and higher all-cause mortality, cardiovascular mortality, cardiovascular disease incidence and type-2 diabetes incidence (8, 35, 65, 87). For example: - meta-analysis (n= 36 383; mean age 62.6 years; 72.8% women): increasing time spent in sedentary behaviour was significantly associated with all-cause mortality. - meta-analysis (more than 1 million participants (87)) showed associations for total sedentary behaviour with all-cause mortality, and cardiovascular disease mortality, after adjustment for physical activity (87), although in this study the associations with cancer mortality were not statistically significant after adjustment for physical activity (87). - meta-analysis (8) reported significant associations between sedentary behaviour (assessed as sitting) and cardiovascular disease and cancer mortality, with results indicating a 9–32% (p for trend < 0.001) higher risk of cardiovascular disease mortality with higher levels of sedentary behaviour when measured as sitting time in the “inactive”, lowest quartile of physical activity (~ 5 min/day). Adults who were sedentary (sitting) for more than 8 hours per day had a higher risk of cardiovascular disease mortality, except for those who were “most active” (i.e. > 35.5 MET-hours/week, or ~ 60–75 mins/day), where the association was mitigated. - Evidence supports an association between sedentary behaviour (measured as total sitting time) and increased incident cardiovascular disease (HR= 1.29 [95% CI: 1.27 to 1.30]) which was attenuated following adjustment for potential covariates, including level of physical activity (HR= 1.14 [95% CI: 1.04 to 1.23]) (88). Conclusion of the GDG: - There is moderate certainty evidence of an association between greater time spent in sedentary behaviour and higher all-cause mortality, cardiovascular disease mortality, cancer mortality and incidence of cardiovascular disease and type-2 diabetes. - The benefits of limiting sedentary behaviour outweigh any potential risks.

World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. 2020 [cited: 2023-02-23]. https://apps.who.int/iris/rest/bitstreams/1315866/retrieve. Laufnummer: #33331	
	Is there a dose-response association (total volume, frequency, duration, intensity of interruption)? - moderate certainty evidence indicates a nonlinear dose-response relationship between sedentary time (sitting or television viewing time assessed by self-reporting, or by device-based assessments) and allcause mortality, cardiovascular disease mortality, cancer mortality, and incident cardiovascular disease (8, 35, 87). - meta-analysis: high certainty evidence on the dose-response relationship between accelerometer assessed total sedentary time and all-cause mortality (65) reporting that increasing time spent in sedentary behaviour was significantly associated with all-cause mortality. HR for increasing quartiles of sedentary time were 1.00 (referent; least sedentary); 1.28 (1.09– 1.51); 1.71 (1.36–2.15); and 2.63 (1.94–3.56), after adjustment for potential confounders including time spent in moderate- to vigorous-intensity physical activity (65). For more informatin, see guideline

Powell KE. The Scientific Foundation for the Physical Activity Guidelines for Americans, 2nd Edition. Journal of physical activity & health 2018:1–11. https://www.ncbi.nlm.nih.gov/pubmed/30558473	
Zitate	- U.S. Department of Health and Human Services. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. 2018 [cited: 2023-03-13]. https://health.gov/sites/default/files/2019-09/PAG_Advisory_Committee_Report.pdf. [3] Laufnummer: #33405 - U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. 2018 [cited: 2023-03-13]. https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf. Laufnummer: #33404
Fragestellung	The **2018 Physical Activity Guidelines Advisory Committee** Scientific Report provides the evidence base for the Physical Activity Guidelines for Americans, 2nd Edition. **Fragestellungen:** 38 questions and 104 subquestions. Für Fragestellung der NVL-Recherche relevant: Chapter 10, Question 4. In people with type 2 diabetes, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression? a) Is there a dose-response relationship? If yes, what is the shape of the relationship? b) Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status? c) Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?
Zeitpunkt der Suche	Pubmed 11/2017
Population	Individuals of all ages with diagnosed type 2-DM
Exposure	All types and intensities of physical activity, including sedentary behavior
Comparison	Comparison Individuals with type 2 diabetes who participate in varying levels of physical activity
Endpunkte	siehe Fragestellung: Im Weiteren für NVL-Recherche betrachtet: - risk of co-morbid conditions, - health-related quality of life, - disease progression (wenn zur Fragestellung NVL passend)

Powell KE. The Scientific Foundation for the Physical Activity Guidelines for Americans, 2nd Edition. Journal of physical activity & health 2018:1–11. https://www.ncbi.nlm.nih.gov/pubmed/30558473	
Sources of evidence	Systematic reviews, meta-analyses, pooled analyses reports published from 2011–2016 Assess Quality for Existing SRs, MAs, and Pooled Analyses: modified version of AMSTAR
Bewertung der Evidenz	**GRADE** the Evidence (Physical Activity Guidelines Advisory Committee Grading Criteria (S. 115/779): Grading the strength of the evidence was based on - applicability of the populations, exposures, and outcomes studied; - generalizability to the population of interest; - risk of bias and study limitations; - quantity and consistency of findings across studies; - magnitude and precision of effect.
Results (Abstract)	Newly described benefits of physical activity include reduced risk of excessive weight gain in children and adults, incidence of 6 types of cancer, and fall-related injuries in older people. Physical activity is associated with enhanced cognitive function and mental health across the life span, plus improved mental health and physical function. There is no threshold that must be exceeded before benefits begin to accrue; the accrual is most rapid for the least active individuals. Sedentary time is directly associated with elevated risk of all-cause and cardiovascular mortality, incident cardiovascular disease and type 2 diabetes, and selected cancer sites. A wide range of intervention strategies have demonstrated success in increasing physical activity. (Ergebnisse, siehe Beschreibung der WHO Guideline)
Methodische Bewertung	AMSTAR-2: Nur eingeschränkt anwendbar (Umbrella review): Y-nicht erwähnt, war aber wahrscheinlich vorhanden-N-PY-Y-Y-Y-N-na-na-na-na-na-na-na-? Na= nicht anwendbar (kein SR, Umbrella-Review).
Kommentar	Evidence review wird für die WHO-Guideline 2020 als Grundlage genutzt und ggf. aktualisiert. - SR von SRs, Metaanalysen und pooled analyses - keine Darstellung der Einzelstudien - Keine Beschränkung auf die Betrachtung von RCTs, auch SR von Kohortenstudien betrachtet.

3.1.2 Diabetesremission

Zhang et al., 2023

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Zhang Y. The effectiveness of lifestyle interventions for diabetes remission on patients with type 2 diabetes mellitus: A systematic review and meta-analysis. Worldviews Evid	**Suchzeitraum:** from inceptions to 03/2021 **Fragestellungen:** effectiveness of lifestyle interventions for diabetes remission among patients with type 2 diabetes mellitus.	**RESULTS** - 12 studies (7 RCTs, 5 quasi-experimental studies) with 3 997 patients with T2DM included. - Lifestyle interventions mainly divided into diet-only interventions and diet combined with physical activity interventions. - types of diet: o low-energy diet, o low carbohydrate diet, and o Mediterranean diet. - physical activity interventions:	Critically low y-y-n-py-y-y-n-py-y-n-n-n-y-y-y-y nicht-erfüllte kritische Do-	Daten von einzelnen Follow-Ups der Studien werden in die Metaanalyse einzeln eingeschlossen, als

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Based Nurs 2023; 20(1):64–78. https://www.ncbi.nlm.nih.gov/pubmed/36480153. #33329	**Population:** participants with T2DM Exclusion: Patients after bariatric surgery; with injectable insulin, or with serious complications. **Interventions:** Lifestyle interventions: diet or physical activity interventions (≥ 12 weeks). Exclusion: interventions involving medication, surgery, or single diet components. **Control:** usual care (standard care with no formalized, structured, or tailored intervention for adherence) or no intervention. **Outcome:** - diabetes remission (defined as: absence of glucose-lowering therapy, normoglycaemia, for a duration of ≥ 3 months), - weight, - quality of life score (measuring - tools of QoL include HRQOL, EQ-5D, and SF-36). **Studies:** randomized controlled trials and quasi-experimental studies Quality assessment: risk of bias was assessed by the Cochrane and Joanna Briggs Institute's tool.	○ Moderate-intensity aerobic and resistance physical activity, ○ walking, and ○ maintaining habitual physical activity Lifestyle intervention: - 3 studies: diet only ((Gow et al., 2017; Umphonsathien et al., 2019; Unwin et al., 2020). - 9 studies: diet combined with physical activity (3 types of diets, see above) Duration of lifestyle interventions varied from 12 weeks to 4 years. **Risk of Bias Assessment:** - 7 RCTs: performance bias (blinding of participants ans personel) high in all RCTs, Allocation concealment und detection bias high in jeweils zwei RCTs. - 5 quasi-experimental trials: 2 were before-after studies with no control group, the follow-up information of three studies were incomplete or absent. **effect of lifestyle interventions on diabetes remission** 11 studies: - RCTs: Lifestyle intervention 1420/9792 vs. 534/9713, OR = 4.03, 95% CI [3.02, 5.38], p < .001; - quasi-experimental studies: Lifestyle intervention 146/268 vs. control 0/268; OR = 109.16, 95% CI [33.18, 359.14], p < .001; **Anmerkung ÄZQ: Im Forest plot Daten für jedes follow-up einzeln eingeschlossen. So gehen die Ergebnisse mehrfach ein.** **Analyse nach follow-up duration (RCTs)** ≤ 12 months: OR 6,09 (95% KI 3,14; 11,79), p<0,001 13-36 months: OR 4,04 (95% KI 2,76; 5,92), p< 0,001 >36 months: OR 2,79 (95% KI 1,71; 4,32), p<0,001 For quasi-experimental studies, diabetes remission rate follow-up >36 months (OR = 122.64, 95% CI [16.66, 902.63], p < .001), follow-up ≤36 months (OR = 102.36, 95% CI [23.21, 451.4], p < .001); **Betrachtung der Einzelstudien** (nur RCTs (n=7), nur Studien, bei denen PA zur Intervention gehörte): **Esposito 2009:** n= 215 (108 intervention, 107 control) Diabetesremission Timepoint 1: OR 3,21 (0,85; 12,22) Timepoint 2: OR 2,28 (1,20; 4,31) Timepoint 3: OR 2,44 (1,39; 4,28) Timepoint 4: OR 1,91 (1,10; 3,32) **Esposito 2014:** n= 2015 (108 interventino, control 107)	männen: Ausgeschlossene Studien nicht aufgelistet, Methodik der Metaanalyse nicht nachvollziehbar,	seien es unterschiedliche Studien: Verzerrung durch mehrfache Wertung. Betrachtung der Einzelstudien. - Metaanalysen trotz großer Heterogenitäten gerechnet; Heterogenitäten in interventions - Lifestyle intervention meist als Kombination aus diet und PA - in der Recherche zur mediterranen Diät wurde ein SR zum Effekt von Diäten auf die Diabetesremission (Churuangsuk et al., 2022) identifiziert. Dieser identifiziert annähernd die gleichen Studien. Bei zwei Studien unklar (einmal

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Diabetesremission Timepoint 1: OR 1,78 (0,95; 3,30) Timepoint 2: OR 2,47 (1,07; 5,72) Timepoint 3: OR 27,85 (1,63; 476, 68) Timepoint 4: OR 11,43 (0,62; 209,23) **Gregg 2012 (Look-AHEAD)**: n= 4503 (2241 intervention, 2262 control) Diabetesremission: Timepoint 1: OR 6,4 (4,6; 8,9) Timepoint 2: OR 4,98 (3,62; 6,85) Timepoint 3: OR 4,22 (3,03; 5,87) Timepoint 4: OR 3,84 (2,70; 5,46) **Lean 2018 (DiRECT)**: n= 306 (157 intervention, 149 control), Diabetesremission: OR 21,75 (9,01; 52,47) **Lean 2019 (DiRECT)**: n= 306 (157 intervention, 149 control) Diabetesremission: OR 15,9 (6,13; 41,22) **Ried-Larsen 2019 (U-TURN):** n= 93 (62 Intervention, 31 control), Diabetesremission: timepoint 1: OR 5,5 (1,5; 20,14) timepoint 2: OR 2,84 (0,75; 10,78) timepoint 3: OR 4,23 (0,9; 19,96) **Taheri 2020 ((DIADEM-I):** n= 147 (70 intervention, 77 control) Diabetesremission: OR 2,76 (1,23; 6,18) **Effect of lifestyle interventions on QoL** 5 studies reported efficacy of lifestyle interventions on total score of QoL (SF-36 questionnaire, Equation 5-D scale, and HRQOL). - SMD and random-effect models were used due to differences in the measurement of different rating scales and the existence of heterogeneity (p < .001, I2 = 92%). intervention vs. control: SMD = 1.10, 95% CI [0.49, 1.70], p = .007). **Subgroup analysis:** - RCTs: intervention vs. control: SMD = 0.17 (95% CI 0.02, 0.32), p = 0.02) with a low heterogeneity (p = 0.52, I2 = 0%), - quasi-experimental studies: intervention vs. control: SMD = 2.09 (95% CI 0.70, 3.47), p < .001		ggf. Publikation nach Zeitpunkt der Recherche). Da die ausgeschlossenen Studien nicht mit Ausschlussbegründung aufgeführt werden, kann es für eine Studie nicht nachvollzogen werden.

3.1.3 Diabetische Retinopathie

Yusufu et al., 2019

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Yusufu M. How to perform better intervention to prevent and control diabetic retinopathy among patients with type 2 diabetes: A meta-analysis of randomized controlled trials. Diabetes Res Clin Pract 2019; 156:107834. https://www.ncbi.nlm.nih.gov/pubmed/31550487 .	**Suchzeitraum:** 01/1980 to 06/2019 **Fragestellungen:** - could interventions targeting modifiable risk factors of DR (blood glucose, blood pressure, lipid, dietary, **physical activity** and smoking) reduce the risk of developing DR and/or its worsening among patient with type 2 diabetes? - what type of intervention is most effective? - Best follow-up interval of interventions? **Population:** T2DM **Interventions:** interventions targeting modifiable risk factors of DR (including blood glucose, blood pressure, lipid, dietary, physical activity and smoking) **Outcome:** prevention and control of DR. **Studies:** RCTs **Quality/RoB-assessment:** RoB-Tool Cochrane, GRADE	22 RCTs (n = 22,511) included. - In all studies ophthalmologists diagnosed and/or evaluated DR based on on-site ophthalmoscopy or report from primary care physicians. Interventions classified into 5 categories based on modifiable risk factors: (1) Blood-pressure-control intervention, (2) Glycemic-control intervention, (3) Lipid-control intervention, (4) Dietary-control intervention, and (5) Multi-factorial intervention (interventions targeting >1 risk factors) Results of intervention (all) effects on **DR prevention (New onset DR)** - interventions targeting modifiable risk factor of DR (all): Intervention 220/3013 (7,3%) vs. Control 260/2868 (9,1%), OR = 0.60 (95% CI 0.45 to 0.79), 11 RCTs, I^2 = 26.7%; Results of intervention (all) effects on **DR worsening** OR = 0.62 (95% CI 0.47 to 0.80; P < 0.001), I2 = 0.0%; **Subgroup-Analyses:** Keine Einzelauswertung zu physical activity, nur in multi-factorial intervention enthalten: Multifactorial intervention reduced the **risk of developing DR** significantly (OR = 0.27; 95% CI 0.14 to 0.53; P = <0.001, 3 studies). Effects on **DR worsening**: no pooled results of multifactorial intervention because only one study in this subgroup. 1 study: OR 0,13 (95% CI 0,01; 2,83), **Risk of progression:** multifactorial intervention: 0,39 (95% CI 0,23; 0,65), 2 studies	Critically low Y-n-n-py-y-y-n-y-py-n-y-n-n-y-y-y Nicht-erfüllte kritische Domänen: kein Protokoll, ausgeschlossenen Studien nicht aufgeführt, RoB bei der Interpretation der Ergebnisse nicht ausreichend diskutiert.	**Keine Einzelauswertung zu physical activity (PA).** Es wurden nur Studien zu multifaktoriellen Interventionen identifiziert. Wie groß der Anteil an physical activity war, ist nicht ersichtlich.

3.1.4 Diabetische Neuropathie / Fußkomplikationen

Matos et al., 2018

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Matos M. Physical activity and exercise on diabetic foot related outcomes: A systematic review. Diabetes Res Clin Pract 2018; 139:81–90. https://www.ncbi.nlm.nih.gov/pubmed/29477503. #33066	**Zeitpunkt der Suche:** 02/2017 (07/2017) **Fragestellung:** effects of exercise and physical activity interventions on diabetic foot outcomes. **Population:** patients with a diagnosis of diabetes regardless of etiology, or a clinical diagnosis of diabetic peripheral neuropathy, polyneuropathy or diabetic foot ulcer; **Intervention:** any form of supervised physical activity at a care center or at home; **Comparator:** daily-life physical activity (absence of supervised physical activity or exercise regimen) and/or usual foot care education. **Studies:** controlled clinical trials, ≥ 10 participants **Outcomes:** diabetic foot outcomes **Secondary outcomes:** (im Methodenteil nicht definiert, aus Ergebnisteil: glycaemic control, functional fitness, quality of life, BMI, lipid profile and others) **Study quality assessment:** PEDro critical appraisal tool (at least 5 points: low risk of bias)	6 studies (n=418 patients with diabetes) included. - 2 studies only aerobic exercise; - 2 studies combined aerobic, resistance and balance exercise; - 2 studies combined aerobic and balance exercise by Thai Chin Chuan methods. - Intervention programs ranged from 8 weeks to 4 years - 3/6 studien type 1 or 2 eingeschlossen, 3 studien patients with T2DM - vorbestehende Neuropathie: 4 studies with PN, 1 study without symptoms of PN, 1 study 6/28 in intervention group with PN Heterogenity in type of intervention, outcome measurement, duration: Outcome measurement - nerve velocity conduction (3 studies), different nerves - peripheral sensory function (2 studies) (vibration perception threshold, Semmes-Weinstein 10-g monofilament) - Michigan neuropathy Screening Instrument (MNSI) (2 studies), Michigan Diabetic Neuropathy Score (MDNS) - peak pressure, time to peak pressure and center of pressure over plantar surface by the Pedar-X System - incidence rate of foot lesions **Anmerkung ÄZQ: Hier nur incidence rate of foot lesions und quality of life extrahiert (für die NVL priorisierte Endpunkte, für andere Endpunkte siehe Originalpublikation)** **Rate of foot lesions:** - 1 study (diabetic patients type 1 or 2 with PN, n= 79): Improvements: Incidence rate (IR) of all foot lesions from 6 months to 12 months: Intervention group (IG) - 44.6%, Control group (CG) - 31.1% IR: lesion episodes IG - 43.0%, CG - 37.8% IR of full-thickness ulcer episodes: IG - 47.2%, CG - 19.0% IR of weight-bearing full thickness plantar ulcers decreased in intervention by 60.0% and increased in controls by 76.0%, showing a risk of 0.02 ulcers/person-year in the intervention group and a risk of 0.12 ulcers/person-year in controls. **Quality of life:** 1 study (The Korean SF-36 v2 instrument) - better results in life scores on domains of physical functioning (7.0%, p = 0.028), bodily pain (17.6%, p = 0.009), physical role limitation (29.0%, p = 0.006), emotional role limitation (30.3%, p = 0.002), and social functioning (15.6%, p = 0.001) in diabetic patients who did the Tai Chi Chuan program.	Critically low y-n-n-py-y-y-n-y-py-n-noMa-noMa-y-y-n-y nicht erfüllte kritische Domänen: kein Protokoll, ausgeschlossene Studien nicht aufgeführt, Publikationsbias nicht berücksichtigt	Keine Subgruppenanalyse zwischen Typ-1- und Typ-2-Diabetes möglich - Keine Subgruppenanalyse nach vorbestehender Neuropathie Endpunkte/outcome measures wie Scores (MDNS) siehe Originalpublikation

3.1.5 Lebensqualität

Jayedi et al., 2022

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Jayedi A. Dose-Dependent Effect of Supervised Aerobic Exercise on HbA1c in Patients with Type 2 Diabetes: A Meta-analysis of Randomized Controlled Trials. Sports Med 2022; 52(8):1919–38. https://www.ncbi.nlm.nih.gov/pubmed/35362859. #33327	**Suchzeitraum:** to May 2021 **Fragestellung:** dose-dependent effect of supervised aerobic training (SAT) on HbA1c. **Population:** adults with type 2 diabetes mellitus **Interventions:** Supervised aerobic exercise training. **Comparisons:** no exercise intervention. **Ausschlusskriterien:** - combined exercise program (aerobic and resistance training combined); - unsupervised aerobic exercise program; **Outcomes:** Primary outcome: HbA1c Secondary outcomes: - quality of life, - change in hypoglycemic medications, - adverse events. **Studies:** randomized trials, ≥12 weeks **Subgroup:** baseline weight and health status, exercise, modality and intensity, intervention duration, presence of dietary co-intervention, and risk of bias assessment. **Risk of bias assessment:** Cochrane Risk of bias tool	26 trials, n=1253 participants **Change in hypoglyaemic medication** - decreased antidiabetic medications: Intervention 37/211 (17,5%) vs. Comparison 11/174 (6,3%), RR 1,09 (1,02; 1,15), risk difference 0.13, 95% CI 0.02-0.23, absolute effect: 13 more per 100 patients (from 2 more to 23 more); 7 trials, n = 375, I^2: 67%; **GRADE = moderate** (imprecision), “Of the trials included in the present review, three trials reported significant reduction either in the dosage or the number of hypoglycemic medications in the intervention group as compared with the control group [32, 48, 54]. Of those, two trials reported a non-significant reduction in HbA1c levels [48, 54]. Therefore, the effect of aerobic exercise on improving glycemic control in these trials appeared as a reduction in hypoglycemic medications rather than a reduction in HbA 1c levels.” **hypoglycemic events** - Intervention 18/139 (12,9%) vs. comparison 2/124 (1,6%), RR 1,08 (1,05; 1,15), risk difference: 0.10, 95% CI 0.03-0.17; absolute effect: 10 more per 100 patients (from 3 more to 17 more); 4 trials, n = 263, I2: 14,7%; **GRADE = low** (RoB, imprecision). **Adverse events:** - Increased adverse events by 4 per 100 patients (risk difference: 0.04, 95% CI − 0.02 to 0.11; 2 trials, n = 236; **GRADE = low**) **Seriours adverse events** - Intervention 10/132 (7,6%) vs. comparison 3/104 (2,9%), RR 1,05 (0,99; 1,11); absolute effect: 1 more per per 1000 patients; 2 trials, n = 236, I2:20,8%; **GRADE = low** (indirectness, imprecision). **Quality of life** Limited evidence is available for quality of life. 2 trials reported effect of SAT on HRQoL. - 1 trial: SAT significantly improved physical functioning and mental health after a 12-week intervention (n=64). - 1 trial indicated that aerobic training did not change HRQoL significantly as compared with the control group (n=123). **RoB:** - 9 trials: low risk of bias, - 14 trials: some concerns,	**Moderate** y-py-n-py-y-y-y-y-py-n-y-y-y-y-y-y (Begründung für Studiendesign-Wahl nicht gegeben und Funding in Studien nicht berichtet.)	Quality of life als einer der in der NVL priorisierten Endpunkte für die NVL Recherche nicht primärer Endpunkt (Erhebung des HbA1c als obligates Einschlusskriterium) Anmerkung ÄZQ: Die angegebenen relativen Risiken scheinen bei den Zahlen zu gering. Aufgrund der Unsicherheit werden diese Zahlen im HGT nicht genannt, sondern die absoluten Zahlen.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		- 3 trials: high risk of bias. The analysis of trials with a low risk of bias indicated the same finding as the main analysis. **Limitations:** - High degree of statistical heterogeneity, exercise intensity and baseline weight status partially explained the observed inconsistency. However, all trials showed a reducing effect, and 13 trials reported a significant reduction in HbA1c. Observed heterogeneity may be mainly due to differences in the magnitude of effect rather than differences in direction of effect. - Some differences in baseline characteristics of participants including baseline weight, number of medications used, pre-existing comorbidities, and duration of diabetes, which may have affected the results. - Insufficient evidence regarding the long-term (> 6 months) effect of aerobic training on HbA1c.		

