Verantwoording/Totstandkoming

Richtlijn Prikkelbaredarmsyndroom

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Nederlands
Huisartsen
Genootschap

Verantwoording/Totstandkoming Richtlijn Prikkelbaredarmsyndroom

INITIATIEF
Nederlands Huisartsen Genootschap (NHG)
Nederlandse Vereniging van Maag-Darm-Leverartsen (NVMDL)

IN SAMENWERKING MET
Nederlandse Vereniging van Diëtisten (NVD)
Prikkelbare Darm Syndroom Belangenorganisatie (PDSB)

MET ONDERSTEUNING VAN
Kennisinstituut van de Federatie Medisch Specialisten
Nederlands Huisartsen Genootschap

Colofon

CONCEPTRICHTLIJN PRIKKELBAREDARMSYNDROOM

Nederlands Huisartsen Genootschap
Nederlandse Vereniging van Maag-Darm-Leverartsen

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Inhoudsopgave

1. Samenstelling werkgroep

Werkgroep

Prof. dr. A.A.M. (Ad) Masclee, mdl-arts, (voorzitter) NVMDL
J. (Jacintha) Van Balen, huisarts, (voorzitter) NHG
Prof. dr. J. (Jean) Muris, huisarts, (vice-voorzitter) NHG
Dr. C.H.M. (Cees) Clemens, mdl-arts, NVMDL
B.J.T. (Bertram) Haarhuis, mdl-arts, NVMDL
Prof. dr. D. (Daniel) Keszthelyi, mdl-arts, NVMDL
Prof. dr. N. (Niek) de Wit, huisarts, NHG
Dr. A.O. (Otto) Quartero, huisarts, NHG
Dr. C.E. (Carla) Flik, klinisch psycholoog (niet praktiserend), op persoonlijke titel
D.D (Dyana) Loehr, patiëntvertegenwoordiger, PDSB
J.H.M. (Jenny) Brouns, diëtist, NVD
Dr. M. Minnaard, wetenschappelijk medewerker, NHG
Dr. A.E. Schep - Akkerman, epidemioloog, NHG
Dr. ir. N.L. van der Zwaluw, senior adviseur, Kennisinstituut van de Federatie Medisch Specialisten
Dr. E. Belfroid, adviseur, Kennisinstituut van de Federatie Medisch Specialisten

Met ondersteuning van:
C. (Carla) Sloof, medisch informatiespecialist, cluster Richtlijnontwikkeling NHG
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A. (Amanda) van Walraven, apotheker, wetenschappelijk medewerker farmacotherapie, cluster Richtlijnontwikkeling NHG
Dr. L. (Lonneke) van der Mark, huisarts, wetenschappelijk medewerker implementatie, cluster E-learning NHG
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M. (Marianne) Berkelaar, projectsecretaresse, Kennisinstituut van de Federatie Medisch Specialisten

2. Inleiding

2.1 Aanleiding herziening en definitie 'richtlijn'

Op initiatief van het Nederlands Huisartsen Genootschap (NHG) en de Nederlandse Vereniging van Maag-Darm-Leverartsen (NVMDL) is in september 2020 gestart met de herziening van de multidisciplinaire richtlijn en de NHG-Standaard Prikkelbaredarmsyndroom (PDS). Aanleiding voor het gezamenlijk oppakken van de herziening van deze richtlijnen, is de wens tot nadere afstemming van het aanbevolen beleid tussen eerste en tweede lijn. De tweedelijnsrichtlijn bestaat uit een set van modules waarin de aanbevelingen staan met onderbouwing. De NHG-Standaard bestaat uit een volledige tekst met aanbevelingen, waarbij voor de onderbouwing wordt verwezen naar de details. Een deel van deze details komt inhoudelijk overeen met de modules uit de tweedelijnsrichtlijn. Wanneer in deze totstandkoming wordt gesproken over 'de richtlijn' dan worden hiermee de tweedelijnsrichtlijn én de NHG-Standaard bedoeld.

2.2 Doel van de richtlijn

Deze richtlijn geeft adviezen over diagnostiek, behandeling, begeleiding en voorlichting in de eerste en tweede lijn voor patiënten met een prikkelbaredarmsyndroom. De modules zijn onderverdeeld in 3 overkoepelende onderwerpen:

- diagnostiek
- begeleiding en behandeling
- organisatie van zorg

2.3 Afbakening van het onderwerp

Deze richtlijn beschrijft de zorg voor alle patiënten met prikkelbaredarmsyndroom, zowel voor de eerste als voor de tweede lijn.

2.4 Werkwijze

Voor het herzien van de multidisciplinaire richtlijn en de NHG-Standaard is een multidisciplinaire werkgroep en een klankbordgroep ingesteld, bestaande uit vertegenwoordigers van alle relevante specialismen die betrokken zijn bij de zorg voor patiënten met PDS. In de multidisciplinaire werkgroep zijn de modules uitgewerkt die onderdeel zijn van de tweedelijnsrichtlijn én de NHG-Standaard. In een aparte vergadering met de huisartsen en een van de medisch specialisten van de multidisciplinaire werkgroep zijn de 'extra' onderdelen van de NHG-Standaard besproken (volledige tekst, details die niet als module in de multidisciplinaire werkgroep besproken zijn).
Een kerngroep bestaande uit de 2 voorzitters van de multidisciplinaire werkgroep, de wetenschappelijk medewerkers van het NHG en de adviseurs van het Kennisinstituut van de Federatie Medisch Specialisten (Kennisinstituut) was verantwoordelijk voor de afstemming binnen het project.

Het NHG en het Kennisinstituut hebben de richtlijnontwikkeling zowel procesmatig als methodologisch ondersteund.

2.5 Gebruikers van de richtlijn

De richtlijn is bedoeld voor alle zorgverleners die betrokken zijn bij de zorg aan patiënten met prikkelbaredarmsyndroom. De NHG-Standaard is primair bedoeld voor de huisartsen, de tweedelijnsrichtlijn is primair bedoeld voor alle zorgverleners die de medische specialistische zorg verlenen, zoals mdl-artsen, internisten, (klinisch) psychologen en diëtisten. Waar mdl-arts wordt genoemd in deze richtlijn kan ook internist met specialisatie in gastro-enterologie worden gelezen.

2.6 Betrokkenheid beroeps- en patiëntenorganisaties

Voor het ontwikkelen van de richtlijn zijn een multidisciplinaire werkgroep en een klankbordgroep ingesteld, bestaande uit vertegenwoordigers van alle relevante specialismen (zie hiervoor de paragraaf 'Samenstelling van de werkgroep') die betrokken zijn bij de zorg voor patiënten met PDS.

Er werd aandacht besteed aan het patiëntperspectief door zitting van een afgevaardigde van de patiëntenorganisatie (PDSB) in de werkgroep. De Patiëntenfederatie Nederland en PDSB werden uitgenodigd voor de *invitational conference*/knelpunteninventarisatie. De verkregen input is meegenomen bij het opstellen van de uitgangsvragen, de keuze voor de uitkomstmaten en bij het opstellen van de overwegingen. De richtlijn is tevens voor commentaar voorgelegd aan de PDSB en de Patiëntenfederatie.

2.7 Presentatie

De tweedelijnsrichtlijn wordt gepresenteerd in de Richtlijnendatabase van de Federatie Medisch Specialisten en de NHG-Standaard op de NHG-richtlijnenwebsite. Deze databases/sites verschillen qua structuur en opbouw iets van elkaar, en dit maakt dat sommige onderdelen uit de richtlijn specifiek zijn voor of de Richtlijnendatabase, of de NHG-richtlijnenwebsite. Daarnaast is een vertaling van de richtlijn gemaakt naar informatie op Thuisarts.nl, zodat de actuele informatie ook voor patiënten beschikbaar is.

2.8 Implementatie

In de verschillende fasen van de richtlijnontwikkeling heeft de werkgroep rekening gehouden met de implementatie van de richtlijn en de uitvoerbaarheid van de aanbevelingen. Daarbij heeft de werkgroep expliciet gelet op factoren die de invoering van de richtlijn in de praktijk kunnen bevorderen of belemmeren. Bij elke module is een implementatietabel opgesteld. Bij elke aanbeveling is een inventarisatie gedaan van de mogelijke bevorderende en belemmerende factoren voor het naleven van de aanbevelingen. Daarbij heeft de werkgroep een advies uitgebracht over het tijdspad voor implementatie, de daarvoor benodigde randvoorwaarden en de acties die door de verschillende partijen ondernomen dienen te worden.

2.9 Juridische status van richtlijnen

Richtlijnen bevatten geen wettelijke voorschriften, maar aanbevelingen die zo veel mogelijk op bewijs gebaseerd zijn. Zorgverleners kunnen aan de aanbevelingen voldoen in het streven om kwalitatief goede of 'optimale' zorg te verlenen. Aangezien deze aanbevelingen gebaseerd zijn op 'algemeen bewijs voor optimale zorg' en de inzichten van de werkgroep hierover, kunnen zorgverleners op basis van hun professionele autonomie zo nodig in individuele gevallen afwijken van de richtlijn. Afwijken van richtlijnen is, als de situatie van de patiënt dat vereist, zelfs noodzakelijk. Wanneer zorgverleners van deze richtlijn afwijken, wordt het aanbevolen om dit beargumenteerd, gedocumenteerd en waar relevant in overleg met de patiënt te doen. Wij verwijzen voor huisartsen naar de *disclaimer* en voor medisch specialisten naar het rapport *Medisch Specialistische Richtlijnen 2.0.*

2.10 Belangenverstrengeling

De *Code ter voorkoming van oneigenlijke beïnvloeding door belangenverstrengeling* is gevolgd. Alle werkgroepleden hebben een verklaring ingevuld. Een overzicht van de belangen van werkgroepleden en het oordeel over het omgaan met eventuele belangen vindt u in de tabel. De volledige belangenverklaringen zijn op te vragen via het secretariaat van het Kennisinstituut en het NHG.

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen actie
Masclee, Voorzitter richtlijnwerk-groep	Hoofd MDL-ziekten en hoogleraar MDL-ziekten, Maastricht UMC+ (t/m oktober 2021)	- Vicevoorzitter Medisch Ethische Toetsingscommissie (METC), Maastricht UMC+, vergoeding 0.2 fte binnen Maastricht UMC+ verrekend - Voorzitter Commissie Neurogastro-enterologie en Motiliteit, NVMDL, onbetaald	- Eenmalig deelname aan advisory board meeting over IBS, georganiseerd door firma Bayer; 4 mei 2018, München, Duitsland. -ZonMw subsidie Goed Gebruik Geneesmiddelen: Peppermint oil for the treatment of irritable bowel syndrome: optimalisation of anti-nociception through targeted delivery in the large bowel. - Grunenthal GmbH: financiering van investigator initiated onderzoek (2014-2019): Experience Sampling Method voor klachten registratie (app) bij prikkelbare darmsyndroom: internationaal samenwerkingsverband	Geen. (alternerend) voorzitterschap lag bij mede-voorzitter tijdens bespreking pepermuntolie
Van Balen, Voorzitter richtlijnwerk-groep	Senior wetenschappelijk medewerker Nederlands Huisartsen Genootschap (0,7 fte) en huisarts (0,2 fte)	Geen	Geen	Geen acties nodig
Muris	Hoogleraar Huisartsengeneeskunde Universiteit Maastricht, 1,0 fte Vervangende werkzaamheden in huisartsen-praktijk Geulle (1-2 × per maand 1 dag)	- Invaller huisartsenpraktijk (15 dagen per jaar); betaald. - Secretary-general van de European Society for Primary Care Gastroenterology (ESPCG) - Lid Primary Care Committee van de Rome Foundation for Functional Digestive Disorders	Geen	Geen acties nodig
Haarhuis	Mdl-arts Bernhoven te Uden	Geen	Geen	Geen acties nodig
Loehr	Coördinator social media en lid medische commissie bij de Prikkelbare Darm Syndroom Belangenorgani-satie (als vrijwilliger, ± 8 uur per week)	- Betaalde baan: senior communicatieadviseur bij het EnergieCollectief Utrechtse Bedrijven (ECUB) (24 uur per week) - Tweede vrijwilligersfunctie: vrijwilliger bij Klimaatneutraal IJsselstein (1 uur per week)	Geen	Geen acties nodig

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen actie
Clemens	Mdl-arts Alrijne Zorggroep	Geen	Geen	Geen acties nodig
Keszthelyi	Mdl-arts Maastricht UMC+ (1,0 fte)	- Medische Adviesraad Prikkelbare Darmsyndroom Belangenorganisatie (onbetaald). - Raad van Aanbeveling, POS therapeuten (onbetaald). - Voorzitter Sectie Neurogastro-enterologie en Motoriek, Nederlandse Vereniging voor Gastro-enterologie (NVGE, onbetaald). - Lid Editorial board, Neurogastroenterology and Motility (onbetaald). - Klankbord Zinnige Zorg Spijsvertering programma, Zorginstituut Nederland (onbetaald). - Lid richtlijncommissie perioperatieve voeding (vacatiegeld). - Lid richtlijncommissie chronische buikpijn (onbetaald). - Lid richtlijncommissie Europese UEG/ESNM richtlijn functionele dyspepsie en gastroparese (onbetaald).	- ZonMw Goed Gebruik Geneesmiddelen grantnr. 836031017 (pepermuntolie bij prikkelbare darmsyndroom, projectleider). - Will Pharma BV: confinancierder van ZonMw projectnr. 836031017 (projectleider). - ZonMw Goed Gebruik Geneesmiddelen grantnr. 848016005 (nortriptyline bij functionele dyspepsie, projectleider). - ZonMw Doelmatigheidsonderzoek grantnr. 852001924 (online versus. conventionele hypnotherapie bij prikkelbare darmsyndroom, projectleider). - Maag-Lever-Darm Stichting MDL Innovaties grant lmp 17-1: kenniscentra PDS (hoofdaanvrager). - Stichting Sint Annadal: hersenimaging bij viscerale pijn (projectleider). - EU Horizon 2020 onderzoek naar psychopathologie bij PDS (mede-aanvrager). - Grunenthal GmbH: onderzoek van nieuwe meetmethoden van buikpijn (ESM technologie, projectleider). - Allergan Ltd.: onderzoek naar nieuwe meetmethode van klinische respons bij PDS (ESM technologie, projectleider).	Geen trekker bij module over Pepermuntolie. Restricties t.a.v. besluitvorming over pepermuntolie.
De Wit	- Voorzitter divisie Julius Centrum voor Gezondheidswe-tenschappen en Eerstelijns Geneeskunde	Onbezoldigd: - Lid wetenschappelijke commissie KWF - Lid programmacommissie ZON programma Kwaliteit van Zorg - Lid Executive Committee,	- Projectleider van het CEDAR onderzoek; ZonMw project naar kosteneffectiviteit van coloscopie aanvragen door de huisarts bij onderbuikspijnklachten.	Restricties t.a.v. module over hypnotherapie

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen actie
	UMC Utrecht - Hoogleraar Huisartsgenees-kunde UMC Utrecht	European Society for Primary Care Gastroenterology (ESPCG) - Lid Primary Care Committee, Rome Foundation for Functional digestive disorders - Lid NHG-werkgroep Maagklachten - Lid NFU-programmacommissie Doen of Laten - Lid NFU-kwartiermakersoverleg Onderzoek en Innovatie voor de regio - Lid International Advisory Board, Norwegian Primary Care Research Network Praxisnett - International partner CANTEST consortium rondom diagnostisch onderzoek naar kanker in de eerstelijn - Lid wetenschappelijke commissie WONCA 2021, Amsterdam - Lid van international advisory board BMBF program Primary Care research networks, Ministry of Health, Germany - Lid Utrecht Development board - Lid Raad van Toezicht hospice Demeter, de Bilt Bezoldigd - Lid Raad van Commissarissen coöperatie Huisartsen Gelderse Vallei, Ede (tot 1.1.2020) - Lid Raad van Commissarissen huisartsencoöperatie Rho-go, Hilversum	- Projectleider van de IMAGINE studie naar de effectiviteit van hypnotherapie bij PDS - Co-applicant van de vervolgstudie, het SUCCEED onderzoek, naar effectiviteit van implementatie van de CEDAR beslisregel in de praktijk (aanvraag MDLS 2020)	
Quartero	Huisarts, vrijgevestigd	Voorzitter huisartsencoöperatie HCDO; hiervoor ontvang ik per kwartaal vacatiegeld (afhankelijk van gedraaide uren €1300-€1500 per kwartaal)	Geen	Geen acties nodig
Flik	Gepensioneerd klinisch psycholoog (n.p.)	Eigenaar van de digitale verbeteringen Hypnotherapie gemaakt in het kader van mijn onderzoek	Geen	Restricties t.a.v. hypnotherapie (opstellen uitgangsvraag en geen leidende rol in schrijven van de module)
Brouns	Diëtist met specifieke deskundigheid MDL waaronder PDS,	- Lid netwerk diëtisten MDL/NVD (onbetaald) - Lid commissie voeding	Geen	Geen acties nodig

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen actie
	28 uur per week (24 uur patiënt gerelateerde zorg, 4 uur MDL innovatie) UMC+ Maastricht	NVMDL (onbetaald)		

2.10 Financiering

Het Nederlands Huisartsen Genootschap heeft de totstandkoming van de NHG-Standaard gefinancierd, met aanvullende financiering van ZonMw.

Voor de ontwikkeling van de tweedelijnsrichtlijn is financiering verkregen bij de Stichting Kwaliteitsgelden Medisch Specialisten (SKMS).

2.11 Kwalitatieve raming van mogelijk financiële gevolgen in het kader van de Wkkgz

Bij de richtlijn is conform de Wet kwaliteit, klachten en geschillen zorg (Wkkgz) een kwalitatieve raming gedaan of de aanbevelingen mogelijk leiden tot substantiële financiële gevolgen. Bij het uitvoeren van deze beoordeling zijn richtlijnmodules op verschillende domeinen getoetst.

Uit de kwalitatieve raming blijkt dat de aanbeveling(en) breed toepasbaar zijn (> 40.000 patiënten), maar dat er waarschijnlijk geen substantiële financiële gevolgen zijn. Zie **tabel 1** voor een overzicht van uitkomsten van de kwalitatieve raming met bijbehorende toelichting.

Tabel 1 Kwalitatieve raming in het kader van de Wkkgz

Module	Uitkomst raming	Toelichting
Calprotectinetest	Geen financiële gevolgen	Het betreft geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen substantiële financiële gevolgen verwacht.
Fecaal Immunochemische test (FIT)	Geen financiële gevolgen	De aanbeveling heeft een kostenbesparend effect, omdat de diagnostiek minder zal worden ingezet dan in de huidige situatie. Er worden daarom geen substantiële financiële gevolgen verwacht.
Coloscopie	Geen financiële gevolgen	De aanbeveling heeft een kostenbesparend effect, omdat de diagnostiek minder zal worden ingezet dan in de huidige situatie. Er worden daarom geen substantiële financiële gevolgen verwacht.
Voeding	Geen financiële gevolgen	De aanbevelingen betreffen geen toename in het aantal in te zetten voltijdsequivalenten aan zorgverleners en geen wijziging in het opleidingsniveau van zorgpersoneel betreft. Er worden daarom geen financiële gevolgen verwacht.
Probiotica	Geen financiële gevolgen	De aanbeveling is zwak negatief geformuleerd. Er worden daarom geen substantiële financiële gevolgen verwacht. Bovendien betalen patiënten zelf voor het middel.
Pepermuntolie	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling geen toename in het aantal in te zetten voltijdsequivalenten aan zorgverleners betreft en het geen wijziging in het opleidingsniveau van zorgpersoneel betreft.

Module	Uitkomst raming	Toelichting
Linaclotide	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling geen toename in het aantal in te zetten voltijdsequivalenten aan zorgverleners betreft en het geen wijziging in het opleidingsniveau van zorgpersoneel betreft.
Antidepressiva	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling geen toename in het aantal in te zetten voltijdsequivalenten aan zorgverleners betreft en het geen wijziging in het opleidingsniveau van zorgpersoneel betreft.
Psychologische behandelingen	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling geen toename in het aantal in te zetten voltijdsequivalenten aan zorgverleners betreft en het geen wijziging in het opleidingsniveau van zorgpersoneel betreft.
Organisatie van zorg	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbevelingen breed toepasbaar zijn. Echter, uit de toetsing volgt ook dat de aanbevelingen volgens de criteria beschreven in het uitvoeringsbesluit Wkkgz 2.1b en 2.1c ten opzichte van de huidige situatie geen substantiële financiële investering vragen, en geen wijziging in het opleidingsniveau van zorgpersoneel en geen toename (> 5% fte) in het aantal in te zetten voltijdsequivalenten aan zorgverleners betreffen. Er worden daarom geen substantiële financiële gevolgen verwacht.
Patiëntvoorlichting	Geen financiële gevolgen	De aanbevelingen volgend uit deze module zijn voorlichtend van aard en bevorderen hoogstens in enige mate de zelfredzaamheid van de patiënt. Er worden daarom geen substantiële financiële gevolgen verwacht.

3. Methoden

Deze richtlijn is ontwikkeld volgens de *Handleiding Ontwikkelen van NHG-richtlijnen* (verkorte versie *Totstandkoming NHG-Standaarden | NHG-Richtlijnen*) en het rapport *Medisch Specialistische Richtlijnen 2.0.* Op punten waar deze van elkaar verschilden is overeenstemming gezocht tussen NHG en Kennisinstituut.

3.1 Voorbereidingsfase

Knelpuntenanalyse

Tijdens de voorbereidende fase is een *invitational conference* georganiseerd, waarvoor betrokken verenigingen en organisaties zijn uitgenodigd. Voorafgaand aan de invitational conference zijn door het NHG knelpunten in de huisartsenzorg verzameld. Het conceptraamwerk met geïdentificeerde onderwerpen gedeeld met aanwezigen, en aanwezigen hebben kunnen reageren op het raamwerk. Tijdens de invitational conference zijn de onderwerpen besproken en was er gelegenheid te reageren. Een verslag van de invitational conference is opgenomen als bijlage in de richtlijn. Het NHG en het Kennisinstituut hebben samen met de voorzitters vervolgens op basis van de resultaten van de knelpunteninventarisatie de onderwerpen geselecteerd die opgenomen zouden kunnen worden in de richtlijn. Na bespreking in de werkgroep zijn concept-uitgangsvragen opgesteld en definitief vastgesteld.

Opstellen van uitgangsvragen

De werkgroep heeft aan het begin van het traject besloten voor welke uitgangsvragen een literatuursamenvatting met GRADE-beoordeling geschreven kon worden (dit betreft vooral diagnostische of therapeutische vragen), en voor welke uitgangsvragen geen literatuursamenvatting of een literatuursamenvatting zonder GRADE-beoordeling zou worden opgenomen. In het geval van een diagnostische of therapeutische vraag is de uitgangsvraag vertaald naar een PICO of PIRO (*patient, intervention, control/reference test, outcome*). Aan het begin van het traject heeft de werkgroep per uitgangsvraag de patiëntrelevante uitkomstmaten vastgesteld. Deze uitkomstmaten zijn vervolgens geprioriteerd: ze werden gelabeld als cruciaal, belangrijk en niet-belangrijk.

Voor de onderwerpen die niet geselecteerd zijn, is de onderbouwing onveranderd overgenomen uit de vorige versie van de richtlijn/standaard.

3.2 Ontwikkelingsfase – uitgangsvragen met GRADE-beoordeling

Zoekstrategie en selectie van literatuur

Voor elke PICO voerde een medisch informatiespecialist van het NHG of het Kennisinstituut een literatuursearch uit. De gevonden literatuur is gescreend op basis van titel en abstract. De relevante literatuur werd geselecteerd en de volledige tekst van het artikel werd aangevraagd. De resultaten van de literatuurselectie van iedere PICO zijn samengevat in PRISMA-stroomdiagrammen.

In eerste instantie zijn systematische reviews (SR's) en (buitenlandse) richtlijnen van goede kwaliteit gebruikt voor de beantwoording van de uitgangsvragen. De kwaliteit van de SR's of van de samenvattingen van het wetenschappelijk bewijs die deel uitmaakten van een richtlijn werd beoordeeld; alleen SR's die aan enkele minimale eisen voldeden (componenten PICO beschreven; PICO aansluitend bij uitgangsvraag; systematische search uitgevoerd; geïncludeerde artikelen beschreven; recente zoekdatum) werden gebruikt. Indien er voor een uitgangsvraag een geschikte SR werd gevonden, zijn aanvullend individuele onderzoeken van na de sluitingsdatum van de zoekactie van deze SR gescreend.

Indien er geen SR beschikbaar was, werd naar individuele onderzoeken gekeken, waarbij werd gefilterd op methodologie (bijvoorbeeld RCT's bij interventievragen).

Samenvatting van het wetenschappelijke bewijs
Indien er voor een uitgangsvraag een geschikte SR werd gevonden, werd de samenvatting van het wetenschappelijk bewijs uit deze SR gebruikt. Anders werden de resultaten van individuele primaire onderzoeken samengevat. Indien mogelijk werden de resultaten gepoold. Van iedere geïncludeerde studie werd het risico op vertekening beoordeeld.

Beoordeling en gradering van het wetenschappelijke bewijs
Het beoordelen en graderen van het bewijs heeft plaatsgevonden met de GRADE-methode. GRADE beoordeelt de zogenoemde *body of evidence*: de verzameling van alle gevonden onderzoeken per uitkomstmaat. De onderverdeling van de kwaliteit van het wetenschappelijk bewijs kent 4 niveaus: hoog, redelijk, laag of zeer laag. Een hoge kwaliteit wil zeggen dat het geschatte en het werkelijke effect dicht bij elkaar liggen. Naarmate de kwaliteit van bewijs lager is, neemt de onzekerheid daarover toe (zie **tabel 2**).

Tabel 2 Definitie kwaliteit van bewijs

Kwaliteit	Interpretatie
Hoog	Het werkelijke effect ligt dicht in de buurt van de schatting van het effect.
Redelijk	Het werkelijke effect ligt waarschijnlijk dicht bij de schatting van het effect, maar er is een mogelijkheid dat het hier substantieel van afwijkt.
Laag	Het werkelijke effect kan substantieel verschillend zijn van de schatting van het effect.
Zeer laag	We zijn onzeker over het werkelijke effect.

Bij het beoordelen van het verschil in effecten tussen interventies is gelet op het bestaan van klinisch relevante verschillen tussen interventies. Daarvoor wordt bij voorkeur gelet op absolute verschillen (indien deze gegevens beschikbaar zijn). De werkgroep heeft per uitkomstmaat bepaald wat de grens voor een klinisch relevant verschil (voor- of nadeel) is.

Van bewijs naar aanbeveling (overwegingen)
Na de samenvatting en beoordeling van het wetenschappelijk bewijs volgt de vertaling van de resultaten naar aanbevelingen voor de praktijk, oftewel de zogenoemde vertaalslag 'Van bewijs naar aanbeveling'. Ook praktische en contextuele factoren spelen een rol om tot goed toepasbare aanbevelingen te komen. De volgende zes factoren komen hierbij aan de orde:

- Voor- en nadelen
- Kwaliteit van bewijs
- Waarden en voorkeuren van patiënten
- Kosten (NB De werkgroep heeft geen formele kosteneffectiviteits- of budgetimpactanalyses gedaan)
- Aanvaardbaarheid
- Haalbaarheid en implementatie

In de GRADE-methodiek wordt onderscheid gemaakt tussen sterke en zwakke (of conditionele) aanbevelingen. De sterkte van een aanbeveling verwijst naar de mate van zekerheid dat de voordelen van de interventie opwegen tegen de nadelen (of vice versa), gezien over het hele spectrum van patiënten waarvoor de aanbeveling is bedoeld. De sterkte van een aanbeveling heeft duidelijke implicaties voor patiënten, behandelaars en beleidsmakers (zie **tabel 3**). Een aanbeveling is geen dictaat, zelfs een sterke aanbeveling

gebaseerd op bewijs van hoge kwaliteit (GRADE-gradering HOOG) zal niet altijd van toepassing zijn, onder alle mogelijke omstandigheden en voor elke individuele patiënt.