Mohammad Rahimi et al., 2022

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Mohammad Rahimi GR. The Effect of Exercise Interventions to Improve Psychosocial Aspects and Glycemic Control in Type 2 Diabetic Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Biological research for nursing 2022; 24(1):10–23. https://www.ncbi.nlm.nih.gov/pubmed/34235949 .	Suchzeitraum: up to 01/2021 Fragestellung: to investigate the impacts of exercise training interventions to improve psychosocial aspects and glycemic control in T2DM patients. Population: adult T2DM patients without regular exercise (less than 150 min per week) before study enrollment Intervention: exercise intervention (aerobic, resistance, or combined (aerobic + resistance) exercise intervention) with or without dietary advice for more than 4 weeks Outcome: - quality of life (dimensions of bodily pain, mental health, and social functioning), depression and glycemic control (i.e., HbA1c and fasting blood glucose)	17 RCTs with 2,127 participants. - **depression**, standard mean difference (SMD) -0.65 (95% confidence interval (CI) -1.03 to -0.28, p = 0.0006), 11 RCTs, I^2=87%, Aussagesicherheit der Evidenz: very low (RoB, Inkonsistenz, Publication bias) - **mental health** SMD: 0.53 (95% CI 0.31 to 0.76, p < 0.00001, I2= 47%), 9 RCTs, n=870, Aussagesicherheit der Evidenz: low (RoB, Publikation bias) - no significant differences between the intervention and control groups for bodily pain, social functioning, and fasting glucose (all p > 0.05). The overall quality of included RCTs was estimated to be moderate to good, with a median TESTEX score of 9 (range 7–12) out of a maximum 15 CONCLUSION Our systematic review and meta-analysis displayed that exercise training interventions decreased depression and HbA1c and increased mental health in individuals with T2DM. Further longer-term and high-quality clinical trials are required to additional assess and confirm the findings presented here.	Critically low Y-n-y-py-y-y-y-y-n-n-y-n-n-y-y-y Nicht-erfüllte kritische Domänen: kein Protokoll, Blinding der Teilnehmenden in der RoB nicht erhoben (bei Sport relevant?), Einfluss des RoB in der Metaanalyse und	low number of included RCTs, some included studies have small sample sizes. Einige Studien von kurzer Interventionsdauer Many of the included studies did not provide information regarding the

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	Studies: RCTs	Bewertung der Aussagesicherheit der Evidenz: RoB: -1 (Blinding der Teilnehmenden nicht erhoben) Päzision: 0 Inkonsistenz: -1 bei Depression Direktheit: 0 Publication bias: -1	bei der Interpretation der Ergebnisse nicht berücksichtigt.	energy expenditure.

Cai et al., 2017

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentare
Cai H. Effect of exercise on the quality of life in type 2 diabetes mellitus: A systematic review. Quality of life research an international journal of quality of life aspects of treatment, care and rehabilitation 2017; 26(3):515–30. https://www.ncbi.nlm.nih.gov/pubmed/27990609. #33070	**Suchzeitraum:** until 01/2016. **Fragestellung:** effect of exercise on the quality of life of people with T2DM **Population:** adult people with T2DM **Intervention:** exercise **Comparison:** usual care **Outcome:** quality of life **Ausschlusskriterien:** exercise training as part of an intervention with multiple components (e.g. combined with a diet intervention) **Studies:** all clinical trials **Assessment of study quality:** Downs and Black Quality Index (QI)	30 studies (2785 participants) - No Metaanalysis performed due to heterogeneity in type of intervention exercise, programme duration, of study designs and outcome measurement and others. - exercise was divided into four modes: aerobic, resistance, a combination of aerobic and resistance and yoga. **Aerobic exercise:** 15/20 studies reported a significant effect on quality of life in patients with T2DM compared with control group. (quality: 8 good, 3 moderate, 4 poor; Qualität der 5 Studien, die keinen Effekt gezeigt haben: 1 good, 3 moderate, 1 poor) **Resistance exercise:** 3/6 studies reported a significant effect on quality of life in patients with T2DM compared with control group (quality of studies: 2 poor, 1 good). (Quality of studies showing no effect: 1 poor, 1 moderate, 1 good) **Combined exercise:** 4/9 studies reported a significant effect on quality of life in patients with T2DM compared with control group. **Yoga:** One study reported a significant effect of yoga on quality of life. **Quality assessment:** Most studies: good reporting quality; most studies: high risk of bias in terms of study design. Quality of the majority of the studies was moderate, with a mean score of 21. - 8 studies: poor quality, - 11 studies: moderate quality, - 11 studies: high quality CONCLUSIONS (authors of the review) The effect of aerobic exercise on the quality of life in people with type 2 diabetes was safe and effective. Then, most of the studies on aerobic exercise were of good methodological quality. The effects of resistance exercise and combined exercise on the quality of life in people with type 2 diabetes were mixed, and the effect of yoga on quality of life still need more research.	Critically low y-n-n-py-y-y-n-py-py-n-noMa-noMa-n-y-n-y Nicht-erfüllte kritische Domänen: Kein Protokoll, keine Angabe der ausgeschlossenen Studien, RoB-bei der Interpretation der Ergebnisse nicht berücksichtigt, Publikatonisbias nicht betrachtet.	Limitations: - some included studies did not provide supervised exercise (participants completed training program or reached moving targets?), - Studiendesign der Einzelstudien nicht ausreichend angegeben - most of the included studies performed 12–16 weeks (duration of exercise too short?) - could not observe long-term effects.

Acosta-Manzano et al., 2020

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Acosta-Manzano P. Beyond general resistance training. Hypertrophy versus muscular endurance training as therapeutic interventions in adults with type 2 diabetes mellitus: A systematic review and meta-analysis. Obes Rev 2020; 21(6):e13007. https://www.ncbi.nlm.nih.gov/pubmed/32067343. #33095	**Suchzeitraum:** 01/1998, to 07/ 2019 **Fragestellung:** effects of HT (hypertrophy training) and MERT (muscular endurance training) in patients with T2DM **Population:** adults with T2DM **Intervention/Comparison:** HT and MERT Comparisons (a) HT vs control group, (b) MERT vs control group, (c) HT vs AT (aerobic training), and d) MERT vs AT Ausschluss: Resistance training (RT) complemented with other interventions, patients with major chronic comorbidities **Outcomes:** **primary** - glycaemic control, - physical fitness, **secondary** - body composition, - lipid profile, - blood pressure, - C-reactive protein, - **quality of life** (Anmerkung ÄZQ: im Folgenden nur QoL in RCTs berichtet, da andere Endpunkte für die NVL-Recherche nicht priorisiert wurden; non-RCTs wurden in dem Review auch nicht näher beschrieben). **Studies:** RCTs and non-RCT (resistance training ≥ 4 weeks) **Risk of bias assessment:** RCT: Cochrane RoB-Tool	82 studies included (qualitative synthesis), of those 43 RCTs were included in meta-analysis. **Quality of life:** 8 sudies, SF-36 and SF-12: 6 studies, ADDQoL: 2 studies Methodical quality: 4 medium quality, 3 low quality, 1: nicht sicher zuordnenbar **Ergebnisse:** **within-group changes from the hypertrophy or muscular endurance group minus the control group** **General quality of life**: - HT vs control group (ADQOL: The Audit of Diabetes-Dependent Quality of Life): 1 study, n=30, pooled Difference: 0,13 (95% CI -4,18; 4,44) - MET vs. control group (ADQOL): 1 study, n=26; pooled difference -0,18 (95% CI -0,3; -0,06) **within-group changes from the hypertrophy or muscular endurance group minus the aerobic group** **Physical component score (standardized):** - HT vs. AT: 3 studies, n=127, pooled difference 0,25 (95% CI -0,34; 0,84), I2=76,1% - MERT vs. AT: 1 study (SF-36), n=60: pooled difference -0,09 (95% CI -0,6; 0,41) - RT vs. AT: 4 studies, n=187, pooled difference 0,16 (95% CI -0,28; 0,6), I2= 68,9% **Mental component score (standardized):** - HT vs. AT: 3 studies, n=127; pooled difference -0,06 (95% CI -0,59; 0,48), I2=71,7% - MERT vs. AT: 1 study (SF-36), n=60: pooled difference 0,19 (95% CI -0,31; 0,7) - RT vs. AT, 4 studies, n=187, pooled difference: 0,00 (95% CI -0,4; 0,4), I2= 63,1%. **General quality of life:** no studies.	**Moderate** (unkritische Kriterien nicht erfüllt: keine Begründung zur Wahl des Studientyps, Extraktion einzeln, Funding der Studien nicht berichtet) y-y-n-py-y-n-y-y-py(?)-n-y-y-y-y-y-y	Wenig Daten zum betrachteten Endpunkt (Quality of life), keine statistisch signifikanten Unterschiede (nur MET vs. Control: klinisch relevant?, n=26) - Kleine Studien

Miranda et al., 2018

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Miranda S. Pilates in noncommunicable diseases: A systematic review of its effects. Complement Ther Med 2018; 39:114–30. https://www.ncbi.nlm.nih.gov/pubmed/30012382. #33075	**Suchzeitraum:** je nach Datenbank von 1960-1999 bis November 2016 **Fragestellung:** effects of Pilates in the four major groups of noncommunicable diseases (including diabetes) **Population:** participants with most common NCDs, i.e., chronic respiratory diseases, chronic cardiovascular diseases, cancer or diabetes **Intervention:** pilates **Comparison:** control (e.g. usual care) **Outcomes:** at least one clinical or patient –reported outcome **Studies:** quantitative studies **Risk of bias assessment:** Quality assessment tool effective public health practice project (EPHPP)	12 studies included, 491 participants (78.6% females; age range 13.7-70 years old), diabetes (3 studies: 1 study T1DM, 2 studies T2DM) Im Weiteren nur Extraktion T2DM (nur für die NVL-Recherche relevante Outcomes: QoL): **1 Study (Yucel 2015):** RCT, n=45, Duration 12 weeks, moderate quality - Intervention versus Control (usual care) SF-36: Mental health: Exercise group (EG) Pre 29.0 ± 5.0, Post 35,0 ±3.0, p=0,001 Control group (CG): Pre 29.0±11.0; Post 35.0±1.0, p=0.132 Effect size (ES)=0,00 Physical heath: EG: Pre 40.0±3.0; Post 41.0±4.0, p=0.120 CG: Pre 40.0±0.0; Post 41.0±4.0, p=0.42 Effect size=0,00 HADS (Hospital anxiety depression scale) Anxiety: EG: 8.0±3.0; Post 7.0±3.0, p=0.023, CG: Pre 8.0±1.0; Post 7.0±1.0, p=0.162 ES=0.00 Depression: EG: Pre 9.0±2.0; Post 8.0±2.0, p=0.019, CG: Pre 9.0±2.0; Post 8.0±1.0, p=0.08 ES= 0.00 **1 Study (Torabian 2013):** weak quality, 2 groups pre-post design, n=70, duration 8 weeks. (eingegraut, da nicht priorisierter EP in der Recherche. - Intervention versus Control (usual care) GHQ-28: General health questionnaire – 28 (general health, depression); Physical symptoms: EG: Pre 43.1±2.1; Post 4.3±1.8, p=0.001, CG: Pre 12.2±3.1; Post 11.9±2.7, p=0.23 EG vs. CG p=0.01 ES=-12.70 (Anmerkung ÄZQ: Baseline-Score zwischen den Gruppen sehr unterschiedlich) Anxiety: EG: Pre 11.0 ±2.0; Post 5.9±2.2, p=0.04, CG: Pre 10.6±3.3; Post 0.7±2.6, p=0.11 EG vs. CG p= 0.003 ES= -1.52 Depression: EG: Pre 11.1±2.6; Post 6.4±2.0, p=0.01, CG: Pre 11.5±2.9; Post 11.3±3.0, p=0.47 EG vs. CG p=0.04 ES=-1.38 Social dysfunction: EG: Pre 13.0±2.3; Post 6.2±2.2, p=0.02, CG: Pre 12.4±3.5; Post 11.5±2.9, p=0.50 EG vs. CG p=0.001, ES= -1.73	**Critically low** y-y-n-py-n-y-y-y-n-n-noMa-noMa-n-y-n-y	Nur wenige Daten (n=45, 12 weeks) zu den in den NVL-Rechere betrachteten Outcomes

Tai Chi

Qin et al., 2020

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Qin J. Effect of Tai Chi on Quality of Life, Body Mass Index, and Waist-Hip Ratio in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne) 2020; 11:543627. https://www.ncbi.nlm.nih.gov/pubmed/33542702. #33109	**Suchzeitraum:** inception to February 2020 **Fragestellung:** effect of Tai Chi on improving quality of life (QoL), body mass index (BMI) and waist-hip ratio (WHR) in patients with T2DM. **Population:** patients with T2DM **Interventions:** Tai Chi **Comparisons:** control group (wait list; no intervention; usual care; sham exercise), other exercise (ÄZQ: sham exercise?) **Outcomes:** QoL, BMI and /or WHR **Studies:** RCTs and quasi-experimental studies **Risk of bias assessment:** PEDro scale	18 trials included (total). 8 trials assessed Effect on QoL - Assessment-tool: DSQoL: 1 RCT (tai chi versus walking); SF-36: 7 RCTs. QoL (SF-36): Tai Chi statistically improved QoL compared with control group (wait list; no intervention; usual care; sham exercise), 7 RCTs - physical function (PF): MD = 7.73, 95% confidence interval (CI) = 1.76 to 13.71, 6 RCTs, n=447, p = 0.01; GRADE: very low - role-physical function (RP): MD = 9.76 (95% CI 6.05; 13.47), 6 RCTs, n=447, p < 0.001; GRADE: low - body pain (BP): MD = 8.49 (95% CI 1.18; 15.8), 6 RCTs, n=447, p = 0.02; GRADE: very low - general health (GH): MD = 9.80 (95% CI 5.77; 13.82), 6 RCTs, n=447 p <0.001; GRADE: Low - vitality (VT): MD = 6.70 (95% CI 0.45, 12.94), 6 RCTs, n=447 p = 0.04; GRADE: very low - social function (SF): MD = 9.1 (95% CI 4.75; 13.45), 7 RCTs, n=484, p < 0.001; GRADE: low - role-emotional function (RE): MD = 7.88 (95% CI 4.03; 11.72), 6 RCTs, n=447, p < 0.001; GRADE: low - mental health (MH): MD = 5.62 (95% CI 1.57; 9.67), 6 RCTs, n=447 p = 0.006), GRADE: very low The lower limits of 95% CI in the two SF-36 domains of GH and RP were greater than the minimal clinically important difference, but not in the other six SF-36 domains of PF, BP, VT, SF, RE, and MH. For the DSQoL, the trial demonstrated favorable effects of Tai Chi when compared with walking. methodological quality (studies assessing QoL): ranged from 3 to 6/10 points. 5 of "good" quality (6/10), 2 "fair" quality (5/10), and one study "poor" quality (3/10). Blinding of participants, therapists, and evaluators was not conducted in most trials. No trial reported concealed allocation. --- Bewertung der Aussagesicherheit in Anlehnung an GRADE (Bewertung oben mit Indirektkeit -1): - RoB: -1 (Verblindung nicht möglich, no concealed allocation) - Inkonsistenz: für PF, BP, VT, MH: -1, für RP, GH, SF, RE: 0	Critically low y-n-n-py-y-y-n-y-py-n-y-n-y-y-y nicht-erfüllte kritische Domänen: kein Protokoll, ausgeschlossene Studien nicht aufgelistet	Clinically important differences "only" in two domains (minimal clinically important differences for eight SF-36 domains defined as ≥5 points) - style, time, frequency, and duration of treatment of Tai Chi were variable. 14/18 studies conducted in China (auf deutschen Versorgungsalltag übertragbar?)

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		- Indirektheit: 0 bis -1 (14/18 Studien aus China, auf deutschen Kontext übertragbar? In mehreren Studien angeblich kein drop out., Interventionen unterschieden sich) - Präzision: 95%KI-Intervall überlappt die Bereiche, in denen es keinen klinisch relevanten Effekt gibt: PF, BP, VT, SF, RE und MH: -1 - Publication bias: kein funnel plot, da weniger als 10 Studien für den betrachteten Endpunkt, viele kleine Studien		

3.2 Assoziation physical activity and morbidity/mortality: Kohortenstudien, Querschnittsstudien

Rietz et al., 2022

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar

Rietz M. Physical Activity and Risk of Major Diabetes-Related Complications in Individuals With Diabetes: A Systematic Review and Meta-Analysis of Observational Studies. Diabetes Care 2022; 45(12):3101–11. https://www.ncbi.nlm.nih.gov/pubmed/36455117.
 	
#33328
	Suchzeitraum: up to July 2021
	
	Fragestellung: association of physical activity and macro- and microvascular complications in adults with diabetes mellitus
	
	Population: adults with diabetes (type-1- or Type-2-diabetes)
	
	Intervention/Factor: physical activity
	
	Outcomes: incidence of and mortality from diabetes-related complications, i.e.,
	- cardiovascular disease (CVD),
	- coronary heart disease,
	- cerebrovascular events,
	- heart failure,
	- major adverse cardiovascular events,
	- microvascular complications such as retinopathy and nephropathy
	
	Studies: prospective observational studies
	
	certainty of evidence and risk of bias: GRADE, ROBINS-I.
		Overall, 31 studies included.
		- Diabetes type in included studies:
		  - 14 studies type 2 diabetes,
		  - 6 studies type 1 diabetes,
		  - 5 studies type 1 and type 2 diabetes,
		  - 6 studies type of diabetes was not specified.
		- Physical activity recorded via self-reports in all studies.
		- RoB: 6 studies moderate RoB, 25 studies serious RoB. Main sources of bias included bias: confounding (not all relevant confounders were considered in the primary study), misclassification of exposure (physical activity was assessed with nonvalidated tools).
		
		<u>High versus low levels of physical activity:</u>
		CVD incidence: summary risk ratio (SRR) 0.84 [95% CI 0.77, 0.92], 7 studies, n=34503, I^2:0%, **GRADE* moderate** (very serious RoB, positive: dose response gradient)
		
		CHD incidence: SRR 0,84 (0,76; 0,93), 5 studies, n=31768, I2:0%, **GRADE* low** (very serious RoB)
		
		Cerebrovascular event incidence: SRR 0,74 (0,65; 0,84), 6 studies, n=928076; I2: 26%, GRADE* low (very serious RoB)
		
		Heart failure incidence: SRR 0,76 (0,65; 0,88), 3 studies, n=3047, I2:0%, GRADE* low (very serious RoB)
		
		Major adverse cardiovascular events: SRR 0,82 (0,70; 0,97), 2 trials, n=11617, I2: 0%, **GRADE* low** (very serious RoB)
		
		CVD mortality: SRR 0.62 [0.55, 0.69], 11 trials, n=51804, I2: 0%, **GRADE* moderate** (very serious RoB, positive: dose response gradient)
		
		CHD mortality: SRR 0,90 (0,54; 1,51), 3 studies, n=1327, I2: 42%, **GRADE* very low** (very serious RoB, serious imprecision**)**
		
		microvascular complications: SRR 0.76 [0.67, 0.86], 8 studies, n=27645, I2: 0%. **GRADE*** (Autor*innen des Reviews): **moderate certainty of evidence** (very serious RoB, positive: dose response gradient)
		
		Diabetic retinopathy incidence: SRR 0,68 (0,55; 0,84), 5 studies, n=14041, I2: 0%, **GRADE* moderate** (very serious RoB, positive: dose response gradient)
			Moderate
			
			y-py-n-py-y-y-y-py-y-n-y-y-y-y-y
			
			2 nicht-kritische Domänen nicht erfüllt: Auswahl des Studiendesign nicht begründet, Funding in den Studien nicht angegeben.
				Kohortenstudien
				
				Unterscheidung zwischen T1DM und T2DM?

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Diabetic renal disease incidence: SRR 0,97 (0,46; 2,07), 2 studies, n=2464, I2: 75%, **GRADE* very low** (very serious RoB, serious imprecision, serious inconsistency) **<u>Linear dose-response meta-analysis (physical activity per 10 MET-h/week)</u>** **CVD incidence:** SRR 0.97 [95% CI 0.93, 1,00], 4 studies, n=16040, I^2: 6%, **CHD incidence**: SRR 0,89 (0,77; 1,03), 3 studies, n=15871, I2:45%, **Cerebrovascular event incidence:** SRR 0,92 (0,80; 1,04), 2 studies, n=13229; I2: 1%, **Heart failure incidence:** Linear dose-response meta-analyses could not be conducted because of lack of data from primary studies **Major adverse cardiovascular events:** Linear dose-response meta-analyses could not be conducted because of lack of data from primary studies **CVD mortality:** SRR 0.82 [0.74, 0.90], 7 trials, n=29822, I2: 82%, **CHD mortality:** Linear dose-response meta-analyses could not be conducted because of lack of data from primary studies **microvascular complications:** SRR 0.93 [0.88, 0.98], 3 studies, n=14472, I2: 45%. **Diabetic retinopathy incidence:** SRR 0,95 (0,91; 0,98), 2 studies, n=3332, I2: 0%, **Diabetic renal disease incidence:** Linear dose-response meta-analyses could not be conducted because of lack of data from primary studies ***:** GRADE-Bewertung durch Autor*innen des Reviews; “Dose-response meta-analyses showed that physical activity was associated with lower risk of diabetes-related complications even at lower levels.” There was an inverse dose response relation between physical activity and incidence of the investigated outcomes. However, the relationship was nonlinear for CVD mortality and incidence of MVD. **Subgroups: Summary relative risks (SRRs) of high versus low levels of physical activity and incidence of cardiovascular diseasein individuals with diabetes** All studies: SRR 0,84 (0,77; 0,92), trials =7, I2: 0%, Risk of bias: - Moderate: SRR 0,87 (0,76; 0,96), 2 trials - Serious: SRR 0,82 (0,73; 0,93), 5 trials Type of diabetes: - Type 1 diabetes: SRR 0,84 (0,77;0,92), 2 trials		

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		- Type 2 Diabetes: SRR 0,84 (0,77; 0,92), 5 trials For other subgroups see supplement. no differences between subgroups after stratification for ROB, sex, type of diabetes, geographic location, and adjustment of relevant confounders for the outcomes CVD, CHD, cerebrovascular event, HF incidence, CVD and CHD mortality, and incidence of retinopathy LIMITATIONS - Most included studies had a serious ROB, mainly due to insufficient adjustment for potential confounders (e.g., socioeconomic status and diabetes duration) or assessment of physical activity with nonvalidated tools. - findings are at a substantial risk of reverse causation (it is likely that healthier individuals with diabetes are more active than those with more severe diabetes and/or other medical conditions). - studies relied on self-reported physical activity, studies were at risk for measurement error - most studies did not include repeated recording of physical activity and only included recording of baseline physical activity. changes in physical activity may have distorted results - many studies did not differentiate between type 1 and type 2 diabetes		
Schlesinger S, Neuenschwander M, Ballon A, et al. Adherence to healthy lifestyles and incidence of diabetes and mortality among individuals with diabetes: A systematic review and meta-analysis of prospective studies. J Epidemiol Community Health 2020; 74(5):481–7. DOI: 10.1136/jech-2019-213415. http://www.ncbi.nlm.nih.gov/pubmed/32075860. Laufnummer: 33321	**Suchzeitraum:** up to September 2019 **Fragestellung:** quantify association between lifestyle indices and incident T2D as well as mortality in individuals with T2D. **Population:** Adults (> 18 years) from the general population. Adults (> 18 years), with type 2 diabetes. **Intervention/Exposure:** Adherence to healthy lifestyle index, including combination of factors, such as dietary behaviour, physical activity, smoking status, alcohol intake, being overweight or obese, etc.; at least three factors. **Coparator/Control:** Non-adherence to a healthy lifestyle index. **Studies:** prospective cohort studies ≥ 1 year follow-up **Outcome:** - Incidence of T2DM (general population)	19 studies included, 14 focussing on T2D prevention, 5 on mortality in individuals with T2D (17 155 participants) **Lifestyle indices and all-cause mortality in individuals with type 2 diabetes** Adhering to healthy lifestyle versus low adherence to healthy lifestyle: Mortality: summary relative risk (SRR) 0.43 (95% CI: 0.31 to 0.58); I^2=65,9%, 5 studies, n=17 155 (2 115 cases of death) Dose-response analyses: adherence to every additional healthy lifestyle factor was associated with a reduced relative risk of 21% (95% CI: 15% to 26%) for mortality. Adherence to one, two, three or four healthy lifestyle factors was associated with a relative risk reduction of mortality by 22% (SRR: 0.78; 95% CI: 0.72 to 0.85), 39% (SRR: 0.61; 95% CI: 0.53 to 0.71), 52% (SRR: 0.48; 95% CI: 0.39 to 0.58) and 62% (SRR: 0.38; 95% CI: 0.28 to 0.49) compared with low adherence to a healthy lifestyle. Limitations: high statistical heterogeneity between studies Quality assessment: studies included rated to be at moderate or serious risk of bias: - residual confounding - mearsurement of lifestyle risk factors only conducted at baseline - definitions of lifestyle factors varied Heterogeneity in assessment, definition of single lifestyle factors as well as the different combinations of lifestyle factors included in the index may have influenced the results.	moderate y-py-n-py-n-y-y-y-y-n-y-y-y-y-y nicht erfüllte nicht-kritische Domänen: Auswahl der Studientypen nicht begründet, Studienselektion nicht berichtet, Funding in den Studien nicht berichtet	Kohortenstudien, keine Interventionsstudien Intervention: healthy lifestyle index, nicht körperliche Aktivität. Kommentar des Reviews zu Zhang et al 2020: However, the authors combined studies investigating lifestyle indices and cardiovascular

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	- All-cause mortality (T2DM) **Quality assessment:** Risk of bias was assessed using the Cochrane Risk of bias in Non-randomised Studies of Interventions (ROBINS-I) tool **Auswertung:** 2 meta-analyses: - high vs low risk, - linear and non-linear dose-responses.	---------- Bewertung der Aussagesicherheit (Mortalität bei Personen mit Typ-2-Diabetes) in Anlehnung an GRADE: sehr niedrig RoB: -1 Konsistenz: -1 Direktheit: 0 Präzision: 0 Publication bias: 0		risk markers such as blood pressure, blood lipids and blood glucose. These surrogate markers are influenced by lifestyle factors as well as genetic predisposition, and cannot be considered as lifestyle factors by itself.
Geidl W. Dose-response relationship between physical activity and mortality in adults with non-communicable diseases: A systematic review and meta-analysis of prospective observational studies. Int J Behav Nutr Phys Act 2020; 17(1):109. https://www.ncbi.nlm.nih.gov/pubmed/32843054.	**Suchzeitraum:** from inception to August 2018 **Fragestellung:** relationship between post-diagnosis physical activity (PA) and mortality in patients with selected noncommunicable diseases, including type 2 diabetes. **Intervention/Factor/Comparison:** PA (at least three categories (e.g. low, moderate, high) **Primary outcome:** Mortality **Studies:** prospective observational studies **Quality assessment:** ROBINS-I	28 studies included in the meta-analysis: 6 for type 2 diabetes, 10 metabolic equivalent task hours increase of physical activity per week: 4% lower mortality rate in T2DM (HR, 0.96; 95% CI: 0.93, 0.99; I^2: 71.8%), 6 studies, n=32.221 (observational studies; metaregression). **GRADE:** Certainty of evidence: **low** (downgraded -2: five studies judged as serious risk of bias regarding confounding or selection bias; Downgraded -1: differences in the assessment and calculation of physical activity levels, Upgraded by one level due to the dose-response gradient) CONCLUSION (Review) Higher levels of post-diagnosis PA are associated with lower mortality rates in breast cancer, type 2 diabetes, ischemic heart disease and COPD patients, with indication of a no-threshold and non-linear dose-response pattern.	Low y-y-n-py-y-n-n-y-y-n-y-y-y-y-y-y nicht-erfüllte kritische Domänen: ausgeschlossene Studien nicht aufgelistet.	- Observationsstudien - selbstberichtete Level of PA, Verzerrungsrisiko Nicht im Hintergrundtext zitiert.