Tabel 3 Implicaties van sterke en zwakke aanbevelingen voor verschillende richtlijngebruikers

	Sterke aanbeveling	Zwakke (conditionele) aanbeveling
Voor patiënten	De meeste patiënten zouden de aanbevolen interventie of aanpak kiezen en slechts een klein aantal niet.	Een aanzienlijk deel van de patiënten zouden de aanbevolen interventie of aanpak kiezen, maar veel patiënten ook niet.
Voor behandelaars	De meeste patiënten zouden de aanbevolen interventie of aanpak moeten ontvangen.	Er zijn meerdere geschikte interventies of aanpakken. De patiënt moet worden ondersteund bij de keuze voor de interventie of aanpak die het beste aansluit bij zijn of haar waarden en voorkeuren.
Voor beleidsmakers	De aanbevolen interventie of aanpak kan worden gezien als standaardbeleid.	Beleidsbepaling vereist uitvoerige discussie met betrokkenheid van veel stakeholders. Er is een grotere kans op lokale beleidsverschillen.

Synthese van bewijs en opstellen van aanbevelingen
De aanbevelingen geven antwoord op de uitgangsvraag en zijn gebaseerd op het beschikbare wetenschappelijke bewijs en de belangrijkste overwegingen, en een weging van de gunstige en ongunstige effecten van de relevante interventies. De kracht van het wetenschappelijk bewijs en het gewicht dat door de werkgroep wordt toegekend aan de overwegingen, bepalen samen de sterkte van de aanbeveling. Conform de GRADE-methodiek sluit een lage bewijskracht van conclusies in de systematische literatuuranalyse een sterke aanbeveling niet a priori uit, en zijn bij een hoge bewijskracht ook zwakke aanbevelingen mogelijk. De sterkte van de aanbeveling wordt altijd bepaald door weging van alle relevante argumenten tezamen. De werkgroep heeft bij elke aanbeveling opgenomen hoe zij tot de richting en sterkte van de aanbeveling zijn gekomen.

Randvoorwaarden (organisatie van zorg)
In de knelpuntenanalyse en bij de ontwikkeling van de richtlijnmodule is expliciet aandacht geweest voor de aspecten die randvoorwaardelijk zijn voor het verlenen van zorg (zoals coördinatie, communicatie, (financiële) middelen, mankracht en infrastructuur). Randvoorwaarden die relevant zijn voor het beantwoorden van deze specifieke uitgangsvraag zijn genoemd bij de overwegingen.

3.3 Ontwikkelingsfase – overig
Voor een aantal modules/details is geen literatuursamenvatting of een literatuursamenvatting zonder GRADE-beoordeling opgenomen. Dit is het geval bij modules/details die meer achtergrondinformatie geven (epidemiologie, etiologie en pathofysiologie) of gericht zijn op de organisatie van zorg. Indien er wel een systematische zoekactie is uitgevoerd, dan vond er geen systematische selectie, beoordeling en gradering van de evidence plaats, maar is de literatuur narratief beschreven. Daarnaast worden er in de volledige tekst (NHG-Standaard) naast de aanbevelingen ook praktische adviezen gegeven die niet worden onderbouwd (in een detail), zoals de onderdelen anamnese, lichamelijk onderzoek, evaluatie, controles en verwijzingen. Deze teksten zijn – na discussie door de werkgroep – op basis van consensus tot stand gekomen.

Kennislacunes
Tijdens de ontwikkeling van deze richtlijn is systematisch gezocht naar onderzoeksbevindingen die nuttig konden zijn voor het beantwoorden van de uitgangsvragen. Een deel (of een onderdeel) van de hiervoor opgestelde PICO's is met het resultaat van deze zoekacties te beantwoorden, een groot deel echter niet. Door gebruik te maken van de evidence-based methodiek (EBRO) is duidelijk geworden dat er nog

kennislacunes bestaan. De werkgroep is van mening dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk. Om deze reden heeft de werkgroep per module aangegeven op welke vlakken nader onderzoek gewenst is. Hierbij heeft er een prioritering plaatsgevonden waarbij is uitgegaan van maximum van 5 lacunes. Deze kennislacunes zijn gepubliceerd op *Lacunes & onderzoeken | NHG-Richtlijnen* en als bijlage van de richtlijnmodules op de *Richtlijnendatabase*.

3.4 Commentaar- en autorisatiefase

De conceptrichtlijnmodule werd in het voorjaar van 2022 aan de NHG-Autorisatiecommissie (NHG AC), de betrokken (wetenschappelijke) verenigingen en (patiënt)organisaties voorgelegd ter commentaar.
Twee leden van de NHG-Adviesraad Standaarden (NAS) hebben tijdens de commentaarronde de standaard beoordeeld. Tien huisartsen gaven via het HAweb-ledenforum commentaar op de NHG-Standaard.

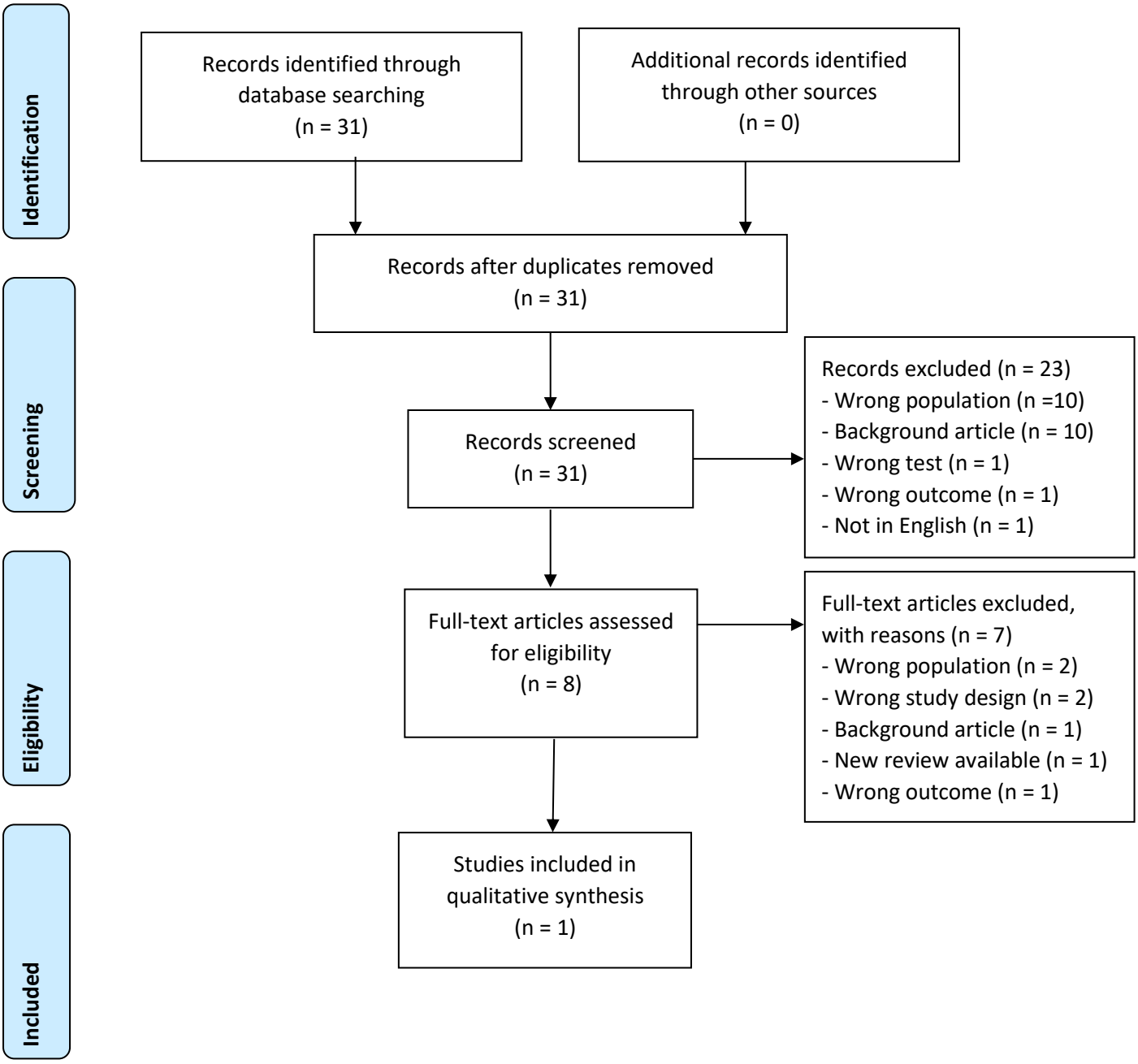
De commentaren werden verzameld en besproken met de werkgroep. Naar aanleiding van de commentaren werd de conceptrichtlijn aangepast en definitief vastgesteld door de werkgroep. De definitieve richtlijn werd na bespreking voorgelegd aan de NHG AC, de deelnemende (wetenschappelijke) verenigingen en (patiënt)organisaties voor (bestuurlijke) goedkeuring en werd door hen geautoriseerd dan wel geaccordeerd.

3.5 Procedure voor herziening

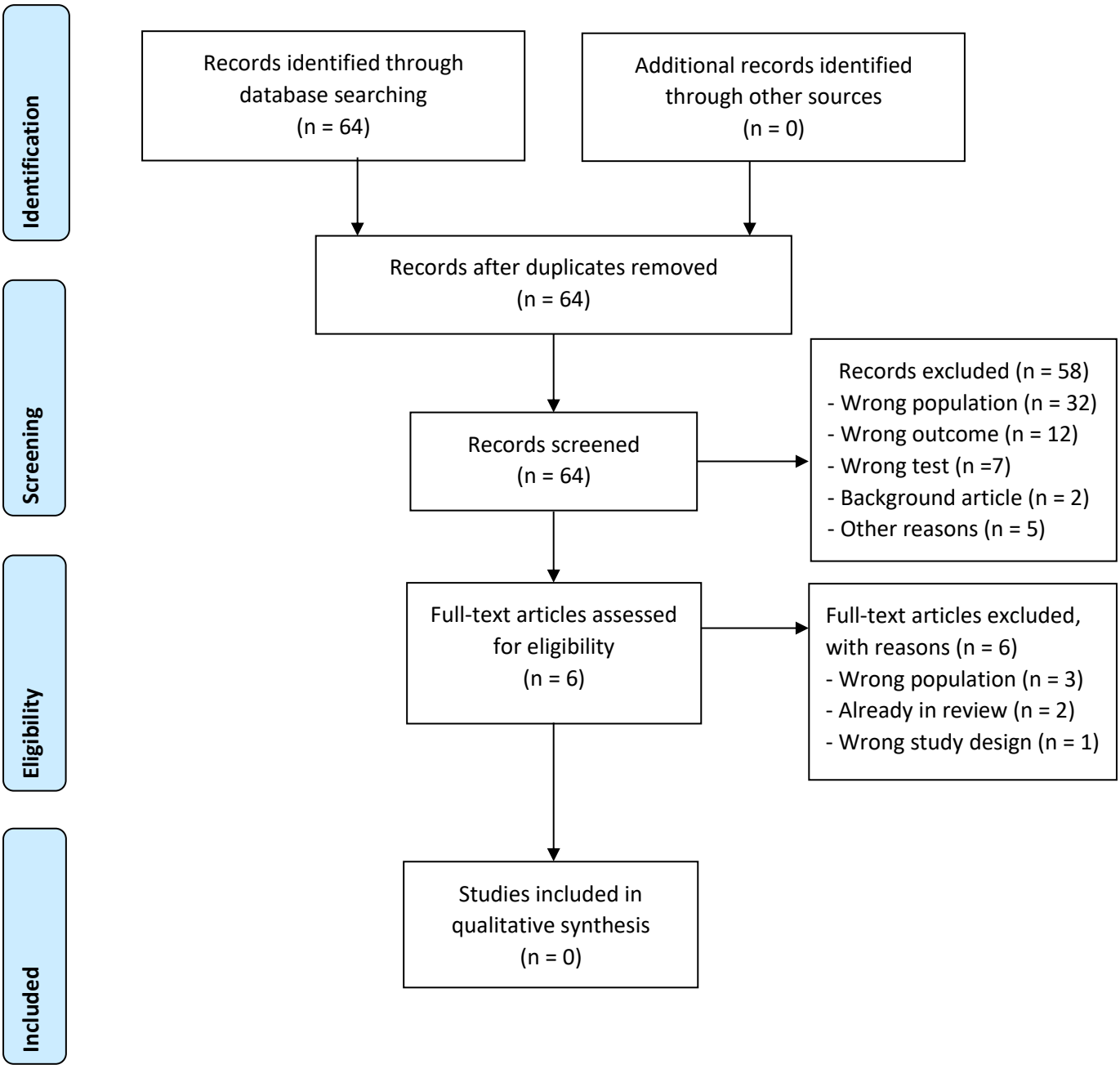
Deze richtlijn wordt periodiek herzien. Uiterlijk in 2026 bepalen het NHG en de NVMDL of deze richtlijn nog actueel is. Zo nodig wordt een nieuwe werkgroep geïnstalleerd om de richtlijn te herzien. De geldigheid van deze richtlijn komt eerder te vervallen indien nieuwe ontwikkelingen aanpassing aan de aanbevelingen nodig maken, en daarmee aanleiding zijn om een herzieningstraject te starten.

Bijlage 1: Prisma flowcharts en exclusietabellen full-textartikelen

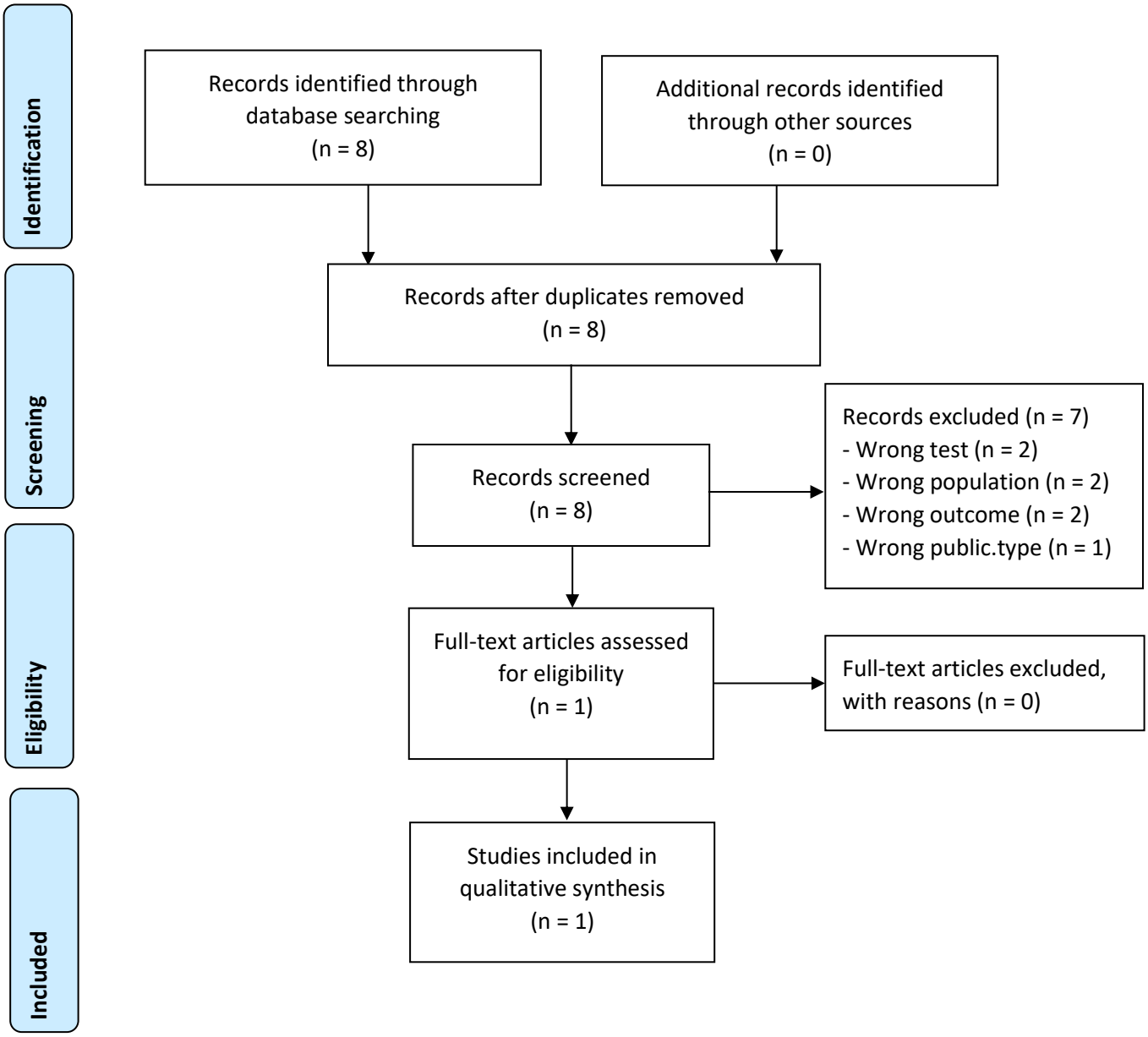
PRISMA flowchart– Calprotectin test (systematic reviews)



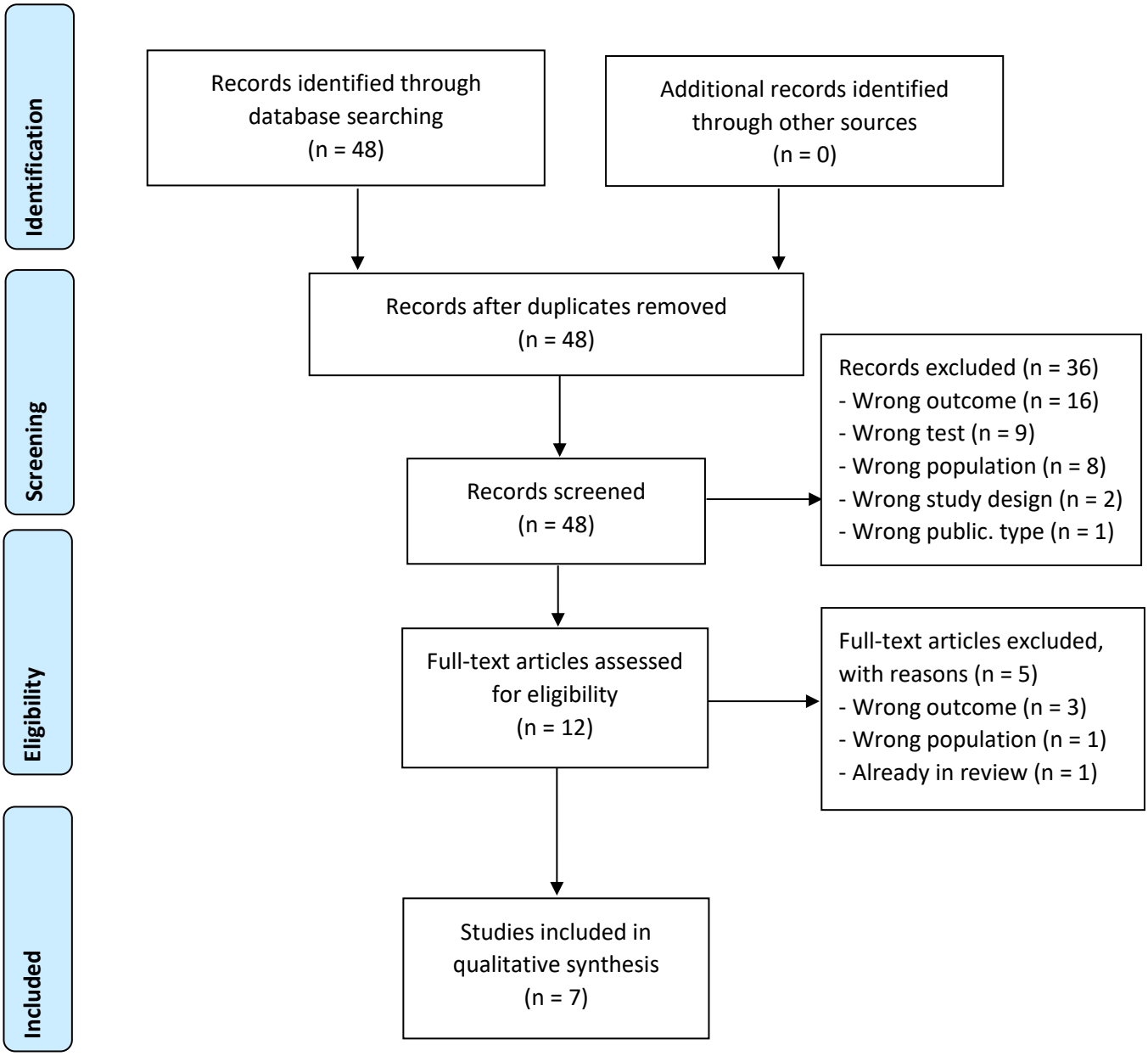
PRISMA flowchart Calprotectin test (other studies, published after January 2018)



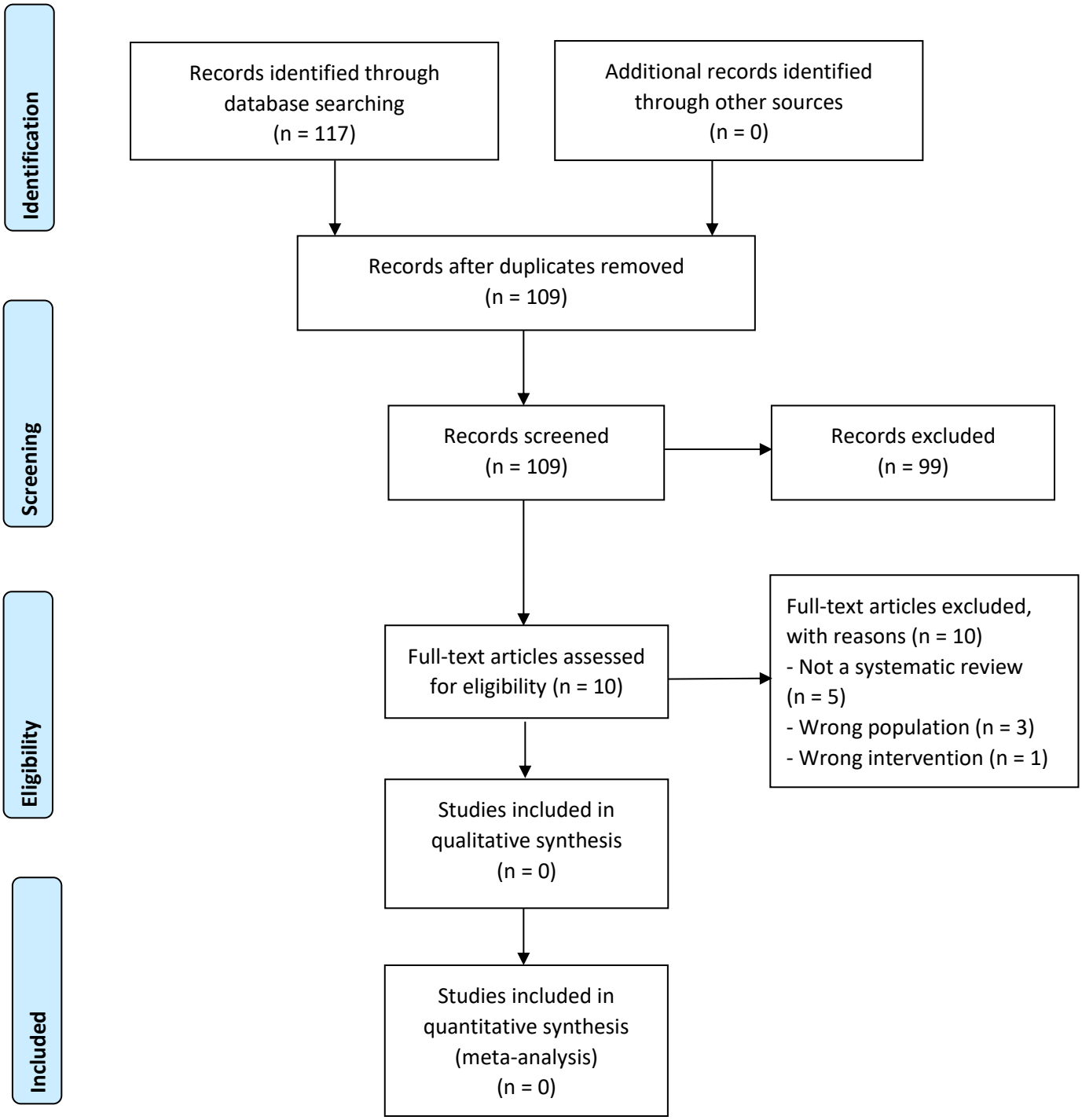
PRISMA flowchart – Fecal Immunochemical Test (FIT)-test (Systematic reviews)



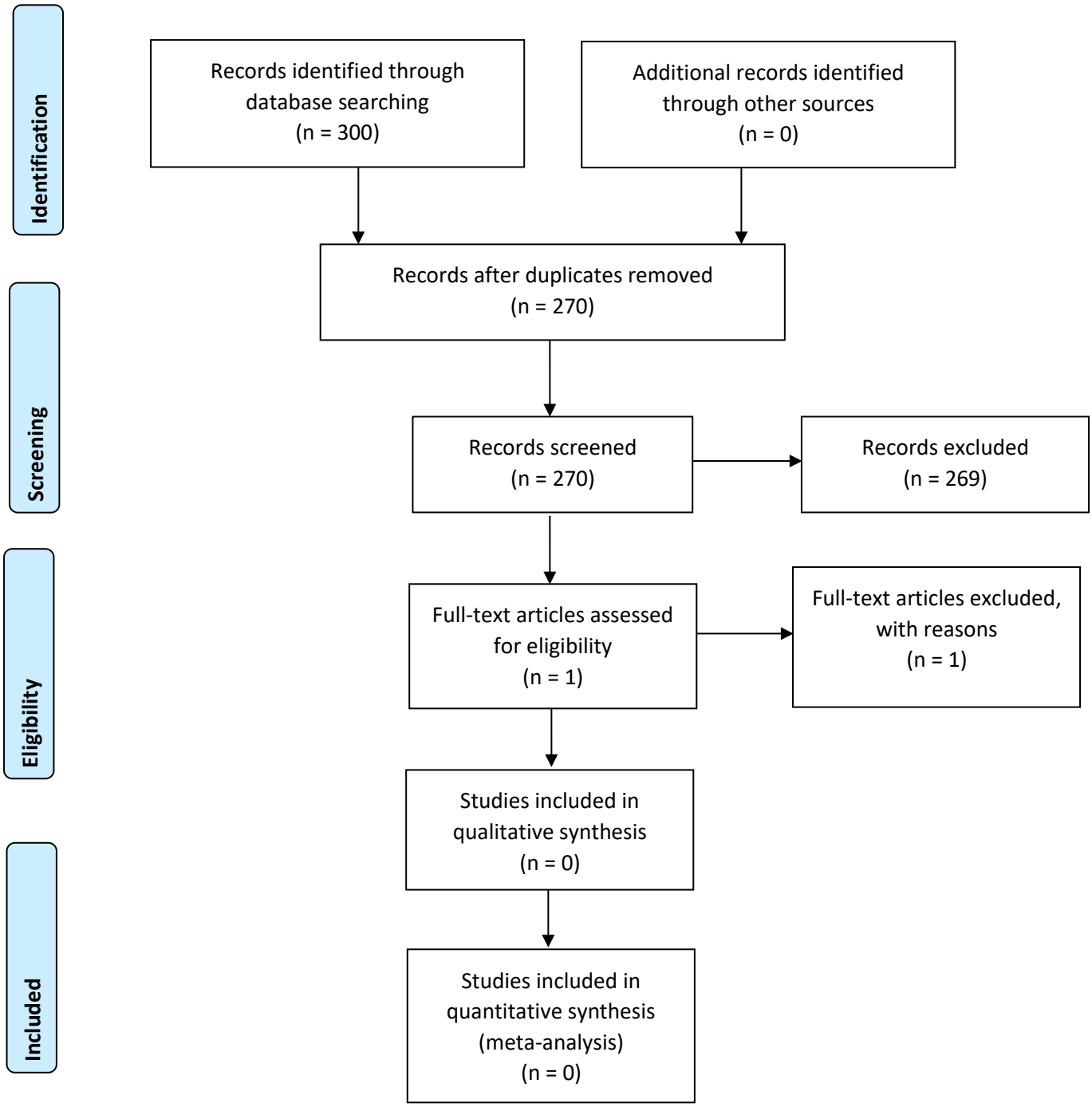
PRISMA flowchart – Fecal Immunochemical Test (FIT)-test (other studies, published after January 2016)