3.3 Von der Leitliniengruppe eingebrachte Literatur

Selektiv von der Leitliniengruppe eingebrachte Literatur wurde kritisch bewertet und in der Gruppe diskutiert.

Zitat	Kommentar
Kelly, Sarah; Martin, Steven; Kuhn, Isla; Cowan, Andy; Brayne, Carol; Lafortune, Louise (2016): Barriers and Facilitators to the Uptake and Maintenance of Healthy Behaviours by People at Mid-Life: A Rapid Systema-tic Review. In: PloS one 11 (1), e0145074. DOI: 10.1371/journal.pone.0145074.	Körperliche Aktivität
Korkiakangas, Eveliina E.; Alahuhta, Maija A.; Laitinen, Jaana H. (2009): Barriers to regular exercise among adults at high risk or diagnosed with type 2 diabetes: a systematic review. In: Health promotion international 24 (4), S. 416–427. DOI: 10.1093/heapro/dap031.	Körperliche Aktivität
World Health Organization (WHO) (2024): Global level s of physical inactivity in adults. Off track 2030.[4]	
Deutsche Gesellschaft für Sportmedizin und Prävention (DGSP); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2024): S2k-Leitlinie Sportmedizinische Vorsorgeuntersuchung. Registernummer 066 - 002, Version 1.0. Online verfügbar unter https://register.awmf.org/de/leitlinien/de-tail/066-002, zuletzt geprüft am 01.07.2024.	

Literaturverzeichnis

1. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie Typ-2-Diabetes, Ergänzung zu Version 3: Kapitel Nicht-medikamentöse Therapie. 2024 [cited: 2024-11-20]. DOI: 10.6101/AZQ/000518. https://register.awmf.org/de/leitlinien/detail/nvl-001.
2. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans. 2018 [cited: 2023-03-13]. https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf.
3. U.S. Department of Health and Human Services. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. 2018 [cited: 2023-03-13]. https://health.gov/sites/default/files/2019-09/PAG_Advisory_Committee_Report.pdf.
4. World Health Organization (WHO). Global levels of physical inactivity in adults: Off track for 2030. Geneva: WHO; 2024. https://www.who.int/publications/i/item/9789240096905.

NATIONALE VERSORGUNGS LEITLINIEN

Nationale VersorgungsLeitlinie

Typ-2-Diabetes

Recherchedokumentation + Evidenztabellen
zum Kapitel Nicht-medikamentöse Therapie
Teil 4: Alkoholkonsum und Neuropathie, Interventionen zur Stressbewältigung

Ergänzung zu Version 3

AWMF-Register-Nr. nvl-001

Träger:

Bundesärztekammer

Kassenärztliche Bundesvereinigung

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften

BUNDESÄRZTEKAMMER KBV AWMF

Inhaltverzeichnis

1 Aufbau der Recherche-/Evidenz-Dokumente

Zur leichteren Handhabung der umfangreichen Evidenzrecherchen werden die Recherchedokumentationen und Evidenztabellen in verschiedenen Teilen dargestellt:

- Teil 1
  - Evidenzbasis des Kapitels Nicht-medikamentöse Therapie
  - Themenübergreifende systematische Recherche
  - Themenverwandte AWMF-Leitlinien
  - Nationale und internationale Konsensuspapiere (von der Leitliniengruppe eingebrachte Literatur)
- Teil 2
  - Systematische Recherche zum Gewichtsmanagement
  - Systematische Recherche zu Formuladiäten
  - Systematische Recherche zu Mediterraner Diät
- Teil 3
  - Systematische Recherche zu körperlicher Aktivität und strukturierten Bewegunsprogrammen
- Teil 4 (vorliegendes Dokument)
  - Systematische Recherche Alkoholkonsum und Neuropathie
  - Systemtische Recherche Interventionen zur Stressbewältigung

2 Recherchedokumentation

2.1 Systematische Recherche: Alkoholkonsum und Neuropathie

2.1.1 PICO-Fragestellung

P: Erwachsene Personen mit Typ-2-Diabetes mit oder ohne vorbestehende diabetische Polyneuropathie

I: Intervention/Faktor: Alkoholkonsum

C: jegliche Vergleiche (z. B. kein Alkoholkonsum/moderater Alkoholkonsum)

O: für Personen mit vorbestehender Polyneuropathie:

- Verschlechterung einer Polyneuropathie,
- kardiovaskuläre Morbidität / Mortalität, Gesamtmortalität,
- Lebensqualität,
- Adverse events

(Für Personen ohne vorberstehende Polyneuropathie: vorrangig betrachteter Endpunkt: Entwicklung einer Polyneuropathie. Evidenz zu den weiteren oben genannten Endpunkten wurden ggf. nicht alle gefunden; AND-Verknüpfung zwischen Diabetes und Polneuropathie).

S: Systematische Übersichtsarbeiten und Primärstudien (z. B. Kohortenstudien) ab 2013

Sprache: deutsch, englisch

2.1.2 Recherchestrategien

Medline via Pubmed (www.pubmed.gov) (13.06.2023)

Search		
#19	**Search: #18 NOT #17 Filters: from 2013/1/1 - 3000/12/12**	**269**
#18	Search: #12 AND #13 Filters: from 2013/1/1 - 3000/12/12	280
#17	**Search: #14 AND #15 Filters: from 2013/1/1 - 3000/12/12**	**11**

Search		
#16	Search: #14 AND #15	18
#15	Search: (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation study[pt] OR validation study[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	655,984
#14	Search: #12 AND #13	634
#13	Search: #3 AND #7	38,256
#12	Search: #8 OR #9 OR #10 OR #11	547,663
#11	Search: "Alcoholic Beverages"[Mesh]	23,148
#10	Search: Ethanol[MeSH]	118,133
#9	Search: Ethanol[tiab]	137,214
#8	Search: Alcohol*[tiab]	398,990
#7	Search: #4 OR #5 OR #6	182,224
#6	Search: "Diabetic Neuropathies"[Mesh]	26,533
#5	Search: Polyneuropath*[tiab]	16,790
#4	Search: Neuropath*[tiab]	160,121
#3	Search: #1 OR #2	788,122
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	170,093
#1	Search: diabet*[tiab]	775,358

Epistemonikos (www.epistemonikos.org) (14.06.2023)

Advanced search

Search	Most Recent Queries	Result
#1	(title:((title:(diabet*) OR abstract:(diabet*))) OR abstract:((title:(diabet*) OR abstract:(diabet*)))) AND (title:(neuropath* OR polyneuropath*) OR abstract:(neuropath* OR polyneuropath*)) AND (title:(alcohol* OR ethanol) OR abstract:(alcohol* OR ethanol)) **Publication year: from 2013 to 2021** **Publication type: all (inkl. 12 Systematic Reviews)**	36

Cochrane Datenbank (www.cochranelibrary.com) 14.06.2023

Search	Most Recent Queries	Result
#16	**#13 AND #14 in Trials, from 2013**	**82**
#15	**#13 AND #14 in Cochrane Reviews, Cochrane Protocols, from 2013-01-01**	**1**
#14	#3 AND #8	6567
#13	#9 OR #10 OR #11 OR #12	39670
#12	MeSH descriptor: [Alcohol Drinking] explode all trees	5081
#11	MeSH descriptor: [Alcoholic Beverages] explode all trees	672
#10	(Ethanol):ti,ab,kw (Word variations have been searched)	6379
#9	(alcohol*):ti,ab,kw (Word variations have been searched)	37396
#8	#4 OR #5 OR #6 OR #7	18907
#7	MeSH descriptor: [Polyneuropathies] explode all trees	663
#6	MeSH descriptor: [Diabetic Neuropathies] explode all trees	2783
#5	(Polyneuropath*):ti,ab,kw (Word variations have been searched)	1708
#4	(Neuropath*):ti,ab,kw (Word variations have been searched)	17010
#3	#1 OR #2	114213
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	23067
#1	(Diabet*):ti,ab,kw (Word variations have been searched)	114213

Anmerkung ÄZQ: Auch wenn bei der Fragestellung keine Trials aus der Cochrane Library (randomisierte und quasi-randomisierte Trials) zu erwarten sind, wurden diese wegen des systematischen Vorgehens mit gesucht.

2.1.3 Übersicht der eingeschlossenen Treffer

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	11	12	1	**24**
Sonstige	269	24	82	**375**
GESAMT				**399**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 34

A2 (nicht englisch/deutsch): 17

A3 (Conference Abstract): 2

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 346

Handsuche:

- Papanas, Nikolaos; Ziegler, Dan (2015): Risk Factors and Comorbidities in Diabetic Neuropathy. An Update 2015. In: *Rev Diabet Stud* 12 (1-2), S. 48–62. DOI: 10.1900/RDS.2015.12.48.[1]
- Andersen, Signe T.; Witte, Daniel R.; Dalsgaard, Else-Marie; Andersen, Henning; Nawroth, Peter; Fleming, Thomas et al. (2018): Risk Factors for Incident Diabetic Polyneuropathy in a Cohort With Screen-Detected Type 2 Diabetes Followed for 13 Years. ADDITION-Denmark. In: Diabetes Care 41 (5), S. 1068–1075. DOI: 10.2337/dc17-2062 [2]
- Risk factors for neuropathic pain in diabetes mellitus, Harry L. H ´ebert*, Abirami Veluchamy, Nicola Torrance, Blair H. Smith, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5359789/pdf/jop-158-560.pdf
- DOLORisk: Research on Risk Factors and Determinants for Neuropathic Pain, https://classic.clinicaltrials.gov/ct2/show/NCT04888455; https://pubmed.ncbi.nlm.nih.gov/30756091/

2.1.4 TiAB-Screening

TiAb-Tabelle		
	Einschluss	**Ausschluss**
Population	Erwachsene mit Typ 2 Diabetes mit oder ohne diabetische Neuropathie	- Diabetes bei besonderen Patientengruppen (Cystische Fibrose, nach Transplantation); Alter < 18 Jahre, Diabetes in und um die Schwangerschaft
Intervention/Faktor	- Alkoholkonsum	
Comparison	Jeglicher Vergleich	
Outcome	- Mortalität - Kardiovaskuläre und diabetische Morbidität - Lebensqualität - Verschlechterung der Neuropathie - (Glykämische Kontrolle (HbA1c), wenn dadurch Medikamente eingespart werden können, Diabetesremission.)	- *Andere Laborwerte* - *Lipide* - *Andere Stoffwechselparameter (HOMA-Index)* - *Körpergewicht, Änderung Körpergewicht* - *RR*
Studientyp	- Systematische Übersichtsarbeiten - Primärstudien: RCTs, Register, Kohortenstudien	- *Kongressbeiträge* - *Zusammenfassungen ohne systematische Recherche, etc.*

2.1.5 Flow-Chart

Legende TiAb-Screening:

A: Ausschluss, Thema nicht passend, Population nicht passend

As: methodisch nicht ausreichend, oder kein systematischer Review und keine Primärstudie

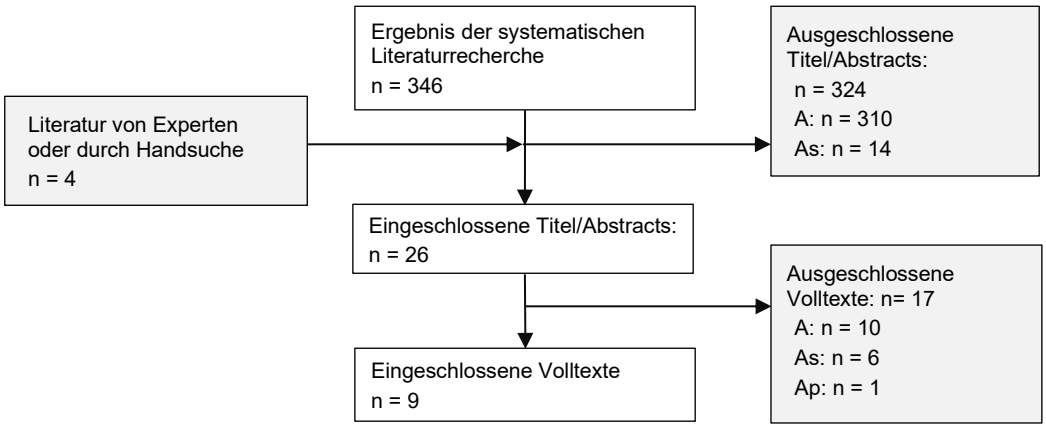
E: Einschluss

Legende Volltextscreening:

A: Ausschluss, Thema nicht passend, Population nicht passend

As: methodisch nicht ausreichend

Ap: Ausschluss, Protokoll



Eingeschlossene Studien

- Geng 2023
- Kamalarathnam 2022
- Huang 2021
- Shrestha 2017
- Christensen 2020
- Yokoyama 2020
- Christensen 2018
- Bansal 2014
- Andersen 2018

2.1.6 Evidenzzusammenfassung

Es erfolgte eine systematische Recherche zum Einfluss der Höhe des Alkoholkonsums auf die Entstehung bzw. Verschlechterung einer diabetischen Neuropathie und andere patientenrelevante Langzeitendpunkte bei Menschen mit Typ-2-Diabetes. In der Recherche wurden **keine relevanten systematischen Übersichtsarbeiten** mit ausreichender methodischer Berichtsqualität identifiziert. Es liegen wenige prospektive und retrospektive longitudinale Studien und Querschnittstudien vor, in denen die Assoziation von Alkoholkonsum und der Entwicklung bzw. Verschlechterung einer (diabetischen) Polyneuropathie bei Personen mit Typ-2-Diabetes untersucht wurde.

Zur Evidenzbeschriebung siehe Kapitel Nicht-medikamentöse Therapie (Ergänzung zu Version 3) [3].

2.2 Systematische Recherche: Interventionen zur Stressbewältigung

2.2.1 PICO-Fragestellung

P: erwachsene Personen mit Typ-2-Diabetes

I: Interventionen zur Stressbewältigung, Entspannungsverfahren, psychologische Kurzinterventionen

C: keine spezifischen Interventionen zur Stressbewältigung (z. B. usual care, Warteliste)

O: Kardiovaskuläre und diabetesassoziierte Morbidität / Mortalität, Gesamtmortalität, Lebensqualität, Diabetes-Distress, Depression, (glykämische Kontrolle, nur wenn dadurch Medikamente eingespart werden können);

Sprache: deutsch, englisch

Publikationstyp: aggregierte Evidenz von RCTs ab 2014

Es wurden systematische Übersichtsarbeiten (bereits publizierte sowie Protokolle) zu Interventionen zur Stressbewältigung bei Typ-2-Diabetes gesucht. Die Recherche zielte nicht auf die Therapie von Depressionen bei Personen mit Typ-2-Diabetes ab. Hierzu verweist die NVL Typ-2-Diabetes auf die NVL Unipolare Depression.

Das Screening und die Extraktion und Bewertung erfolgten mit dem aktuellen Jahr beginnend, bis ausreichend Lieratur identifiziet wurde. Es wurden die Jahre bis 2021 gescreent und die eingeschlossenen Studien extrahiert und bewertet.

2.2.2 Recherchestrategien

Medline via Pubmed (www.pubmed.gov) (29.11.2023)

Search	Most Recent Queries	Results
#14	**Search: #11 AND #12 Filters: from 2014/1/1 - 3000/12/12**	**334**
#13	Search: #11 AND #12	430
#12	Search: (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation study[pt] OR validation study[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	687,109
#11	Search: #3 AND #10	3,382

Search	Most Recent Queries	Results
#10	Search: #4 OR #7 OR #8 OR #9	131,328
#9	Search: Mindfulness[mesh]	6,757
#8	Search: Mind-body[tiab]	4,253
#7	Search: #5 AND #6	109,981
#6	Search: Support[tiab] OR intervention[tiab] OR therap*[tiab]	5,370,405
#5	Search: Psychologic*[tiab]	313,266
#4	Search: mindfulness*[tiab] OR MBI[tiab] OR MBSR[tiab] OR MBCT[tiab] OR MB-EAT[tiab] OR meditation[tiab]	20,854
#3	Search: #1 OR #2	809,568
#2	Search: "Diabetes Mellitus, Type 2"[Mesh]	174,785
#1	Search: diabet*[tiab]	796,755

MBCT: Mindfulness-Based Cognitive Therapy, MBSR: Mindfulness-Based Stress Reduction, MB-EAT: Mindfulness-Based Eating Awareness Training.

Epistemonikos (www.epistemonikos.org) (30.11.2023)

Advanced search

Search	Most Recent Queries	Result
#4	**Publication year: from 2014 to 2024** **Publication type: Systematic review**	**97**
#3	#1 AND #2	369
#2	Title/Abstract: (Mind-body OR "Psychological therapy" OR "Psychological therapies" OR "Psychological intervention" OR "Psychological interventions" OR "Psychological support" OR meditation OR MB-EAT OR MBCT OR MBSR OR MBI OR Mindfulness)	16.535
#1	Title/Abstract: Diabet*	143.340

Cochrane Datenbank (www.cochranelibrary.com) 29.11.2023

Search	Most Recent Queries	Result
#17	**#3 AND #15 in Cochrane Protocols; Custom Range: from 2014-01-01**	**1**
#16	**#3 AND #15 in Cochrane Reviews; Custom Range: from 2014-01-01**	**33**
#15	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	109592
#14	(psychological support):ti,ab,kw (Word variations have been searched)	26173
#13	(psychological therapy):ti,ab,kw (Word variations have been searched)	65386
#12	(psychological intervention):ti,ab,kw (Word variations have been searched)	59560
#11	MeSH descriptor: [Psychosocial Intervention] explode all trees	234
#10	(Meditation):ti,ab,kw (Word variations have been searched)	4599
#9	(MB-EAT):ti,ab,kw	13
#8	(MBCT):ti,ab,kw	709
#7	(MBSR):ti,ab,kw	1106
#6	(MBI):ti,ab,kw	1142
#5	(mindfulness):ti,ab,kw (Word variations have been searched)	14199

Search	Most Recent Queries	Result
#4	MeSH descriptor: [Mindfulness] explode all trees	2169
#3	#1 OR #2	116667
#2	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	23475
#1	(Diabet*):ti,ab,kw	116667

2.2.3 Übersicht der eingeschlossenen Treffer

	Medline	Epistemonikos	Cochrane	Summe
Aggregierte Evidenz	**334**	**97**	**34**	**465**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 84

A2 (nicht englisch/deutsch): 10

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 371

2.2.4 TiAb-Screening

TiAb-Tabelle		
	Einschluss	**Ausschluss**
Population	Erwachsene mit Typ 2 Diabetes mit oder ohne Folge- und Begleiterkrankungen	- Studien, die nicht zwischen Typ-1- und Typ-2-Diabetes unterscheiden - Diabetes bei besonderen Patientengruppen (Cystische Fibrose, nach Transplantation); Alter < 18 Jahre, Diabetes in und um die Schwangerschaft
Intervention	- Stressbewältigung, Entspannungsverfahren, psychotherapeutische Kurzinterventionen	
Comparison	Keine spezielle Intervention zur Stressbewältigung	
Outcome	- Mortalität - Kardiovaskuläre und diabetische Morbidität - Lebensqualität - (Glykämische Kontrolle (HbA1c), wenn dadurch Medikamente eingespart werden können, Diabetesremission.)	- *Andere Laborwerte* - *Lipide* - *Andere Stoffwechselparameter (HOMA-Index)* - *Körpergewicht, Änderung Körpergewicht* - *RR*

2.2.5 Flow-Chart

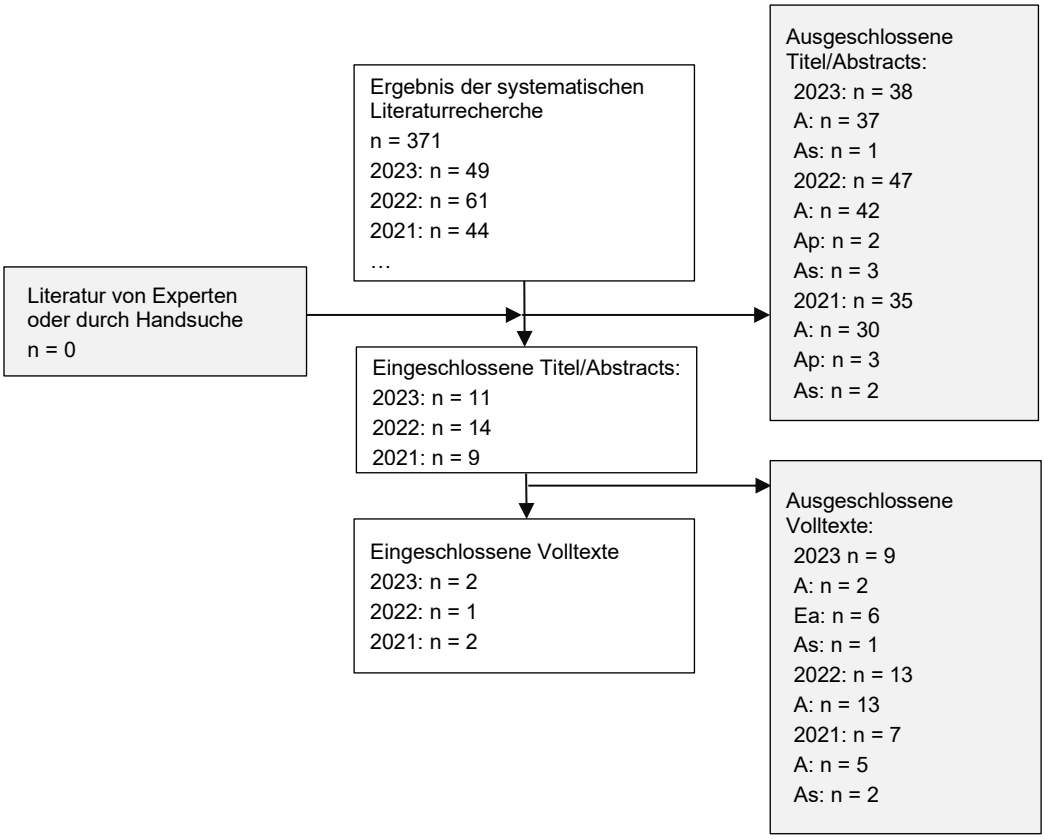
Legende TiAb/VT:

A: Ausschluss, Thema nicht passend, Population nicht passend

As: Methodisch nicht ausreichend

E: Einschluss

Ea (VT-Screening): Endpunkte nicht passend (z. B. intermediäre Endpunkte)



Eingeschlossene Studien:

- Fisher 2023
- Kayser 2023
- Jenkinson 2022
- Ni 2021
- Ngan 2021

Zusätzlich aus der themenübergreifenden systematischen Recherche eingeschlossen: Chew et al., 2017

2.2.6 Evidenzzusammenfassung

In der systematischen Recherche wurde der Nutzen von Interventionen zur Stressbewältigung bei Personen mit Typ-2-Diabetes auf partientenrelevante Langzeitendpunkte (kardiovaskuläre Morbidität, Mortalität, Gesamtmortalität), Diabetes-Distress, Depression und Lebensqualität untersucht.

Folgende Einschränkungen sind bei der Betrachtung der Ergebnisse der identifizierten systematischen Übersichtsarbeiten (SR) zu berücksichtigen: Die SRs hatten überwiegend eine geringe Berichtsqualität gemäß der Bewertung durch AMSTAR 2. In einem Großteil der Reviews wurden die ausgeschlossenen Studien nicht aufgeführt und das Publikations-Bias nicht adäquat erhoben.

- In vielen Studien wurden unterschiedliche Diabetestypen (Typ-1-, Typ-2-Diabetes, Gestationsdiabetes) zusammen betrachtet. Weiterhin zeigte sich oftmals eine hohe Heterogenität der eingeschlossenen Studien bezüglich Art und Durchführung der Intervention (MBSR, MBCT; Gruppentreffen oder einzeln; Follow-Up; Dosis) und vorbestehender psychischer Belastung (Depression, Diabetes-related-distress). Die Zusammenfassung der Ergebnisse in einer Metaanalyse scheint in einigen Reviews bei hoher Heterogenität nicht sinnvoll.
- Die in der NVL-Recherche priorisierten Endpunkte waren häufig sekundäre Endpunkte in den Studien und SRs oder wurden nicht betrachtet.
- In einigen der identifizierten SRs ergaben sich Hinweise auf einen positiven Effekt von achtsamkeitsbasierte Interventionen (mindfulness-based interventions, MBI) auf diabetesbezogene Belastungen (diabetes-related distress, DRD) und Depression [4–6]. Die Höhe der Effekte unterschied sich unter anderem je nach der betrachteten Intervention bzw. den zusammen betrachteten Interventionen und den eingeschlossenen Patientenpopulationen.

Ein SR (nach AMSTAR 2 kritisch niedrig) untersuchte die Effekte achtsamkeitsbasierter Interventionen auf die Glukosekontrolle und psychologische Endpunkte bei Menschen mit Diabetes (Typ-1- und Typ-2-Diabetes) {Ni 2021: 34532}. Es ergaben sich positive Effekte für DRD gemessen mittels Problem Areas in Diabetes Survey scale (PAID) (Mean Difference (MD) -5.81 (95% KI -10,10; -1.52), p = 0,008, I^2=28%, 5 Studien, n=431, niedrige bis moderate Aussagesicherheit, herabgestuft wegen Verzerrungsrisiken der Studien). Positive Effekte wurden auch für Depression (standardized mean difference (SMD) -0,56 (95% KI -0,82; -0,30), p <0,0001; I^2=59%; 8 Studien, n=648, niedrige Aussagesicherheit) und Stress (SMD -0,53 (KI -0,75; -0,31); p <0,00001, I^2=47%, 7 studies, n=652, moderate Aussagesicherheit) in den Studien beobachtet. In den Subgruppenanalysen zu den beiden letztgenannten Endpunkten wurden größere Effekte beobachtet, wenn psychische Erkrankungen (psychological disorders) vorbestanden. Für den HbA1c-Wert wurde eine MD von -0.25% ((95% KI -0.43 to -0.07), p=0,006, 7 studies, n=665, I^2=0%) berichtet. Einschränkend sind die Verzerrungsrisiken der Studien, die gerignge Anzahl und Größe der Studien und die Heterogenität der Interventionen und Populationen zu berücksichtigen [4].

Ein Review (AMSTAR 2 kritisch niedrig), der neben achtsamkeitsbasierten Interventionen (mindfulness-based interventions) auch Akzeptanz- und Commitmenttherapie (acceptance-based interventions) an Personen mit Typ-2-Diabetes untersuchte, fand einen positiven Effekt für Diabetes-distress (SMD −0,37 (95% KI −0,63; −0,12); p <0,01, niedrige Aussagesicherheit) und den HbA1c-Wert (MD -0,35 (95% KI -0,67; -0,04), p = 0,03, niedrige Aussagesicherheit) bis zu einen Monat nach Intervention. Auch hier waren die Studien heterogen und klein [5].

Eine systematische Übersichtsarbeit betrachtete “Mindfulness based stress reduction” (MBST) bei Personen mit Diabetes (AMSTAR 2 kritisch niedrig) [6]. Unterschiedliche Diabetestypen (Typ-1-DM, Typ-2-Diabetes mellitus und Gestationsdiabetes) wurden zusammen betrachtet. Der Review berichtet über statistisch signifikante positive Effekte je nach Follow-Up für die Endpunkte Angst, Depression und Stress. Metaanalysen scheinen allerdings bei derart hoher Heterogenität der Studien nicht sinnvoll. Für den HbA1c-Wert ergaben sich weder post-interventionell noch nach Follow-Up signifikante Effekte [6].

Ein SR untersuchte den Effekt traditioneller kognitiver Verhaltenstherapie und kognitiver Verhaltenstherapie der “dritten Welle”, wie Akzeptanz- und Commitmenttherapie und MIB, auf Diabetes-related distress (AMSTAR 2 niedrig) [7]. In 14 von 22 eingeschlossenen Studien wurde als Einschlusskriterium nach erhöhtem DRD oder Depression gescreent. Dabei erfolgten jeweils getrennte Auswertungen, je nachdem ob DRD primärer oder ein sekundärer Endpunkt war. In der Metaanalyse mit Studien zu kognitiven Verhaltenstherapien der “dritten Welle” waren die Effekte aus DRD, Depression und den HbA1c-Wert nicht statistisch signifikant. Als methodisch einschränkend ist unter anderem die Heterogenität der Studien zu berücksichtigen. Die Studien hatten überwiegend ein unklares oder hohes Verzerrungsrisiko [7].

Eine in der Recherche identifizierte systematische Übersichtsarbeit von Cochrane untersuchte den Nutzen verschiedener psychologischer Interventionen auf Diabetes-related distress (DRD) bei Menschen mit Typ-2-Diabetes (AMSTAR 2 hoch) [8]. Die psychologischen Interventionen wurden unterteilt in emotion-focused (EF), cognition-focused (CF) oder eine Mischung beider Komponenten (emotion-cognition, EC). Sie wurden untereinander oder im Vergleich zu einer usual-care-Gruppe untersucht. Hier erfolgt nur die Darstellung der Vergleiche gegen Usual-care-Gruppen. Im Vergleich zur Standardtherapie (usual care) zeigte sich in der gemeinsamen Betrachtung aller psychologischen Interventionen kein statistisch signifikanter Effekt auf Diabetes-related distress (DRD) (SMD -0,07 (95% KI -0,16; 0,03), p=0,17, 12 Studien, n=3 315, niedrige Aussagesicherheit), die Health related quality of life (HRQoL) (SMD 0,01 (95% KI -0,09; 0,11), p=0,87; 5 trials, n= 1 932, niedrige Aussagesicherheit) oder die Gesamtmortalität (RR 1,01 (95% KI 0,17; 6,03), p=0,99, 3 Studien, n=1 376, niedrige Aussagesicherheit).

Es wurden keine Studien identifiziert, die Emotion-focused Interventionen gegen usual care untersuchten. Auch für die Vergleich von cognition-focused Interventionen oder emotion-cognition focused Interventionen mit usual-care wurden keine statistisch signifikanten Effekte auf DRD, HRQoL oder Gesamtmortalität beobachtet [8].

3 Evidenztabellen: Alkoholkonsum und Neuropathie

3.1 Systematische Recherche – aggregierte Evidenz

In der Recherche wurden keine relevanten systematischen Übersichtsarbeiten identifiziert.

3.2 Systematische Recherche – Primärstudien

3.2.1 Prospektive und retrospektive Kohortenstudien

Geng et al., 2023

Geng T. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. PLoS Med 2023; 20(1):e1004135. https://www.ncbi.nlm.nih.gov/pubmed/36626356.	
Studiendesign	"retrospective cohort study" using electronic health records, 15.104 patients*, median follow-up of 8.1 years, *UK Biobank: large community-based prospective cohort study for common diseases, >500,000 participants aged 37 to 73 years from 22 sites across England, Scotland, and Wales between March 2006 and October 2010; data obtained through touchscreen questionnaires, physical measurements, and biological samples at recruitment
Fragestellung	to examine associations of combined lifestyle factors with risks of total and individual microvascular complications among patients with type 2 diabetes (T2D) and to explore the potential mediation effects of metabolic biomarkers.
Population	patients with T2DM from UK Biobank* free of macro- and microvascular complications at baseline
Intervention/Factor	Healthy lifestyle behaviors included: - noncurrent smoking, - recommended waist circumference, - regular physical activity, - healthy diet, - moderate alcohol drinking (1–28 g/day for men; 1–14 g/day for women)
Datenerhebung	- The frequency of all types of alcohol intake was reported using 6 predefined categories, between never to daily or almost daily. For participants who reported to drink alcohol, data on the average monthly or weekly alcohol intake from 6 types of alcohol beverages were collected. We calculated the average units of alcohol intake using the abovementioned information and defined low-risk drinking as moderate drinking (1 to 14 g/day for women or 1 to 28 g/day for men). - Ascertainment of outcomes: microvascular disease cases were identified through linking the cohort database with the hospital inpatient admissions and death registries

Geng T. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. PLoS Med 2023; 20(1):e1004135. https://www.ncbi.nlm.nih.gov/pubmed/36626356.	
Comparison	participants adhering to 4 to 5 low-risk lifestyle behaviours versus 0 to 1.
Outcomes	- diabetic retinopathy, - diabetic neuropathy, - diabetic kidney disease, - composite microvascular complication (diabetic retinopathy, diabetic neuropathy, diabetic kidney disease) cases were identified through linking the cohort database with the hospital inpatient admissions and death registries
Multivariable adjustment	for sociodemographic characteristics, history of hypertension, glycemic control, and medication histories
Ergebnisse	
Baseline-Charkteristika	60.3% male; mean age, 59.3 years, low-risk lifestyle behaviors (number of low-risk lifestyle behaviours): - 0 or 1 low-risk lifestyle behaviors: 3,406 persons (22.6%), - 2 low-risk lifestyle behaviors: 6,080 (40.3%), - 3 low-risk lifestyle behaviors: 4,062 (26.9%), - 4 or 5 low-risk lifestyle behaviors: 1,556 (10.3%)
	1,296 cases of the composite microvascular complications occurred - 558 diabetic retinopathy, - 625 diabetic kidney disease, - 315 diabetic neuropathy, with some patients having 2 or 3 microvascular complications simultaneously. HR for the participants adhering 4 to 5 low-risk lifestyle behaviors versus 0 to 1 **Diabetic retinopathy:** HR 0.65 (0.46, 0.91) **diabetic kidney disease:** 0.43 (0.30, 0.61) **diabetic neuropathy**: HR 0.46 (0.29, 0.74) **composite outcome (all Ps-trend ≤0.01):** HR 0.54 (0.43, 0.68) **Population-attributable fraction** of diabetic microvascular complications for poor adherence to the overall healthy lifestyle (<4 low-risk factors): from 25.3% (95% CI 10.0%, 39.4%) to 39.0% (95% CI 17.7%, 56.8%). In addition, albumin, HDL-C, triglycerides, apolipoprotein A, C-reactive protein, and HbA1c collectively explained 23.20% (12.70%, 38.50%) of the associations between overall lifestyle behaviors and total diabetic microvascular complications.

Geng T. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. PLoS Med 2023; 20(1):e1004135. https://www.ncbi.nlm.nih.gov/pubmed/36626356.

HRs (95% Cis) of microvascular complications according to the overall lifestyle behaviors among individuals with T2D.					
	Number of low-risk lifestyle behaviours				
	0-1	**2**	**3**	**4-5**	**HR (continu-ous)**
Composite microvascular complications					
Cases/person years	378/25.684	507/47.476	312/31.985	99/12.301	-
unadjusted	1.0	0.71 (0.67, 0.76)	0.65 (0.61, 0.69)	0.54 (0.48, 0.59)	0.82 (0.80, 0.84)
Model 1	1.0	0.70 (0.62, 0.80)	0.62 (0.53, 0.72)	0.51 (0.40, 0.63)	0.80 (0.76, 0.85)
Model 2	1.0	0.71 (0.62, 0.81)	0.63 (0.54, 0.74)	0.53 (0.42, 0.67)	0.81 (0.77, 0.86)
Model 3	1.0	0.71 (0.62, 0.81)	0.65 (0.56, 0.76)	0.54 (0.43, 0.68)	0.82 (0.77, 0.87)
PAF, %	-	-	-	25.3 (10.0, 39.4)	-
Diabetic Neuropathy					
Cases/person years	110/26,409	122/48,553	61/32,742	22/12,533	-
unadjusted	1.0	0.60 (0.53, 0.67)	0.44 (0.38, 0.51)	0.42 (0.34, 0.51)	0.71 (0.68, 0.75)
Model 1	1.0	0.59 (0.46, 0.77)	0.43 (0.32, 0.60)	0.41 (0.26, 0.65)	0.71 (0.63, 0.80)
Model 2	1.0	0.61 (0.47, 0.79)	0.46 (0.34, 0.64)	0.48 (0.30, 0.76)	0.74 (0.65, 0.83)
Model 3	1.0	0.61 (0.47, 0.79)	0.47 (0.34, 0.64)	0.46 (0.29, 0.74)	0.73 (0.65, 0.83)
PAF, %	-	-	-	26.4 (−6.5, 54.1)	-
PAFs based on Model 3 were calculated to theoretically estimate the proportion of each outcome in this study population that could have been prevented if the population had ≥4 low-risk lifestyle behaviors					

Model 1: age (continuous, years), sex (male, female), Townsend Deprivation Index (continuous), and race/ethnicity (White, others).
Model 2: Model 1 + education attainment (college or university degree, A/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, or none of the above), sleep duration (<6, 6–8, or ≥9 hours/day), family history of CVD (yes, no), family history of hypertension (yes, no), and prevalence of hypertension (yes, no).

Geng T. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. PLoS Med 2023; 20(1):e1004135. https://www.ncbi.nlm.nih.gov/pubmed/36626356.

Model 3: Model 2 + diabetes duration (continuous, years), HbA1c (continuous, mmol/mol), use of diabetes medication (none, only oral medication pills, or insulin or others), use of antihypertensive medication (yes, no), use of lipid-lowing medication (yes, no), and use of aspirin (yes, no).

HRs (95% Cis) of microvascular complications according to individual lifestyle behaviors in individuals with type 2 diabetes (für Retinopathie und Nephropathie siehe Originalarbeit)						
	Microvascular complications			**Diabetic neuropathy**		
Alcohol intake	**Person-years**	**Cases**	**HR**	**Person-years**	**cases**	**HR**
Model 1						
others	39.646	526	1.0	40.741	151	1.0
1-28 g/day (men) or 1-14 g/day (women)	77.799	770	0.74 (0.71; 0.78)	79.497	164	0.57 (0.51; 0.62)
Model 2						
others	39.646	526	1.0	40.741	151	1.0
1-28 g/day (men) or 1-14 g/day (women)	77.799	770	0.73 (0.65; 0.82)	79.497	164	0.54 (0.43; 0.68)

Model 1: individual lifestyle factors were mutually adjusted
Model 2: age (continuous, years), sex (male, female), ethnicity (White, others), education attainment (college or university degree, A/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, or none of the above), Townsend Deprivation Index (continuous), sleep duration (<6, 6-8, or ≥9 hours/day), family history of CVD (yes, no), family history of hypertension (yes, no), prevalence of hypertension (yes, no), diabetes duration (continuous, years), use of diabetes medication (none, only oral medication pills, or insulin or others), use of antihypertensive medication (yes, no), use of lipid-lowing medication (yes, no), use of aspirin (yes, no), and HbA1c (continuous, mmol/mol). Individual lifestyle factors were mutually adjusted.

Geng T. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. PLoS Med 2023; 20(1):e1004135. https://www.ncbi.nlm.nih.gov/pubmed/36626356.

Sensitivity analysis

HRs (95% CIs) of microvascular complications according to the healthy lifestyle score using moderate drinking and non-drinking as the low-risk behavior in individuals with type 2 diabetes					
	Number of low-risk lifestyle behaviours				
	0-1	**2**	**3**	**4-5**	**HR (continuous)**
Microvascular complications					
Cases/person years	196/14,089	596/51,577	376/36,970	128/14,809	-
Model 1	1.0	0.83 (0.77, 0.89)	0.73 (0.67, 0.79)	0.62 (0.56, 0.68)	0.86 (0.84, 0.89)
Model 2	1.0	0.80 (0.68, 0.94)	0.70 (0.59, 0.84)	0.61 (0.49, 0.77)	0.86 (0.81, 0.91)
Diabetic Neuropathy					
Cases/person years	56/14,461	147/52,811	86/37,832	26/15,134	-
Model 1	1.0	0.72 (0.63, 0.83)	0.59 (0.51, 0.68)	0.44 (0.36, 0.55)	0.78 (0.74, 0.83)
Model 2	1.0	0.74 (0.54, 1.01)	0.63 (0.45, 0.89)	0.51 (0.32, 0.82)	0.82 (0.72, 0.93)

Model 1: unadjusted model.
Model 2: age (continuous, years), sex (male, female), ethnicity (White, others), education attainment (college or university degree, A/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, or none of the above), Townsend Deprivation Index (continuous), sleep duration (<6, 6-8, or ≥9 hours/day), family history of CVD (yes, no), family history of hypertension (yes, no), prevalence of hypertension (yes, no), diabetes duration (continuous, years), use of diabetes medication (none, only oral medication pills, or insulin or others), HbA1c (continuous, mmol/mol), use of antihypertensive medication (yes, no), use of lipid-lowing medication (yes, no), and use of aspirin (yes, no).
Low-risk alcohol drinking was defined as <28 g/d for men and <14 g/d of ethanol intakes for women.

Methodische Bewertung: Newcastle Ottawa Scale (für Kohortenstudien)

Selektion der Studienteilnehmer*innen: ***

1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja/Wahrscheinlich ja**.
- large community-based prospective cohort study for common diseases, >500,000 participants (37 to 73 years) from 22 sites across England, Scotland, and Wales

2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Nein**

Geng T. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. PLoS Med 2023; 20(1):e1004135. https://www.ncbi.nlm.nih.gov/pubmed/36626356.	
	- die nicht-exponierte Kohorte stammt aus der vergleichbaren Grundgesamtheit wie die exponierte Kohorte, allerdings ist die Kategorie des Alkoholkonsums (siehe auch Kommentare) ungünstig gewählt. „Others“ umfassen sowohl Personen ohne Alkoholkonsum als auch Personen mit Alkoholkonsum >14 bzw. 28g/d. 3) Erfolgte eine valide Erfassung der Exposition? **Ja** (soweit möglich; siehe Datenerhebung (data obtained through touchscreen questionnaires)) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Eher **Ja** (ggf. underreporting, Questionaire and interview) **Vergleichbarkeit: *** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Kann nicht beantwortet werden; eine Auswertung, wie sich die unterschiedlichen Gruppen (moderater Alkoholkonsum versus others) unterscheiden, gibt es nicht. Es fand aber eine Adjustierung zu einer Reihe von Faktoren statt. 2) **Endpunkterfassung: *** 1) Erfolgte eine valide Erfassung der Endpunkte? **Nein**: objektive Erfassung anhand record linkage (ICD-Kodierung), aber erhebliches underreporting möglich, da überwiegend hospital inpatient records ausgewertet wurden. 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? **Ja** (follow up 8,1years) 3) Wurden fehlende Daten adäquat berücksichtigt? **Nein** (fehlende Daten ergeben sich auch aus der Art der Datenerhebung – hospital inpatient records) Gesamtbewertung 5/9 Punkte, die unten genannten Limitationen beschränken die Aussagesicherheit.
Kommentare	**Limitationen:** - retrospective sampling from the UK Biobank study - UK Biobank is not representative of the general population of the UK, healthy volunteer selection bias - self-reported one-time assessment of lifestyle-behaviour; behavior may change over time - microvascular complications were identified via hospital inpatient records and death registries, underreporting of the cases, for example, primary care data were not completely available. - Berichtete Kategorie des Alkoholkonsums ungünstig: in der Analyse (HRs of microvascular complications according to individual lifestyle behaviors) wurde non-drinking nicht in die low-risk Kategorie eingeschlossen. Bei dem Vergleich moderate drinking 1-14 bzw. 1-28g/d versus others, gehört non-drinking zu others. 65,4% der Kohorte haben einen moderaten Alkoholkonsum angegeben. Ob die restlichen 34,6%Eine differenzierte Analyse auch zu stärkerem Konsum nach Kategorien wäre hilfreich. - residual or unknown confounding could not be excluded due to the observational study design,

Andersen et al., 2018

Andersen, Signe T.; Witte, Daniel R.; Dalsgaard, Else-Marie; Andersen, Henning; Nawroth, Peter; Fleming, Thomas et al. (2018): Risk Factors for Incident Diabetic Polyneuropathy in a Cohort With Screen-Detected Type 2 Diabetes Followed for 13 Years. ADDITION-Denmark. In: Diabetes Care 41 (5), S. 1068–1075. DOI: 10.2337/dc17-2062 B348	
Studiendesign	observational, prospective cohort analysis of data from the Danish arm of the Anglo-Danish-Dutch study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION) - General practices randomized to deliver either routine care for diabetes or an intensive multifactorial targetdriven care until the trial was concluded in 2009 and subsequently follow the current guidelines for diabetes care. Since the closure of ADDITION, participants followed observationally via questionnaires, registers, and a clinical follow-up examination carried out between 2015 and 2016 - 13 years after the trial baseline
Fragestellung	To study incident diabetic polyneuropathy (DPN) prospectively during the first 13 years after a screening-based diagnosis of type 2 diabetes and determine the associated risk factors for the development of DPN.
Population	Patients with previously undiagnosed diabetes (aged 40–69 years) via a stepwise screening program in primary care starting with a self-administered risk score questionnaire
Intervention/Factor	- Für NVL Recherche: Alkoholkonsum
Datenerhebung	- Michigan Neuropathy Screening Instrument questionnaire (MNSIQ), defining DPN with scores ≥ 4. MNSIQ completed by participants at baseline and at the 6- and 13-year clinical examination; it was also mailed to participants at 12 years - Risk factors present at the diabetes diagnosis associated with the risk of incident DPN were estimated using Cox proportional hazard - records of alcohol consumption: self-completed questionnaires (units of alcohol per week). Alcohol consumption dichotomized: above or below the recommended weekly intake according to the Danish national health care authorities (<7 units alcohol per week for women and <14 units alcohol per week for men)
Outcomes	Incident DNP
Multivariable adjustment	models adjusted for trial randomization group, sex, and age.
Ergebnisse	
Baseline-Chrarkteristika	median age 60.8 years [interquartile range 55.6; 65.6], 59% of whom were men. Baseline characteristics of participants by incident DPN status during 13 years of follow-up: ADDITION-Denmark Alkohol (<7 units alcohol per week for women and <14 units alcohol per week for men: Participants without incident DPN: 330 (31%) Participants with incident DPN: 19 (27,5%)

Andersen, Signe T.; Witte, Daniel R.; Dalsgaard, Else-Marie; Andersen, Henning; Nawroth, Peter; Fleming, Thomas et al. (2018): Risk Factors for Incident Diabetic Polyneuropathy in a Cohort With Screen-Detected Type 2 Diabetes Followed for 13 Years. ADDITION-Denmark. In: Diabetes Care 41 (5), S. 1068–1075. DOI: 10.2337/dc17-2062 B348

12-year mal (ADDITIION study): n=720, 57% completing MNSIQ
13-year follow-up (ADDITION study): n=479 (38%) completing MNSIQ

total cohort: n=1,533 people, 1,445 completed the MNSIQ at baseline
- 189 (13.1%) had DPN at baseline.
- remaining 1,256 without DPN entered this study

cumulative incidence of DPN 10% during 13 years of diabetes.

Risk of incident DPN by dichotomous potential risk factors for incident DPN present at the diagnosis of type 2 diabetes found by screening, the ADDITIONDenmark study (supplemental material)		
Alcohol *		0.87 (0.51;1.47)
Smoking		
	Former-smoker	0.77 (0.43;1.38)
	Current-smoker	0.92 (0.54;1.59)
Risk of incident DPN expressed by HR (95%CI) from Cox proportional hazard models adjusted for trial randomization-group, sex and age. * Alcohol: Weekly alcohol consumption exceeding recommended intake (>7 units in woman and >14 units in men). Dichotomous risk factors reference group: participants without the respective risk factor. Former and current smokers are compared to participants of never-smokers.		

Sensitivity analyses of the associations of potential risk factors with the risk of incident DPN by multivariate logistic regression models, the ADDITION-Denmark study (supplemental material)	
	OR of incident DPN (95% CI)
Alcohol	0.88 (0.50;1.54)
Risk of incident DPN is expressed by OR (95% CI) from multivariate logistic regression models adjusted for trial randomization-group, sex and age. * P-value<0.05; dichotomous risk factors have as a reference group participants without the respective risk factor. Alcohol: Weekly alcohol consumption exceeding the recommended intake (>7 units in women and >14 units in men).	