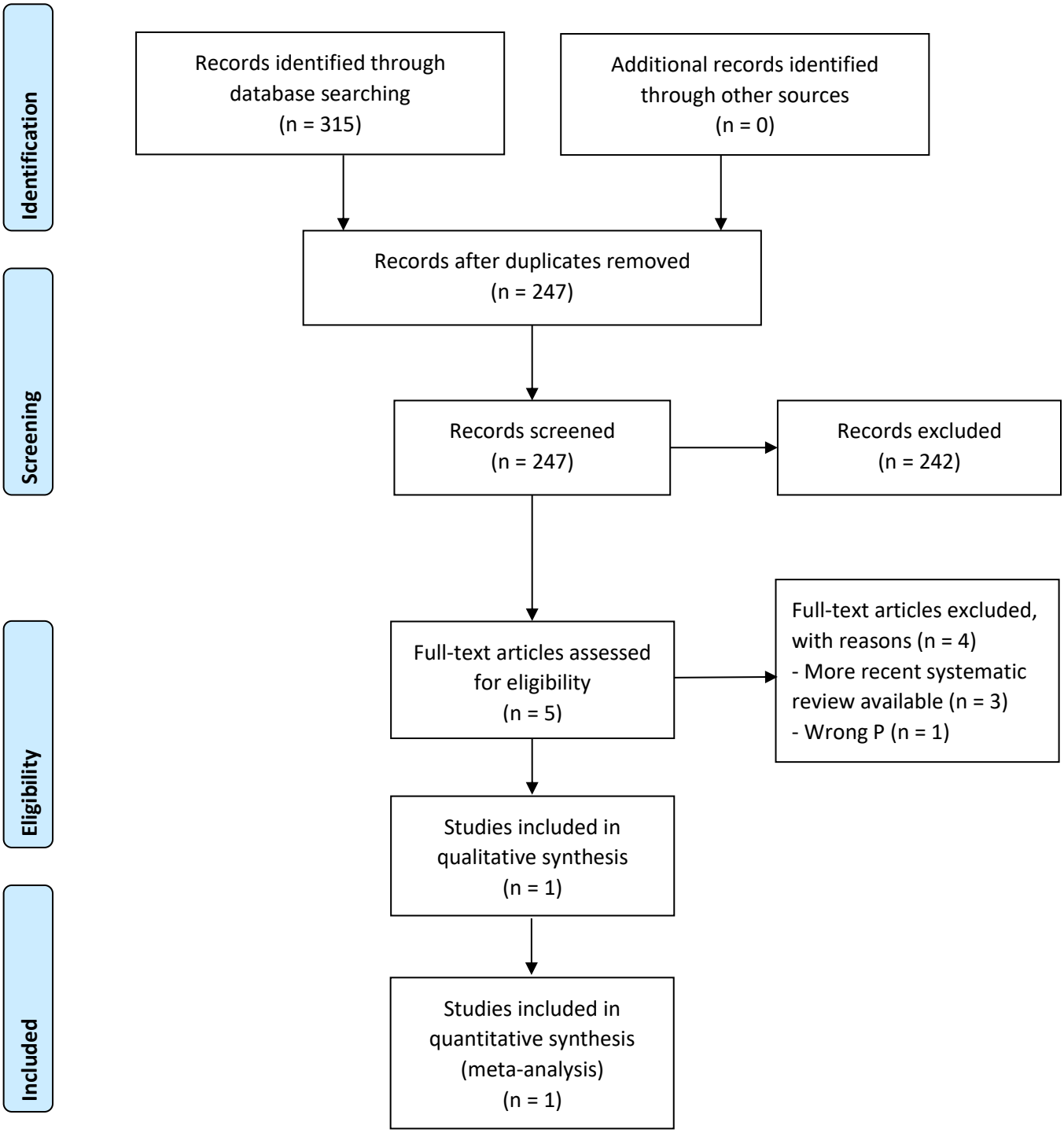
PRISMA flowchart – Coloscopy (systematic reviews)



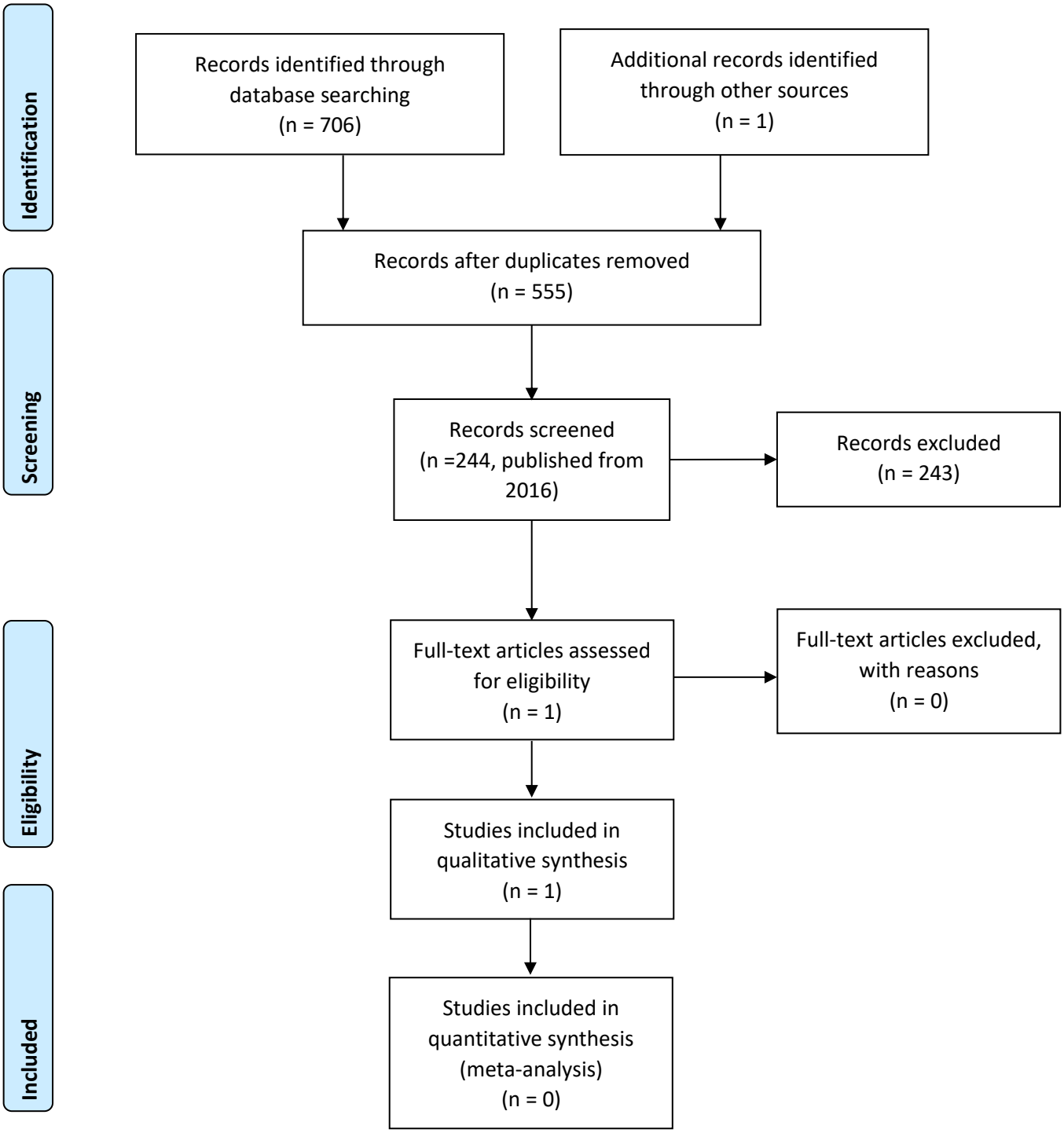
PRISMA flowchart – Coloscopy (RCT's, published from 2000)



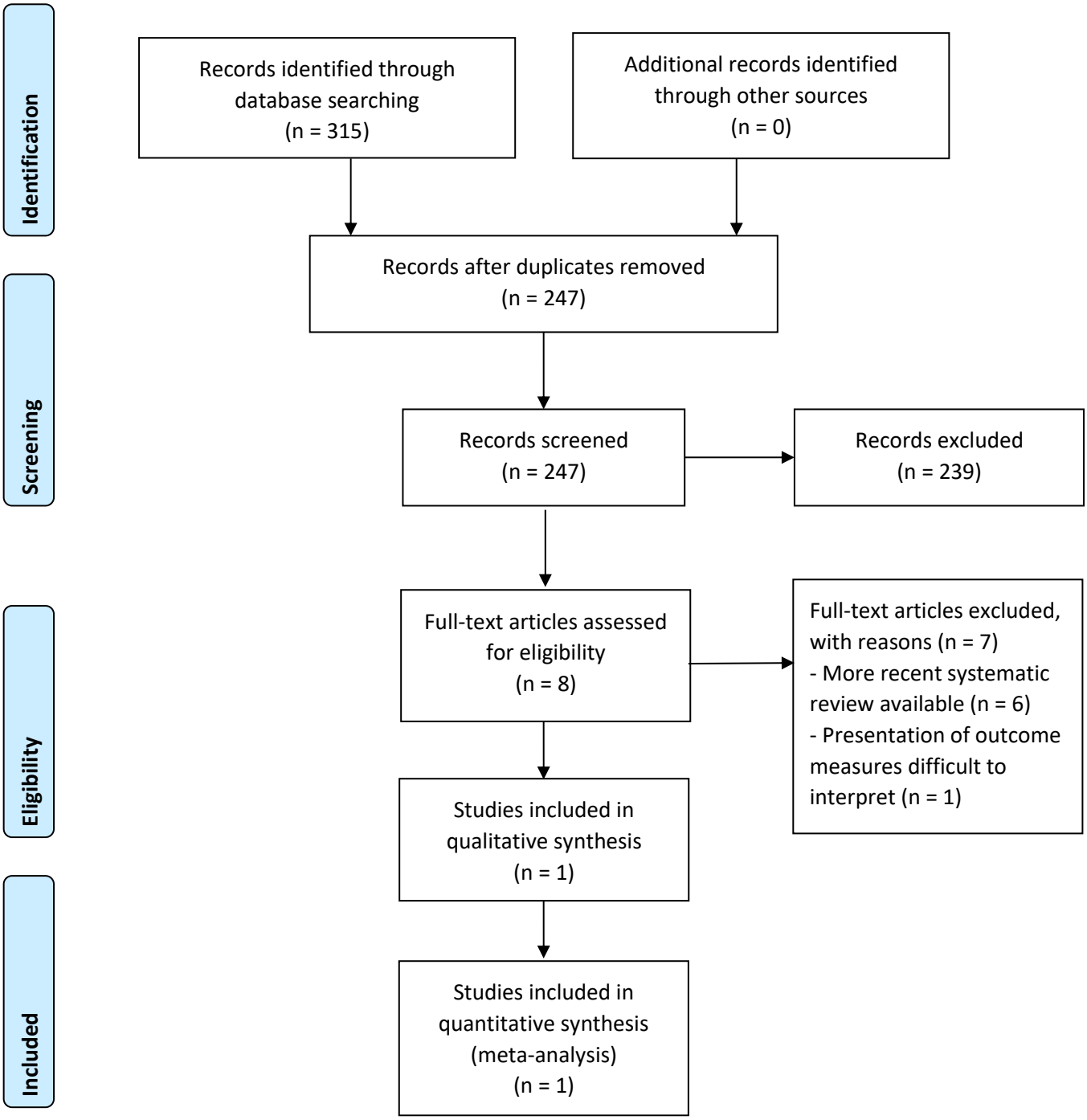
PRISMA flowchart – Diet – Gluten free (systematic reviews)



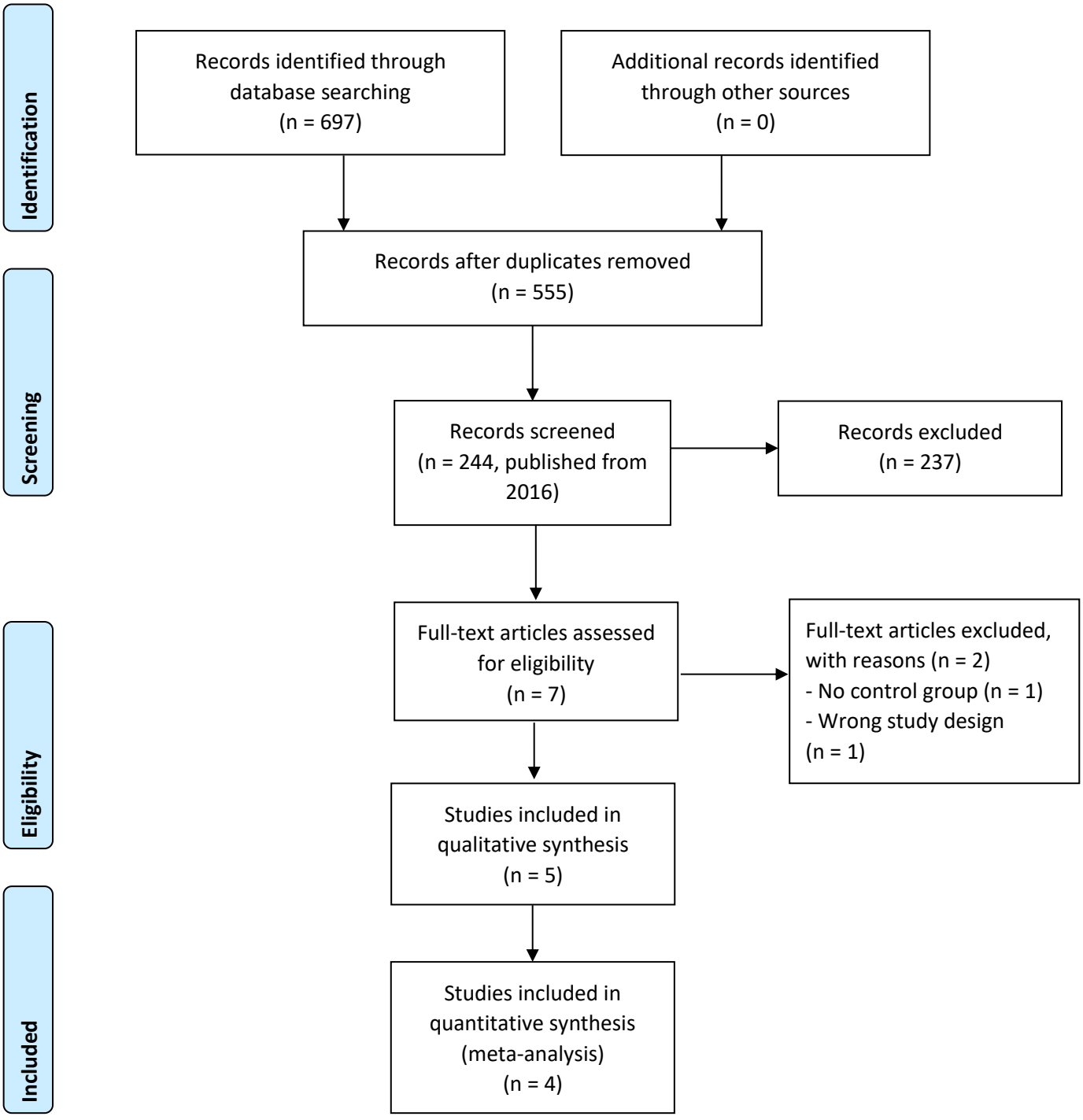
PRISMA flowchart – Diet – Gluten free (RCT's)



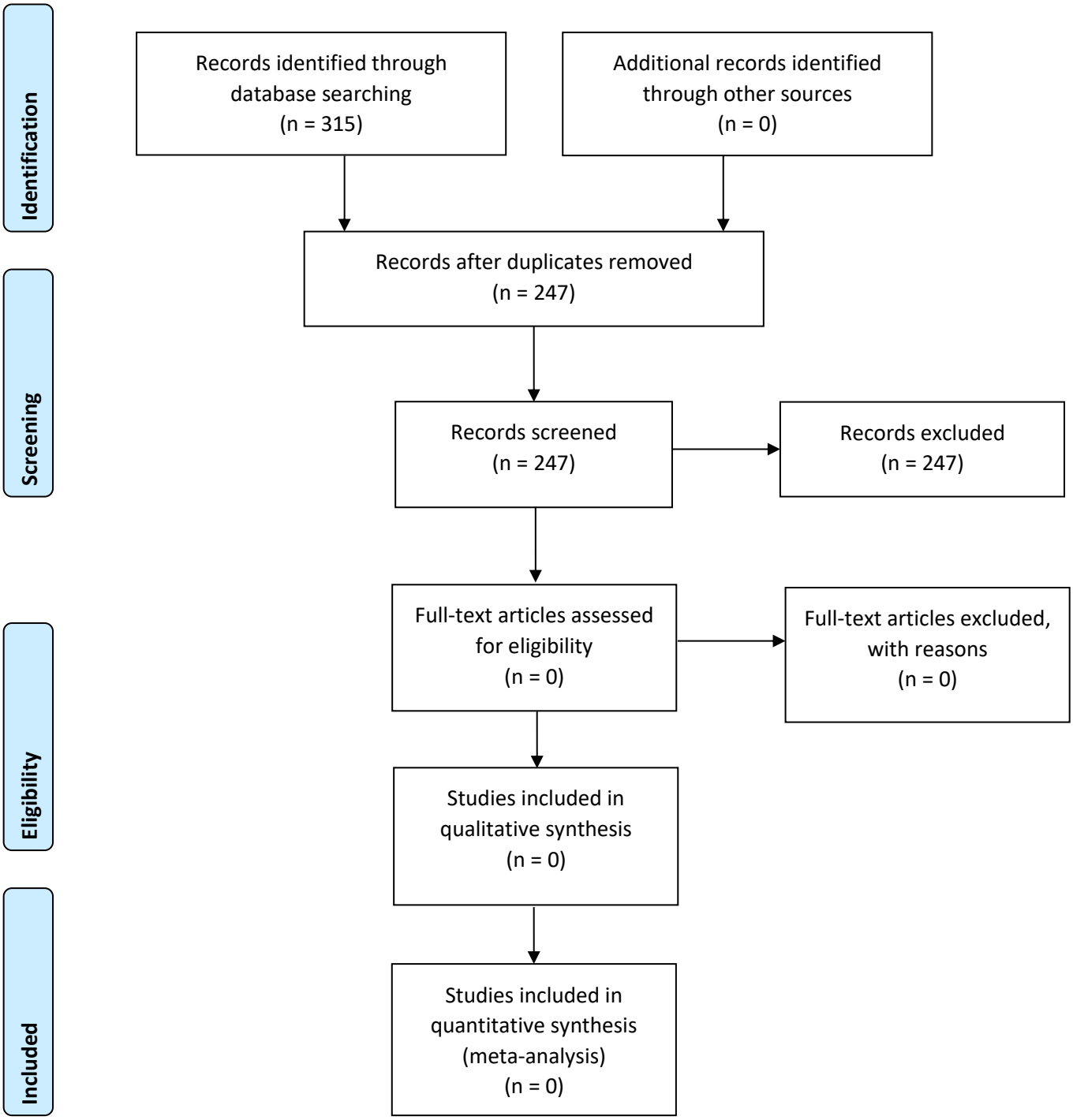
PRISMA flowchart – Diet – Low FODMAP (systematic reviews)



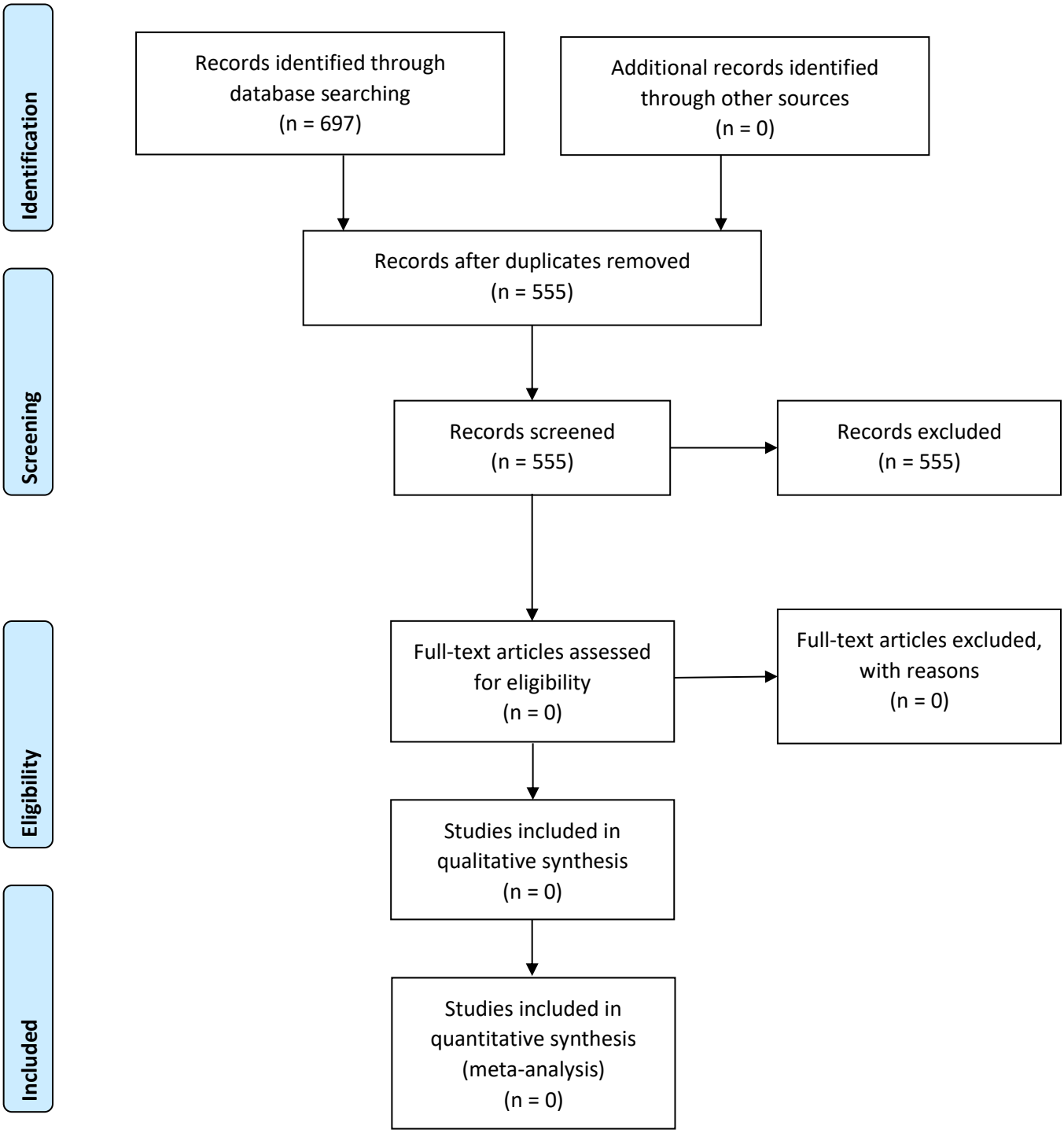
PRISMA flowchart – Diet – Low FODMAP (RCT's)



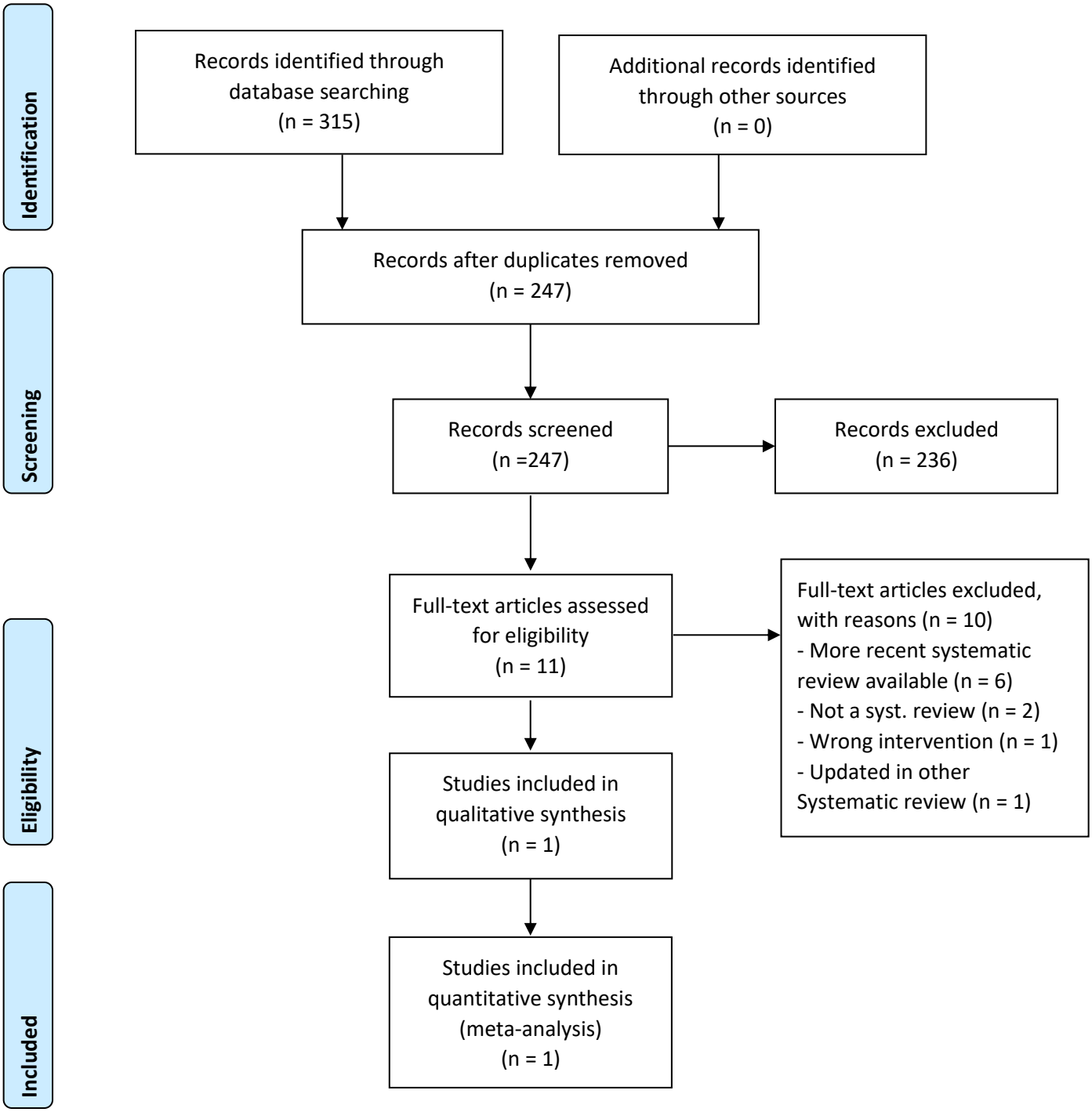
PRISMA flowchart – Diet – NICE diet (systematic reviews)