Risk of incident DPN by clinically relevant changes in continuous potential risk factors for incident DPN at the diagnosis of type 2 diabetes found by screening: ADDITION-Denmark
- Age (hazard ratio [HR] 1.03 [95% CI 1.00; 1.07]) (unit = 1 year),
- weight (HR 1.09 [95% CI 1.03; 1.16]) (unit = 5 kg),
- waist circumference (HR 1.14 [95% CI 1.05; 1.24]) (unit = 5 cm),
- BMI (HR 1.14 [95% CI 1.06; 1.23]) (unit = 2 kg/m2),
- HDL cholesterol (HR 0.82 [95% CI 0.69; 0.99]) (unit = 0.25 mmol/L),

Andersen, Signe T.; Witte, Daniel R.; Dalsgaard, Else-Marie; Andersen, Henning; Nawroth, Peter; Fleming, Thomas et al. (2018): Risk Factors for Incident Diabetic Polyneuropathy in a Cohort With Screen-Detected Type 2 Diabetes Followed for 13 Years. ADDITION-Denmark. In: Diabetes Care 41 (5), S. 1068–1075. DOI: 10.2337/dc17-2062 B348	
	- LDL cholesterol (HR 0.92 [95% CI 0.86; 0.98]) (unit =0.25mmol/L) The risk of incident DPN is expressed by HR (95% CI) fromCox proportional hazard models adjusted for trial randomization group, sex, and age. In the current study, we found **no support for smoking status or alcohol consumption as risk factors for DPN**.
Methodische Bewertung: Newcastle Ottawa Scale (für Kohortenstudien)	**Selektion der Studienteilnehmer*innen: ****** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja/Wahrscheinlich ja**. - large prospective cohort study (participants from general practices) 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja** - die nicht-exponierte Kohorte stammt aus der vergleichbaren Grundgesamtheit wie die exponierte Kohorte, 3) Erfolgte eine valide Erfassung der Exposition? **Ja** (soweit möglich, questionnaires) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Eher **Ja** (gleiches Erhebungsinstrument, Teilnehmende wurden untersucht, im vorliegenden Artikel aber nicht berichtet, dass eine neurologische Erhebung erfolgte)) **Vergleichbarkeit: -** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Kann nicht beantwortet werden; eine Auswertung, wie sich die unterschiedlichen Gruppen (Kategorien des Alkoholkonsums) unterscheiden, gibt es nicht. Es fand eine Adjustierung zu einigen Faktoren statt (nur age, sex, trial randomization). **Endpunkterfassung: ** bis ***** 1) Erfolgte eine valide Erfassung der Endpunkte? **MNSIQ ausreichend?** 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? **Ja** (aber relativ geringe Inzidenz der DPN über 13 Jahre) 3) Wurden fehlende Daten adäquat berücksichtigt? **Ja** (censoring) Gesamtbewertung 6-7/9 Punkte, die unten genannten Limitationen beschränken die Aussagesicherheit.
Kommentare	- use of MNSIQ rather than a neurological history and examination in conjunction with nerve conduction studies or validated small-fiber measures (possible underestimation of DPN) - Screen-detected Diabetes, ggf. Beobachtungszeit für die Entwicklung einer DPN zu gering? - participants lost to follow-up prior to the second MNSIQ may introduce selection bias resulting in an underestimation of the true incidence of DPN, as they are typically older and have higher BMIs (nach 12 und 13 Jahren: completion of MNSIQ 57 bzw. 38%) - Änderung der Risikofaktoren über den Verlauf der Studie nicht betrachtet.

Huang et al., 2021

Huang L. Identification of independent risk factors for diabetic neuropathy progression in patients with type 2 diabetes mellitus. J Int Med Res 2021; 49(9):3000605211044366. https://www.ncbi.nlm.nih.gov/pubmed/34559575.	
Studiendesign	Retrospective Kohortenstudie (n=376 patients with T2DM at the First Affiliated Hospital of Fujian Medical University, China between 01/2013-10/2016)
Fragestellung	To identify independent risk factors for diabetic neuropathy (DN) in patients with T2DM.
Population	T2DM, duration > 1 year and age >18 years. - exclusion criteria were serum creatinine level of >2 mg/dL, **alcoholism**, stroke, other causes of neuropathy, or loss of the dorsalis pedis artery pulse.
Assessment	baseline characteristics of patients obtained from electronic medical records, Screening for DN using the Michigan Neuropathy Screening Instrument and through nerve conduction studies using an evoked potential recorder. The diagnostic criteria for DN: - abnormal clinical symptoms, including patient-reported discomfort, pain, or numbness in the lower limbs; - Neuropathy Symptom Score (NSS); - Neuropathy Disability Score (NDS); - nerve conduction velocities; and quantitative sensory test results. DN was defined as a NDS score of ≥6 or a NDS score of 3 to 5 in conjunction with a NSS score of ≥5.
Ergebnisse	
Baseline-Chrarkteristika	

	Patients without DN (n=214)	Patients with DN (n=162)	p-value
Age (years), median (IQR)	61,00 (52; 68)	61 (53; 67)	0,939
Hospital stay (days), median (IQR)	11 (8; 15)	12 (9; 15)	0,190
Duration of DM (years, median (IQR)	6 (2; 10)	9,5 (5; 14)	<0,001
Duration of alcohol consumption (years), median (IQR)	0.0 (0.00; 0.00) Continuous variables were compared between groups using Kruskal–Wallis tests because of non-normality.	0.00 (0.00; 0.00) Continuous variables were compared between groups us-ing Kruskal–Wallis tests because of non-normality	0.004

Huang L. Identification of independent risk factors for diabetic neuropathy progression in patients with type 2 diabetes mellitus. J Int Med Res 2021; 49(9):3000605211044366. https://www.ncbi.nlm.nih.gov/pubmed/34559575.	
	prevalence of DN in patients with T2DM: 43.1% (n=162). Associations (multivariate logistic regression): - retinopathy (OR: 2.755, 95% CI: 1.599-4.746); - diabetic nephropathy (OR: 2.196, 95% CI: 1.279-3.772); - longer duration of T2DM (OR: 1.081, 95% CI: 1.045-1.120); - use of insulin (OR: 1.091, 95% CI: 1.018-1.170); - **longer history of alcohol consumption: OR: 1.034 (95% CI: 1.010-1.059);** - higher blood urea nitrogen (OR: 1.081, 95% CI: 1.009-1.159) CONCLUSIONS (Authors of the article): Retinopathy, diabetic nephropathy, longer duration of T2DM, use of insulin, longer history of alcohol consumption, and higher blood urea nitrogen were independent risk factors for DN.
Methodische Bewertung in Anlehnung an die Newcastle Ottawa Scale für Kohortenstudien	Selektion der Studienteilnehmer*innen: - 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Nein**, hospitalisierte Personen. 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Nein** - die nicht-exponierte Kohorte stammt aus der vergleichbaren Grundgesamtheit wie die exponierte Kohorte, 3) Erfolgte eine valide Erfassung der Exposition? **nein** (wahrscheinlich wurde die Exposition vallide erfasst, aber es wird in dem Artikel nicht gezeigt. (keine absoluten Werte) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Retrospektive Studie Vergleichbarkeit: * 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Kann nicht beantwortet werden; eine Auswertung, wie sich die unterschiedlichen Gruppen (Alkoholkonsum) unterscheiden, gibt es nicht. Es fand eine Adjustierung zu einigen Faktoren statt Endpunkterfassung: * 1) Erfolgte eine valide Erfassung der Endpunkte? **Ja** (ausführliche Diagnostik) 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Nicht zutreffend, retrospective Analyse 3) Wurden fehlende Daten adäquat berücksichtigt? Wird nicht berichtet Gesamtbewertung 2/9 Punkte, die unten genannten Limitationen beschränken die Aussagesicherheit.
Kommentar:	- Höhe des Alkoholkonsums nicht erhoben bzw. angegeben, nur die Dauer; die Dauer des Alkoholkonsums wird in Tabelle 1 für beide Gruppen mit 0.00 angegeben (continuierliche variable). OR legen einen geringen Effekt nahe. Absolute Zahlen sind aus den Daten nicht nachvollziehbar. - hospitalisierte Patientenpopulation **Zusammenfassung:** In einer retrospektiven Kohortenstudie an 376 hospitalisierten Personen mit T2DM wurde der Einfluss unterschiedlicher Faktoren auf die Entwicklung einer diabetischen Neuropathie untersucht. Die Erhebung der Baselinecharakteristika erfolgte aus elektronischen Gesundheitsdaten.

Huang L. Identification of independent risk factors for diabetic neuropathy progression in patients with type 2 diabetes mellitus. J Int Med Res 2021; 49(9):3000605211044366. https://www.ncbi.nlm.nih.gov/pubmed/34559575.	
	Die Prävalenz der diabetischen Neuropathie lag bei 43,1%. Ein länger bestehender Alkoholkonsum war in der Studie mit einem leicht erhöhten Risiko verbunden (OR 1,034 (95% KI 1,010-1,059)), allerdings wurde die Dauer des Alkoholkonsums oder die Höhe nicht beschrieben, die Studie kann daher nach Einschätzung der Leitlininegruppe nicht empfehlungsbegründend herangezogen werden {Huang 2021: 33713}.

Christensen et al., 2020

Christensen DH. Metabolic Factors, Lifestyle Habits, and Possible Polyneuropathy in Early Type 2 Diabetes: A Nationwide Study of 5,249 Patients in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Cohort. Diabetes Care 2020; 43(6):1266–75. https://www.ncbi.nlm.nih.gov/pubmed/32295810**.**	
Weitere Zitate	Christensen DH. Danish Centre for Strategic Research in Type 2 Diabetes (DD2) project cohort of newly diagnosed patients with type 2 diabetes: A cohort profile. BMJ Open 2018; 8(4):e017273. https://www.ncbi.nlm.nih.gov/pubmed/29627803.
Studiendesign	Prospective cohort study, - investigators linked the DD2 cohort with a range of other medical databases to comprehensively investigate the association of various metabolic and lifestyle factors at diabetes diagnosis with occurrence of DPN and neuropathic pain at a median of 2.8 years later - DD2 cohort: nationwide cohort of individuals with newly or recently diagnosed type 2 diabetes (median diagnosed diabetes duration at enrollment time 1.3 years [interquartile range (IQR) 0.3–2.9]) enrolled from hospital specialist outpatient clinics and from general practitioners' offices in Denmark since November 2010. - The unique civil personal registration number assigned to all Danish citizens links the DD2 cohort to other Danish health registries, including a complete hospital contact history from the Danish National Patient Registry, filled drug prescriptions from the Danish National Health Service Prescription Database, and information on vital status and migration from the Danish Civil Registration System. **Aktuell:** In June 2016, a median of 2.8 years (IQR 1.8–3.7) after the DD2 enrollment date, a detailed questionnaire on neuropathy and pain was sent out to all 6,726 living DD2 participants enrolled from November 2010 to February 2016.
Fragestellung	Investigate association of metabolic and lifestyle factors with possible diabetic polyneuropathy (DPN) and neuropathic pain in patients with early T2DM
Population	Recently diagnosed diabetes
Assessment	detailed questionnaire on neuropathy, including the Michigan Neuropathy Screening Instrument questionnaire (MNSIq), to identify possible DPN (score ≥4) and the Douleur Neuropathique en 4 Questions (DN4) questionnaire for possible associated neuropathic pain (MNSIq ≥4 + pain in both feet + DN4 score ≥3). alcohol consumption (≤ or ≥ 21/14 units per week for males/females - the recommended safe dose in 2010 when the DD2 was initiated)

Christensen DH. Metabolic Factors, Lifestyle Habits, and Possible Polyneuropathy in Early Type 2 Diabetes: A Nationwide Study of 5,249 Patients in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Cohort. Diabetes Care 2020; 43(6):1266–75. https://www.ncbi.nlm.nih.gov/pubmed/32295810.

Ergebnisse	
Baseline-Charkteristika	5,249 patients included with data on both DPN and pain, - 17.9% (n = 938) had possible DPN, including 7.4% (n = 386) with possible neuropathic pain. - Median age 65 years (IQR 57–72), 42% were female, - median diabetes duration: 4.6 years (IQR 3.5–5.7) at DPN assessment - At baseline, 7% (n=472) consumed more alcohol per week than the recommended maximum safe amount in Denmark (maximum of 14/21 drinks per week for women/men).
	Prevalence Ratios (PRs) of DPN: Alcoholc consumption (units of alcohol per week, male/female) baseline: total n=5247 ≤ 21/14 units: n=4904, events 872, adjusted prevalence ratios (PR) 1,0 > 21/14 units: n=343, events 66, adjusted prevalence ratios 1,19 (0,95; 1,49) - All estimates are adjusted for age, sex, and diabetes duration. **Prevalence Ratios (PRs) of <u>neuropathic pain</u> occurrence** among 938 patientes with DNP: Alcohol (units alcohol per week, male/female): DNP, total n=938 ≤ 21/14: n=872: painful DPN, n (%): 352 (40,4%), adjusted Prevalence Ratio: 1 (Reference) > 21/14: n=66: painful DPN n (%): 34 (51.5%), adjusted Prevalence Ratio: 1,31 (1,01; 1,69). (Anmerkung ÄZQ: Aussagesicherheit der Evidenz aufgrund des Studiendesigns und der Frage, ob die Personen in den verschiedenen Kategorien von den anderen Faktoren (auch BMI, HbA1c) her vergleichbar waren: sehr niedrig) The fact that high alcohol intake at baseline (defined as >21/14 units for males/females) but not as defined at the later questionnaire (>14/7 units for males/females) associated with neuropathic pain may suggest a dose-response relationship. In another sensitivity analysis, we excluded patients with alcohol overconsumption because peripheral neuropathy may result from DPN, alcoholic polyneuropathy, or a mixture in these patients. CONCLUSIONS (Autor*innen der Publikation): Possible DPN was associated with metabolic syndrome factors, insulin resistance, inflammation, and modifiable lifestyle habits in early type 2 diabetes. Notably, we found clear evidence that high alcohol intake, tobacco smoking, and failure to increase activity after diabetes diagnosis associated with higher prevalence of painful DPN.
Methodische Bewertung in Anlehnung an die	Selektion der Studienteilnehmer*innen: *** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja** 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja**

Christensen DH. Metabolic Factors, Lifestyle Habits, and Possible Polyneuropathy in Early Type 2 Diabetes: A Nationwide Study of 5,249 Patients in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Cohort. Diabetes Care 2020; 43(6):1266–75. https://www.ncbi.nlm.nih.gov/pubmed/32295810**.**	
Newcastle Ottawa Scale (für Kohortenstudien)	3) Erfolgte eine valide Erfassung der Exposition? **Ja** (interview data) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? **Fraglich**: zwar erfolgte eine Auswertung anhand von Daten aus dem Danish National Patient Registry (DNPR) aber keine Fragebögen zu Beginn der Studie. Unknown DPN and pain status at baseline. Vergleichbarkeit: * 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Ja (nur einen Punkt vergeben, da die Charakteristika Personen in den verschiedenen Alkoholkategorien nicht angegeben sind; All estimates are adjusted for age, sex, and diabetes duration). Endpunkterfassung: - bis * 1) Erfolgte eine valide Erfassung der Endpunkte? Wahrscheinlich Ja (detailed questionnaire but no neurological examination, Diagnostik ausreichend?) 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Eher **nein** (Beobachtungszeit 2,8 Jahre zu kurz) 3) Wurden fehlende Daten adäquat berücksichtigt? Keine ausreichenden Informationen zur Beantwortung vorhanden. Gesamt 5/9 Punkten
Kommentar:	- DPN and painful DPN assessment relied on the MNSIq and DN4 questionnaires and not on neurological examinations, nerve conduction studies, or validated small-fiber measures. - unknown DPN and pain status at baseline, uncertainty about temporal relationships and the possibility for reverse causality - self-reported factors may be subject to recall errors.

3.2.2 Querschnittstudien

Kamalarathnam et al., 2022

Kamalarathnam SR. Diabetic peripheral neuropathy in diabetic patients attending an urban health and training centre. Journal of family medicine and primary care 2022; 11(1):113–7. https://www.ncbi.nlm.nih.gov/pubmed/35309653.	
Studiendesign	Querschnittstudie, n=204, Dauer: 1 Monat
Fragestellung	- To screen Diabetic patients attending an Urban Health and Training Centre of a medical college in Tamilnadu for Diabetic Peripheral Neuropathy. - To assess association between DPN and selected variables such as socio-demographic factors, glycaemic control, duration of diabetes, physical activity, body mass index, smoking and consumption of alcohol.

Kamalarathnam SR. Diabetic peripheral neuropathy in diabetic patients attending an urban health and training centre. Journal of family medicine and primary care 2022; 11(1):113–7. https://www.ncbi.nlm.nih.gov/pubmed/35309653.	
Population	All (consecutive) diabetic patients attending an Urban Health and Training Centre were eligible for the study.
Assessment	Michigan Neuropathy Screening Instrument (MNSI), which involves using a questionnaire followed by a physical examination.
Ergebnisse	
Baseline-Chrarkteristika	204 patients, 58.8% male, mean age 54.8 years (SD = 8.8 years), 79.9% employed of which 29.4% skilled labourers, mean duration of diabetes 6.2 years (SD = 5.3 years).
	Proportion of diabetics screened positive for PN was 23% and 45.6% using MNSI questionnaire and examination, respectively. **Alcohol consumption (total):** Yes n=36 (17,6%), no 168 (82,4%) Association between Alcoholism and Diabetic peripheral neuropathy: Alcoholism present: Screened positive for DPN by MNSI: n=14 (38,9%), Alcoholism absent: Screened positive for DPN by MNSI: n=79 (47%), OR 0,72 (95% CI 0,34; 1,5), p=0,38 An age of 60 years and above was associated with DPN (OR = 2.505, P value = 0.003). A duration of more than 4 years of diabetes was also associated with DPN (OR = 1.872, P value = 0.02820).
Methodische Bewertung: in Anlehnung an Newcastle Ottawa scale für Kohortenstudien	**Selektion der Studienteilnehmer*innen**; ** (*) 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja** (für diese Studie ja, aber fraglich für die Patientenpopulation der NVL – medical training centre in Indien) 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja** (die nicht-exponierte Kohorte stammt aus einer vergleichbaren Grundgesamtheit wie die exponierte Kohorte, wie sich die Baselinecharakteristika unterschieden, kann aber nicht nachvollzogen werden) 3) Erfolgte eine valide Erfassung der Exposition? Fraglich **Ja** (Questionaire, undereporting möglich; auf die Menge des Alkoholkonsums wird im Artikel nicht eingegangen) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Nicht passend, da Querschnittsstudie **Vergleichbarkeit**: - 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Not applicable, eine Auswertung, wie andere Faktoren bezogen auf die Kategorien des Alkoholkonsums verteilt waren, liegt nicht vor. **Endpunkterfassung**: * 1) Erfolgte eine valide Erfassung der Endpunkte? **Ja** (MNSI questionnaire and examination) 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Not applicable (Querschnittsstudie) 3) Wurden fehlende Daten adäquat berücksichtigt? Nein (keine Angaben vorhanden, ob Daten fehlten)

Kamalarathnam SR. Diabetic peripheral neuropathy in diabetic patients attending an urban health and training centre. Journal of family medicine and primary care 2022; 11(1):113–7. https://www.ncbi.nlm.nih.gov/pubmed/35309653.	
	3 bis 4 von 9 Punkten im NOS (nur eingeschränkt anwendbar, da Querschnittstudie)
Kommentar:	- Keine Angaben über die Menge des tatsächlichen Alkoholkonsums. - Ursache der PNP ausreichend abgeklärt? - Protokoll nicht aufgefunden. - Studiendesign: Querschnittstudie, keine kausalen Rückschlüsse möglich.

Shrestha et al., 2017

Shrestha HK. Prevalence and Risk Factors of Diabetic Peripheral Neuropathy in T2DM Patient Presenting to Community Hospital in Nepal. Kathmandu Univ Med J (KUMJ) 2017; 17(58):146–9. https://www.ncbi.nlm.nih.gov/pubmed/34547847.	
Studiendesign	cross sectional study in a University Teaching Hospital.
Fragestellung	prevalence and risk factors of Diabetic Peripheral Neuropathy (DPN) among type 2 diabetes mellitus (T2DM) patients.
Population	T2DM patients (age ≥30 years) with diabetes duration > 6 months
Assessment	Michigan Neuropathy Screening Instrument Scoring was used to diagnose DPN. Examination of foot.
Ergebnisse	
	Total n=160 patients **Characteristics of study population:** mean age 57.32 years, female 90 (56%). Alcohol history: 40 (25%) DPN: 61 (38.1%) DPN within 1 year of being diagnosed with diabetes: 26 (16%) Mean Diabetes duration: 5.56 years mean HbA1c was 8.33%; No statistically significant risk factors are evident on multivariate analysis. Conclusion: Diabetic peripheral neuropathy was found to be highly prevalent in patients with type 2 diabetes including the patients with relatively shorter diabetes duration.

Shrestha HK. Prevalence and Risk Factors of Diabetic Peripheral Neuropathy in T2DM Patient Presenting to Community Hospital in Nepal. Kathmandu Univ Med J (KUMJ) 2017; 17(58):146–9. https://www.ncbi.nlm.nih.gov/pubmed/34547847.	
Methodische Bewertung in Anlehnung an NOS für Kohortenstudien	Selektion der Studienteilnehmer*innen: - bis * 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? Fraglich: patients presenting at community hospital. 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? Auch hospitalisierte Personen und Kategorien des Alkoholkonsums nicht ausreichend beschrieben. Die nicht-exponierte Kohorte stammt aber aus der vergleichbaren Grundgesamtheit wie die exponierte Kohorte, 3) Erfolgte eine valide Erfassung der Exposition? nein (ggf. wurde die Exposition vallide erfasst, aber es wird in dem Artikel nicht ausreichend beschrieben) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Nicht anwendbar, Querschnittstudie Vergleichbarkeit: - 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Kann nicht beantwortet werden; eine Auswertung, wie sich die unterschiedlichen Gruppen (Alkoholkonsum) unterscheiden, gibt es nicht. Endpunkterfassung: * 1) Erfolgte eine valide Erfassung der Endpunkte? Ja (MNSIQ and foot examination) 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Nicht zutreffend, Querschnittstudie 3) Wurden fehlende Daten adäquat berücksichtigt? Wird nicht berichtet Gesamtbewertung 2/9 Punkte, die unten genannten Limitationen beschränken die Aussagesicherheit.
Kommentar	- keine nummerische Auswertung zur Assoziation zwischen Alkoholkonsum und DNP. Nur im Fließtext, dass es keine Assoziationen gab. Daten nicht gezeigt. - Hospitalisierte Personen repräsentativ für NVL? - Relativ geringe Teilnehmerzahl - Querschnittstudie; kausale Rückschlüsse nicht möglich.

Yokoyama et al., 2020

Yokoyama H. Factors associated with diabetic polyneuropathy-related sensory symptoms and signs in patients with polyneuropathy: A cross-sectional Japanese study (JDDM 52) using a non-linear model. J Diabetes Investig 2020; 11(2):450–7. https://www.ncbi.nlm.nih.gov/pubmed/31314173	
Studiendesign	cross-sectional survey - 17 primary care clinics (specialized in diabtes) across various regions of Japan. Of overall population of 13,039 patients a total of 9,914 patients had neuropathy evaluated within 1 year of attendance at the clinic and were registered in the present study.
Fragestellung	prevalence of diabetic polyneuropathy (DPN)-related sensory symptoms/signs and associated factors in patients with polyneuropathy, considering non-linear effects for numerical variables

Yokoyama H. Factors associated with diabetic polyneuropathy-related sensory symptoms and signs in patients with polyneuropathy: A cross-sectional Japanese study (JDDM 52) using a non-linear model. J Diabetes Investig 2020; 11(2):450–7. https://www.ncbi.nlm.nih.gov/pubmed/31314173

Population	patients with type 2 diabetes mellitus from 17 primary care clinics across Japan
Assessment	DPN and DPN-related sensory symptoms/signs were diagnosed according to the Diabetic Neuropathy Study Group in Japan criteria. Two or more of three components (1) subjective symptoms in the bilateral lower limbs or feet; (2) loss of or decreased ankle jerk reflex and (3) decreased vibration perception, assessed using a C128 tuning fork and bilaterally measured at the medial malleoli. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5051339/pdf/bmjdrc-2016-000294.pdf) Neuropathic sensory symptoms/signs were defined as bilateral spontaneous pain; hypoesthesia, including decreased perception to pinprick and temperature (cold tuning fork); or paresthesia of the legs Information on alcohol consumption was collected from medical records (Kategorien in der Methodenbeschreibung nicht angegeben).
Ergebnisse	
Baseline-Chrarkteristika	Total: 9,914 patients with type 2 diabetes mellitus - 2,745 had DPN and 1,689 had DPN-related sensory symptoms/signs (61.5% of patients with DPN). - median age (all participants) 66 years, - 62.3% of patients were male - median BMI of 24.5 - median SBP of 127 mmHg - median duration of diabetes (all patients) 13.0 years, - median HbA1c of 6.9%. - The median age, sex distribution, BMI, SBP, smoking status, alcohol consumption status and median eGFR were similar in the subgroups of patients with DPN and DPN-related sensory symptoms/signs.
	- Analyses of factors associated with DPN-related sensory symptoms/signs among patients with DPN: Correlations between DPN-related sensory symptoms/signs and alcohol consumption (OR 2.02 (95% CI 1,247; 3,271) for former/never; P = 0.004).