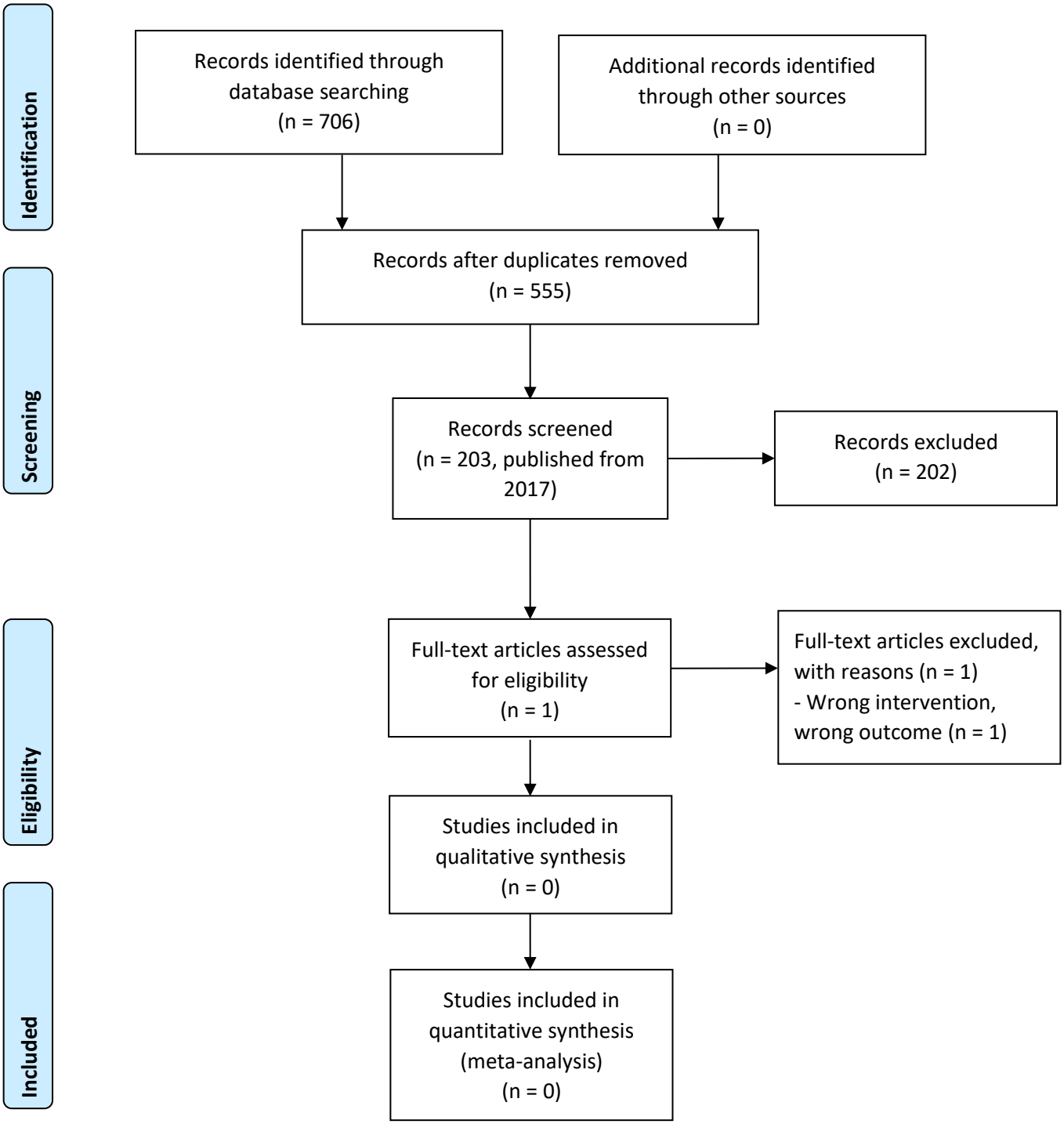
PRISMA flowchart – Diet – NICE diet (RCT's)



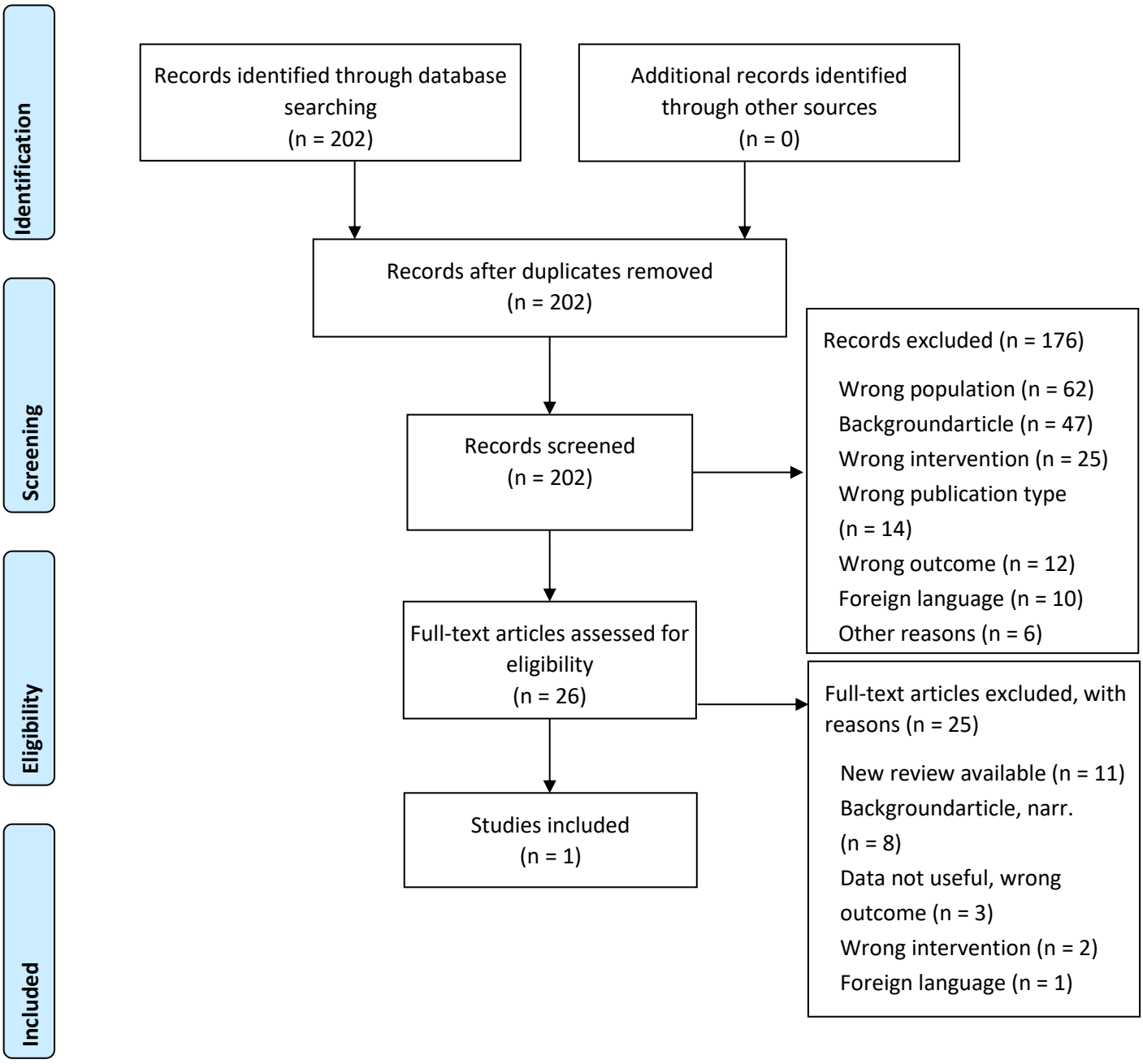
PRISMA flowchart – Diet – Psyllium fibre (systematic reviews)



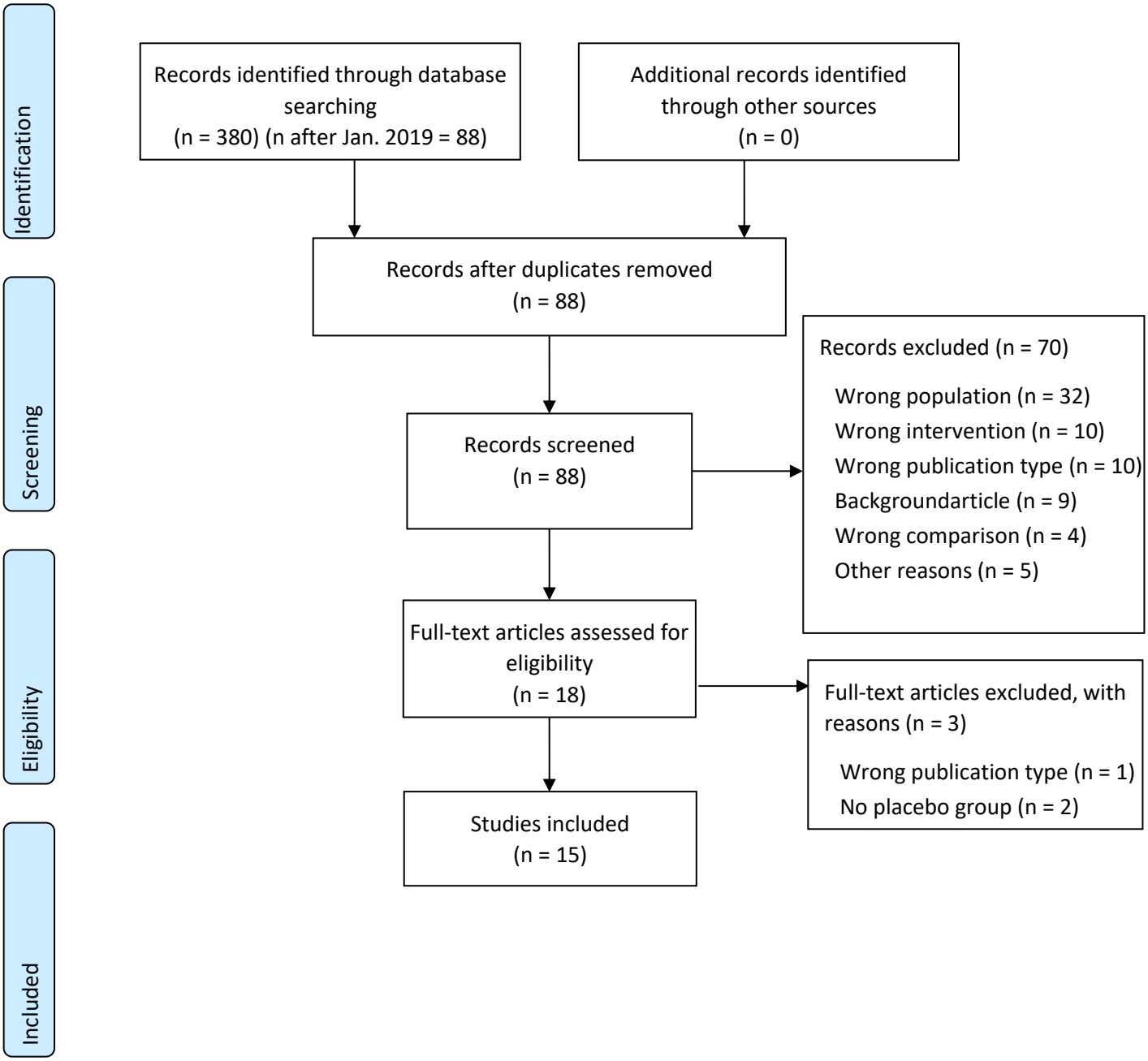
PRISMA flowchart – Diet – Psyllium fibre (RCT's)



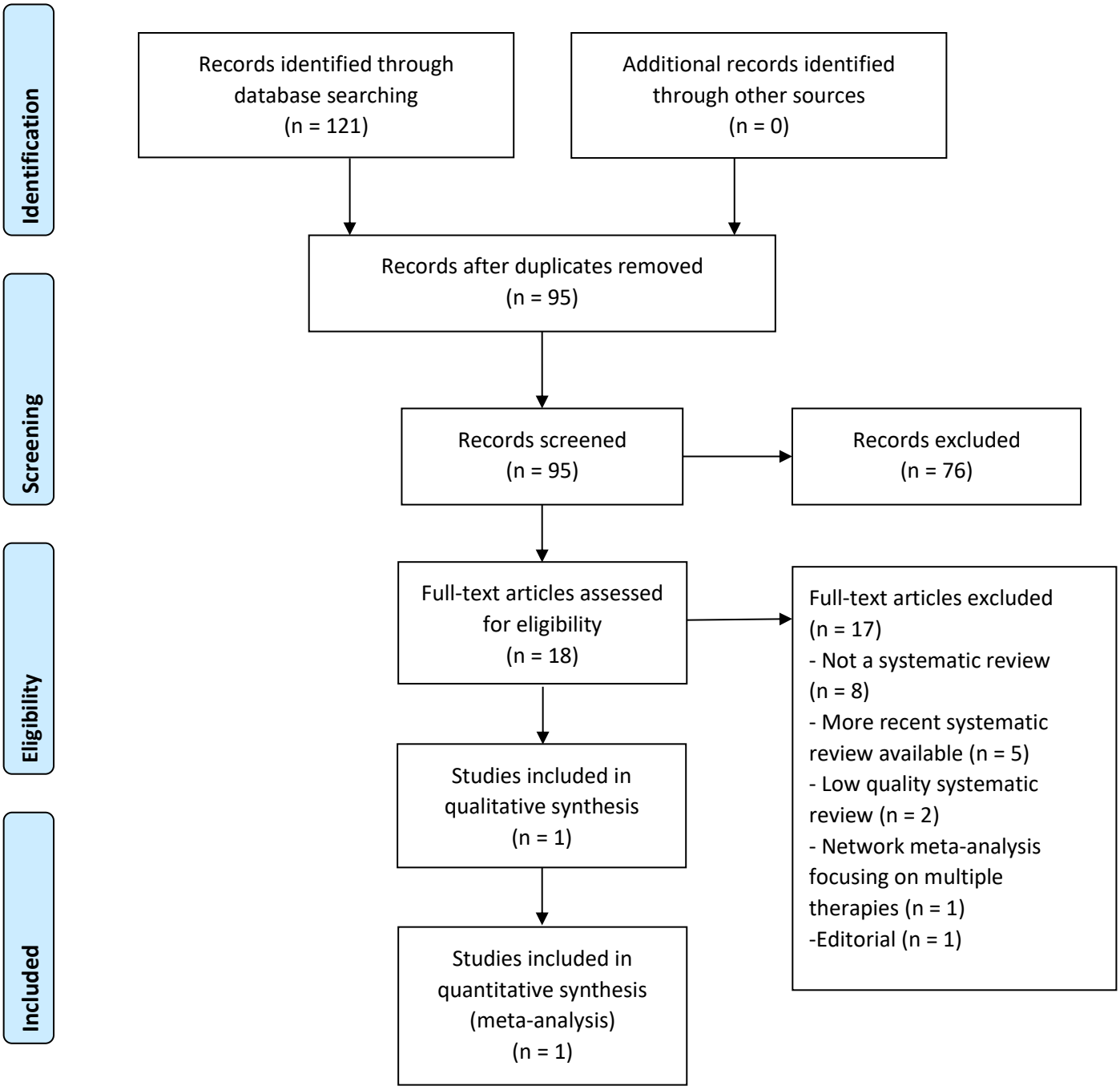
PRISMA Flowchart – Probiotics (systematic reviews)



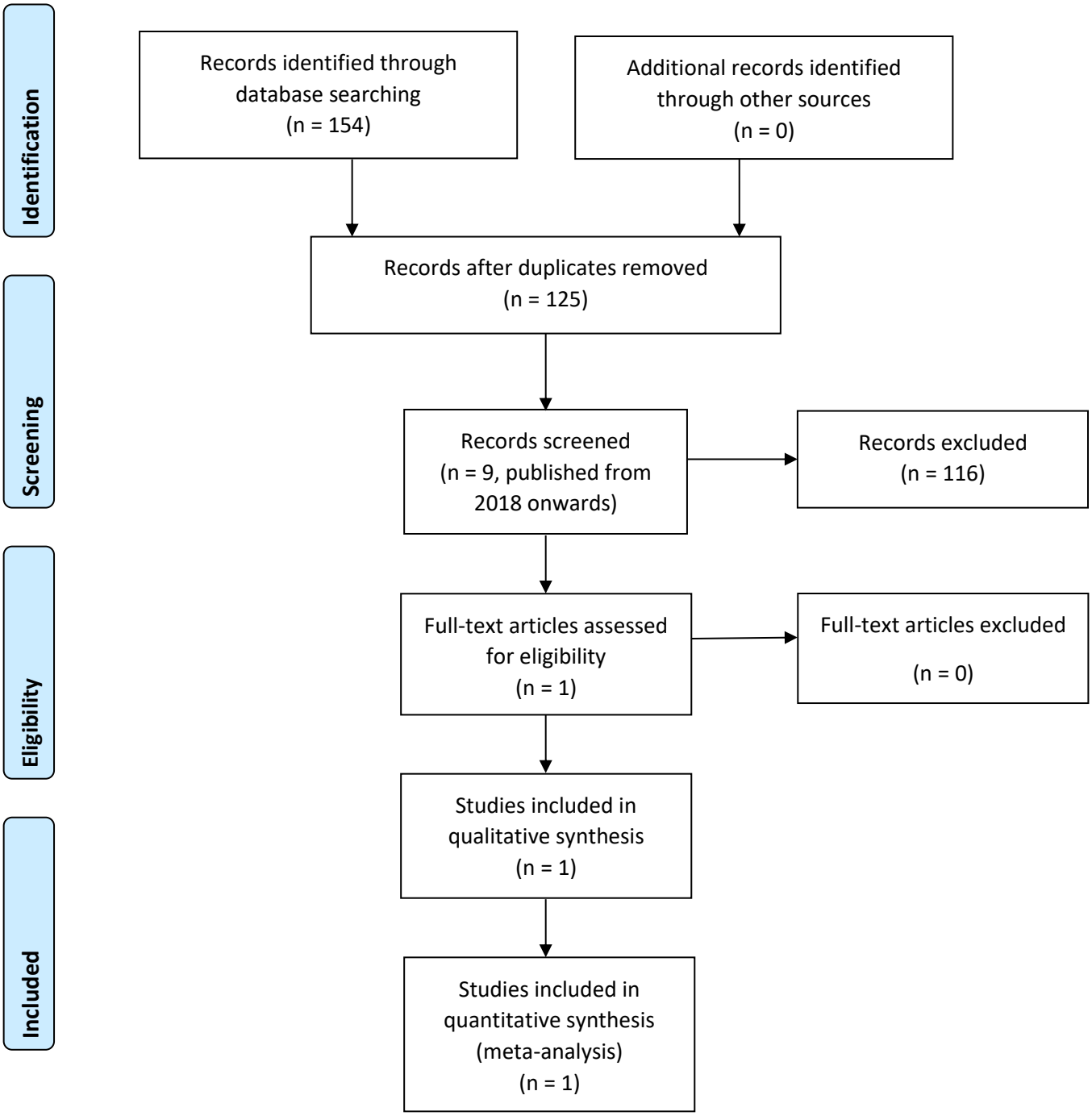
PRISMA Flowchart – Probiotics (RCT's, published after January 2019)



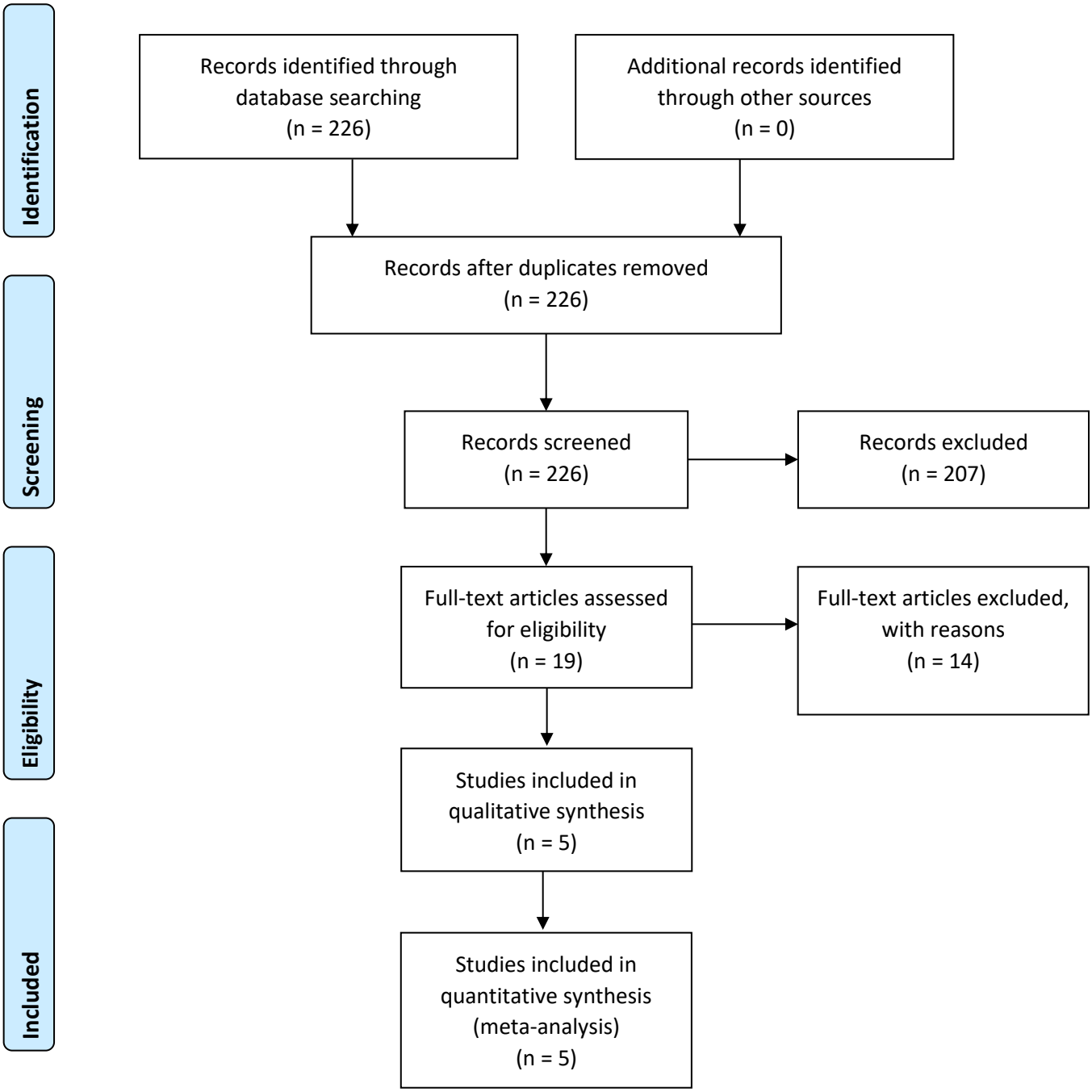
PRISMA flowchart– Peppermint oil – Systematic reviews



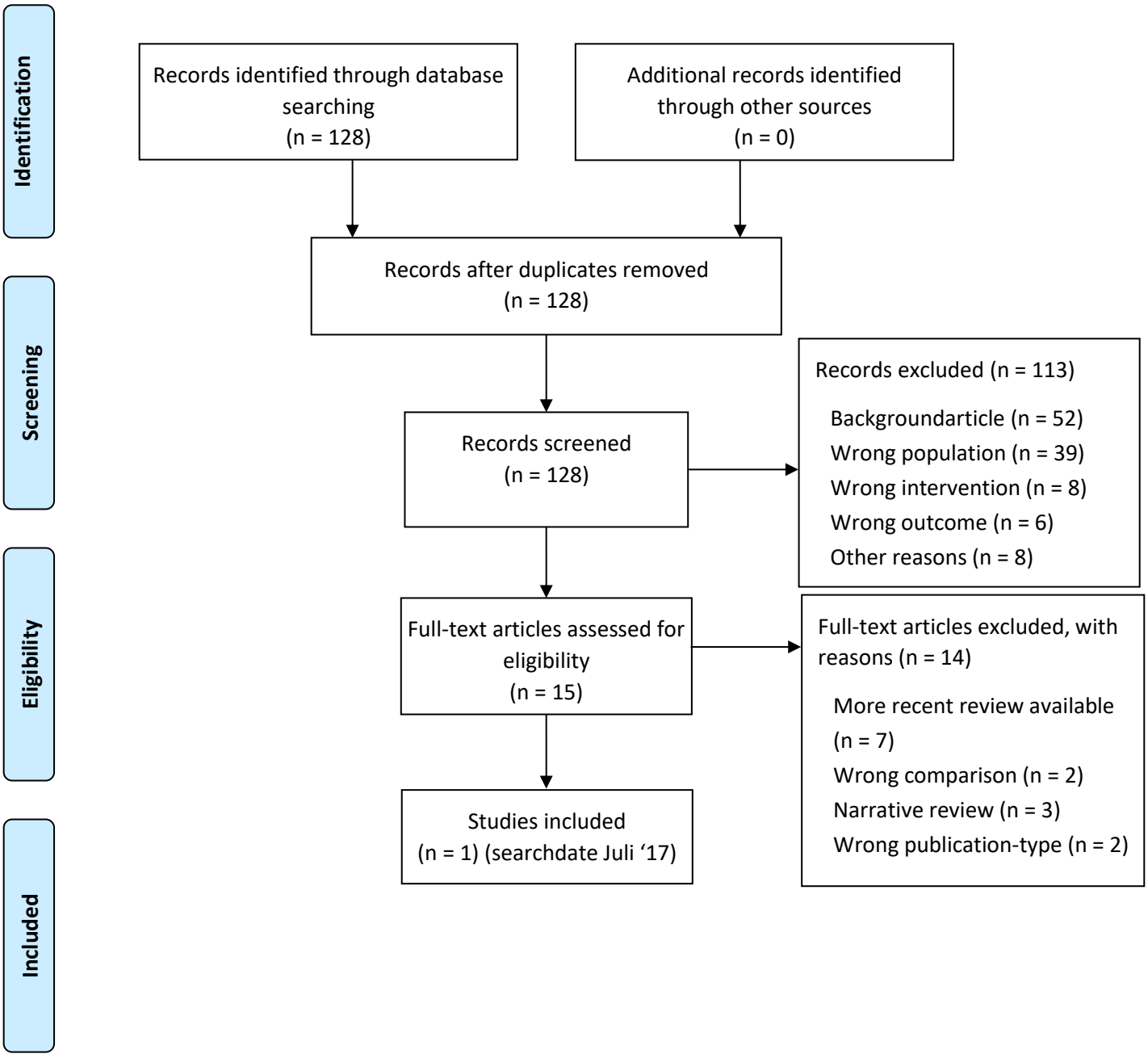
PRISMA flowchart– Peppermint oil – RCT's