	Patients with T2DM (n=9914)				
	Overall population (n=9914)	Patients without DPN (n=6180)	Patients with DPN (n=2745)		Patients with unknown status of DPN (n=989)
			Overall (n=2745)	With DPN-related sensory symptoms/signs (n=1689)	
Alkohol use, n (%)					
Current	2477 (31,6)	1530 (31,8)	703 (29,3)	475 (32,7)	244 (39,9)
Former	264 (3,4)	157 (3,3)	95 (4,0)	74 (5,1)	12 (2,0)
Never	5087 (65,0)	3128 (65,0)	1604 (66,8)	905 (62,2)	355 (58,1)

Yokoyama H. Factors associated with diabetic polyneuropathy-related sensory symptoms and signs in patients with polyneuropathy: A cross-sectional Japanese study (JDDM 52) using a non-linear model. J Diabetes Investig 2020; 11(2):450–7. https://www.ncbi.nlm.nih.gov/pubmed/31314173	
	Aus der Veröffentlichung: “As no similar association was observed with current alcohol consumption in the present study, the association between DPN-related sensory symptoms/signs and former alcohol consumption might be an artifact due to the small number of patients in this subgroup, a causal relationship reversal or another confounding variable not detected.”
Methodische Bewerteung in Anlehnung an NOS für Kohortenstudien	Selektion der Studienteilnehmer*innen: *** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja**, in Japan schon (Primärversorgung, große Kohortenstudie) 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja** (die nicht-exponierte Kohorte stammt aus einer vergleichbaren Grundgesamtheit wie die exponierte Kohorte, allerdings ist die Art der Erfassung ggf. nicht ausreichend, underreporting) 3) Erfolgte eine valide Erfassung der Exposition? **Ja** (anhand der Patient*innenakte, aber unklar, ob die Kategorien im Interview wirklich adäquat angegeben werden; Für die Recherche der NVL nicht ausreichend, da keine quantitative Erfassung erfolgt ist.) 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? **Nicht zutreffend**, Querschnittsstudie Vergleichbarkeit: - 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Keine Aussage möglich, da ein Vergleich der Gruppen nicht erfolgt ist. Endpunkterfassung: ** 1) Erfolgte eine valide Erfassung der Endpunkte? **Ja**, klinische Untersuchung, neurologische Tests 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Keine Angabe möglich: Querschnittsstudie. 3) Wurden fehlende Daten adäquat berücksichtigt? **Ja,** All missing data were imputed by the multiple imputation method using the “aregImpute” function in the “rms” package of R software version 3.3.0. Gesamt 5/9 Punkten.
Kommentare:	- Limitatinen: Studiendesign (Querschnittstudie) - Übertragbarkeit auf deutsche Versorgunsbereiche (Studie aus Japan)? - In den Kategorie Alcohol use gibt es keine quantitative Erfassung.

Bansal et al., 2014

Bansal D. Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting. J Diabetes Investig 2014; 5(6):714–21. https://www.ncbi.nlm.nih.gov/pubmed/25422773.	
Studiendesign	cross-sectional study in an outpatient setting of an endocrinology clinic of a public tertiary care hospital in north India

Bansal D. Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting. J Diabetes Investig 2014; 5(6):714–21. https://www.ncbi.nlm.nih.gov/pubmed/25422773.

Fragestellung	- To assess the prevalence of diabetic peripheral neuropathy (DPN), - To compare the prevalence between known diabetes mellitus (KDM) and newly detected diabetes mellitus (NDDM), - To identify risk factors associated, its prevalence pattern and to assess if any sex-specific differences are present.
Population	Patients with duration of diabetes ≤6 months were considered to be newly detected diabetes mellitus (NDDM)
Assessment	DPN was diagnosed by the combination of >1 abnormal result of 10-g monofilament, pinprick sensations and ankle reflexes, and categorized according to the severity level using vibration perception threshold. Thereafter, the patient underwent VPT (Vibration perception threshold) test to categorize them according to the severity level of DPN. Quantification of DPN was assessed by VPT using a Biothesiometer in a standardized manner Information regarding Alcohol consumption were collected by interviewing the participants.
Ergebnisse	
Baseline-Chrarkteristika	Total: n=2006, 49,3% male, - newly detected diabetes mellitus (NDDM): 369 (18,4%) - known diabetes mellitus (KDM): 1637 (81,6%)

DNP-prevalence (total): 586 participants, 29.2% (95% confidence interval [CI] 27.2-31.2).
Prevalence (DNP): KDM 33.7% (95% CI 31.42-36.01) vs NDDM 9.2% (95% CI 6.3-12.2); P < 0.001.
Prevalence of mild, moderate, and severe neuropathies was 8.06, 14.55 and 6.63%, respectively.

Diabetic peripheral neuropathy prevalence in study cohort

Group	Severity of Neuropathy n (%), [95% CI]			
	Overall neuropathy	Mild neuropathy	Moderate neuropathy	Severe Neuropathy
Total (n=2006)	586 (29,2) [27,2; 31,2]	161 (8,06) [6,7; 10,2]	292 (14,55) [12,6; 16,4)	133 (6,63) [4,4; 8,2]
KDM (n=1637)	552 (33,7) [31,4; 36,0]	132 (8,06) [5,7; 10,5]	285 (17,4) [15,1; 19,8]	135 (8,3) [5,9; 10,7]
NDDM (n=369)	34 (9,2) [6,3; 12,2]	23 (6,2) [3,3; 9,1]	11 (2,98) [0,2; 5,9]	-

Clinical characteristics of study participants

Variables	DNP present (n=586)	DNP absent (n=1420)	p-value
Duration of Diabetes (years)	10,8 (7,5)	6,6 (6,9)	<0,001
Age (years)	57,1 (9,7)	52,5 (10,4)	<0,001
Alcohol, n (%)	146 (24,9)	289 (20,3)	0,024
Retinopathy, n (%)	245 (41,8)	260 (18,3)	<0,001
Nephropathy, n (%)	123 (20,9)	54 (3,8)	<0,001

Bansal D. Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting. J Diabetes Investig 2014; 5(6):714–21. https://www.ncbi.nlm.nih.gov/pubmed/25422773.

Risk factors for DPN in multivariate logistic regression

Variables	Odds ratio (95% CI)	p-value
Duration of Diabetes	1,04 (1,03; 1,06)	<0,001
Alcohol, n (%)		
- non-drinker	1 (reference)	
- drinker	1,46 (1,03; 2,07)	0,033
Smoking		
- Non-Smoker	1 (ref)	
- Smoker	0,71 (0,47; 1,06)	0,096
Hypertension		
- absent	1 (ref.)	
- present	2,02 (1,56; 2,61)	<0,001
Macrovascular complications		
- absent	1 (reference)	
- present	1,6 (1,18; 2,19)	<0,01
Microvascular complications		
- absent	1 (ref.)	
- present	3,45 (2,65; 4,5)	<0,001

CONCLUSIONS (authors of the article): The study showed a high prevalence (29.2%) of DPN among north Indian type 2 diabetes mellitus patients. Thus, timely screening with earlier detection and intervention would be useful in preventing the progression of neuropathy.

Methodische Bewertung in Anlehnung an NOS (für Kohortenstudien)

Selektion der Studienteilnehmer*innen: ** bis ***

1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? Für die Studie ja (outpatiend clinic Indien)
2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? Wahrscheinlich Ja (die nicht-exponierte Kohorte stammt aus einer vergleichbaren Grundgesamtheit wie die exponierte Kohorte)
3) Erfolgte eine valide Erfassung der Exposition? Fraglich, Interview der Teilnehmenden ggf. underreporting Für die Fragestellung der NVL nicht ausreichend, da keine quantitative Erfassung erfolgt ist)
4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Nicht zutreffend, Querschnitts-studie

Vergleichbarkeit: -
1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Keine Aussage möglich, da ein Vergleich der Gruppen (verschiedene Kategorien des Alkoholkonsums) nicht erfolgt ist.

Endpunkterfassung: *
1) Erfolgte eine valide Erfassung der Endpunkte? Ja, klinische Untersuchung, neurologische Tests

Bansal D. Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting. J Diabetes Investig 2014; 5(6):714–21. https://www.ncbi.nlm.nih.gov/pubmed/25422773.	
	2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Keine Angabe möglich: Querschnittsstudie. 3) Wurden fehlende Daten adäquat berücksichtigt? Keine ausreichenden Angaben. Gesamt 3-4/9 Punkten.
Kommentar:	- Kohorte aus Indien - Querschnittsstudie - Kategorisierung des Alkoholkonsums in drinker vs. Non-drinker

3.2.3 Zurückgestellt

3.2.3.1 Art der Auswertung für Fragestellung der NVL nicht passend

Liu G. Adherence to a Healthy Lifestyle in Association With Microvascular Complications Among Adults With Type 2 Diabetes. JAMA Netw Open 2023; 6(1):e2252239. https://www.ncbi.nlm.nih.gov/pubmed/36701156.	
Studiendesign	Analyse von zwei prospektiven Kohortenstudien
Fragestellung	association between adherence to a healthy lifestyle before and after diabetes diagnosis and the risk of subsequent microvascular complications among adults with diabetes
Population	incident patients with type 2 diabetes who were free of cardiovascular disease and cancer at the time of diabetes diagnosis and completed the diabetes supplementary questionnaires in the Nurses' Health Study (in 2000 and 2005) and the Health Professionals Follow-Up Study (in 2000, 2004, and 2008) in the US.
Intervention/Factor	- Diet and lifestyle factors before and after diabetes diagnosis (validated questionnaires). healthy lifestyle: - nonsmoking, - body mass index of ≥18.5 or <25, - engaging in moderate-to-vigorous physical activity (≥150 minutes per week), - consuming a high-quality diet (top 40th percentile of the Alternative Healthy Eating Index), - moderate alcohol drinking (5-15 g/d for women and 5-30 g/d for men).
Comparison	4 or more low-risk lifestyle factors before diabetes diagnosis compared with zero

Liu G. Adherence to a Healthy Lifestyle in Association With Microvascular Complications Among Adults With Type 2 Diabetes. JAMA Netw Open 2023; 6(1):e2252239. https://www.ncbi.nlm.nih.gov/pubmed/36701156.	
Outcomes	Physician-diagnosed microvascular complications including diabetic neuropathy, retinopathy, nephropathy, and foot disorders were self-reported at questionnaire surveys.
Multivariable adjustment	multivariable model: adjusted for age at diabetes diagnosis (years), sex (men or women), ethnicity (White or non-White), total energy intake (in quartiles), aspirin use (yes or no), presence of hypertension or hypercholesterolemia (yes or no), and use of antihypertensive or cholesterol-lowering drugs (yes or no).
Ergebnisse	
Baseline-Chrarkteristika	7077 patients with T2DM included (4982 women in NHS and 2095 men in HPFS), mean age [SD]: 61years [8.8], 94.2% White. proportion of participants with low-risk lifestyle factors at diabetes diagnosis 0 low-risk lifestyle factors 8.5% 1 low-risk lifestyle factors 33.5%, 2 low-risk lifestyle factors 35.4%, 3 low-risk lifestyle factors 16.9%, 4 or more low-risk lifestyle factors 5.7%,
	2878 patients developed microvascular complications. - 1796 cases of diabetic neuropathy, - 1415 cases of diabetic retinopathy, - 383 cases of diabetic nephropathy, - 452 cases of diabetic foot disorders. adherence to a healthy lifestyle before and after diabetes diagnosis were both associated with a lower risk of developing microvascular complications. **4 or more low-risk lifestyle factors before diabetes diagnosis compared with zero:** Any microvascular complication: RR 0.73 (95% CI, 0.60-0.91) diabetic neuropathy: RR 0.71 (95% CI, 0.54-0.93) diabetic retinopathy: RR 0.76 (95% CI, 0.57-1.01) diabetic nephropathy: RR 0.42 (95% CI, 0.23-0.79) Diabetic foot disorders: RR0.60 (95% CI, 0.35-1.00) **4 or more low-risk lifestyle factors after diabetes diagnosis compared with zero:** any microvascular complications: RR of 0.68 (95% CI, 0.55-0.83) diabetic neuropathy: RR 0.67 (95% CI, 0.51-0.88) diabetic retinopathy: RR 0.65 (95% CI, 0.48-0.86) diabetic nephropathy: RR 0.57 (95% CI, 0.34-0.98)

Liu G. Adherence to a Healthy Lifestyle in Association With Microvascular Complications Among Adults With Type 2 Diabetes. JAMA Netw Open 2023; 6(1):e2252239. https://www.ncbi.nlm.nih.gov/pubmed/36701156.	
	diabetic foot disorders: 0.62 (95% CI, 0.37-1.05) In addition, greater improvement in lifestyle factors from before to after diabetes diagnosis was also significantly associated with a lower risk of neuropathy or total microvascular complications. Each increment in number of low-risk lifestyle factors was associated with a 6% (RR, 0.94; 95% CI, 0.90-0.98) lower risk for any microvascular complications and a 9% (RR, 0.91; 95% CI, 0.86-0.96) lower risk for diabetic neuropathy. Consistent results were observed when analyses were stratified by age at diabetes diagnosis, sex/cohort, or lifestyle factors before diabetes diagnosis.
Kommentare	- Healthy lifestyle in Bezug auf Alkohol definiert als: moderate alcohol drinking (5-15 g/d for women and 5-30 g/d for men). Was ist mit Alkoholkonsum 0-5g/d? Kein Vergleich zwischen hohem und niedrigem Alkoholkonsum möglich. - Datenerhebung: Endpunkterhebung: self-reported at questionnaire surveys, Erhebung der Lifestyle-Faktoren: assessed by validated questionnaires - Keine Einzelauswertung, was moderater Alkoholkonsum alleine bringt, nur als zusätzlicher Faktor zu bereits drei “helathy lifestyle factors”.

4 Evidenztabellen: Stressbewältigung

4.1 Systematische Recherche (Ergebnisse 2022/2023/2021)

Ni et al., 2021 – Mindfulness-based interventions (MBI)

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Ni Y-X, Ma L, Li J-P. Effects of mindfulness-based intervention on glycemic control and psychological outcomes in people with diabetes: A systematic review and meta-analysis. J Diabetes Investig 2021; 12(6):1092–103. DOI: 10.1111/jdi.13439.	**Suchzeitraum:** from inception to October 2019 **Fragestellung:** effects of MBI on glycemic control and psychological outcomes in people with diabetes **Intervention**: mindfulness-based intervention (MBI) **Population:** adults with type 1 and type 2 diabetes **Intervention:** any interventions that MBI was	Eight studies (n=841 participants) included - 4 studies: mixture of T1DM and T2DM, 4 studies only included T2DM. - various forms of mindfulness-based intervention, including MBSR (3 studies), MBCT (2 studies), mindful eating (1 study), combination of MBSR and MBCT (1 study), and unspecific mindfulness-based intervention (1 study). - All studies delivered the sessions face-to-face, except one study through audio compact disc. - 5 studies: group-based intervention and 3 studies: individual intervention - Psychological outcomes were measured by different tools	**Critically low** y-py-y-py-y-y-n-y-y-n-y-n-n-y-y-y Kritische nicht erfüllte Domänen: Ausgeschlossene Studien nicht	Small number of trials and samples Es gibt einen weiteren Artikel von dem gleichen Autor aus 2020: http://www.ncbi.nlm.nih.g

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
http://www.ncbi.nlm.nih.gov/pubmed/33064926.	a major component of, such as MBSR, MBCT and MB-EAT; **Comparator:** usual care, wait-list control, no intervention or health education without any mindful component; **Outcomes:** depression, stress, anxiety, distress and glycemic control (HbA1c); **Studies:** RCTs published in English. **Exclusion criteria:** exercise-focused intervention programs with mindfulness as a component, mixed interventions (i.e., Tai Chi and meditation), dialectical behavior therapy, and acceptance and commitment therapy, **Studienqualität:** RoB	- 6 studies reported attrition rates of <20%, and 2 studies reported attrition rates of >20%, but no significant difference between groups regarding attrition rates Meta-analysis: Effectiveness of mindfulness-based intervention on: - **diabetes-related distress:** Mean Difference (MD) -5.81 (95% CI -10.10; -1.52) P = 0.008, I^2 = 28%, 5 studies, n=431 - **depression:** standardized mean difference (SMD) -0.56 (95% CI -0.82; -0.30), P < 0.0001; I^2 = 59%; 8 Studien, n=648 - **stress:** SMD: -0.53 (CI -0.75; -0.31); P < 0.00001, I^2: 47%, 7 studies, n=652 - Mixed effects were observed for **anxiety.** - **HbA1c:** mean difference -0.25% (95% CI -0.43 to -0.07), p = 0,006, 7 studies, n=665, I^2 = 0% ---------- Bewertung der Aussagesicherheit der Evidenz: Diabetes related distress: **moderate to low** RoB: -1 (allocation bei 2/5 RCTs unclear, Blinding patients 3/5 high, blinding outcome assessment: 3/5 unclear, 1/5 high, 1/5 low, selective reporting 1/5 high, 1/5 unclear) Inkonsistenz: 0 (bis -1; Punktschätzer und KI überwiegend überlappend, hier nicht abgewertet) Indirectness: ± 0 bis -1 (Personen mit und ohne vorbestehende psychische Erkrankung bzw. Belastung betrachtet) Imprecision: ± 0 Publication bias: ± 0 (funnel plot bei < 10 Studien nicht durchgeführt, zwar keine Recherche nach grauer Literatur aber auch kein Hinweis auf Publication bias) **Depression:** Aussagesicherheit der Evidenz: **low** RoB: -1 Inkonsistenz: -1 (Punktschätzer und KI teilweise nur wenig überlappend, Heterogenität I^2=59%)	aufgeführt, RoB nicht bei der Interpretation berücksichtigt (auch keine Sensitivitätsanalysen gerechnet) Weitere Anmerkung: Es wird eine Prospero Registrierung angegeben, diese passt aber vom Titel nicht mit dem Artikel überein. Der Prospero-Eintrag wurde nicht aktualisiert (Abweichungen wie main und secondary outcomes, duration od follow-up etc.).	ov/pubmed/32406186. Mit ähnlicher Fragestellung (QoL als zusätzlichen Endpunkt).

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Indirectness: ± 0 Imprecision: ± 0 Publication bias: ± 0 (funnel plot bei < 10 Studien nicht durchgeführt) **Stress:** Aussagesicherheit der Evidenz: **moderate to low** RoB: -1 Inkonsistenz: 0 bis -1 (I^2= 47%) Indirectness: ± 0 Imprecision: ± 0 Publication bias: ± 0 **Subgruppenanalysen:** - larger effect sizes for depression and stress in combined studies involving participants with baseline psychological disorders than those involving participants without baseline psychological disorder. o studies with baseline psychological disorder (3 studys): depression: SMD -0.72 (95% CI -0.93 to -0.51; P < 0.00001), stress: SMD -0.79 (95% CI -1.04 to -0.55; P < 0.00001)) o without baseline psychological disorder: depression: SMD -0.37 (95% CI -0.85, -0.10; P = 0.13); stress: SMD -0.37 (95% CI -1.04, -0.55; P = 0.001) 3 studies recruited participants with a certain baseline level of depression (1 study), diabetes-related distress (1 study) or low levels of emotional well-being (1 study), hence, participants in those studies were considered to have a psychological disorder. - nach Diabetestyp war geplant: However, no study included in the present review reported outcomes on people only with type 1 diabetes, making it impossible to identify diabetes type-specific effects of MBI. Conclusions (Review): MBI appears to have benefits on HbA1c, depression, stress and diabetesrelated distress in people with diabetes.		

Ngan et al., 2021 – Mindfulness- and acceptance-based interventions

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Ngan HY. Effects of mindfulness- and acceptance-based interventions on diabetes distress and glycaemic level in people with type 2 diabetes: Systematic review and meta-analysis. Diabet Med 2021; 38(4):e14525. https://www.ncbi.nlm.nih.gov/pubmed/33438251.	**Suchzeitraum:** from inception to June 2020 **Fragestellung:** effects of mindfulness- and acceptance-based interventions on diabetes distress and glycaemic level in community-dwelling adults with type 2 diabetes. **Population:** community-dwelling adults with type 2 diabetes. **Intervention:** any intervention that included mindfulness and/or acceptance training as the main component and aimed to relieve emotional distress by cultivating mindful skills such as focusing on the present moment, raising awareness and enhancing acceptance. Studies that used yoga exercises were excluded. **Comparison:** usual care, including diabetes education **Outcomes:** diabetes distress and/or glycaemic level; Diabetes distress was assessed using the Problem Areas in Diabetes Scale or the Diabetes Distress Scales **secondary outcomes:** diabetes self management (i.e. measured using the 11-item Summary of Diabetes Self-Care Activities Measure and symptoms of psychological conditions such as depression, anxiety and stress (i.e. as measured using the 21-item Depression, Anxiety and Stress Scale26 and Hospital Anxiety and Depression Scale) **Studies:** RCTs	Nine RCTs (801 participants) examining the effects of acceptance and commitment therapy, mindfulness-based cognitive therapy, mindfulness-based stress reduction and self-directed mindfulness practice were included. - Baseline characteristics: mean age: 50-66 years, average disease duration: 4-10 years), diabetes control (HbA1c >7.0%, 53 mmol/mol). - RoB: only 3 studies were rated as having 'some concerns' regarding the RoB, and the remaining 6 studies were judged as having a 'high risk of bias' - 4/9 RCTs evaluated acceptance and commitment therapy. 5/9 adopted interventions based on the principles of mindfulness, including mindfulness-based stress reduction (n = 2), mindfulness-based cognitive therapy (n = 2) and self-directed mindfulness practice (n = 1). **diabetes distress (intervention vs. control):** - 5 studies assessed diabetes distress: n=2 mindfulness-based cognitive therapy, n=1 mindfulness-based stress reduction, n=1 acceptance and commitment therapy and n=1 selfdirected mindfulness practice - Diabetes distress immediately to 1 month post-intervention: SMD = −0.22 (95% CI: −0.59, 0.14), p = 0.23, 5 RCTs, 368 participants, I^2=64%, **GRADE low** (RoB, Inconsistency, indirectness, imprecision), Anmerkung ÄZQ: nach Anzahl der "Abwertungen" eigentlich very low. - Diabetes distress (therapist-led) 4 RCTs, n=319 (without Pearson et al) Standardised mean difference (SMD) = -0.37 (95% CI: -0.62, -0.11), p = 0.002, **GRADE low** (RoB, Indirectness, Imprecision) **HbA1c** - HbA1c (immediately post-intervention): MD -0,35 (95% CI -0,67; -0,04), p = 0,03, 3 studies, n= 306, I^2=0%, **GRADE low** - HbA1c (3-6 months post-intervention): SMD -0,21 (95% CI -0,47; 0,05), p=0,05, 3 trials, n=312, I^2=0-24%, **GRADE low** **Diabetes self management:** - 4 studies, 1 study failed to report overall questionaire score, The authors of the remaining 3 studies, which evaluated acceptance and commitment therapy, failed to demonstrate significant effects of the	Critically low y-n-y-y-y-y-n-y-y-n-y-n-y-y-n-y kritische nicht-erfüllte Domänen: Keine Information, ob es ein Protokoll für den Review gab, Ausgeschlossene Studien nicth aufgeführt. Publication bias: Es wurde die Wahrscheinlichkeit des selective reportings in den Studien diskutiert, aber es erfolgte kein funnel-plot oder sttistischer test,	hetero-geneity of the interventions in the included studies (intervention hours, structure and dose) small number of included studies with small sample of people with type 2 diabetes substantial risks of bias in the included studies, this review included 2 studies in which 30%–40% of the participants had type 1

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar

	Qualitätsbewertung der Studien: Cochrane RoB-tool, 2.0, GRADE-Bewertng der Aussagesicherheit	interventions on diabetes self management (p = 0.14) after 3–6 months, compared with diabetes education
		
		Psychological Symptoms:
		- 5 studies assessed effects on psychological symptoms, 2 studies did not report means and SDs.
		- meta-analysis of 3 studies of mindfulness-based cognitive therapy (n=2) and self-directed mindfulness practice (n=1):
		  ○ anxiety (SMD = −0.41, 95% CI: −0.66, −0.15, p = 0.002, 3 RCTs, 250 participants) immediately after the intervention, compared with usual care
		  ○ depression (SMD = −0.53 (95% CI: −0.82, −0.25), p ≤ 0.001, 3 RCTs, 250 participants), immediately after the intervention, compared with usual care
		  ○ pooled effect on stress at the same time point was non-significant (p = 0.77)
		
		Limitations: underpowered studies may have led to overestimation, the interventions for diabetes distress and HbA1c were heterogeneous.
				diabetes.
				