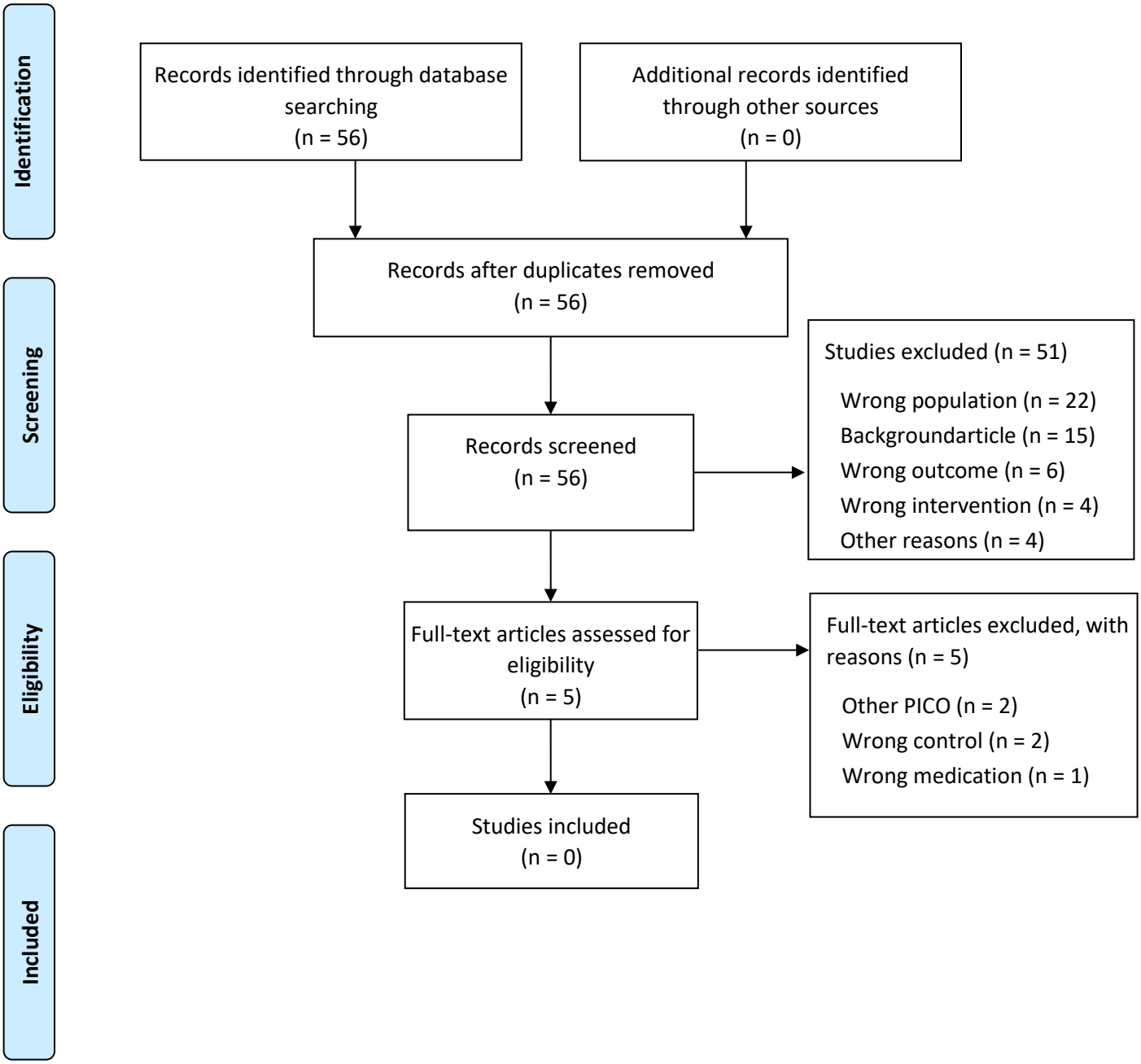
PRISMA flowchart – Linaclotide



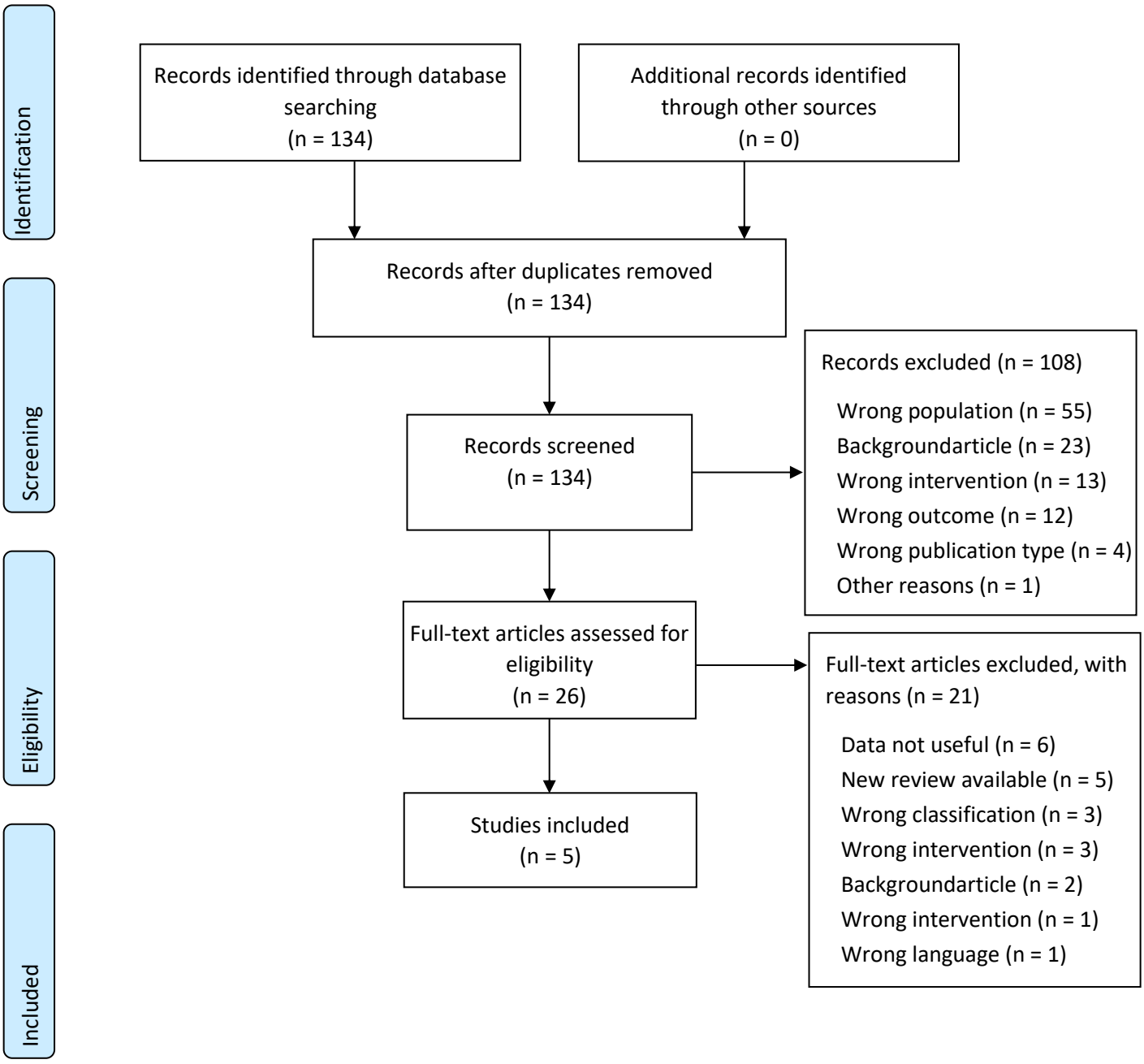
PRISMA flowchart – Antidepressants (systematic reviews)



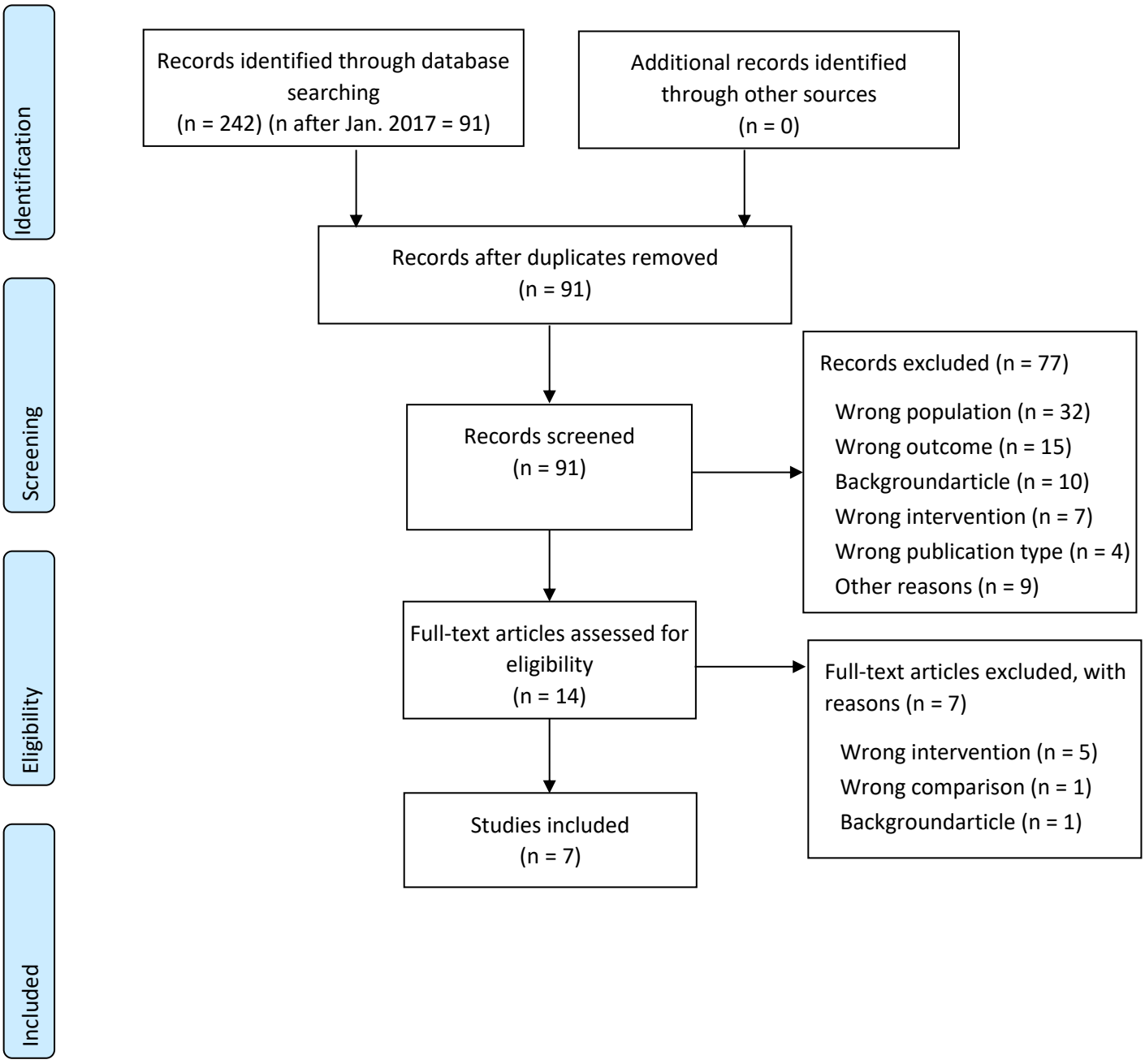
PRISMA flowchart – Antidepressants (RCT's and other studies, published after January 2017)



PRISMA Flowchart – Psychological therapies (systematic reviews)



PRISMA Flowchart – Psychological therapies (RCT's, published after January 2017)



Bijlage 2: Geëxcludeerde artikelen na full-textbeoordeling

Calprotectin: Table of excluded studies (SR and other studies)

Author and year	Reason for exclusion
Systematic reviews	
Petryszyn 2019	Wrong population
Mari 2019	Backgroundarticle
Carrasco 2019	Wrong population
McFarlane 2016	Wrong study design
McFarlane 2016	Wrong study design
Menees 2015	Wrong outcome measure
Waugh 2013	New review available
Other studies	
Vicente 2020	Wrong population
Turvill 2020	Wrong study design
Campbell 2020	Wrong population
Walker 2018	Already in review
Sharbatdaran 2018	Wrong population
Conroy 2018	Already in review

FIT: Table of excluded studies (SR and other studies)

Author and year	Reason for exclusion
Systematic reviews	
n.a.	
Other studies	
McSorley 2020	Wrong outcome
Khan 2020	Wrong population
Hogberg 2020	Wrong outcome
Lord 2018	Wrong outcome
Godber 2016	Already in review

Coloscopy: Table of excluded studies

Author and year	Reason for exclusion
Jahnsen (2009)	Wrong I (not endoscopy)
Whitehead (2010)	A non systematic literature review
Petryszyn (2019)	Wrong P (patients with IBD)
Brandt (2008)	A non systematic literature review
Schusselé Filliettaz (2009)	Wrong P (included patients do not fulfill rome criteria without alarm symptoms)
Burbige (2010)	No systematic literature search

Adelstein (2011)	Wrong P (included patients do not fulfill rome criteria without alarm symptoms)
Furman (2011)	A non systematic literature review
Brandt (2002)	Updated in Brandt 2008
Kamp (2016)	A non systematic literature review
Kok (2013)	No Comparision

Diet: Table of excluded studies (SR and RCT's) gluten free

Author and year	Reason for exclusion
Systematic reviews	
Ford (2015)	More recent systematic review available
Moayyedi (2015)	More recent systematic review available
Singh (2018)	More recent systematic review available
Scarpato (2019)	Wrong P (functional gastrointestinal disorders)
RCT's	
x	x

Diet: Table of excluded studies (SR and RCT's) low FODMAP

Author and year	Reason for exclusion
Systematic reviews	
Ford (2015)	More recent systematic review available
Moayyedi (2015)	More recent systematic review available
Rao (2015)	More recent systematic review available
Altobelli (2017)	More recent systematic review available
Korgsgaard (2017)	More recent systematic review available
Varju (2017)	More recent systematic review available
Schumann (2018)	Presentation of outcome measures difficult to interpret
RCT's	
Guerreiro (2020)	Wrong study design
Gravina (2020)	No control group

Diet: Table of excluded studies NICE diet

Author and year	Reason for exclusion
x	x

Diet: Table of excluded studies (SR and RCT's) psyllium fiber

Author and year	Reason for exclusion
Systematic reviews	
Zuckerman	Not a systematic review (search strategy unknown, databases unknown)
Spiller	Not a systematic review (search strategy unknown, databases unknown)
Moayyedi (2014)	Updated in Ford 2018
Enck (2010)	Wrong intervention
Bijkerk 2004	More recent systematic review available
Bijkerk 2004	More recent systematic review available
Bijkerk 2005	More recent systematic review available
Quartero 2005	More recent systematic review available
Ford 2008	More recent systematic review available
Ruepert (2011)	More recent systematic review available
RCT's	
Oskouie (2018)	Wrong intervention, wrong outcome

Probiotics: Table of excluded studies (SR and RCT's)

Author and year	Reason for exclusion
Systematic reviews	
Wen 2020	Wrong outcome
Sun 2020	More recent review available
Pratt 2020	Wrong (too specific) intervention
Li 2020	More recent review available
Gendi 2020	Background article, narrative
Asha 2020	More recent review available
Ohkusa 2019	Background article, narrative
Liang 2019	More recent review available
Dale 2019	More recent review available
Anbari 2019	Background article, narrative
Lacy 2018	Background article
Hungin 2018	Background article, narrative
Ford 2018	More recent review available
Domingo 2017	Foreign language
Zhang 2016	More recent review available
Tiequn 2015	Wrong (too specific) intervention
Didari 2015	Data not useful
Vitetta 2014	Background article
Ford 2014	More recent review available
Ortiz 2013	More recent review available
Ritchie 2012	Data not useful
Korpela 2012	Background article
Clarke 2012	Background article, narrative
Botschinsky 2010	More recent review available
Moayyedi 2010	More recent review available

RCT's	
Maixent 2020	Wrong publication type
Caviglia 2020	No comparison/ placebo group
Leventogiannis 2019	No comparison/placebo group

Peppermint oil: Table of excluded studies

Author, year	Reason of exclusion
Black 2020	Network meta-analysis, not only peppermint oil; wrong outcome (response/no response)
Camilleri 2017	Not a systematic review
Chang 2006	Not a systematic review
Chumpitazi 2018	Focus is on mechanism, search in only 1 database
Enck 2010	Not a systematic review
Ford 2008	More recent systematic review available
Grigoleit 2005	The search strategy and databases are not described
Hawrelak 2020	Almost same studies as Alammar (2019), but with also with a study in children
Khanna 2014	More recent systematic review available
Kligler 2007	Not a systematic review
Mann 2012	Editorial
McKay 2006	Not a systematic review
Pittler 1998	More recent systematic review available
Ruepert 2011	More recent systematic review available
Sali 2007	Not a systematic review
Shen 2009	Not a systematic review
Vanuytsel 2014	Not a systematic review

Linaclotide: Table of excluded studies

Author and year	Reason for exclusion
Lee 2012	Narrative review
Chey 2012	Described in systematic review (Atluri, 2014)
Rao 2012	Described in systematic review (Atluri, 2014)
Quigley 2013	Pooled meta-analysis of previous described studies
Lacy 2014	Pooled meta-analysis of previous described studies
Rao 2014	Pooled meta-analysis of previous described studies
Camilleri 2015	Pooled meta-analysis of previous described studies
Black 2018	Systematic review, included also other interventions than linaclotide, relevant studies are described elsewhere. Network meta-analysis
Shah 2018	Systematic review, relevant studies are described elsewhere
Fukudo 2018 (dose finding study)	Wrong study population (chronic constipation)
Fukudo 2018	Systematic review, relevant studies are described elsewhere
Yiannakou 2018	Wrong study design (observational study)
Pohl 2019	Wrong study design (observational study)
Rao 2020	Wrong population: IB-C patients with rectal hypersensitivity (not representative for the general IBS-C population)
Chey 2020	Wrong intervention: delayed release linaclotide (not available in the Netherlands)

Antidepressants: Table of excluded studies (SR and RCT's)

Author and year	Reason for exclusion
Systematic reviews	
Black 2020	More usable review available
Cangemi 2019	Narrative review
Xiong 2018	Wrong comparison
Lacy 2018	More recent review available
Kulak 2017	Narrative review
Xie 2015	More recent review available
Hughes 2015	Wrong publication type
Vanuytsel 2014	Narrative review
Ford 2014	More recent review available
Bundeff 2014	More recent review available
Chao 2013	Wrong comparison
Shah 2012	More recent review available
Lai 2012	Wrong publication type
Ruepert 2011	More recent review available
RCT's	
Seddighnia 2020	Wrong medication
Tavakoli 2019	Other PICO
Tadyon 2019	Wrong control
Li 2019	Wrong control
Dehkordi 2017	Other PICO

Psychological therapies: Table of excluded studies (SR and RCT's)

Author and year	Reason for exclusion
Systematic reviews	
Shah 2020	Wrong intervention
Gendi 2020	Data not useful
Black 2020	Data not presented in useful way for our PICO
Cangemi 2020	Data not useful
Thakur 2018	Data not useful
Laird 2017	Wrong classification, no subdivision in CBT, hypnotherapy and relaxation
Flik 2017	Backgroundarticle
Surdea 2016	Data not useful
Laird 2016	Wrong classification
Hauser 2016	Backgroundarticle
Peters 2015	Data not useful
Altayar 2015	Wrong classification
Schaefert 2014	New review available
Ford 2014	New review available
Pajak 2013	New review available
Grundmann 2013	New review available
Sinagra 2012	New review available
Hefner 2009	Wrong language
Shumann 2016	Wrong intervention
Aucoin 2014	Wrong intervention

Lakhan 2013	Wrong intervention
RCT's	
Sibelli 2017	Backgroundarticle
Dehkordi 2017	Wrong comparison
Kashyap 2020	Wrong intervention
Henrich 2020	Wrong intervention
Schumann 2018	Wrong intervention
Ghandi 2018	Wrong intervention
Thakur 2017	Wrong intervention

Bijlage 3: Samenvatting onderzoekskarakteristieken (evidencetabellen)

Fecal Immunochemical Test (FIT): Evidence table for diagnostic studies (baseline characterics)

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison/ control (C) [3]	Follow-up	Comments
Nicholson, 2020	Type of study: Retrospective cohort study Setting and country: Primary care, UK Funding and conflicts of interest: JEE was funded by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre. BDN is an NIHR Academic Clinical Lecturer and is supported by the NIHR Oxford Medtech and In-Vitro Diagnostics Co-operative and Macmillan Cancer Support. The views expressed are those of the author(s) and not necessarily those of the National Health Service, the NIHR or the Department of Health.	Inclusion criteria: consecutive FIT samples sent to OUH clinical biochemistry laboratory from primary care for adults (≥18 years old) during the period March 2017 to March 2020. Exclusion criteria: less than 6 months of follow-up. N total at baseline: 9896 patients Important prognostic factors[2]: *Age (range): 60 (18 – 101) years* *Sex: 58.6 % women* *Clinical features*: Abdominal pain, anaemie, blood in stools, inflammation, iron deficiency, thrombocytosis, change in bowel habit, tired all the time, weight loss. *Groups comparable at baseline*: A larger proportion of FITs were positive (≥7 µg Hb/g faeces) in men (13.4%) than women (9.6%), and in older patients (eg 18.8% of women aged	Index test: Samples were collected into standard collection pots by patients in primary care and analysed for FIT using the HM-JACKarc analyser (Hitachi Chemical Diagnostics Systems Co., Ltd) a method that has been independently evaluated with respect to analytical performance16 and is recommended in the context of use for samples from primary care.1 The method had a calibration range of 7-450 µg Hb/g faeces and immunoassay reproducibility, assessed across 12 months was between 4.5% and 8.7% when expressed as a percentage coefficient of variation. Sample preparation prior to analysis on the FIT instrument utilized the	Reference test: To confirm the presence or absence of disease, OUHT clinical and diagnostic databases were searched for evidence of cellular pathology for up to 36 months following the FIT test for all patients. Histology, endoscopy and CT colonoscopy reports were retrieved by searching by both hospital and NHS number.	Patients were classified individually then by discussion between members of the research team (BS, BN, TJ, JE) having colorectal cancer, normal cellular pathology findings, colorectal polyps, inflammation of the colon or no further follow-up investigation for between 6 and 36 months. Patients who had no further investigation were categorised as negative for serious pathology as any serious pathology would be expected to have presented to secondary care within this time period.	Outcome CRC: 91% (real high!)

		≥80 years compared to 8.7% aged 18-39 years).	Extel Hemo-Auto MC device, a process which introduced additional variation, with overall analytical imprecision observed to be between 7.0% and 13.5% when specimens had been homogenised and sampled by laboratory staff.			
Lue, 2020	Type of study: prospective observational study Setting and country: Funding and conflicts of interest:	Inclusion criteria: Symptomatic patients aged 18 years or older, referred for colonoscopy between June 2015 and April 2017 from either primary or secondary care (gastroenterology clinic or other specialists) with a complete colonoscopy performed in the Endoscopic Unit of HCU Lozano Blesa (Zaragoza), and with a stool sample available were enrolled prospectively and consecutively into the study. Exclusion criteria: Patients were excluded from the study if the colonoscopy was requested for indications other than gastrointestinal symptoms (e.g. CRC screening, follow up of adenomas, polyposis, and previous diagnosed IBD), or if the stool sample returned was insufficient or unsuitable for the analysis (i.e. if the sample was stored without refrigeration or if it was collected during bowel preparation).	Index test: FOBT was performed using the SENTiFIT 270 FOB Gold® (Sysmex-Sentinel Ch SpA, Barcelona, Spain) test, and results were considered positive above 20 µg/g. FC was analysed using the EliATM Calprotectin 2 immunoassay (Thermo Fisher Scientific, Uppsala, Sweden), at a cut-off of 50 µg/g.	Reference test: All diagnoses were confirmed histologically; and all patients also underwent a colonoscopy.	Length of follow-up: n.a.	Outcome CRC: 3,9%

		N total at baseline: 404 Important prognostic factors[2]: *Age*: *59 years (interquartile range: 47-69)* *Sex: 59% women* Almost half of the patients were referred for colonoscopy because of a recent history of rectal bleeding (41.2%), followed by a change in bowel habits, abdominal pain, diarrhoea and anaemia. Most colonoscopies were requested by general practitioners (60.2%).				
Mowat, 2019	Type of study: prospective cohort study Setting and country: primary care, UK. Funding and conflicts of interest: This study has been funded by Detect Cancer Early initiative (Scottish Government) and Chief Scientist Office. CGF has undertaken paid consultancy with Immunostics, Ocean, NJ, USA, and Kyowa Medex, Tokyo, Japan, and has received support for attendance at conferences from Alpha Labs, Eastleigh, Hants, UK.	Inclusion criteria: If patients presented with new-onset bowel symptoms, general practitioners (Gps) were recommended to request f-Hb as an adjunct to history taking. Exclusion criteria: One hundred and fifty-two of the samples (2.7%) were unsuitable for analysis (most commonly due to faecal contamination) in whom 40 patients did not complete a repeat test. Ten patients had known IBD. In total, therefore, 50 patients were excluded from further analysis N total at baseline: 5422 patients with 5660 FIT samples. After exclusions leaving a cohort of 5372 patients.	Index test: f-Hb was measured using an HM-JACKarc (Kyowa Medex) with an analytical working range of 7–400 µg Hb/g faeces. Practice nurses distributed a FIT kit to each patient. Patients were instructed to collect a single sample of faeces and to return the FIT device immediately in person to the GP surgery and from here they were delivered to Blood Sciences, Ninewells	Reference test: Patients referred to endoscopy were investigated within 6 weeks of referral. All findings were recorded on the endoscopy reporting system by the endoscopists. The diagnoses of CRC, HRA and IBD were confirmed by a gastrointestinal pathologist.	Length of follow-up: 1 year.	Outcome CRC: 6,6%

		Important prognostic factors[2]: *Median age: 65 years (range: 2-99, IQR: 51-75)* *Sex: 56,4% female*	Hospital and Medical School, Dundee, at ambient temperature via the GP surgery routine sample collection service (a daily courier service) and stored at 4°C prior to analysis to ensure f-Hb stability.			
Juul, 2018	Type of study: prospective cohort study. Setting and country: general practice / primary care, Denmark. Funding and conflicts of interest: This study was funded by the Central Denmark Region, the Committee for Quality Improvement and Continuing Medical Education (KEU) for general practice of the Central Denmark Region and the Danish Cancer Society. None of the funding bodies has been involved in designing the study or writing the article, nor in the collection, analyses and	Inclusion criteria: all individuals aged ≥30 years who had performed a valid FIT (defined as a FIT result within the measuring range of the OC Sensor DIANA) in general practice during the study period. Faecal immunochemical testing was aimed at individuals aged ≥30 years who presented in general practice with non-alarm symptoms of CRC. It was left to the GPs' clinical knowledge and judgement to decide on which patients to request a FIT, but GPs were provided with a clinical instruction containing suggested symptoms and signs. These included: change in bowel habits, abdominal pain, unexplained anaemia, and unspecific symptoms (e.g. fatigue or weight loss). Furthermore, faecal immunochemical testing was	Index test: FIT measured with the OC Sensor DIANA. The FIT was used as a rule-in test, and the cut-off value for a positive FIT in general practice was set at 10 µg Hb/g faeces. A single FIT sample was collected from each patient containing 10 mg faeces in 2 ml buffer solution. The FITs were sent with prioritised mail for analyses to the Department of Clinical Biochemistry at Randers Regional Hospital. The FITs were analysed daily by trained staff with expertise in FIT analyses, using the	Reference test: colonoscopy. The doctors performing the colonoscopy were not blinded to FIT results, but had no affiliation with the project.	Length of follow-up: A follow-up time of 3 months was used because individuals with a positive FIT should be urgently referred to diagnostic investigation.	Outcome CRC: 1,5%

	interpretation of data. The authors declare no competing interests.	recommended as part of the diagnostic work up of irritable bowel syndrome (IBS). Exclusion criteria: Invalid FIT results were defined as a FIT without a quantified value and excluded from analyses. N total at baseline: During the study period, 3745 FITs were requested. Of these, 91 (2.4%) FITs were invalid and 192 (5.1%) additional FITs were excluded to ensure only one test per individual. Thus, a total of 3462 (92.5%) FITs were included in the analyses. Important prognostic factors[2]: *Age: 30 – >80 years. 25% between 60 en 69 years of age.* *Sex: 56% female*	automated analyser OC-Sensor DIANA (Eiken Chemical Company, Ltd, Japan).			
Hogberg, 2017	Type of study: prospective cohort study Setting and country: primary care, Sweden. Funding and conflicts of interest: This work was supported by unrestricted grants from the Region J€amtland H€arjedalen [JLL-467441, JLL-557111, JLL-	Inclusion criteria: All patients aged 20 years and over were eligible for the study when a physician ordered a FIT and/or a FC test during the period of 30 January 2013– 31 May 2014. Exclusion criteria: N total at baseline: In total, 510 patients were eligible for the study, and 384 returned both tests. Of these, five died of other conditions before endoscopy, and six moved away from	Index test: FIT. The nurses instructed patients to collect one sample from each of three consecutive stools for the FIT, and to sample one of the stools for the FC test. Patients were instructed to store the samples in a refrigerator prior to returning them as soon as possible to the health care	Reference standard: Physicians were instructed to refer patients with a positive FIT or a FC 100 lg/g to the endoscopy unit at Ostersund € Hospital for a colonoscopy. The test results were available to the	Length of follow-up: 2 year.	Outcome CRC: 2,1%

	601081], Northern County Councils (Visare Norr) [VisareNorr467541, VisareNorr557151], Regional Cancer Centre North, Swedish Society of Medicine, [SLS-324961, SLS-412311], Lions Cancer Research Foundation Umeå University [AMP14-765, LP15-2092]. The authors report that they have no conflicts of interest.	the area during the 2-year follow-up. The final analysis included 373 patients. Important prognostic factors[2]: *Median age: 63 year.* *Sex: 65% women.*	centre. The dipstick, visually read, qualitative test Actim Faecal Blood (Oy Medix Biochemica Ab, Finland) [30] was used for the sample collection and the analysis. And faecal calprotectin. The samples for FC were sent to the accredited Department of Laboratory Medicine, Umeå University Hospital, where they were analysed with the CALPROVR Calprotectin ELISA Test according to manufacturer instructions (Calpro AS, Norway).	endoscopists. All colonoscopy findings were recorded in the regional electronic medical records. CRC, HRAs and IBD were diagnosed by experienced pathologists.		
Elias, 2016	Type of study: cross-sectional / prospective diagnostic study Setting and country: primary care, the Netherlands Funding and conflicts of interest: This work was financially supported by grants from the Netherlands Organization for Health Research and Development (grant numbers 170992101	Inclusion criteria: patients from 266 Dutch primary care practices referred for endoscopy from July 2009 through January 2012. Patients were eligible if suspected of SCD, defined by lower abdominal complaints for at least 2 weeks, combined with rectal bleeding, change in bowel habit, abdominal pain, fever, diarrhoea, weight loss, and/or a sudden onset of abdominal complaints at > 50 years of age. Exclusion criteria: Patients were	Index test: we analysed faecal samples for faecal Hb by a qualitative POC FIT (Clearview® iFOBT One Step Faecal Occult Blood Test Device, Alere Health), yielding either a positive or negative test result. We analysed the faecal samples for calprotectin concentration by a quantitative POC test (Quantum Blue®; dynamic range 30–300 µg/g) and	Reference test: Experienced gastroenterologists from three high-volume centres (i.e. > 1000 endoscopies annually) performed endoscopy in all patients, i.e. colonoscopy or sigmoidoscopy. A final diagnosis was established according to routine	Length of follow-up: 3 months.	Outcome CRC: 4,6%

	and 91810615), and non-financially by Bühlmann Laboratories AG that provided the calprotectin tests, and Alere Health BV that provided the POC FIT tests. None of the authors have any financial or non-financial competing interests with regard to this study. Bühlmann Laboratories AG provided the calprotectin tests and Alere Health BV provided the POC FIT tests. The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report, nor in the decision to submit the article for publication.	excluded if aged below 18, known with SCD, or with confirmed parasitic bowel infection. <u>N total at baseline</u>: Of 843 enrolled patients, 810 could be evaluated. <u>Important prognostic factors</u>[2]: *Age: 61 years (19-92 years)* *Sex: 55% female*	by an enzyme-linked immunosorbent assay (ELISA; EK-CAL Calprotectin ELISA, both from Bühlmann Laboratories), both yielding estimates of µg calprotectin/g faeces.	clinical practice, including histopathology of biopsies if required, and 3 months follow-up after negative endoscopy.		

Diet – Evidence table for intervention studies (baseline characteristics) – Gluten free diet

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up
Biesiekierski, 2011	Type of study: double blind randomized placebo controlled trial Setting and country: patients recruited through advertisements and by referral in private dietetic practice, Australia Funding: the Helen Macpherson Smith Trust, the National Health and Medical Research Council (NHMRC) of Australia, and the Vera and Les Erdi Foundation Conflicts of interest: Susan J. Shepherd has published cookbooks directed toward issues of dietary fructan restrictions, fructose malabsorption, and celiac disease. She has also published shopping guides for low FODMAPs and low fructose and fructan foods.	Inclusion criteria: age > 16 years, symptoms of IBS fulfilling Rome III criteria that have improved on a gluten-free diet, and adherence to the diet for at least 6 weeks immediately before screening Exclusion criteria: Celiac disease, significant gastrointestinal disease (such as cirrhosis or inflammatory bowel disease), excessive alcohol intake, intake of non-steroidal anti-inflammatory agents, and unable to give written informed consent N total at baseline: Intervention (gluten): 19 Control (gluten free): 15 Important prognostic factors[2]: *Median age (range):* *Gluten: 40 (29-55)* *Gluten free:49 (33-51)* *Sex:* *Gluten: 16%* *Gluten free: 7%* Number with predominant	Before participating in the study patients had to adhere to a gluten free diet for at least 6 weeks immediately before screening. Patients were randomized to either the gluten or the placebo treatment group. Participants continued on a gluten-free diet throughout the study, but were asked to consume one study muffin and two study slices of bread containing gluten (total intake of 16 g / day) every day for 6 weeks.	Before participating in the study patients had to adhere to a gluten free diet for at least 6 weeks immediately before screening. Patients continued their gluten free diet and received one study muffin and two study slices of bread containing no gluten every day for 6 weeks. .	*Length of follow-up:* *9 weeks (three weeks after completion of the intervention)* *Loss-to-follow-up:* *Gluten:* *N: 6, withdrew after a median of 7 (range 2 – 18) days* *Reasons (describe)* *Gluten free:* *N: 3, withdrew after a median of 16 (range 11 – 21) days* *There were no statistical differences between the groups in frequency and timing of withdrawal.* *Incomplete outcome data:* *NA*

		bowel habit Gluten: constipation (16%), diarrhea (58%), alternation (26%) Glutenfree: Constipation (20%), diarrhea (33%), alternating (47%) Groups comparable at baseline? No statistical analysis were performed to compare groups at baseline			
Zanwar, 2016	Type of study:: a prospective, randomized, double blinded placebo controlled trial Setting and country: tertiary health care center in the gastroenterology outpatient clinic affiliated to a University Medical College in Mumbai, India Funding: None Conflicts of interest: None	Inclusion criteria: patients aged >16 years, symptoms of IBS as per the Rome III criteria, willing to adhere to the prescribed diet Exclusion criteria: Patients already on a gluten free diet, presence of cirrhosis or inflammatory bowel disease, excessive alcohol intake, patients currently prescribed and using systemic immunosuppressants, nonsteroidal anti-inflammatory agents, or medications affecting gastrointestinal motility, abnormal thyroid function tests, presence of a psychiatric disease, pregnancy, inability to give written informed consent N total at baseline: 180 patients started a gluten free diet. 65 Patients	At the beginning of the study, a dietician provided advice to all patients on following a gluten free diet for 4 weeks. Patients who responded adequately to the gluten free diet and had improvement in their symptoms, defined as a 30% decrease in symptom VAS from the baseline for at least 50% of the time, were included in the study. Patients who did not respond to the GFD were allowed to withdraw from the study. After 4 weeks of the washout (elimination diet) period, the responding patients were randomly assigned into two groups for a double-blind, placebo-controlled rechallenge. Rechallenge: The patients in the gluten group consumed two slices of bread containing gluten each morning for the course of the	At the beginning of the study, a dietician provided advice to all patients on following a gluten free diet for 4 weeks. Patients who responded adequately to the gluten free diet and had improvement in their symptoms, defined as a 30% decrease in symptom VAS from the baseline for at least 50% of the time, were included in the study. Patients who did not respond to the GFD were allowed to withdraw from the study. After 4 weeks of the washout (elimination diet) period, the responding patients were randomly assigned into two groups for a double-blind, placebo-controlled rechallenge. Rechallenge: Patients in the gluten free group consumed consumed two slices of gluten-free breads, each morning for the	*Length of follow-up:* until week 4 of the rechallenge *Loss-to-follow-up:* In total 180 patients started a gluten free diet, 65 responded to the diet and 16 were unable to tolerate a gluten free diet. 65 patients were included in the randomization. Gluten: 34 patients were allocated to the gluten intervention, 4 were lost to follow-up Gluten free: 31 patients were allocated to the intervention, 1 was lost to follow-up *Incomplete outcome data:* NA

		responded to the gluten free diet. Those 65 patients were randomized. 5 patients were lost to follow up. N total = 60 Gluten: N = 30 Gluten free: N=30 <u>Important prognostic factors</u>[2]: *Age mean (+- SD)* *Gluten: 37 (18-60)* *Gluten free 35 (18-56)* *Male Sex:* *Gluten: 17 (56%)* *Gluten free: 18 (60%)* Groups comparable at baseline? Yes (based on age, gender, bmi, duration of illness, IgA tTG antibody level, ESR)	rechallenge. Rechallenge lasted 4 weeks and the patients were advised to maintain a gluten free diet throughout this period.	course of the rechallenge. Rechallenge lasted 4 weeks and the patients were advised to maintain a gluten free diet throughout this period.	
Shahbazkhani, 2015	Type of study: double-blind randomized placebo-controlled trial Setting and country: suburban, outpatient, private-practice gastroenterology clinic in Imam Khomeini hospital, Tehran, Iran Funding: not reported Conflicts of interest: None	<u>Inclusion criteria</u>: newly diagnosed IBS based on the Rome III criteria, >16 years of age <u>Exclusion criteria</u>: diagnosis of celiac disease (CD), ever tried a gluten free diet and whether this diet was currently in place, patients with self-exclusion of wheat from the diet without a known diagnosis of celiac disease, inflammatory bowel disease and diabetes; use of drugs for depression and/or anxiety, use of non-steroidal	All patients started a gluten free diet. Patients in both groups consumed powder for six weeks, while both groups were on gluten-free diets. The gluten containing group), was given a packet (100 g) containing a gluten meal (free of fermentable oligo di-monosaccharides and polyols and proteins including 2.3% non-gluten, 52% gluten and/or gliadin and 27.7 g glucose)	All patients started a gluten free diet. Patients in both groups consumed powder for six weeks, while both groups were on gluten-free diets. The gluten free group was given packets (100 g) containing powder of gluten-free foods (rice flour, corn starch and glucose).	*<u>Length of follow-up</u>: 6 weeks* *<u>Loss-to-follow-up</u>:* Not mentioned *<u>Incomplete outcome data</u>:* NA

		anti-inflammatory drugs, abnormal levels of: glucose, urea, creatinine, sodium, potassium, hemoglobin, ESR) and thyroid function tests, and those who did not sign the consent form to participate in the study <u>N total at baseline</u>: 102 patients started the gluten free diet 22 were withdrawn (found it difficult to follow gluten free diet). 80 patients responded to the diet and achieved significant improvement. 8/80 did not follow a strict gluten free diet and were excluded. 72 patients were included in the study. N gluten = 35 N gluten free = 37 <u>Important prognostic factors</u>[2]: *Mean age (+- SD)* *Gluten: 44.5 (10)* *Gluten free: 43.2 (17)* *Male sex (%)* *Gluten: 6 (17.1%)* *Gluten free: 13 (35.1%)* Kind of IBS Gluten Constipation: 10 (28.6%) Diarrhea: 19 (54.3%) Mixed: 6 (17.1%)			

		Gluten free Constipation: 6 (16.2%) Diarrhea: 18 (48.6%) Mixed: 13 (35.1%) Groups comparable at baseline? Yes (for age, sex, kind of IBS, Anti-tTG IgA, Anti-tTg IgG, AGA IGA, AGA IgG, Positive DQ2/8 HLA)			

Diet – Evidence table for systematic reviews (baseline characteristics) – Gluten free diet and low FODMAP

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up
Dionne, 2018	SR and meta-analysis of RCT's *Literature search up to November 2017* **A**: Biesiekierski, 2011 **B**:Shahhbazkhani, 2015 **C**: Bohn (2015) **D**: Eswaran (2015) **E**: Halmos (2014) **F**: McIntosh (2017) **G**: Staudacher (2017) **H**: Staudacher (2012) **I**:Husthof (2017) Study design: **A**: RCT **B**: RCT **C**: RCT **D**: RCT **E**: RCT **F**: RCT **G**: RCT, 2x2 factorial design **H**:RCT **I**:RCT Setting and Country: Source of funding and conflicts of interest: the American College of Gastroenterology Institute and the Canadian Institute for Health Research,	Inclusion criteria SR: Parallel-group RCT's (or first arm of cross-over) adults (participants aged >17 years), Diagnosis of IBS based on either a clinician's opinion or meeting specific diagnostic criteria. Compared dietary exclusion of gluten or FODMAPs with placebo diet or usual diet. Alternatively, all patients received GFD or low FODMAP diet and then randomized to challenge or continue on diet. Minimum duration of therapy and follow-up 7 days. Dichotomous assessment of response to therapy in terms of effect on global IBS symptoms or abdominal pain following therapy Exclusion criteria SR: Insufficient data, no comparator arm, did not include outcome of interest, drug comparator, duplicates, not RCT, not a clinical study, psychiatric intervention, not IBS, IBS/IBD overlap. *9 studies included, 2*	**A**: Gluten free diet **B:** Patients randomized to packages containing powdered gluten **C**: Low FODMAP **D**: Low FODMAP **E**: Low FODMAP **F**: Low FODMAP **G**: Low FODMAP **H**: Low FODMAP **I**: Low FODMAP	**A**: Gluten free plus study bread and muffin containing 16 g of gluten/ day) **B**: Patients randomized to packages containing gluten free powder **C**: traditional IBS diet advise (3 meals and 3 snacks per day with even fiber distribution) **D**: modified NICE guidelines diet **E**: typical diet **F**: High FODMAP **G**: sham diet, or low FODMAP/probiotics, or low FODMAP/placebo, sham diet/probiotic, sham diet/placebo **H**: usual diet **I**: High FODMAP	End-point of follow-up: **A**: 6 weeks **B**: 6 weeks **C**: 4 weeks **D**: 4 weeks **E**: 3 weeks **F**: 3 weeks **G**: 4 weeks **H**: 4 weeks **I**: 9 weeks For how many participants were no complete outcome data available? NA

	one of the authors has conducted one of the included trials.	*concerning gluten free diet, 7 concerning low FODMAP diet* <u>Important patient characteristics at baseline</u>: *NA* We were unable to assess if groups were comparable at because this data is not provided in the SR			

Diet – Evidence table for intervention studies (baseline characteristics) – low FODMAP diet

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison/control (C) [3]	Follow-up
Zahedi (2017)	Type of study: RCT (single blinded) Setting and country: patients referred to the gastroenterology department Funding: grant from Vice Chancellor for Research, Kerman University of Medical Sciences, Kerman, Iran Conflicts of interest: None declared	Inclusion criteria: IBS-D (Bristol stool form scale ≥ 5) and age 20–60 years old Exclusion criteria: having a confounder medical condition such as celiac disease, inflammatory bowel disease, or presence of cardiovascular, liver, kidney, neurologic diseases, diabetes, and thyroid disorders, consumption of ω-3 fatty acids and other nutritional supplements in the last 3 months, and pregnancy during the study N total at baseline: N=110 I: 55 C: 55 Important prognostic factors[2]: *Age (median ± SD)* *I: 37.60 ±11.09* *C: 37.43±13.27* *Gender (%male)* *I: 52%* *C: 47.05%*	Dietary education: LFD (<0.5 g of FODMAPs per meal)	Traditional IBS diet (British Dietetic Association)	*Length of follow-up:* *6 weeks* *Loss-to-follow-up:* *I: 3 noncompliance, 2 lost to follow-up* *C: 2 excluded because of travel, 2 lost to follow-up* *Incomplete outcome data:* *NA*

		There was no statistically significant difference in age, gender, BMI, HADS, IBS-SSS, QoL and stool frequency at baseline. For Stool consistency there was a statistically significant difference (I: 5.92±0.45 C: 5.67±0.61)			
Eswaran (2017)	Type of study: RCT Setting and country: patients recruited from the gastroenterology and primary care clinics, USA Funding: Michigan Nutrition Obesity Research Center Grant (P30 DK089503), Clinical and Translational Science Award Grant (2UL1TR000433-06), Prometheus Therapeutics and Diagnostics (San Diego, CA). Conflicts of interest: William D. Chey has served as a consultant for and received grant funding	Inclusion criteria: IBS-D patients meeting the Rome III criteria with an average daily abdominal pain score of 4 or higher on an 11-point numerical rating scale, and an average daily stool consistency, assessed by the Bristol Stool Form Scale, of >5 Exclusion criteria: NA N total at baseline: 171 subjects enrolled and screened 84 completed the study. I: 45 C: 39 Important prognostic factors[2]: *Median age (range):* *Gluten: 40 (29-55)* *Gluten free:49 (33-51)* *Age (mean±sd):* *I: 41.6±14.7* *C: 43.8±15.2* Sex (% male) I: 34% C: 23.8%	Low FODMAP diet Instruction was administered in a standardized manner according to published materials from Monash University. Subjects were given teaching materials created from the University of Michigan.	modified diet recommended by the National Institute for Health and Care Excellence (mNICE) Using standardized instructions, the mNICE group was instructed to eat small frequent meals, avoid trigger foods, and avoid excess alcohol and caffeine	*Length of follow-up:* *4 weeks* *Loss-to-follow-up:* *I: 5* *C: 2* *Incomplete outcome data:* *NA*

		Demographics and baseline QOL measures were similar between groups, except that there were more obese patients in the mNICE group.			
Harvie (2017)	Type of study: RCT, parallel design study Setting and country: subjects recruited through gastroenterology outpatient clinics, GP practices and by advertising, New Zealand Funding: NA Conflicts of interest: None reported	Inclusion criteria: meeting the Rome III criteria Exclusion criteria: coeliac disease, inflammatory bowel disease (IBD), pregnancy or lactation, major abdominal surgery and inability to understand English N total at baseline: I: 23 C: 27 Important prognostic factors[2]: *Age (mean±sd):* *I: 43.3±13.8* *C: 40.6±13.3* *Sex (%male)* *I: 26%* *C: 4%* Information on comparability of the groups is not reported, only that groups were different regarding sex.	Low FODMAP Dietary advice was provided to individual participants in a standardized fashion by an experienced registered dietitian. At the initial consultation (approx. 1 h duration) all participants were advised to significantly reduce their intake of excess fructose, lactose, sorbitol, mannitol, FOS and GOS. Participants then purchased and prepared their own food There was a 16.5 ± 15.6 g/d ($p < 0.01$) reduction in total FODMAP intake of participants in this group	Regular diet	*Length of follow-up:* *3 months* *Loss-to-follow-up:* *NA* *Incomplete outcome data:* *NA*
Patcharatrakul (2019)	Type of study: RCT Setting and country: enrolled from the gastroenterology outpatient clinic Thailand	Inclusion criteria: Adult patients (18–70 years of age) who were diagnosed as IBS by Rome III criteria with moderate-to-severe GI	Low FODMAP High-FODMAP items that might aggravate the patient's	Patients received 5 min of dietary advice from an investigator, which included reducing certain foods that have been	*Length of follow-up:* *4 weeks* *Loss-to-follow-up:* *I: 3*

	Funding: Ratchadapiseksompotch Fund, Chulalongkorn University and a grant from The Gastroenterological Association of Thailand Conflicts of interest: None declared	symptoms Exclusion criteria: previous surgery of the GI tract except for appendectomy and hemorrhoidectomy; inflammatory bowel disease; celiac disease; GI malignancy; and severe heart, liver, lung, neurological, or psychiatric diseases N total at baseline: I: 33 C: 33 Important prognostic factors[2]: *Age (mean±sd):* *I: 50.0±13.7* *C: 52.0±14* *Sex (%female):* *I: 76.7%* *C: 75%* Groups were comparable at baseline (for age, gender, BMI, education, global IBS severity score, Symptom severity score, HAD score anxiety, HAD score depression, total high-FODMAPs per week)	symptoms were identified from an individual 7-day food diary. Then, the investigator discussed with the patients to avoid high-FODMAP items and modify recipe/menu with the commonly available low-FODMAP items. The items low in FODMAPs in our country with an example food menu using these low-FODMAP items were listed in the pamphlets provided to the patients.	traditionally recognized as triggers for gas, bloating, or abdominal pain, including fruits, vegetables, nuts, beans, and garlic, and avoidance of large meals.	*C: 1* *Incomplete outcome data: NA*
Pederson (2014)	Type of study: unblinded RCT Setting and country: IBS patients from Herlev Hospital, Denmark Funding: NA	Inclusion criteria: Meeting Rome III criteria for IBS, a negative outcome of colonoscopy, negative transglutaminase antibodies and lactose intolerance gene test prior to study	Low FODMAP Each patient allocated to the LFD was instructed in the diet during a one hour session by nutritionists or	An unchanged normal (Danish/Western)	*Length of follow-up: 6 weeks* *Loss-to-follow-up:* I: 8 C: 3 *Incomplete outcome data:*

	Conflicts of interest: NA	enrolment <u>Exclusion criteria</u>: Patients with a BMI<18 <u>N total at baseline</u>: I: 42 C: 40 <u>Important prognostic factors</u>[2]: *Age mean (range):* *I: 37 (18-71)* *C: 32 (18-73)* *Sex (male/female):* *I: 8/34* *C: 11/29* Baseline characteristics were similar in both groups (age, gender, BMI, smoking, disease duration, subtype, ibs related medication, IBS-SSS, IBS-QOL).	dietitians with a special interest in IBS and the LFD. All patients were requested not to eat food components with a high content of FODMAPs and a list of these was provided at the session with the dietitian. All patients were encouraged to contact the dietitian in case of any uncertainties regarding the diet.		NA

Diet – Evidence table for systematic reviews (baseline characteristics) – psyllium fibre

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up	Comments
Ford (2018)	SR and meta-analysis of RCT's *Literature search up to July 2017* **A**: Ritchie, 1979 **B**: Longstreth, 1981 **C**: Arthurs, 1983 **D**: Nigam, 1984 **E**: Prior, 1987 **F**: Jalihal, 1990 **G**: Bijkerk, 2009 Study design: RCT Setting: **A**: tertiary care **B**: secondary care **C**: secondary care **D**: secondary care **E**: tertiary care **F**: secondary care **G**: primary care Source of funding and conflicts of interest: Unrestricted educational grant. Several of the authors were consultant for Allergan or Ironwood or Nestle.	Inclusion criteria SR: Randomized controlled trials, Adults (participants aged > 16 years), Diagnosis of irritable bowel syndrome (IBS) based on either a clinician ' s opinion or meeting specific diagnostic criteria (Manning, Kruis score, Rome I, II, or III), Compared fiber supplementation with placebo or no therapy, Minimum duration of therapy 7 days, Minimum duration of follow-up 7 days, Dichotomous assessment of response to therapy in terms of effect on global IBS symptoms or abdominal pain following therapy Exclusion criteria SR: NA *7 studies included* Important patient characteristics at baseline: N, IBS definition, IBS type **A**: 100, Author-defined IBS, NA **B**: 77, Author-defined IBS, NA	Describe intervention: **A**: Ispaghula husk **B**: Ispaghula **C**: Ispaghula husk **D**: Ispaghula husk **E**: Ispaghula husk **F**: Ispaghula husk **G**: 20 g Ispaghula husk	Describe control: **A**: placebo **B**: placebo **C**: placebo **D**: placebo **E**: placebo **F**: placebo **G**: placebo	End-point of follow-up: **A**: 3 months **B**: 8 weeks **C**: 4 weeks **D**: 3 months **E**: 12 weeks **F**: 4 weeks **G**: 12 weeks For how many participants were no complete outcome data available? NA	Author's conclusions: Poorly fermentable, soluble fiber remains an evidence-based treatment for IBS. The low cost and lack of significant side effects makes soluble fibre a reasonable first-line therapy for IBS patients.