				Could only evaluate short-term effects

Fisher et al., 2023 – Mindfulness-based stress reduction (MBSR)

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Fisher V. The effectiveness of mindfulness-based stress reduction (MBSR) on the mental health, HbA1C, and mindfulness of diabetes patients: A systematic review and meta-analysis of randomised controlled trials. Appl Psychol	**Suchzeitraum:** inception to July 2022 **Fragestellung:** effectiveness of mindfulness-based stress reduction (MBSR) on the mental health, haemoglobin A1c (HbA1C), and mindfulness of diabe-tes patients. **Population:** diabetes patients **Intervention:** standardised mindfulness-based stress reduction (MBSR)* **Comparator:** control groups **Outcome:** Primary outcome: mental health outcomes	10 studies (718 participants) included in systematic review, 9 studies included in meta-analysis. - Type of diabetes: 48 type 1 diabetes, 474 type 2 diabetics, 124 either type 1 or type 2 diabetes, 94 unspecified diabetes, 88 pregnant women with gestational diabetes. - control groups included treatment as usual (TAU), diabetes education, diabetes support, and waiting list. In the meta-analysis, outcomes at post-intervention and follow-up were compared between the MBSR intervention and control groups with an adjustment of the baseline values. **pooled effect sizes comparing the MBSR and control group post-test scores (post-intervention)**	**Critically low** y-n-y-py-y-y-n-py-n-n-y?-y-y-y-y-y Nicht-erfüllte kritische Domänen: Protokoll nach Extraktion erstellt, aus-	Metaanalyse wegen hoher Heterogenität nicht sinnvoll nicht nur Typ-2-Diabetes, sondern auch T1DM und Gestationsdiabetes betrachtet.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Health Well Being 2023; 15(4):1733–49. https://www.ncbi.nlm.nih.gov/pubmed/36855248.	(e.g. stress, anxiety, and depression), Secondary outcome: HbA1C, and mindfulness **Studies:** RCTs **Assessment of risk of bias:** Prediction Model Study Risk of Bias Assessment Tool (PROBLAST) *MBSR is a clinically standardised intervention that supports participants to adopt the perspective of openness, curiosity, and acceptance of what is occurring in the present moment with a nonjudgmental attitude (Kabat-Zinn, 1982). The intervention delivers eight 2.5-h weekly group sessions and a full-day retreat after the sixth week (Kabat-Zinn, 2017).	- **anxiety**: Hedges' g = -2.407, 95% CI [-3.631, -1.183], p = .000, I^2 = 98.773, p < .001, 3 studies (1x T2DM, 1x unspecified, 1x Gestationsdiabetes) - **depression:** Hedges' g = -1.110, 95% CI [-1.988, -0.232], p = .013, I^2 = 94.075, p < .001, 6 studies - **stress:** Hedges' g = -0.409, 95% CI [-1.287, 0.469], p = .361, I^2 = 85.118, p < .001 at post-intervention, 6 studies - **HbA1C:** Hedges' g = −0.118, 95% CI [−1.345, 1.110], p = .851, I^2 = 72.221, p = .027, 3 studies. - **Mindfulness:** Hedges' g = 1.834, 95% CI [0.278, 3.391], p = .021, I^2 = 85.118, p < .001, 2 studies. **pooled effect sizes comparing the MBSR and control group at follow-up** - **Depression:** Hedges' g = −2.717, 95% CI [−4.504, −0.930], p = .003, I^2 = 97.646, p < .001, 4 studies - **Stress:** Hedges' g = −1.876, 95% CI [−3.643, −0.109], p = .037), I^2 = 95.682, p < .001, 4 studies - **HbA1C:** Hedges' g = −1.165, 95% CI [−3.650, 1.320], p = .358), I^2 = 95.511, p < .001, 2 studies - **Mindfulness:** Hedges' g = 2.683, 95% CI [0.149, 5.216], p = .038, I^2 = 96.417, p < .001, 2 studies Review: The results showed that MBSR demonstrated effects at post-intervention and follow-up (in a period between one to 12 months with a mean length of 4.3 months) in reducing anxiety and depressive symptoms, and enhancing mindfulness, with large effect sizes. However, the effect of MBSR on reducing stress was observed at follow-up, but not at post-intervention. Effects of MBSR on HbA1C were not detected at post-intervention and follow-up. The findings suggest that MBSR appears to be an effective treatment for improving mental health conditions and mindfulness in people with diabetes.	geschlossene Studien nicht aufgelistet	Hohe Heterogenität (unterschiedliche Patientengruppen (Diabetestypen), unterschiedliche Erhebungsinstrumente für die Outcomes.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		The first two authors independently rated the included articles as being at low risk --- GRADE-Bewertung (nur eingeschränkt möglich, da Metaanalyse wegen hoher Heterogenität nicht sinnvoll): RoB (für alle Endpunkte): ±0 (nach Angabe der Autor*innen des Reviews low, Bewertung wird aber nicht gezeigt) Anxiety (post-intervention): low to very low Inkonsistenz: -1 bis -2 Indirectness: -1 (Population) Präzision der Effekte: 0 Publication bias: 0 Depression (post-intervention, follow-up): very-low Inkonsistenz: -1 bis -2 Indirectness: -1 (Population) Präzision: -1 Publication bias: 0 Stress (post-intervention, follow-up): very-low Inkonsistenz: -1 bis -2 Indirectness: -1 (Population) Präzision: 0 (post-intervention), -1 (follow-up) Publication bias: 0 Mindfullness (post-intervention, follow-up): very low Inkonsistenz: -1 bis -2 (hohe Heterogenität I^2) Indirectness: -1 (Population) Präzision: -1 Publication bias: 0		

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		HbA1c (post-intervention, follow-up): very low Inkonsistenz: -1 (post intervention) -2 (follow-up) Indirectness: -1 (Population) Präzision: -1 Publication bias: 0		

Kayser et al., 2023 – Mindfulness Interventions in older adults

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Kayser J. A Systematic Review of the Impact of Select Mindfulness Interventions on Psychological Outcomes among Older Adults with Chronic Health Conditions. Clin Gerontol 2023; 46(3):302–14. https://www.ncbi.nlm.nih.gov/pubmed/35585039 .	**Suchzeitraum:** 01/1990 to 09/2021 **Fragestellung:** to examine MI (Mindfulness intervention) studies that focused on older adults (≥60 years old) with chronic health conditions. **Population:** older adults (≥60 years old) with chronic health conditions **Intervention:** acceptance and commitment therapy (ACT), mindfulness-based stress reduction (MBSR), or mindfulness-based cognitive therapy (MBCT); **Comparator:** standard of care, treatment as usual, historical pre/post, or waitlist condition; **Outcome:** anxiety, depression, well-being, quality of life, or other condition-related psychological outcomes (e.g., diabetes-related distress). **Studies:** study design was either RCTI, quasi-experimental, or another form of historic pre-post comparison; a follow-up period beyond study completion was not required.	17 studies, chronic health conditions including chronic pain, stroke, type 2 diabetes, insomnia, cancer, and chronic obstructive pulmonary disease. 1 RCT for Type-2-Diabetes: Maghsoudi, 2019 (Daten aus der Originalpublikation). - N=80, Participants with at least a one-year history of type 2 diabetes without complications (e.g., amputation or diabetic ketoacidosis, exclusion criteria were: having severe mental problem such as major depression disease, receiving any psychological treatment in the past year) were recruited from a specialized care center, average age of study participants: 63,1 years, - Intervention: ACT, n=80, 8 sessions, 90 minute weekly sessions, no detailed setting information provided, Clinical psychologist and nurse led; pre/post, follow-up 2 months, Intervention group had significant lower diabetes related distress in post intervention and 2-month follow-up (mental wellbeing). **Aus der Originalstudie Maghsoudi, et al., 2019 (**https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6802537/**):** Mean And Standard Deviation Of Emotional Distress Score In The Intervention And Control Group In Different Times In The Study Time of measurement / Group / Before (mean ± / Immediately after (mean ± / 2 months after (mean ± / p-value	**Critically low** y-y-n-py-y-y-n-y-y-no-noMa-noMa-y-y-n-y nicht erfüllte kritische Domänen: ausgeschlossene Studien nicht aufgeführt, Publication bias nicht erhoben	Nur eine Studie zu Personen mit Typ-2-Diabetes identifiziert. Betrachtung der Daten. Diese Studie wurde auch in der Metaanalyse von Ngan et al., 2021 [5] eingeschlossen. Der Review wird daher nicht im Hintergrundtext zitiert.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
		<table><tr><td></td><td>SD)</td><td>SD)</td><td>SD)</td><td></td></tr><tr><td>Inter-vention</td><td>52.75±13.63</td><td>47.60±2.61</td><td>49.28±12.60</td><td><0.000 1</td></tr><tr><td>Control</td><td>54.73±12.11</td><td>54.13±12.34</td><td>55.40±12.60</td><td>0.21</td></tr></table> RoB-2-Bewertung der Studie (gemäß SR): random sequence generation: some concerns, Deviation from the intended intervention: low, missing outcome: some concerns, mearsurement of the outcome: low, selection of the reported result: low, overall risk of bias: some concerns		

Jenkinson et al., 2022 – CBT and third wave cognitive behavioural interventions

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Jenkinson E. The effectiveness of cognitive behavioural therapy and third-wave cognitive behavioural interventions on diabetes-related distress: A systematic review and meta-analysis. Diabet Med 2022; 39(11):e14948. https://www.ncbi.nlm.nih.gov/pubmed/36031793.	**Suchzeitraum:** bis April 2021 **Fragestellung/Objectives** (relevant für NVL Fragestellung)**:** **Objective 3:** effectiveness of all third-wave CBT interventions on DRD alone. **Objective 4:** effectiveness of third-wave CBT interventions that target DRD primarily on DRD, depression, anxiety and HbA1c. **Intervention:** CBT interventions that include both cognitive and behavioural techniques, such as cognitive restructuring, problem solving, goal setting, guided discovery, behavioural activation and exposure. Interventions that are described as third-wave CBT interventions, such as Acceptance and Commitment	- 22 RCTs included - 10 trials included participants with T2DM, the remainder included participants with T1DM or participants with both type 1 and 2 diabetes. - Control: bis auf eine Studie (active control: Blood Glucose Awareness Training) entweder Treatment-as-usual, placebo oder wait-list - elevated distress als Einschlusskriterium in 14 Studien. **Objective 3: Meta-analysis of all third-wave CBT on diabetes-related distress diabetes-related distress** SMD: −0.135, p=0.504 (95% CI −0.532; 0.262), I2 =73.1%, p=0.005; 5 studies. Einschätzung Aussagesicherheit der Evidenz (NVL): very low RoB: -1 (high or unclear risk of bias in the studies) Inkonsistenz: -1 (Punktschätzer und KI nur teilweise überlappend, I^2: 73%) Indirectness: ± 0 Imprecision: -1 (KI schneidet den Nullpunkt, sowohl Nutzen als auch Schaden möglich) Publication bias: ± 0 **Objective 4: Meta-analysis of third-wave CBT interventions targeting diabetes-related distress primarily on outcomes**	**Low bis critically low** y-y-n-py-n-y-n-y-y-n-y-n-(y)-y-y-y Kritische nicht erfüllt Domänen: ausgeschlossene Studien nicht aufgelistet. Die RoB-Bewertung wurde zwar beschrieben, aber der Einfluss mögli-	Heterogenitäten innerhalb der Studien (Diabetes-Typ, DRD vorbestehend ja/nein, Art der Therapie: Einzeltherapie oder Gruppe, face-to-face…) Verschiedene Auswertungen vorgenommen, je

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	therapy (ACT) and mindfulness-based therapy. **Population:** Adult participants (18 years and over) with either T1DM or T2DM **Comparator:** Usual care, waitlist control, placebo control, active control **Outcomes:** diabetes-related distress (DRD) (primary or secondary outcome in the study). Primary outcome of this review: DRD (measured by validated scales such as PAID or DDS). Secondary outcomes of this review: i) psychological outcomes; Depression and anxiety measured through validated scales. ii) physical outcomes; Glycaemic control (HbA1c). **Study design:** RCT's or quasi-RCT's; where 'random' is used to describe the method for assigning subjects to groups	**Diabetes-related distress** SMD: −0.122, p = 0.619 (95% CI −0.605; 0.360), I^2 =79.8%, p=0.002; 4 studies. Einschätzung Aussagesicherheit der Evidenz (NVL): very low RoB: -1 (high or unclear risk of bias in the studies) Inkonsistenz: -1 (Punktschätzer und KI nur teilweise überlappend, I^2: 79.8%) Indirectness: ± 0 Imprecision: -1 (KI schneidet den Nullpunkt, sowohl Nutzen als auch Schaden möglich) Publication bias: ± 0 **Depression** SMD: −0.205, p=0.509 (95% CI −0.811; 0.402); I^2=82.7%, p=0.003; 3 studies. Anmerkung ÄZQ: Daten im Text und in Abbildung 7a passen nicht überein. Einschätzung Aussagesicherheit der Evidenz (NVL): very low RoB: -1 (high or unclear risk of bias in the studies) Inkonsistenz: -1 (Punktschätzer und KI nur teilweise überlappend, I2: 82.7%) Indirectness: ± 0 Imprecision: -1 (KI schneidet den Nullpunkt, sowohl Nutzen als auch Schaden möglich) Publicatoin bias: ± 0 **Anxiety** SMD: −0.451, p=0.034 (95% CI −0.867; −0.035); I^2 =52.2%. p=0.148; 2 studies **HbA1c** SMD: 0.016, p=0.910 (95% CI −0.265; 0.297); I^2 =22.6%, p=0.275; 3 RCTs. **RoB analysis Objective 1-4:** Within-study RoB - high prevalence of unclear or high RoB across the included studies. The categories of allocation concealment, blinding of outcome assessment and selective reporting were often not adequately reported. Zusammenfassung aus dem Review: CBT for diabetes-related distress significantly	cher Verzerrungen wurde nicht im Diskussionsteil diskutiert.	nachdem, ob DRD als primary outcome in den Studien betrachtet wurde oder als secondary endpoint. - high prevalence of unclear or high RoB across the included studies

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		reduced distress (SMD = −0.278, p=0.010) and depression (SMD= −0.604, p =0.016). Third-wave CBT for diabetes-related distress significantly reduced anxiety (SMD: −0.451, p=0.034). No significant effect of either intervention on glycated haemoglobin was observed. CBT interventions that included a digital component, were delivered by a psychological practitioner, and included behavioural activation bolstered the effects on diabetes-related distress.		

4.1.1 Zurückgestellt

4.1.1.1 Intervention nicht passend

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Kong L. Effects of traditional Chinese mind-body exercise-Baduanjin for type 2 diabetes on psychological well-being: A systematic review and meta-analysis. Front Public Health 2022; 10:923411. https://www.ncbi.nlm.nih.gov/pubmed/35968439 .	**Zeitpunkt der Suche:** März 2022 **Fragestellung:** to evaluate the effects on psychological well-being of Baduanjin exercises for type 2 diabetes. **Population:** participants diagnosed with type 2 diabetes **Intervention:** Baduanjin exercises as complementary therapy for type 2 diabetes, and all participants received the conventional drugs of type 2 diabetes. **Comparison:** usual care, education, and any complementary and alternative therapies without Baduanjin exercises. **Outcomes:** primary outcomes: - psychological well-being assessed by the Global well-being schedule (GWB) and WHO-5 well-being index (WHO-5); - depression assessed by Hamilton depression scale (HAMD), Montgomery Asberg	27 studies between 2005 and 2019 Most of them exceeded the cutoff score 6 based on the PEDro scale. Baduanjin exercises showed positive effects in: - psychological well-being (SMD, 0.96; 95% CI, 0.57 to 1.36; p < 0.00001), 2 studies, n=122, I^2=10% - depression (SMD, 1.03; 95% CI, 0.08 to 1.97; p = 0.03), 6 studies, n=390, I^2=94% - anxiety (SMD, 0.88; 95% CI, 0.30 to 1.46; p = 0.003), 6 studies, n=397, I^2=85% - mental health (SMD, 0.72; 95% CI, 0.42 to 1.02; p < 0.00001). 10 studies, n=436, I^2=51% **Subgruppenanalyse** Baduanjin vs. Care/education: SMD 0,69 (95% KI 0,33; 1,04), 7 studies, n=360 Subgruppe Baduanjin versus exercise SMD 0,84 (95% KI 0,21; 1,47), 3 studies, n=76, I^2=37% - physical component score: total: SMD 1,03 (95% KI 0,5; 1,56), 10 studies, n=436, I^2= 83% Subgruppenanalyse Baduanjin vs. Care/education: SMD 1,06 (95% KI 0,4; 1,73), 7 studies, n=360 Subgruppe Baduanjin versus exercise SMD 0,94 (95% KI 0,02; 1,87), 3 studies, n=76, I^2=37% Limitations:	Low y-y-n-py-y-y-n-y-py-n-y-n-y-y-y-y nicht-erfüllte kritische Domäne: - ausgeschlossene Studien nicht aufgelistet.	Fragliche Relevanz und Verfügbarkeit in Deutschland. - All studies published in chinese, not popular worldwide - Heterogenität der Studien. Me-

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	depression rating scale (MADRS), and Self-rating depression scale (SDS), - anxiety assessed by Hamilton anxiety scale (HAMA), and Self-rating anxiety scale (SAS). Secondary outcomes: - fasting blood glucose (FBG), - glycosylated hemoglobin (HbA1c), - 2-h postprandial blood glucose (2-hPBG), - quality of life assessed by 36-Item short-form health survey (SF-36), Diabetes specific quality of life (DSQL), and European quality of life 5-dimensions (EQ-5D). Assessement methodological quality based on PEDro scale. Subgroup analysis was conducted based on different control interventions.	- majority of the studies did not use concealed allocation and blinding - high heterogeneity, different frequency, duration, and session of Baduanjin exercises		taanalsen trotz I^2 von 94% gerechnet

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Li Y. The efficacy of cognitive behavioral therapy-based intervention on patients with diabetes: A meta-analysis. Diabetes Res Clin Pract 2022; 189:109965. https://www.ncbi.nlm.nih.gov/pubmed/35718018.	**Suchzeitraum:** from inception to April 2021 **Fragestellung:** to evaluate whether comprehensive CBTbased interventions positively affect physiological and psychological health outcomes, and quality of life in DM patients **Population:** adult patients with T1DM, or T2DM, or gestational diabetes (GDM) **Intervention:** CBT, individual or group-based, and face-to-face or remote **Vergleich:** non-CBT interventions or usual care or waiting list	32 RCTs with 7006 participants included (3603 in the intervention group and 3403 in the control group). - mean age: intervention group (IG) 54.15, control group (CG) 54.55 - mean proportions of females: IG 65.53% and CG 64.10% - All studies included patients with T1DM, T2DM, or GDM, only 1 study involved pregnant women with GDM. **intervention details:** - 20 studies used the single CBT method, 12 studies used CBT combined with either aerobic exercise, motivational enhancement therapy, lifestyle intervention, or treatment as usual therapy. - 26 articles adopted drug therapy, diabetes education or usual inter-	**Low** y-py-n-py-y-n-n-py-py-n-y-y-y-y-y-y nicht-erfüllte kritische Domänen: ausgeschlossene Studien nicht aufgeführt.	Kognitive Verhaltenstherapie ist nicht die in der NVL-Recherche betrachtete Intervention. Verschiedene Diabetestypen kombiniert betrachtet.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
	Endpunkte: primary outcomes: physiological variables, including - HbA1c%, fasting blood glucose (FBS mg/dl), - SBP (mmHg), DBP (mmHg), and - BMI (kg/m2). Secondary outcomes: psychological variables, including - depression, anxiety and distress symptoms, - quality of life, and sleep quality **Studien:** RCTs **Subgroups:** - diabetes type (T1DM; T2DM); - treatment form (individual; group); - treatment course (<12 weeks; ≥12 weeks); - duration of a session (<50 min; ≥50 min); - number of sessions (<10; ≥10); - mode of delivery (face-to-face; remote); - use of a diabetes-specific manual (no; yes); - drop-out rate (<20%; ≥20%); - use of specific techniques of CBT (no; yes;). **Qualitätsbewertung der Studien:** Physiotherapy Evidence Database tool (PEDro)	vention as the control conditions. 6 studies used the waiting list control group. - 8 studies: remote intervention, such as through the internet or telephone, 24 studies: faceto-face intervention - 12 studies adopting an individual CBT intervention, 19 studies conducted the group-based CBT intervention, 1 studie did not report the treatment form. **Effects on psychological factors** **Depression symptoms** - 21 studies (n=3902) - mean pre-treatment scores for depression symptoms: intervention group 17.75; control group 17.13. - average post-treatment scores: intervention group 9.89, control group 14.95. - mean difference -5.67 (95% CI: -9.52 to -1.82, P = 0.004), SMD -0.90 (95% CI: -1.22 to -0.57, P < 0.001), I2 = 100%, P < 0.001) - depression symptoms during the follow-up time with the combined pool mean of -7.99 (95% CI: −15.42 to −0.56, P =0.040) across 10 studies, with large effect size of SMD -1.28 (95% CI: −1.90 to -0.65, P < 0.001), I2 = 100%, P < 0.001) **Anxiety** 8 studies, 2123 participants - mean pre-treatment scores for anxiety symptoms: intervention group 13.21, control group 13.03. - average post-treatment scores: intervention group 9.93; control group 11.57. - Mean difference -1.46 (95% CI: -2.53 to -0.39, P = 0.008), with a small effect size of SMD -0.28 (95% CI: -18 0.50 to -0.07, P = 0.009). I2 = 74%,	Anmerkungen: Prospero-Nummer angegeben, diese ist aber für einen anderen Review, Metaanalysen trotz großer Heterogenitäten gerechnet (I2 teils 100%).	Keine Subgruppenanalysen für die in der NVL priorisierten Endpunkte - Die in der NVL-Recherche betrachteten Endpunkte waren in dem Review sekundäre Endpunkte. Wurden ggf. nur betrachtet, wenn die primäre Endpunkte des Reviews ebenfalls in der jeweiligen Studie berichtet wurden. Hohe Heterogenität zwischen den Studien

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		P < 0.001 **Distress symptoms** - 8 studies, 1426 participants. - mean pre-treatment scores for distress symptoms: intervention group 33.67, control group 32.99. - average post-treatment scores for distress symptoms: intervention group 26.35; control group 28.86. - Mean difference: -1.95 (95% CI: -4.91 to 0.29, P = 0.090), I2 =84%, P < 0.001) Subgruppenanalysen wurden zu den unterschiedlichen Diabetes-Typen für die psychological factors (Endpunkte) nicht durchgeführt. Qualitätsbewertung der Studien: überwiegend moderate bis high (eine mit 4 moderate, ansonsten 5-9 Punkte). Eine Qualitätsbewertung <4 war ein Ausschlussgrund in dem Review. Publication bias: “Egger test (Table 6) results showed that there was a minimal publication bias in SBP (P = 0.598), DBP (P = 0.172), BMI (P = 0.422), depression symptom (P = 0.349), anxiety symptom (P = 0.362), distress symptom (P = 0.169), quality of life (P = 0.732), sleep quality (P = 0.339). However, the publication bias for HbA1c (P = 0.030) and FBS (P =0.012) was significant.”		

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Wicaksana AL. Effect of self-help interventions on psychological, glycemic, and behavioral outcomes in	**Suchzeitraum:** from 1996, 1937, 1947, 1887, and 2000 to 2 June 2023. **Fragestellung:** effects of self-help interventions on psychological, glycemic, and behavioral outcomes in patients with diabetes.	17 eligible studies, 16 provided data for meta-analysis, n=3083 patients with diabetes; women (61.95 %), average age 55.13 years. - Half of the studies (n=10, 58.82%) included patients with diabetes without prior psychological problems, the others included patients with diabetes and comorbid depression - Erhebungsinstrumente: o diabetes distress: Diabetes Distress Scale, Problems Areas	**Low to moderate** y-y-n-py-y-y-n-py-y-n-y-n-y-y-y-y	Self-help als Intervention wird im Artikel nicht als Intervention zur Stressbewältigung

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
patients with diabetes: A meta-analysis of randomized controlled trials. Int J Nurs Stud 2023; 149:104626. https://www.ncbi.nlm.nih.gov/pubmed/37979371 .	**Population:** adults patients with diabetes (T1DM oder T2DM) **Intervention:** self-help intervention (standardized psychological treatments) as the main or an additional intervention. **Comparator:** any kind **Outcomes:** - diabetes distress, - depression, - anxiety, secondary outcomes: - glycemic (HbA1c) and behavioral outcomes (self-management behavior, self-efficacy, and quality of life). **Studies:** RCTs **Qualitätsbewertung der Studien, Aussagesicherheit der Evidenz:** RoB-Tool, GRADE	in Diabetes Scale; ○ Depression: Center for Epidemiologic Studies Depression Scale and Patients Health Questionaire; ○ Anxiety: Generalizied Anxiety Disorder Scale, Hospital Anxiety Depression Scale-anxiety subscale, WHO Composite International Diagnostic Interview; ○ Self-management behaviour: Diabetes Self-management Questionaire, Self management Profile for Type 2 Diabetes; ○ Self efficacy: Generalized Self-efficacy scale, Diabetes management Self-efficacy scale, Stanford Chronic disease Delf-Efficacy Scale; ○ Quality of life: Medical Outcome Study-Short Form, Audit of Diabetes-Dependent Quality of Life Scae, Assessment of Quality of Life, Euro Quality of Life Group 5 domains, WHO Quality of Life BREF Thailand version. **Self-help interventions short-term effects** - **diabetes distress** (*g* = − 0.363; 95 % CI = − 0.554, − 0.173), I2: 71,31%, 7 RCTs, N=783 Intervention/n=806 Control, **GRADE: very low** - **depression** (*g* = − 0.465; 95 % CI = − 0.773, − 0.156), I2: 90,39%, 9 RCTs, Intervention n=878/Control n=902. **GRADE very low** - **anxiety** (*g* = − 0.295; 95 % CI = − 0.523, − 0.068), I2: 64,85%, 5 RCTs, Intervention n=439/Control n=504, **GRADE low** - glycosylated hemoglobin **level** (*g* = − 0.497; 95 % CI = − 0.791, − 0.167), I2: 84,15%, 8 RCTs, Intervention n=680/ Control n=591, **GRADE very low** - **Self-management behaviour**: g= 0,775 (-0,257; 1,807), I2: 98,04%, 5 RCTs, Intervention n=443/Control n=412, **GRADE very low** - **self-efficacy** (*g* = 0.629; 95 % CI = 0.060, 1.197), I2: 93,05%, 4 RCTs, Intervention n=408/Control n=407, **GRADE very low** - quality of life: ○ Overall: (*g* = 0.413; 95 % CI = 0.104, 0.721) I2: 77,42%, 5 RCTs, Intervention n=435/control n=434, **GRADE very low**;	Nicht erfüllt kritische Domänen: ausgeschlossene Studien nicht aufgeführt (hätten aber erfragt werden können).	beschrieben. Typ-2- und Typ-1-Diabetes gemeinsam betrachtet. Keine Subgruppenanalyse. Zur Hälfte jeweils Personen mit vorbestehender Depression Heterogenität der Interventionen, high risk of bias in einigen Studien.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		○ Physical (*g* = 0.182; 95 % CI = 0.031, 0.333), I2: 0%, 5 RCTs, Intervention n=376/Control n=340, **GRADE moderate**; ○ Mental (*g* = 0.469; 95 % CI = 0.156, 0.783), I2: 74,05%, 5 RCTs, Intervention n=576/ control n=340, **GRADE low**. **Self-help interventions mid-term effects:** - **diabetes distress** (*g* = − 0.195; 95 % CI = − 0.374, − 0.016), I2: 51,69%, 4 RCTs, n=467 Intervention /Control n=466, **GRADE low** - **depression** (g= -0,529 (-1,116; 0,069), I2:96,71%, 6 RCTs, Intervention n=668/Control n=710, **GRADE very low** - **Anxiety** (g= -0,223 (-0,548; 0,102), I2:75,64%, 2 RCTs, Intervention n=244/ Control n=296, **GRADE low** - **Glycated hhemoglobin** (g= -0,181 (-0,396; 0,034), I2: 71,11%, 6 RCTs, Intervention n=663/ Control n=608, **GRADE very low** - **self-management behavior** (*g* = 0.305; 95 % CI = 0.155, 0.454), I2: 0%, 2 RCTs, Intervention n=276/ Control n=283, **GRADE high** - **overall** quality of life (*g* = 0.562; 95 % CI = 0.315, 0.810), I2: 0%, 2 RCTs, Intervention n=196/ Control n=142, **GRADE low** - **Physical quality of life** (g= 0,178 (-0,022; 0,378), I2: 0%, 2 RCTs, Intervention n=192/ control n= 184, **GRADE moderate** - **Mental quality of life** (g= 0,417 (-0,122; 0,955), I2: 84,36%, 2 RCTs, Intervention n=192/ Control n=184, **GRADE low** **Self-help interventions long-term effects:** - **Diabetes distress** (g= -0,033 (-0,222; 0,157), I2:0%, 2 RCTs, Intervention n=148/ Control n=213, **GRADE moderate** - **Depression** (g= -0,067 (-0,200; 0,06), I2: 0%, 4 RCTs, Intervention n=413/ Control n=457, **GRADE low** - **Anxiety** (g= -0,107 (-0,277; 0,062), I2: 0%, 2 RCTs, Intervention n=24/ Control n=296, **GRADE high** - **Glycated hemoglobin** (g= -0,276 (-0,586; 0,035), I2: 72,69%, 3 RCTs, Intervention n=317/ Control n=317, **GRADE very low**		