		C: 80, Author-defined IBS, NA **D**: 168, Author-defined IBS, NA **E**: 80, Author-defined IBS, IBS-C 49% **F**: 22, Author-defined IBS, IBS-C 25%, IBS-D 75% **G:** 275, Author-defined or ROME II IBS, IBS-C 56%, IBS-D 25%, IBA-M 19% *<u>Sex (% female)</u>:* **A**: 77% **B**: 83% **C**: 78% **D:** 45% **E**: 90% **F**: 20% **G:** 79% Groups comparable at baseline? NA				

Probiotics – Evidence table for intervention studies (baseline characteristics)

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/ control (C)	Follow-up	Comments
Gupta, 2021	RCT, secondary care, India. This study was solely funded by Advanced Enzyme Technologies Limited, Thane (India). The authors have no conflicts of interest to disclose.	Inclusion criteria: (1) Male and females (18–65 years) with diagnosis of IBS as per Rome IV criteria associated with following symptoms for more than last 3 months; like abdominal discomfort such as mild pain, cramping, bloating, altered bowel habit indicated by frequent diarrhoea or constipation and functional dyspepsia; (2) written informed consent by study participants. Exclusion criteria: Subjects those were on antibiotics or laxatives within the preceding 6 weeks, Symptoms of IBD, acute GI tract infection, fever, abdominal mass, signs of bowel obstruction, history of colon cancer or diverticulitis, infection from human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), celiac disease, scleroderma and gastroparesis and hypothyroidism were excluded from the study (Supplement: Details of Exclusion and Withdrawal Criteria,	The investigational product (IP) was the active ingredient, B coagulans LBSC mixed with the excipient. The strength of the active ingredient was 2 billion spores per gram per sachet, which was supplied by Advanced Enzyme Technologies Ltd., Thane, India.	The placebo contained only excipient, maltodextrin (1.00 g).	Treatment duration was up to 80 days and total study duration did not exceed 90 days. With total 2 patients lost to follow up (dropped out) 1 in each group; trial was completed with total 38 PP population. Reasons not described.	Outcomes: Digestive Symptom Frequency Questionnaire (DSFQ) on 5-point Likert scale (0=never, 1 1 episode/wk; 2 3 episodes/wk; 3≥ 3 episodes/wk; 4=daily episodes), change in gastrointestinal symptom's severity using IBS severity scoring system (IBS-SSS) and change in stool consistency using Bristol stool form scale. Plus adverse events and The QoL was assessed based on yes or no responses for pain scale on abdominal pain, diarrhoea, constipation, bloating and flatulence,

		http://links.lww.com/MD/F368). In addition, subjects having adverse effects or serious adverse effects, pregnancies, disease emergencies, concomitant therapy, and study protocol violation are considered for withdrawal of subjects from the trial. Intervention: 20 patients Control group: 20 patients Groups comparable at baseline for gender: I male 65%, C male 75% Age: I 36 y, C 35 years Also for height, weight, BMI.				vomiting and nausea, perception of mental well-being, and influence on daily life.
Skrzydlo, 2020	RCT, outpatients clinics, Poland. Funding: This research was funded by the grant financed by Biocare, Copenhagen, Denmark (the principal investigator—B. Cukrowska). Conflicts of Interest: B.C. has served as a speaker for Nutricia, Danone, Bayer, Apotex, Polpharma, and Mead Johnson. J.G. is the co-founder of Biocare Copenhagen, a company acquired	Inclusion criteria: female and male patients aged 18–60 years with IBS-D diagnosed according to Rome III criteria (recurrent abdominal pain or discomfort defined as an uncomfortable sensation not described as pain at least three days a month in the past three months, associated with improvement with defecation; IBS onset associated with a change in frequency and form of stool). Exclusion criteria: the use of probiotics (both recommended by a physician and self-taken) and treatment with antibiotics within last three months; a concurrent severe illness (malignancies, uncontrolled hypertension and diabetes mellitus, hepatic, renal or cardiac	The synbiotic preparation in the form of sachets contained multi-strain probiotic mixture of three Bifidobacterium and two Lactobacillus species (Table 1). The total number of colony-forming units (CFU) per sachet was five billion. The composition of probiotic bacteria resulted from an earlier preliminary study in which positive effects in IBD patients were observed [26]. Patients obtained a mixture of four strains (Bifidobacterium lactis, Bifidobacterium longum, Bifidobacterium bifidum and Lactobacillus acidophilus)	The placebo sachets contained 978 mg of maltodextrin comparable in color, texture and taste to the synbiotic mixture.	Length of follow up: 8 weeks. After the 4-week treatment (visit II), three patients from the synbiotic group and five patients from the placebo group were excluded because of antibiotic treatment (n = 1 in the synbiotic groups and n = 2 in the placebo group), no telephone contact (n = 2 in the synbiotic group and n = 2 in the placebo	IBS-SSS, IBS-GIS, IBS-AR , Bristol stool scale (1-7), severity of pain, flatulence stool pressure (5 points likert scale).

	by DSM Nutritional Products in 2017, but was not involved in conducting the study and data analyses. Other authors declare no conflict of interest.	dysfunctions, serious neurological disorders, psychosis, respiratory disorders such as asthma, chronic obstructive pulmonary disease, hyper- or hypothyroidism); chronic bowel disorders other than IBS, including inflammatory bowel diseases, gastroenteritis, stomach and duodenal ulcers, celiac diseases; pregnancy or lactation; diagnosed lactose intolerance; the use of motility drugs or dietary fiber supplements within 2 weeks before study start; plan to have surgery during the time of the study; a history of alcohol or drug abuse, taking anti-coagulant medications, participation in another clinical trial within last three months. Intervention: 40 Control group: 40 There were no statistically significant differences between the synbiotic and the placebo groups in gender, age, physical development and IBS severity. Gender: I 71% female, C 73% female Age: I 43 years, C 37 years. IBS severe: I 60%, C 70% IBS SSS: I 318, C 326	that were used in the present study. Additionally, the probiotic mixture was enriched with Lactobacillus rhamnosus FloraActive 19,070 strain, which when administered to babies with infant colic significantly reduced the time of crying and anxiety compared to the control group [27]. We decided on a dose of 10 billion/day, taking into account the results of the meta-analysis assessing the optimal dose of probiotics in IBS, which showed that the dosage of 109–1010 CFU/day may be a reference range [28]. The synbiotic preparation also contained prebiotic scFOS from Actilight® (Beghin Meiji, Marckolsheim, France) in a dose of 947 mg in each sachet. scFOS was obtained from sugar beet by a bio-enzymatic reaction and contained 44% of glucose linked 2 units of fructose (GF2), 46% GF3, and 10% GF4. The molecular weight of scFOS was 603 g/mol, and purity of scFOS was at least 95% of dry substance.		group) and one urgent hospitalization due to heart failure in the placebo group. In the next 4 weeks, two patients from each group were excluded from the study. Finally, a total of 68 patients (35 receiving the synbiotic preparation and 33 placebo) finished the study.	

Shi, 2020	Type of study: RCT Setting and country: hospital / outpatient department, China Funding and conflicts of interest: This study was funded in full by the Wu Yingkai Foundation for Medical Research and Development, Beijing (grant numbers XD201907). The authors declare no competing interest.	Inclusion criteria:: (1)25-70 years of age; (2) repeated episodes of abdominal pain, abdominal distension, or bowel habit abnormalities (constipation, diarrhea, or mixed constipation and diarrhea), with a period of more than 6 months; (3) no past history of any chronic disease; and (4) no history of abdominal surgery. Exclusion criteria: (1) contraindications for colonoscopy, disable to tolerate colonoscopy and bowel preparation; (2) taking drugs affecting the gut microbiota within a month before the selection (e.g., antibiotics, antiacid drugs, and probiotics) and drinking alcohol; (3) colonoscopy results of colon malignant or benign tumor, colorectal enteritis, colorectal ulcers, and inflammatory bowel disease; and (4) pregnant women. N total at baseline: Intervention: 25 Control: 25 Important prognostic factors[2]: *Age ± SD:* *I: 41 +/- 11* *C: 43 +/- 12* *Sex:*	Describe intervention (treatment/procedure/test): Medilac-S (live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules, 500 mg per time, three times per day, Hanmi Pharm Co. Ltd., Beijing, China) for 4 weeks.	Describe control (treatment/procedure/test): unknown.	Length of follow-up: 4 weeks. Loss-to-follow-up: ?? Intervention: N (%) Reasons (describe) Control: N (%) Reasons (describe)	Gastrointestinal symptom rating scale (GSR'S) covers 15 gastrointestinal symptoms, each classified into four severity categories (score of 0–3).

		I: 64% F *C: 76% F* Groups comparable at baseline? Yes				
Sadrin, 2020	Type of study: RCT Setting and country: office-based physicians and a hospital, France Funding and conflicts of interest: This study was fundedby OSEO Innovation-Bpifrance (MaisonsAlfort, France) and Laboratoire Denel-Codifra (Le Chesnay, France). Stéphane Sadrin is an employee of Laboratoire Denel-Codifra (Le Chesnay, France), which supplied probiotics and the placebo for the research. The remaining authors disclose no competing interests.	Inclusion criteria: aged between 30 and 60 years old; diagnosed for IBS according to Rome III criteria; presented with a negative coprological and inflammatory balance (negative CRP blood test) for over 6 months Exclusion criteria: l if they presented with an organic intestinal disease, a severe or active disease with multiple treatments, intestinal parasitic infection in the last 6 months, inflammatory bowel disease or a history of previous abdominal surgery (except appendectomy, caesarean birth, tubal ligation, hernia). In addition, subjects were excluded if they changed their medication in the last 2 months, took probiotics in the last 2 months or antibiotic therapy in the last 30 days, received current antidepressant or antipsychotic treatment, and received antimycotic and antiseptic treatment or treatment affecting gastrointestinal transit as well as chronic use of antalgic and antispasmodic medications. Additional exclusion criteria are	Describe intervention (treatment/procedure/test): 8 weeks The study product was provided in the form of vegetable capsule containing a blend of two viable lyophilized L. acidophilus strains: L. acidophilus NCFM (FDA GRAS Notice 000357, strain number ATCC SD5221, Danisco Inc. Madison, Wisconsin, United States) and L. acidophilus subsp. helveticus LAFTI L10 (strain number CBS 116.411, Lallemand Health Solutions, Blagnac, France). This mixture of two probiotic strains provides for each 2.5 × 109 colony-forming unit (cfu) for a total of 5 × 109 cfu per capsule. Formulations of the indistinguishable investigational products are detailed in the	Describe control (treatment/procedure/test): 8 weeks Placebo. Unknown.	Length of follow-up: 9 weeks Loss-to-follow-up: Intervention: N 1 (2,5%) Reasons (describe) unknown. Control: N 0 (0%) Reasons (describe)	The primary outcome was abdominal pain score assessed with a 100-mm visual analogue scale. Secondary outcomes included scores of bloating, flatus and rumbling assessed with a 100-mm visual analogue scale, a composite score and bowel habits.

		detailed in the LAPIBSS protocol. N total at baseline: Intervention: 40 Control: 40 Important prognostic factors[2]: *Age ± SD:* *I: 49 +/- 8* *C: 49 +/- 8* *Sex:* *I: 73% F* *C: 70% F* Groups comparable at baseline? Yes for age, weight, sex ratio, abdominal pain, bloating, flatus, rumbling, composite score, stool frequency, stool consistency.	supplementary material (Table S-1). These products were specially manufactured for the study by Laboratoire Denel-Codifra (Le Chesnay, France). The trial dose was 2 capsules/day taken orally; one in the morning and the other one in the evening with a full glass of water half an hour before eating			
Martoni, 2020	Type of study: RCT Setting and country: outpatients, India Funding and conflicts of interest: his research was funded by UAS Laboratories LLC. Christopher J. Martoni and Gregory Leyer are employees of UAS Laboratories but were not	Inclusion criteria: Healthy adults, aged 18 to 70 years, meeting Rome IV diagnostic criteria for IBS were recruited Exclusion criteria: Participants with organic disease, a history of surgical resection of the stomach, small or large intestine, a history of inflammatory bowel disease, complications from infectious enteritis, hyperthyroidism or hypothyroidism, a history of diet-based intolerance, drug or alcohol	Describe intervention (treatment/procedure/test): The probiotic study products consisted of either L. acidophilus DDS®-1 or B. animalis subsp. lactis UABla-12™. L. acidophilus DDS-1 or B. lactis UABla-12 capsules, which each contained a potency of not less than (NLT) 1 × 1010 CFU/capsule, were formulated with lyophilized probiotic and	Describe control (treatment/procedure/test): Placebo capsules were formulated with microcrystalline cellulose.	Length of follow-up: 42 days intervention Loss-to-follow-up: Intervention: N 4 + 4 (%) Reasons (describe) unknown Control: N 3 (%) Reasons (describe) unknown	Abdominal pain severity (APS NRS), IBS symptom severity (IBS SSS), stool form and frequency (Bristol Stool Scale), IBS related quality of life (IBS QoL) and perceived stress (PSS).

	involved in the study conduct, data management or statistical analysis.	abuse within the past 6 months, a history of malignant tumors, severe depression or anxiety disorder, or uncontrolled hypertension were excluded. Additional exclusion criteria included individuals with unstable medical conditions, type I or II diabetes, a history of cancer or abdominal surgery, immunocompromised conditions, or an active eating disorder. Smokers, defined as ≥ 1 cigarette a day and individuals consuming > 2 standard alcoholic drinks daily over the prior 3 months were excluded N total at baseline: Intervention: 110 en 111 Control: 112 Important prognostic factors[2]: *Age ± SD:* *I: 39 (12) en 42 (11)* *C: 38 (10)* *Sex:* *I: 52% en 47% F* *C: 50 % F* Groups also comparable at baseline for BMI, BP, GAD, PHQ, alcohol consumption.	microcrystalline cellulose.			
Lewis, 2020	Type of study: RCT Setting and country: open population,	Inclusion criteria:: aged 18 years or older, IBS diagnosed according to the Rome III criteria, and willingness to discontinue probiotic	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Length of follow-up: 8 weeks Loss-to-follow-up:	IBS symptom severity (IBS-SSS), general health (SF 36), psychological

	Canada Funding and conflicts of interest: This research was funded by Lallemand Health Solutions (LHS). LHS owns Bifidobacterium longum R0175 and Lactobacillus paracasei HA-196. TAT, RB and AP are employees of Lallemand Health Solutions. LHS was involved in the design of the study, revising the manuscript and decision to publish the results but was not involved in data collection and analyses, or writing the manuscript. The corresponding author oversaw collection and analysis of data and had final responsibility for the decision to submit for publication.	consumption for the duration of the study <u>Exclusion criteria</u>: Participants were excluded if they used medications to manage IBS symptoms or narcotics in the past month, history of gastrointestinal surgery, gastrointestinal disease (except hemorrhoids and uncomplicated diverticula) or family history of colorectal cancer, inflammatory bowel disease, or celiac sprue. <u>N total at baseline</u>: Intervention: 84 + 86 Control: 81 <u>Important prognostic factors</u>[2]: *Age ± SD:* *I: 42 (12) and 42 (17)* *C: 42 (16)* *Sex:* *I: 80 and 74% F* *C: 79% F* Groups are comparable at baseline for type of IBS, race, ethnicity, gender and age.	Each probiotic capsule contained 10 × 109 colony forming units (CFU) of either freeze-dried B. longum (Lot Numbers: NH131210-1VB and NH151104-ICP) or L. paracasei (Lot Numbers: NH131217-1VB and NH151106-ICP), with potato starch and magnesium stearate as excipients.	The placebo (Lot Numbers: NH131226-ISC and NH151028-ICP) contained only potato starch and magnesium stearate.	Intervention: N 4 + 3 / 3 + 1 (%) Reasons (describe) Withdrew or withdrawn consent Control: N 5 / 2 (%) Reasons (describe) withdrew or withdrawn consent	well – being. HADS.
Kim, 2020	Type of study: RCT	<u>Inclusion criteria</u>: (a) age between 18 and 75 years, (b) diagnosed with	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedur	<u>Length of follow-up</u>: 8 weeks	IBS symptoms, stool frequency.

	Setting and country: secondary care, Korea Funding and conflicts of interest: This research was supported by research fund from the Clinical Research Institute of the Seoul National University Hospital. This work was also carried out with the support of ''Cooperative Research Program for Agriculture Science & Technology Development (Project No. PJ01123002)'', Rural Development Administration, Republic of Korea. The authors have no financial conflicts of interest to declare.	diarrhea-dominant IBS according to Rome II criteria (c) without any organic abnormalities by physical and laboratory examination during the screening period. <u>Exclusion criteria</u>:: (a) intolerance to probiotics or lactose, (b) pregnancy or lactation, (c) severe systemic illness (liver cirrhosis, congestive heart failure, chronic renal failure, angina, uncontrolled hypertension, endocrine disorder, metabolic disorder, or malignant tumors), (d) history of inflammatory bowel disease or psychiatric disorder, (e) alcohol or drug addiction, (f) previous abdominal surgery other than appendectomy, (g) being judged ineligible for articipation in clinical trials by clinicians <u>N total at baseline</u>: Intervention: 32 Control: 31 <u>Important prognostic factors</u>[2]: in supplement *Age ± SD:* *I:* *C:* *Sex:* *I: % M* *C: % M*	Combined probiotics, which included 5 strains of probiotics (Bifidobacterium longum BORI, Bifidobacterium bifidum BGN4, Bifidobacterium lactis AD011, Bifidobacterium infantis IBS007, and Lactobacillus acidophilus AD031) were used in this study. A capsule was composed of a total of 5 9 109 viable cells in a lyophilized powder form with the other ingredients including maltodextrin, corn starch, and silicon dioxide. 3x daily	e/test): The placebo capsule had almost the same contents as the active medication, even though the bacteria were replaced with maltodextrin. 3x daily	<u>Loss-to-follow-up</u>: Intervention: N 0 (%) Reasons (describe) Control: N 0 (%) Reasons (describe)	IBS sss IBS qol abdominal pain

		Groups comparable at baseline? There were no significant differences in the baseline clinical and laboratory characteristics between the probiotic a placebo groups				
Gayathri, 2020	Type of study: RCT Setting and country: secondary care, India. Funding and conflicts of interest: not reported	Inclusion criteria: Subjects of both sex, aged above 18 years, and meeting ROME III criteria of IBS were included in the study. Exclusion criteria: Subjects with organic intestinal diseases; pregnant women and children; immunocompromised individuals; food allergies; with comorbid conditions like diabetes, hypertension, and cardiovascular diseases; and subjects on prior probiotics therapy were excluded N total at baseline: Intervention: 52 Control: 48 Important prognostic factors[2]: *Age ± SD:* *I: 42(15)* *C: 40 (13)* *Sex:* *I: 39% F* *C: 29% F* *IBS-D 65%*	Describe intervention (treatment/procedure/test): Standard treatment for 2 weeks along with Saccharomyces cerevisiae CNCM I3856 (2 × 109 c.f.u) capsules twice daily for 8 weeks. Standard treatment for IBS included antidiarrheal—loperamide 2 mg BD 2 weeks for diarrhea predominant IBS, antispasmodic—dicyclomine 20 mg QID for 2 weeks for constipation predominant IBS and for IBS-M subjects, treatment depends on the patient's presentation (antidiarrheal/laxative)	Describe control (treatment/procedure/test): standard treatment for IBS for 2 weeks along with placebo twice daily for 8 weeks.	Length of follow-up: 10 weeks Loss-to-follow-up: Intervention: N 4 (%) Reasons (describe) Control: N 4 (%) Reasons (describe)	IBS symptoms (abdominal pain likert scale 1-7) and adverse events.

		Groups comparable at baseline? All the baseline characteristics of the subjects are similar in both the control group and the treatment group and showed no significant differences				
Barraza, 2020	Type of study: pilot RCT Setting and country: secondary care, Mexico Funding and conflicts of interest: This study received no funding. The authors declare that they have no conflicts of interest.	Inclusion criteria: age range 18–59 years, meeting Rome IV criteria for the IBS-D-predominant or mixed subtype [24], accepting participation in the study, and signing of informed consent. Exclusion criteria: e unexplained weight loss, presence of blood in the gastrointestinal system, anemia, use of systemic antibiotics, NSAIDs, or antipsychotics within 3 weeks before the study starts, pregnancy or lactation, a history of gastrointestinal neoplasia, suspicion of celiac disease, inflammatory bowel disease, endometriosis or pelvic inflammatory disease, abdominal surgery in the 2 years prior to the study (3 months for appendectomy or herniorrhaphy), allergy to any of the medications in the formula or using them in the last 3 months, BMI < 18, or not agreeing to signing of informed consent N total at baseline: Intervention: 18 + 19 Control: 18	Describe intervention (treatment/procedure/test): group 1 received 2 g of i3.1 probiotic formulation (effective dose 3 × 109 cfus) once daily for 6 weeks; group 2 received a capsule containing 60-mg alverine and 300-mg simethicone every 8 h (i.e., thrice daily), in combination with 2 g of i3.1 probiotic formulation (effective dose 3 × 109 cfus) once daily, for 6 weeks; The i3.1 probiotic formulation (ABBiotics SA, Barcelona, Spain) was a combination of 3 lactic acid bacteria: L. plantarum CECT 7484, L. plantarum CECT 7485, and P. acidilactici CECT 7483	Describe control (treatment/procedure/test): group 3 received the placebo capsule every 8 h (i.e., thrice daily) for 6 weeks	Length of follow-up: 6 weeks Loss-to-follow-up: Intervention: N 0 (%) Reasons (describe) Control: N 0 (%) Reasons (describe)	QoI (IBS QoL 0-100), abdominal pain (VAS 0-10), stool consistency (Bristol scale 1-7), adverse events

		Important prognostic factors[2]: *Age ± SD:* *I: 45 (9) + 45 (11)* *C: 46 (5)* *Sex:* *I: 67 + 79% F* *C: 56% F* Groups comparable at baseline for age, gender, BMI, Hb, glucose, IBS-type, IBS Qol, Bristol scale, abdominal pain VAS scale.				
Andresen, 2020	Type of study: RCT Setting and country: primary and secondary care, Germany Funding and conflicts of interest: Synformulas funded the study. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. PL has received reimbursement of travel expenses from Falk, outside the submitted work. VA	Inclusion criteria: 18 years and older, criteria for IBS according to Rome III, abdominal pain >=4 on an 11 point numerical rating scale. Exclusion criteria: inflammatory organic gastrointestinal diseases, systemic diseases , cancer, autoimmune diseases, diabetes, lactose intolerance, immune deficiency, abdominal surgery, hyperthyroidism, etc. N total at baseline: Intervention: 221 Control: 222 Important prognostic factors[2]: *Age ± SD:* *I: 40 (13)* *C: 43 (14)* *Sex:*	Describe intervention (treatment/procedure/test): 8 weeks 2 capsules 1x10 9 B fididum	Describe control (treatment/procedure/test): Maltodextrine	Length of follow-up: 12 weeks Loss-to-follow-up: Intervention: N 14 (%) Reasons (describe) Adverse events Non compliance Other Control: N 13 (%) Reasons (describe) Adverse events Non compliance Other	Pain response (abdominal pain 11 point numerical rating scale / IBS SSS), SF 12, global relief response

	has received speaker and consulting fees from Bayer, Falk and others, outside of the submitted work. JG has received consultant fees from Synformulas, outside of the submitted work.	*I: 70% F* *C: 69% F* Groups comparable at baseline for age, gender, height, weight, BMI, abdominal pain, IBD type.				
Stevenson, 2019	Type of study: RCT Setting and country: ?, South Africa Funding and conflicts of interest: This study was funded in part by Nestle Nutrition Institute Africa (www.nnia.org) and the South African National Research Foundation [gun number 2075266]. No potential conflict of interest was reported by the authors.	Inclusion criteria: described in other article. Exclusion criteria: described in another article N total at baseline: Intervention: 19 + 16 Control: 9 + 8 Important prognostic factors[2]: *Age ± SD:* *I: 52 (25-75)* *C: 42-49 (32-72)* *Sex: 51 of 52 female* Groups comparable at baseline? Yes , for age, BMI and duration of IBS symptoms.	Describe intervention (treatment/procedure/test): The test product contained 5 × 109 colony forming units (CFU) of L. plantarum 299v	Describe control (treatment/procedure/test): micro-crystalline cellulose powder (mean content of cellulose per capsule 256 mg),	Length of follow-up: 12 weeks Loss-to-follow-up: 0 Intervention: N (%) Reasons (describe) Control: N (%) Reasons (describe)	IBS symptoms with Francis Severity Score
Oh, 2019	Type of study: RCT Setting and country: secondary care, Korea	Inclusion criteria: Vietnamese individuals living in Korea aged between 19 and 60 years who met the Rome III criteria [27] for the diagnosis of IBS were eligible to participate.	Describe intervention (treatment/procedure/test): The probiotic mixture (Foodis Lactobacillus, Ildong	Describe control (treatment/procedure/test): Placebo capsules contained the	Length of follow-up: 4 weeks Loss-to-follow-up: Intervention:	Overall IBS symptom with SGA (0 (unchanged)-4 (completely relieved)), abdominal pain

	Funding and conflicts of interest: This work was supported by the Korea Institute of Planning and Evaluation for Technology in Food, Agriculture, Forestry and Fisheries (IPET) through the High Value-Added Food Technology Development Program, funded by the Ministry of Agriculture, Food and Rural Affairs (MAFRA) (316061-3). The authors declare that they have no competing interests in association with this paper.	<u>Exclusion criteria</u>: constipation-predominant IBS (IBS-C), previous history of abdominal surgery except appendectomy and caesarian section, inflammatory bowel disease, and concurrent severe illnesses (cancer, cardiovascular, or pulmonary disease). In addition, patients who had used antipsychotics, antibiotics, and probiotics within 2 weeks were also excluded. <u>N total at baseline</u>: Intervention: 28 Control: 27 <u>Important prognostic factors</u>[2]: *Age ± SD:* *I: 33 (27-39)* *C: 33 (28-45)* *Sex:* *I: 64% F* *C: 79% F* Groups comparable at baseline? The two groups were comparable for age, sex, body mass index (BMI), stool form, IBS subtype, and abdominal pain.	Group, Seoul, Korea) contained three strains of the Lactobacillus species, L. paracasei, L. salivarius, and L. plantarum.	excipient (olive oil and pine tree oil) only.	N 2 (%) Reasons (describe) withdrawn consent Control: N 3 (%) Reasons (describe) withdrawn consent	with VAS (0 (none)-10 (very severe))
Madempudi, 2019	Type of study: RCT Setting and country: ?, India.	<u>Inclusion criteria</u>: IBS, fulflling Rome III criteria i.e. abdominal discomfort/pain associated with two or more of the following at least 25% of the time: improvement with	Describe intervention (treatment/procedure/test): B. coagulans Unique IS2	Describe control (treatment/procedure/test): Placebo	<u>Length of follow-up</u>: 8 weeks <u>Loss-to-follow-up</u>: Intervention:	The primary efficacy outcomes were measured by assessing, (a) pain intensity

	Funding and conflicts of interest: Tis study was fully funded by Unique Biotech Ltd., Hyderabad, India. Each of the authors or their respective organizations were financially compensated by Unique Biotech Ltd for their contribution in the study. R.S.M., J.J.A. and J.N. are employed by Unique Biotech Ltd. which is a manufacturer of probiotics. They wish to state that the study was conducted independently with no intervention on their part during the duration of the study	defecation, onset associated with change in frequency of stool/and or in the form (appearance) of stool // (a) patients of either sex in the age group of 18–60 years, (b) fulflling Rome III criteria of IBS, (c) no evidence of infammatory, anatomic and metabolic or neoplastic process, (d) weekly, average worst abdominal pain score of ≥3.0 on 11 point scale, (e) average of less than 3 CSBMs per week (not due to the laxatives), and (f) able to provide informed consent <u>Exclusion criteria</u>: (a) patients with Bristol stool scale score of 7 or 6 for >25% of their bowel movements during the 12 weeks before screening or, during the run-in period (except laxative induce efect). (b) disease that may affect bowel motility other than IBS, (c) presence of rectal bleeding, recent weight loss (>5 kg in the past month) or iron defciency anemia, (d) history of lactose intolerance and other malabsorption syndromes (e.g. fructose), (e) previous abdominal surgery and severe systemic diseases, (f) use of probiotic within 3 months of screening visit, (g) pregnant or breast-feeding or planning on becoming pregnant/women of child-bearing potential not using eff ective contraception, (h) use of any			N (%) Reasons (describe) Control: N (%) Reasons (describe) In total 28; reasons: protocol deviations (11), violations (2), unavailable during follow up (15).	on 11-point numerical rating scale (NRS) and (b) frequency of CSBM/SBM. The secondary efficacy outcomes were measured by (a) severity of symptoms on 6-point Likert scale, (b) stool consistency on Bristol stool scale, (c) patient and physician global assessment. And adverse events.

		antibiotics (e.g. neomycin, rifaximin) within 1 month of screening, (i) daily use of laxative within one month of screening/current usage, or usage from the past 3 months, of narcotics or other medications for IBS management (e.g. alosetron, tegaserod and lubiprostone). N total at baseline: Intervention: 68 Control: 68 Important prognostic factors[2]: *Age ± SD:* *I: 44* *C: 42* *Sex:* *I: 23% F* *C: 33% F* Groups comparable at baseline? Yes, for gender, age, height, weight.				
Helo, 2019	Type of study: RCT Setting and country: secondary care, Jordan. Funding and conflicts of interest: Funding not stated. The authors declare that there is no	Inclusion criteria: Patients included in the study were males and females and the age between 18 and 70, diagnosed with IBS according to the Rome III criteria. Exclusion criteria: Subjects were excluded if they had organic intestinal diseases, underwent treatments that influence is, or taking any medication or herbals or	Describe intervention (treatment/procedure/test): four weeks two tablets of cerevisiae CNCM I-3856 (1000 mg) with a meal	Describe control (treatment/procedure/test): calcium gluconate 500 mg	Length of follow-up: 4 weeks Loss-to-follow-up: Unknown Intervention: N (%) Reasons (describe) Control:	scores of abdominal pain/discomforts, bloating and flatulence, defecation difficulty, stool frequency, and stool consistency. A pain/discomfort scored from 0 to 7

	conflict of interest regarding the publication of this paper.	probiotics. N total at baseline: Intervention: 177 Control: 170 Important prognostic factors[2]: *Age ± SD:* not in article *I:* *C:* *Sex:* not in article *I: % M* *C: % M* Groups comparable at baseline? Yes, for IBS type.			N (%) Reasons (describe)	(Likert scale). Changes in stool frequency and consistency were followed daily using the Bristol Stool Scale from (1) to (7). Adverse events.
Al-Jassim, 2019	Type of study: RCT Setting and country: secondary care?, Iraq. Funding and conflicts of interest: There are no conflicts of interest of any sort. No information about funding.	Inclusion criteria: constipation-predominant IBS-C Rome III, and > 18 years of age Exclusion criteria: Pregnant or breastfeeding females, the presence of uncontrolled cardiovascular disease, diabetes mellitus (type I or II), psychological conditions, renal or hepatic sickness, uncontrolled thyroid disease, Parkinson's disease, previous gastrointestinal surgery, allergy to ginger or S. cerevisiae (Brewer's yeast), and exclude patients taking medications that are frequently	Describe intervention (treatment/procedure/test): 500 mg Brewer's yeast Or 1g ginger Brewer's yeast (S. cerevisiae) 500 mg tablets of Adrien Gagnon Company were used in the study. Ginger root powder (Zingiber officinale Roscoe, Zingiberaceae) was capsulated in a dose of 1 g	Describe control (treatment/procedure/test): The placebo capsules were prepared to contain brown sugar.	Length of follow-up: 20 days Loss-to-follow-up: 0 Intervention: N (%) Reasons (describe) Control: N (%) Reasons (describe)	IBS severity scale (IBS-SS) and visual analog scale of IBS (VAS-IBS) severity of pain, abdominal distention, and constipation (IBS-C) subjects rated on a 0–100 scale, where 0 = none symptom and 100 = more severe symptom

		associated with constipation such as contraceptives, proton-pump inhibitors, beta-blockers, ACE inhibitors, calcium antagonists, statins, diuretics, and barbiturates. <u>N total at baseline</u>: Intervention: 15 + 15 Control: 15 <u>Important prognostic factors</u>[2]: No information in article. *Age ± SD:* *I:* *C:* *Sex:* *I: % M* *C: % M* Groups comparable at baseline?	daily capsule provided by simply organic company.			