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		Risk of bias Bewertung der Studien 4: high, 4: low, 9: some concerns		

4.1.1.2 Unzureichende Berichtsqualität

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
Ruiz-Ariza B. Effects of Mind-Body Training as a Mental Health Therapy in Adults with Diabetes Mellitus Type II: A Systematic Review. J Clin Med 2023; 12(3). https://www.ncbi.nlm.nih.gov/pubmed/36769502 .	**Zeitpunkt der Suche:** 11-12/2022 **Fragestellung:** effectiveness of mind-body training as a therapy for the mental health management of adult patients with type 2 diabetes mellitus (T2DM) **Population:** adult patients with type 2 diabetes **Intervention:** mindfulness and yoga with variable durations of between 8 weeks and 6 months. (Suchbegriffe für die Intervention: pilates, yoga, Tai Chi, Core-based, Mind-body) **Comparison:** wird nicht klar benannt, wahrscheinlich “any” **Outcomes:** anxiety, depression and/or stress **Studies:** RCTs **Qualitätsbewertung der Studien:** PEDro scale	8 Artikel eingeschlossen, n=835, average age 59,57± 7,66 years Interventions: - 3 studies: mindfullness techniques (8, 9 and 12 weeks, approximate 1,5h, 1 session a week) - 4 studies: yoga (duration between 8 weeks, 3 months and 6 months, sessions of 25-30 min from 1/day, 2/day to 1/week) - 1 study: mindfullness techniques combined with yoga (8 weeks) **Anxiety:** - Measurement instruments: Spielberger’s State-Trait Anxiety Inventory, the DASS-21 and the SCL-90 were used. - Statistically significant changes were observed in all of them (4 studies), irrespective of the intervention used. One study used DASS-21 but did not report values for anxiety. **Depression:** - 6 studies - measurement instruments: PHQ, Depression, Anxiety and Stress Scale-21 (DASS-21), Symptom Checklist 90 (SCL-90) and the Beck Depression Inventory. - Statistically significant differences in favor of the intervention groups when compared with the control groups were found in all of them. **Stress:** - 6 studies - Measurement instruments: PHQ, Perceived Stress Scale, Relocation Stress Scale and DASS-21. - The study by Hartmann et al. was the only one that did not find sta-	**critically low** y-y-y-py-y-n-n-py-py-n-noMA-NoMa-y-y-n-y kritische nicht-erfüllt Kriterien: - Ausgeschlossene Studien nicht aufgeführt - Publication bias nicht erhoben	- Keine Metaanalyse gerechnet (Heterogenität), aber auch für die Einzelstudien keine Effektmaße mit 95% KIs angegeben. - Kleine Studien (zwischen 15 und 115 Personen pro Interventions- bzw. Kontrollgruppe) - Heterogene Interventionen (Dauer, Intensität, Gruppe versus Einzelintervention),

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR 2	Kommentar
		tistically significant changes in stress either at the end of the intervention or after 1 year of follow-up when comparing the intervention group (IG) with the control (CG) (PHQ stress score at 8 weeks, IG: 4.90 ± 0.47 / CG: 5.10 ± 0.58, p = 0.751) (PHQ stress score at 1 year of follow up, IG: 5.00 ± 0.42 / CG: 6.20 ± 0.52, p = 0.071). **Qualitätsbewertung der Studien:** - 3 fair quality, - 5 good quality The main weakness in methodological quality was that none of the studies succeeded in blinding the participants or the therapists. Additionally, the study by Sarika et al. was the only one that did not present a baseline comparison. No intention to treat analysis in most studies. **Limitations:** - High level of heterogeneity (instruments used to measure, interventions, 75% of studies conducted in asia) **GRADE-Bewertung** (Nach Einschätzung NVL): low to **very low** RoB: -1 Inkonsistenz: 0 bis -1 (keine Konfidenzintervalle angegeben, alle Effekte deuten in die gleiche Richtung, in wieweit sie KI überlappen, odere heterogen sind, ist unklar) Indirektheit: -1 (viele asiatische Studien, heterogene Interventionen) Unzureichende Präzision: 0 Publikationsbias: 0		unterschiedliche Instrumente zur Erhebung der Endpunkte

4.1.1.3 Endpunkte nicht passend

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Heo S. Effects of Meditation Intervention on Self-management in Adult Patients	**Zeitpunkt der Suche:** 03/2022 **Fragestellung: to examine the** effects of meditation interventions on self-management	Eight studies (9 articles) included (8: 2-arm, 1: 3-arm RCT), n=698, mean ages of each sample in the 9 studies ranged from 42,1 years to 78,9 years; proportaion of men ranged from 0% to 78,2%. **Interventions:**	**Critically low** y-n-n-py-y-y-n-py-y-n-y-n-	Zurückstellen: intermediäre Endpunkte betrachtet.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
With Type 2 Diabetes: A Systematic Literature Review and Meta-analysis. J Cardiovasc Nurs 2023; 38(6):581–92. https://www.ncbi.nlm.nih.gov/pubmed/37816085 .	(ie, control of glucose, blood pressure, cholesterol, and obesity and self-management) **Population:** adults with type-2-DM **Intervention:** meditation interventions (provision and demonstration of common meditation techniques, including breathing relaxation, maintaining attention, and awareness of the mind and body at the present moment, and the request of practicing those techniques). **Comparison:** usual care group of waiting list **Outcomes:** self-management (ie. controlling obesity, blood pressure, glucose level, cholesterol level) **Studies:** RCTs **Quality assessment:** RoB-Tool	- Mindfullness-based stress reduction programs: 5 studies - Mindfullness meditation programms: 3 studies - Mindfullness-based cognitive therapy: 1 study Interventionist, follow-up, mode of intervention delivery varied between studies **Assessed outcomes:** - HbA1c (8 RCTs), Fasting blood glucose (4 RCTs), Blood pressure (2 RCTs), diabetes self-management (1 study), BMI (1 RCTs), total cholesterol (1 RCT), Low-density lipoprotein cholesterol (1 study), high density lipoprotein cholesterol (1 study),triglycerides (1 RCT), diet (1 RCT), exercise (1 RCT), foot care (1 RCT), monitoring of blood glucose (1 study). **Risk of bias assessment:** 4/9 low RoB, 5 showed some concerns **hemoglobin A 1c** Mean difference from baseline to follow-up: intervention group -0,73±0,63, control group -0,12±0,28. effect size = -0.75; 95% confidence interval, -1.30 to -0.21; P = .007), I2: 93,2% **CONCLUSIONS (Review):** Mindfulness-based meditation reduced hemoglobin A 1c levels in adult patients with type 2 diabetes but did not consistently improve other types of self-management in a few studies examined. This may imply the need for additional intervention components to improve different types of self-management.	y-y-y-y nicht erfüllt kritische Domänen: Protokoll, ausgeschlossene Studien nicht aufgeführt.	Als Endpunkt wird Selfmanagement benannt, aber es geht eher um intermediäre Endpunkte wie Gewicht, HbA1c. - Heterogenität der Studien: Follow-up duration ranged from 5 days to 4 years, sample seize. - Different countries - Metaanalyse zu HbA1c mit hoher Heterogenität.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Luo J. Global comparison of the effect of non-pharmacological interventions on glycemic control in patients with type 2 diabetes: A network meta-analysis from 107 randomized controlled trials. J Diabetes Complications 2023; 37(7):108518. https://www.ncbi.nlm.nih.gov/pubmed/37267719 .	**Suchzeitraum:** inception until January 2023. **Fragestellung:** effectiveness of non-pharmacological interventions (NPIs) on glycemic control in patients with type 2 diabetes (T2D) **Population:** patients with T2D. **Intervention:** non-pharmacological interventions (NPIs) **Control:** usual care, waitlist, or other NPIs **Outcome:** primary outcome was HbA1c, secondary outcomes were self-efficacy, QoL, RoCCs, and DRPs. **Studies:** Randomized controlled trials	total of 107 studies (10,496 participants) included. - median sample size of included studies: 64 (range, 10-563) - median duration: 3 months (range, 1-24). 6 types of non-pharmacological interventions were included in this NMA: - 2 studies on acupuncture, - 34 on exercise, - 35 on nutrition therapy, - 13 on meditation therapy, - 16 on support care, - 7 studies on psychological therapy. Compared to usual care, all NPIs except acupuncture (MD: -0.28; 95 % CI: -1.02, 0.26) and psychological therapy (MD: -0.29; 95 % CI: -0.66, 0.08) showed significantly differences in improving glycemic control in patients with T2D. And according to the results of surface under the cumulative ranking analysis and Cluster ranking, meditation therapy was considered to the best choice when balancing the efficacy of glycemic control with self-efficacy and diabetes related problems, while nutrition therapy was considered to the best choice when balancing quality of life with risk of cardiovascular complications. CONCLUSIONS (Review) These findings validate the efficacy of NPIs for glycemic control in patients with T2D and suggest that healthcare-giver should consider both the efficacy of interventions and the psychosocial needs of patients when developing NPIs programs.	*Kann bei Bedarf bewertet werden.*	Zurückgestellt: primär intermediäre Endpunkte betrachtet; Network meta-analysis (NMA)
Chen S. Effects of Yoga on Blood Glucose and Lipid Profile of Type 2 Diabetes Patients Without Complications: A Systematic Review and Meta-Analysis.	**Fragestellung:** effect of yoga training on diabetes-related indicators compared with usual care. **Interventions:** yoga-based intervention (i.e., randomized controlled trial [RCT]; e.g., yogic postures, movements, breathing, and meditation) **Outcomes:**	296 eligible entries, of which 13 were finalized after screening using predefined inclusion and exclusion criteria. **RESULTS** The standardized mean difference for the effects of yoga was significant on HbA1c (MD = -0.47; 95%CI: -0.77, -0.16; Z = 3.02, p = 0.003), FBG (SMD = -0.92; 95%CI: -1.55, -0.29; Z = 2.87, p = 0.004), PPBG (SMD = -0.53; 95%CI: -0.86, -0.21; Z = 3.20, p = 0.001), and TG (SMD = -0.32; 95%CI: -0.54, -0.10; Z = 2.86, p = 0.004). However, yoga effect was not		Endpunkte (glycaemic control) nicht passend.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Front Sports Act Living 2022; 4:900815. https://www.ncbi.nlm.nih.gov/pubmed/35813055.	- glycosylated hemoglobin (HbA1c), - fasting blood glucose (FBG), - postprandial blood glucose (PPBG), - total cholesterol (TC), - triglycerides (TG), - and body mass index (BMI). **Qualitätsbewertung der Studien:** Cochrane Risk of Bias Tool 2.0.	observed on TC (SMD = -0.84; 95%CI: -1.71, 0.04; Z = 1.87, p = 0.06) and BMI (MD = -0.63; 95%CI: -1.42, 0.16; Z = 1.57, p = 0.12). **CONCLUSION** The findings suggest that yoga can improve the biochemical indices of blood glucose and the lipid profile of patients with T2DM. Therefore, yoga can be prescribed as an effective and active complementary treatment for T2DM. However, this study only tested yoga as a short-term treatment. In the future, rigorous RCTs with a larger sample size may be carried out to examine the long-term effect of yoga on T2DM.		

4.1.1.4 Protokoll

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Ee CC, Armour M, Piya MK, McMorrow R, Al-Kanini I, Sabag A.Mindfulness-based interventions for adults with type 2 diabetes mellitus (Protocol).Cochrane Database of Systematic Reviews 2021, Issue 12. Art. No.: CD014881.DOI: 10.1002/14651858.CD014881.	**Suchzeitraum:** nicht angegeben **Fragestellung:** assess effects of mindfulness-based interventions for adults with type 2 diabetes mellitus (T2D) **Population:** adults (> 18 years) with T2D. **Intervention:** (a) Mindfulness-based interventions (MBIs) (b) MBIs plus any other therapy Intervention that describes **mindfulness meditation** as the main component, utilise formal mindful meditation techniques such as the bodyscan, mindful breathing or mindful movement, and where the primary aim of the intervention is to cultivate mindfulness. Mindfulness must be defined as both present-moment awareness and non-judgement. Interventions that are based on mindfulness meditation techniques as the main component, and which include additional components such as psychotherapy will be included (including MBCT). MBIs can be of any type of delivery or frequency. Exclude: ▪ interventions described as yoga or tai chi, even though mindfulness is recognised as a central feature ofthese practices, unless mindfulness was specified as a main component or focus of the practice (e.g. mindful yoga). ▪ psychotherapy interventions as a main component that incorporate a mindfulness component. These include Acceptanceand Commitment Therapy (ACT), and Dialectical BehaviouralTherapy (DBT). These therapies are more commonly associated with traditional cognitive behavioural therapy, although they drawon ‘mindful’ principles		Nicht durchgeführt (Protokoll)	Protokoll Intervention: Mindfulness meditation as the main component. Anfrage per E-Mail gestellt (05.04.2024), under first revision (Stand 06.03.2024), Publikation wahrscheinlich nicht vor Ende 2024.

Referenz	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
	within a larger suite of techniques butwithout an explicit focus on mindfulness meditation practice (Schuman-Olivier 2020; Shonin 2013; Van Dam 2018). ▪ interventions that do not have a primary aim of cultivating mindfulness, such as Mindful Self Compassion which has the primary aim of cultivating self-compassion (Neff 2013). These interventions are considered to be mindfulness-informed interventions rather than mindfulness based (Schuman-Olivier 2020). **Comparator:** • Minimal intervention e.g. single session at baseline compared to (a) - Usual care - Waitlist control - Active control - Psychosocial interventions • Minimal intervention plus any other therapy compared to (b) - Usual care plus any other therapy - Waitlist control plus any other therapy - Active control plus any other therapy - Psychosocial interventions plus any other therapy **Primary outcomes** - Health-related quality of life - Complications of diabetes - Adverse events **Secondary outcomes** - All-cause mortality - Socioeconomic effects - Cardiovascular risk factors - Glycaemic control **Studies:** RCTs **Bewertung der Studien und Aussagesicherheit der Evidenz:** Cochrane RoB-Assessment-Tool, GRADE		

4.2 Themenübergreifende systematische Recherche (Cochrane, AHRQ, IQWiG, NICE)

Cochrane-Recherche: Von 2014 an (n=391). 1. TiAb-Screening (generell für NVL relevant: n=176); Treffer in der Excel-Tabelle gescreent. Die Ergebnisse der Strukturierten Recherche bei AHRQ, IQWiG und NICE wurden gescreent: keine relevanten Treffer für diese Recherche.

Chew et al., 2017 – Psychological interventions for DRD

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
Chew BH, Vos RC, Metzendorf MI, et al. Psychological interventions for diabetes-related distress in adults with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2017(9):CD011469. DOI: 10.1002/14651858.CD011469.pub2. http://dx.doi.org/10.1002/14651858.CD011469.pub2.	**Zeitpunkt der Suche:** last search 12/2014 for BASE and 09/2016 for all other databases **Fragestellung:** effects of psychological interventions for diabetes-related distress (DRD) in adults with T2DM. Secondary objectives: to separately evaluate effects of emotion-focused and cognition-focused psychological interventions for DRD in adults with T2DM (Chew 2015) **Population:** adults (≥18 years) with T2DM **Intervention:** psychological interventions for DRD* Interventions were classified as emotion-focused (EF), cognition-focused (CF) or a mixture of both components – an emotion-cognition (EC) intervention. **Comparison:** different psychological interventions or usual care. **Primary outcome:** - Diabetes-related distress (DRD), - health-related quality of life (HRQoL) - adverse events. **Secondary outcomes**: - self-efficacy, - HbA1c, - blood pressure, - diabetes-related complications, - all-cause mortality	30 RCTs with 9177 participants, 16 parallel two-arm RCTs, 7 three-arm parallel trials. 7 cluster-randomised trials: 2 had 4 arms, 5 had 2 arms. - 11 trials: cognition-focused (CF) psychological interventions versus usual care. - 9 RCTs: emotion-cognition (EC) versus cognition-focused (CF) interventions, - 9 trials: emotion-cognition (EC) focused interventions versus usual care. - 1 trial: emotion-focused (EF) versus cognition-focused (CF) intervention. - No trials compared an emotion-focused intervention to usual care. - Median duration of the intervention: 6 months (range 1 week to 24 months), median follow-up period: 12 months (range 0 to 12 months). - wide spectrum of interventions and were both individual- and group-based. **Results:** **all psychological interventions combined versus usual care** Primary outcomes - **DRD:** standardised mean difference (SMD) in the intervention groups -0.07 (95% CI -0.16 to 0.03); P = 0.17; n=3315; 12 trials; low-quality evidence, - **HRQoL**: SMD in the intervention groups 0.01 (95% CI -0.09; 0.11); P = 0.87; n=1932; 5 trials; low-quality evidence, - **all-cause mortality:** 11/1000 vs 11/1000; risk ratio (RR) 1.01 (95% CI 0.17; 6.03); P = 0.99; n=1376, 3 trials; low-quality evidence - **adverse events:** 41/1000 (psychological intervention) vs. 17/1000 (usual care); RR 2.40 (95% CI 0.78; 7.39); P = 0.13; n=438; 3 trials; low-quality evidence. Secondary outcomes - **self-efficacy:** SMD 0.15 (95% CI 0.00; 0.30); P = 0.05; n=2675; 6 trials; low-quality evidence in favour of psychological interventions; - **HbA1c:** mean difference (MD) -0.14% (95% CI -0.27 to 0.00); P = 0.05; n=3165; 11 trials; low-quality evidence in favour of psychological interventions. - Included trials did not report **diabetes-related complications or socioeconomic effects**.	**High** y-y-n-y-y-y-y-y-y-y-y-y-y-y-y	- Many trials small and at high risk of bias - Possible publication bias for Outcome HbA1c

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
	- socioeconomic effects **Studies:** RCTs, duration of follow-up after the intervention ≥ 6 months. * trials that measure DRD with either the Problem Areas In Diabetes (PAID) questionnaire or the 17-item Diabetes Distress Scale (DDS)	**Emotion-focused interventions versus usual care (EF vs. usual care)** - No trials **Emotion focused intervention versus cognition focused (EF vs. CF)** - 1 trial reporting on adverse events (of 'worried/stressed about what to write') (RR 2,38 (95% CI 0,1; 55,06, p= 0,50, n=41)) **Cognition-focused intervention versus usual care (CF vs. usual care)** 5 trials. Primary outcomes - **DRD**, Interventions lasted from 3 to 12 months, follow-up periods ranged from 10 to 12 months. SMD −0.09 (95% CI −0.27; 0.08); P = 0.29; n=898; - **Health-related quality of life (HRQoL)**, at 6 to 12 months after the intervention. HRQoL: MD 5 points (95% CI −3; 12); n=119; 1 trial; - **Adverse events**: o 1 trial, events at < 6 months (short-term) post intervention: 1/107 death in intervention group vs. 0/56 deaths in control group (163 participants; 1 trial; very low-quality evidence) (Anmerkung ÄZQ: sind hier wirklich “deaths” oder adverse events gemeint? !The trial collated incidence of hypoglycaemia together with all the other adverse events,including hospitalisations and emergency-room visits.” o With the enhanced usual care comparator, Fisher 2011 reported incidence of hypoglycaemia, based on downloaded meter data, to be 1.9% in the intervention group versus 1.8% in the usual care group. o 1 participant in the second intervention group of symptom-focused diabetes intervention with booster reported feeling depressed (Skelly 2009). **Secondary outcomes** - **Self-efficacy**: 2 trials, at 6 to 12 months (medium-term) postintervention: SMD 0.21 (95%CI 0.04 to 0.38); P = 0.02; n=742. - **HbA1c**: 3 trials, at 6 to 12 months (medium-term) postintervention: MD −0.51% (95% CI −1.39; 0.36); P = 0.25; n=831; - **Diabetes-related complications:** included psychological intervention trials did not investigate diabetes-related complications. - **All-cause mortality**:		

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
		○ Combining all comparators for up to and > 12 months: RR 0.79 (95% CI 0.31 to 2.02); P = 0.62; n=1621; 3 trials; moderate-quality evidence ○ all-cause mortality at all times: 10/721 deaths in the intervention groups versus 3/447deaths in the comparator groups; RR 1.81 (95% CI 0.29 to 11.38); P = 0.17; n=1168; 2 trials; low-quality evidence. **Emotion-cognition focused interventions versus usual care (EC vs. usual care)** Primary outcomes - **DRD:** at 6 to 12 months (medium-term) postintervention: SMD -0.07 (95% CI -0.19; 0.06); p=0.30, n=2366, 8 trials - **HRQoL** at 6 to 12 months (medium-term) postintervention: SMD -0.01 (95% CI -0.11; 0.09), p=0.85, n=1813, 4 trials - **Adverse events**, examined in 3 trials, sufficient data for metaanalysis in 2 trials; RR 2,55 (95% CI 0.77; 8.47); p=0.13; n=275, 2 trials, low quality evidence. Secondary outcomes - **Self efficacy** (medium-term): SMD 0.14; 95% CI−0.08 to 0.35; P = 0.22; n=1933; 4 trial - **HbA1c** (medium-term): MD for HbA1c −0.09% (95% CI −0.19 to 0.0; P = 0.06; n=2334; 8 trials; - **Diabetes-related complications:** included psychological intervention trials did not investigate diabetes-related complications. - **All-cause mortality:** 1 trial reported on all-cause mortality at less than 12 months, 1 death reported at 3 months and 2 deaths at 9 months following usual care (3/103 and 9/103 participants, respectively, versus 0/105 in the intervention group); **Emotion-cognition focused interventions versus cognition-focused interventions (EC vs. CF)** Overall there were no substantial differences between these two types of psychological interventions on the outcomes in this review. (see reiew for further information) **Limitations:** - low number of trials per outcome in specific psychological interventions comparisons, - small sample sizes - wide variation in programmes - particularly in emotion-cognition psychological intervention trials - Many trials small and at high risk of bias for incomplete outcome data as well as		

Zitat	Studiencharakteristika	Ergebnisse	AMSTAR-2	Kommentar
		possible performance and detection biases in the subjective questionnaire-based outcomes assessment, and some appeared to be at risk of selective reporting. - **Publication bias:**Trials on the effect of psychologicalinterventions compared to usual care on DRD probably had no reporting bias or small study bias as shown by the funnel plot. However, trials with HbA1c as an outcome might have reporting bias or small study bias as indicated by an asymmetric funnel plot. For ongoing trials or trials awaiting classification see review **Authors' conclusions:** Low-quality evidence showed that none of the psychological interventions would improve DRD more than usual care. Low-quality evidence is available for improved self-efficacy and HbA1c after psychological interventions. This means that we are uncertain about the effects of psychological interventions on these outcomes. However, psychological interventions probably have no substantial adverse events compared to usual care. More high-quality research with emotion-focused programmes, in non-US and non-European settings and in low and middle-income countries, is needed.		

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