Peppermint oil – Evidence table for systematic review of RCT's and observational studies (intervention studies)

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up
Alammar, 2019 [individual study characteristics deduced from Alammar, 2019] PS., study characteristics and results are extracted from the SR (unless stated otherwise)	SR and meta-analysis of RCT's *Literature search up to April 11, 2018* **A**: Alam, 2013 **B**: Cash, 2016 **C**: Capanni, 2005 **D**: Cappello, 2007 **E**: Carling, 1989 **F**: Dew, 1984 **G**: Lech, 1988 **H**: Liu, 1997 **I**: Merat, 2009 **J:** Rees, 1979 **K**: Schneider, 1990 **L:** Weiss, 1988 Setting and Country: **A**: Bangladesh **B**: USA **C**: Italy **D**: Italy **E**: Sweden **F**: Wales **G**: The Netherlands **H**: China **I**: Iran **J:** UK **K**: USA **L:** Germany Source of funding and conflicts of interest: Funding for the SR was not applicable and no conflict of interest.	Inclusion criteria SR: 1. Randomized placebo-controlled trials comparing peppermint oil and placebo for irritable bowel syndrome with a minimum treatment duration of 2 weeks. 2. Adult patients with irritable bowel syndrome as diagnosed using any of the following criteria for IBS: Manning, Rome I, II, III, IV diagnostic criteria. Exclusion criteria SR: 1. Non-randomized trials; observational studies such as cohort study, cross-sectional study, etc. 2. Patients having organic disease or did not have organic disease excluded. 3. Treatment duration of less than 2 weeks. 4. Studies with inadequate data. *12 studies included* Important patient characteristics at baseline: *Number of patients:* **A**: 74 **B**: 72 **C**: 178 **D**: 57 **E**: 40 **F**: 29 **G**: 47 **H**: 110 **I**: 90 **J:** 18 **K**: 60 **L:** 60	Enteric-coated Peppermint Oil Capsules	Placebo	End-point of follow-up: **A**: 6 weeks **B**: 4 weeks **C**: 12 weeks **D**: 4 weeks **E**: 2 weeks **F**: 2 weeks **G**: 4 weeks **H**: 4 weeks **I**: 8 weeks **J:** 3 weeks **K**: 6 weeks **L:** 3 weeks For how many participants were no complete outcome data available? *Number of patients completed:* **A:** 65/70 **B**: 70/72 **C**: 173/178 **D**: 50/57 **E**: 38/40 **F**: 29/29 **G**: 42/47 **H**: 101/110 **I**: 60/90 **J:** 16/18 **K**: 47/60 **L:** 46/60

Peppermint oil – Evidence table for intervention studies (baseline characteristics)

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up
Weerts, 2020	Type of study: randomized, double-blind, placebo-controlled trial Setting and country: 4 hospitals in the Netherlands Funding and conflicts of interest: Funding for this study was provided by a grant received from ZonMw (The Netherlands Organisation for Health Research and Development [Dutch government]), grant number 836031017. The study was initiated by the academic authors in collaboration with WillPharma SA, Wavre, Belgium.	Inclusion criteria: ▪ Patients between 18 and 75 years of age ▪ Rome IV diagnostic criteria for IBS ▪ If alarm symptoms were present (e.g. unexplained rectal blood loss or weight loss), a colonoscopy or other relevant tests were performed to exclude organic disease. Exclusion criteria: ▪ Exclusion criteria were inability to read or understand Dutch ▪ History of GI disorders such as inflammatory bowel disease, celiac disease, or thyroid dysfunction (if not well-regulated) ▪ History of major abdominal surgery or radiotherapy interfering with GI function. An uncomplicated appendectomy, cholecystectomy, or hysterectomy were allowed unless within six months prior to screening ▪ Use of peppermint oil capsules in the three months prior to screening ▪ A known allergic reaction to peppermint oil ▪ Current drug abuse ▪ History of liver or gallbladder/biliary disease ▪ Women had to use contraceptives and have a negative urine pregnancy test, or be postmenopausal for at least two years. ▪ The use of one antidepressant or one PPI was allowed, if a patient had been and would stay on a stable dose. Prohibited concomitant medications included opioids, prokinetics, stimulant laxatives (i.e. bisacodyl), linaclotide, prucalopride, and anti-spasmodic drugs. Regular use of NSAIDs, antibiotics, osmotic laxatives, and antidiarrheal drugs was prohibited. N total at baseline: Intervention 1 (Small-intestinal–release	Eligible patients entered a 14-day pretreatment period during which they scored their daily worst abdominal pain in a digital symptom diary, scored on an 11-point numerical rating scale (NRS) from0 (no pain) to 10 (worst possible pain). Subsequently, those with a mean worst abdominal pain score of at least 3 were then randomly assigned to 182 mg of: 1) **small-intestinal–release peppermint oil** (Tempocol, WillPharma SA, Wavre, Belgium) or 2) **ileocolonic-release peppermint oil** (Tempocol, core capsules, coated with a ColoPulse [WillPharma SA, Wavre, Belgium] coating layer25,27) intake orally. Patients were instructed to self-administer 3 capsules daily, 30 minutes before breakfast, lunch, and dinner, for 8 weeks.	Placebo (microcrystalline cellulose)	Length of follow-up: 6 months Loss-to-follow-up: In total, 11 patients withdrew from the study: 9 discontinued as a result of adverse events, 1 because of insufficient therapeutic response, and 1 for personal reasons. Exact numbers per group were not described.

		peppermint oil): 62 Intervention 2 (Ileocolonic-release peppermint oil): 63 Control: 64 <u>Important prognostic factors</u>[2]: *Age, mean ± SD:* *I1: 32.0 (11.1)* *I2: 34.4 (13.1)* *C: 35.5 (15.2)* *Sex:* *I1: 17.7% M* *I2: 25.5%* *C: 23.4% M* *IBS subtype:* *Diarrhea, n(%)* I1: 25 (40.3%) I2: 29 (46.0%) C: 29 (45.3%) *Constipation, n(%)* I1: 12 (19.4%) I2: 16 (25.4%) C: 14 (21.9%) *Mixed, n(%)* I1: 15 (24.2%) I2: 13 (20.6%) C: 12 (18.8%) *Undefined, n(%)* I1: 10 (16.1%) I2: 5 (9.7%) C: 9 (14.1%) Baseline characteristics were balanced across treatment groups.			

Linaclotide – Evidence table for systematic reviews (baseline characteristics)

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up
Atluri, 2014 [individual study characteristics deduced from [1st author, year of publication]] PS., study characteristics and results are extracted from the SR (unless stated otherwise)	SR and meta-analysis of RCT's *Literature search up to [month/year]* **A**: Johnston, 2010 **B**: Chey, 2012 **C**: Rao, 2012 <u>Study design</u>: RCT [parallel] <u>Setting and Country</u>: **A:** USA **B**: USA **C**: USA <u>Source of funding and conflicts of interest:</u> **A:** Supported by Ironwood Pharmaceuticals; all authors were employees of Ironwoord. **B:** funded by Forest Research Institute and Ironwood Pharmaceuticals, Inc; authors were employees or paid consultants. **C:** funded by Forest Research Institute and Ironwood Pharmaceuticals, Inc; authors were employees or paid consultants.	Inclusion criteria SR: RCT's; Adult patients (≥18 years) with IBS-C based on Rome II or III diagnostic criteria. - Linaclotide 266, 290 or 300 lg once daily dose. Compared to placebo - Reporting clinical outcomes such as relief of abdominal pain and/or abdominal discomfort and bowel habits - Study duration > 12 weeks Exclusion criteria SR: Studies that recruited patients with organic constipation, drug-induced constipation or chronic idiopathic constipation Studies which only reported non-clinical outcomes such as colonic transit time were excluded. *3 studies included about linaclotide and IBS* <u>Important patient characteristics at baseline</u>: *All patients had fewer than 3 spontaneous bowel movements (SBMs) per week and 1 or more of the following symptoms for at least 12 weeks in the 12 months preceding entry into the study: (1) straining during ≥25% of bowel movements (BMs); (2) lumpy or hard stools during ≥25% of BMs; or (3) sensation of incomplete evacuation during 25% of BMs. In addition, during the 2-week pretreatment baseline period, patients were required to report a mean score of ≥2.0 for the daily assessment of nonmenstrual abdominal pain or abdominal discomfort (i.e., at least mild on a 5-point scale ranging from 1 =none to 5 =*	Describe intervention: **A**: Linaclotide, 300 µg/d (also 75, 150 and 600 ug were investigated) **B**: Linaclotide, 290 µg/d **C**: Linaclotide, 290 µg/d	Describe control: **A**: placebo; once daily **B**: placebo; once daily **C**: placebo; once daily	<u>End-point of follow-up</u>: **A**: 12 weeks **B**: 26 weeks **C**: 12 weeks <u>For how many participants were no complete outcome data available?</u> (intervention/control) **A:** **B**: **C**:

		very severe), as well as a mean of <3 complete SBMs (CSBMs) and ≤6 SBMs per week. N, mean age (intervention/ placebo) **A**: 84 patients, 46 yrs / 85 patients, 44 yrs **B**: 401 patients, 45 yrs / 403 patients, 44 yrs **C**: 405 patients, 43 yrs / 395 patients, 44 yrs *Sex (intervention/ placebo):* **A**: 92% / 92% female **B**: 92% / 87% female **C**: 91% / 90% female *IBS-criteria* **A:** Rome II **B**: Modified Rome II **C**: Modified Rome II Groups comparable at baseline? Yes			
Fukudo, 2018a	Type of study: double-blind, placebo-controlled RCT Setting and country: Japan, hospitals and clinics with departments of gastro-enterology Funding and conflicts of interest: This research was funded by Astellas Pharma Inc., Tokyo, Japan.	Inclusion criteria: Male and female outpatients aged 20-79 years were diagnosed as having IBS-C based on the Rome III diagnostic criteria. - for the last 3 months with IBS symptom onset at least 6 months prior to diagnosis. - recurrent abdominal pain or discomfort for at least 3 days/month in the last 3 months associated with two or more of the following: improvement with defecation, onset associated with a change in frequency of stool, and/or onset associated with a change in form (appearance) of stool. - hard or lumpy stools at least 25% of the time, and loose (mushy) or watery stools with fewer than 25% of bowel movements. Exclusion criteria: Organic diseases were excluded by colonoscopy or double-contrast barium enema if these examinations had not been performed within 5 years.	Describe intervention (treatment/ procedure/test): Linaclotide, 0,5 mg, orally taken, before breakfast	Describe control (treatment/ procedure/test): Placebo tablet, orally taken, before breakfast	Length of follow-up: 12 weeks (study continued with an open-label part for 40 more weeks.) Drop-out: Intervention: N=27 (11%) Reasons: adverse event (3%), lost to follow-up (1%), protocol deviation (2%), withdrawal by subject (3%), other (2%). Control: N=33 (13%) Reasons: adverse event (1%), lack of efficacy (4), protocol deviation (1%), withdrawal by subject (4%), pregnancy (1%), other (2%)

		N total at baseline: Intervention: 249 Control: 251 Important prognostic factors[2]: *Age ± SD:* *I: 41.6± 10.7* *C: 42.2±11.3* *Sex:* *I: 10% M* *C: 15% M* Groups comparable at baseline? Yes			
Fukudo, 2018b	Type of study: double-blind, placebo-controlled RCT Setting and country: Japan, hospitals and clinics with departments of gastro-enterology Funding and conflicts of interest: This research was funded by Astellas Pharma Inc., Tokyo, Japan.	Inclusion criteria: Male and female outpatients aged 20-64 years were diagnosed as having IBS-C based on the Rome III diagnostic criteria. - recurrent abdominal pain or discomfort for at least 3 days/month in the last 3 months associated with two or more of the following: improvement with defecation, onset associated with a change in frequency of stool, and/or onset associated with a change in form (appearance) of stool. - IBS symptom onset at least 6 months prior to enrolment - hard or lumpy stools at least 25% of the time, and loose (mushy) or watery stools with fewer than 25% of bowel movements. Exclusion criteria: Organic diseases were excluded by colonoscopy or double-contrast barium enema if these examinations had not been performed within 5 years. N total at baseline: Intervention: 116 + 111 + 112 + 107	Describe intervention (treatment/ procedure/test): Linaclotide, 0.0625, 0.125, 0.25 or 0,5 mg, once daily, orally taken, before breakfast We focused on the 0.25 g group.	Describe control (treatment/ procedure/test): Placebo tablet, once daily, orally taken, before breakfast	Length of follow-up: 12 weeks Drop-out: Intervention: N =13 (12%) Reasons: adverse events, violated the protocol, exacerbation of underlying disease or insufficient effect, other reasons. Control: N=11 (10%) Reasons: violated the protocol, adverse events, withdrew consent, exacerbation of underlying disease of insufficient effect

		Control: 113 Important prognostic factors[2]: *age ± SD:* *I: 41.8±9.8* *C: 41.6±10.8* *Sex:* *I: 11.6% M* *C: 10.7% M* Groups comparable at baseline? Yes			
Yang, 2018	Type of study: double-blind, placebo-controlled RCT Setting and country: China, USA, Canada, Australia and New Zealand, clinical centers Funding and conflicts of interest: This research was funded by AstraZeneca and Ironwood Pharmaceuticals	Inclusion criteria: Men and women ≥ 18 years of age were eligible if they met the Rome III IBS criteria. In the 3 months before screening (with symptom onset ≥ 6 months prior), patients had to report < 3 BMs per week and ≥ 1 additional bowel symptom during > 25% of BMs (straining, lumpy/hard stools, or sensation of incomplete evacuation). Exclusion criteria: Patients were excluded if they reported loose/mushy or watery stool (Bristol Stool Form Scale [BSFS] score of 6 or 7) in the absence of laxative, suppository, enema, or other prohibited medication use, for > 25% of BMs during the 3 months before screening; reported a BSFS score of 6 for > 1 SBM or 7 for any SBM during the 14 days before the randomization visit; or used rescue medicine (bisacodyl tablet or suppository) or other laxative, suppository, or enema on the calendar day before or day of the randomization visit. N total at baseline: Intervention: 417 Control: 422 Important prognostic factors[2]:	Describe intervention (treatment/ procedure/test): Linaclotide, 290µg, once daily, orally taken, ≥30 minutes before breakfast	Describe control (treatment /procedure/test): Placebo tablet, once daily, orally taken, before breakfast	Length of follow-up: 12 weeks Drop-out: Intervention: N =33 (7.9%) Reasons: protocol violation (n=11), withdrew consent (n=10), adverse events (n=7), lost to follow-up (n=3), insufficient therapeutic response (n=1), other (n=1) Control: N=48 (7.8%) Reasons: protocol violation (n=12), withdrew consent (n=25), adverse events (n=6), lost to follow-up (n=1), insufficient therapeutic response (n=4), other (n=0)

		age (range): *I: 41.0 (18-77)* *C: 41.3 (18-80)* *Sex:* *I: 20,1% M* *C: 15.6% M* Groups comparable at baseline? Yes			

Psychological therapies – Evidence table for intervention studies (baseline characteristics)

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/control (C)	Follow-up
Lackner, 2018 and 2019	Type of study: RCT. Setting and country: 2 tertiary centres in USA. The authors disclose no conflicts. The research reported in this article was supported by National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Grant 77738 (J.M.L.). The content is solely the responsibility of the authors and does not necessarily represent the official views of NIH.	Inclusion criteria: Adults (18–70 years) suffering from IBS as defined by Rome III criteria; if GI symptoms were at least moderately severe (i.e., occurred at least twice weekly and caused some self-reported interference in life domains such as work/school, social, household responsibilities). Exclusion criteria: Patients were excluded if they presented evidence of current structural/biochemical abnormalities or other primary GI disease that better explained gastrointestinal symptoms; had been diagnosed with a malignancy other than localized basal or squamous cell carcinomas of the skin in the past 5 years; were undergoing IBS-targeted psychotherapy; could not commit to completing all scheduled follow-up visits; had an unstable extraintestinal condition or a major psychiatric disorder (e.g., depression with severe suicidality, psychotic disorder); reported an active GI infection within 2 weeks before	Standard-CBT (S-CBT) involves 10 weekly, 60 min face-to-face sessions and emphasizes the provision of information regarding brain–gut interactions; self-monitoring of GI symptoms, their antecedents (i.e., triggers) and consequences; muscle relaxation to dampen physiological arousal and increase control over GI symptoms; worry control to challenge and dispute negatively skewed thinking patterns; flexible problem solving to aid in the deployment of more effective ways of managing realistic stressors; and relapse prevention training to maintain treatment gains. As a learning-based program, CBT assigns home exercises to facilitate acquisition of symptom self-management skills introduced in session through didactic instruction. Because minimal contact-CBT (MC-CBT) requires only four clinic visits over the 10-	The education condition (EDU) was equivalent to MC-CBT in time, attention, and the amount of home study materials received. EDU sessions were structured around education and support. Content included information about IBS, its clinical features, epidemiology, diagnostic criteria, medical tests, and treatment options as well as the role of stress, diet, and physical activity. Clinicians were prohibited from prescribing relevant behaviour changes (e.g., stress management skills). To mimic receipt of the MC-CBT patient workbooks, EDU patients received a copy of IBS: Learn to Take Charge Of It which emphasizes the “empowering” therapeutic value of patient education	Follow-up: 24 months. Loss-to-follow-up: Intervention MC CBT: N 17 (12%) Intervention S CBT: N 27 (18%) Control EDU: N 17 (12%) 9% of patients dropped out during treatment (no statistically significant percent differences between conditions). Dropout was unrelated to a range of demographic, psychological, and IBS-related variables measured at baseline, with one exception: an 8% treatment dropout rate for Whites versus a 22% rate for non-Whites (p , 0.05). There were no statistically significant differences between those lost to attrition

		evaluation; and used a gut-sensitive antibiotic during the 12 weeks prior to baseline assessment <u>N total at baseline</u>: 436 Intervention MC CBT: 145 Intervention S CBT: 146 Control EDU: 145 <u>Important prognostic factors</u>[2]: *Age ± SD: 41,4 (14,8)* *I MC CBT: 40,9 (14,6)* *I S CBT: 41,1 (14,4)* *C EDU: 42,2 (15,4)* *Sex: 80% F* *I MC CBT: 86% F* *I S CBT: 77% F* *C EDU: 79% F* All baseline characteristics were comparable across treatment groups.	week period, it relies more extensively on home study materials to cover the same procedures that S-CBT introduces at each session.		versus those retained on multiple demographic and clinical variables assessed at baseline, nor as a function of outcome variables at immediate posttest.
Everitt, 2019a-c	Type of study: RCT Setting and country: 74 general practices and three gastroenterology centres in London and South of England <u>Funding and conflicts of interest</u>: The project ACTI B (Assessing Cognitive–behavioural Therapy in Irritable Bowel syndrome)—a randomised controlled trial of clinical and cost-effectiveness of therapist-delivered cognitive–behavioural therapy and web-	<u>Inclusion criteria</u>: Participants were eligible if they fulfilled criteria for refractory IBS at screening, defined as: fulfilling ROME III criteria for IBS; reported ongoing clinically significant symptoms on IBS Symptom Severity Score (IBS-SSS), that is, ≧75; had been offered first-line therapies (eg, antispasmodics, antidepressants or fibre-based medications);	Two interventions were assessed: therapist TCBT and a low-intensity WCBT—an update of the Regul8 programme developed in MIBS including eight online sessions, with some therapist support. The CBT content of the treatment arms was similar, based on an empirical cognitive–behavioural model	All arms received TAU, control being TAU alone. TAU was a continuation of current medications and usual GP or consultant follow-up with no psychological therapy.	<u>Length of follow-up</u>: 24 months. <u>Loss-to-follow-up</u>: Intervention T CBT: N 67 (36%) Reasons unknown. Intervention W CBT: N 86 (46%) Reasons unknown.

	based self-management in irritable bowel syndrome—was funded by the National Institute for Health Research (NIHR) HTA Project: 11/69/02, with additional support from the NIHR Clinical Research Network. This paper represents independent research with some staff part funded by the NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. Competing interests PL is the director of PGfAR and a member of the Journals Library Board. RMM reports personal fees from training in IBS intervention for Central and North West London NHS Foundation Trust and University of East Anglia, outside the submitted work. TC reports grants from Guy's and St Thomas' Charity. She was a faculty member, Third International Conference on Functional (Psychogenic) Neurological Disorders, September 2017, Edinburgh, member of the IAPT Education and Training ERG (2016–), member of the IAPT Outcomes and Informatics Meeting (2016–) and president of the British Association of Behavioural and Cognitive Psychotherapies (2012–2015) for which she did not receive payment. Workshops were delivered on medically unexplained symptoms, during the conduct of the study (money paid into KCL for future research). TC has a patent background IP—manuals were developed prior to trial starting. SL and KG report grants from NIHR. The TSC chair, PW, was a colleague of TC in the past but he has recently retired. RMM reports personal	and had IBS symptoms ≧12months. Due to the increased risk of bowel cancer, potential participants aged >60years were only included if they had hospital consultant review ≤2years to confirm symptoms were IBS related and exclude serious bowel conditions. <u>Exclusion criteria</u>: Medical exclusion criteria: unexplained rectal bleeding or weight loss, IBD, coeliac disease, peptic ulcer disease, colorectal carcinoma. Other exclusions: patients < 18 years, unable to participate in CBT due to speech or language difficulties, no access to internet computer, received CBT in the last 2years, previous access to Regul8 during MIBS trial, currently participating in another IBS intervention trial. <u>N total at baseline</u>: 558 Intervention T CBT: 186 Intervention W CBT: 185 Control TAU: 187 <u>Important prognostic factors</u>[2]: *Age ± SD: 43,1 (13,2)* *I T CBT: 43,4 (12,5)* *I W CBT: 43,8 (13,6)* *C TAU: 42,0 (13,5)*	of IBS, consisting of education, behavioural and cognitive techniques, aimed at improving bowel habits, developing stable healthy eating patterns, addressing unhelpful thoughts, managing stress, reducing symptom focusing and preventing relapse. Treatments were standardised by provision of training, supervision and manuals for therapists. Participants randomised to TCBT arm received a detailed self-help manual including homework tasks and had six 1-hour telephone sessions with a CBT therapist at weeks 1, 2, 3, 5, 7 and 9. They also received two 1-hour booster sessions at 4 and 8months (total 8hours of therapist support). WCBT participants received online access to Regul8 and three 30min telephone therapy calls at weeks 1, 3 and 5, and two 30min booster sessions at 4 and 8months (2.5 hours of therapist support).		Control TAU: N 82 (44%) Reasons unknown.

	fees from training in IBS intervention for Central and North West London NHS Foundation Trust and University of East Anglia, outside the submitted work. Since this study was submitted, she has received payment for consultancy to Mahana Therapeutics. The CBT patient and the therapist manual used in the telephone CBT arm are freely available on the National Improving Access to Psychological Therapies (IAPT) for LTC/MUS website as part of evidence-based resources for IAPT. The patient manual is background IP developed by CI's RMM and TC in previous work. The therapist manual was developed for the ACTI B trial. These manuals were only made available once the 12-month ACTI B follow-up was complete. HAE, FB, GOR, AS, RH, SL, SH, SW, PMC, NC and RL have nothing to disclose.	*Sex: 76% F* *I T CBT: 75% F* *I W CBT: 78% F* *C TAU: 74% F* All baseline characteristics were well balanced between groups.			
Peter, 2018	Type of study: controlled trial. Setting and country: The study was conducted at the specialist outpatient-clinic for psychosomatics at the Gastroenterology and Hepatology Division, Department for Internal Medicine III, University Hospital of Vienna, Austria. Funding and conflicts of interest: The study was supported by the 2014 Marianne Ringler Award for research in psychotherapy and psychosomatics, www. marianneringlerpreis.eu, to JP. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.	Inclusion criteria: Included were IBS patients diagnosed according to Rome III criteria, aged between 18 and 75, and refractory to other IBS therapies. 'Refractory' here refers to IBS patients who had failed to improve on a variety of therapies (IBS medications, antidepressants, probiotics, psychotherapy), who were unhappy about their care and who had a persistently high rate of healthcare consumption. Antidepressants, anxiolytics and/or ongoing psychotherapy were allowed, since comorbid	The Gut-directed Hypnotherapy (GHT) treatment protocol used was the Manchester protocol of GHT and consisted of 10 weekly sessions (45 min) with six patients per group over a treatment period of 12 weeks. GHT was performed at the University Hospital by two experienced physicians (GM, MM) trained in Manchester (UK).	Untreated patients.	Length of follow-up: d on average 10 months after last GHT session Loss-to-follow-up: Intervention: N 0 (0%) Control: N 0 (0%)

	Conflicts of interest unknown.	psychological diagnoses, a common problem in IBS patients, were present in the study sample. Exclusion criteria: Patients with acute medical complications, pregnancy or insufficient knowledge of German were excluded from this study. N total at baseline: 74 Intervention: 37 Control: 37 Important prognostic factors[2]: *Age (range):* *I: 43 (28-67)* *C: 45 (29-57)* *Sex:* *I: 78% F* *C: 68% F* There were no differences in baseline characteristics between any of the subgroups, except a significantly lower count of known psychological diagnoses in invited non-participants (Mann-Whitney U tests and chi-squared tests).			
Jang, 2017	Type of study: RCT Setting and country: 4 colleges of nursing in the Republic of Korea.	Inclusion criteria: Participants were included if they were diagnosed as IBS-C by a gastroenterologist based on the questionnaire according to the	The CBT intervention consisted of 8 weekly group sessions of 80 minutes per session, with 60 minutes of thematic training and 20	General medical information.	Length of follow-up: 24 weeks. Loss-to-follow-up:

	Funding and conflicts of interest: Financial support: None. Conflicts of interest: None	Rome III criteria. Participants were at least 18 years old. <u>Exclusion criteria</u>: Individuals were excluded if they had a history of digestive or bowel surgery that may have caused similar symptoms; had an accompanying organic digestive disease that had the potential to affect their symptoms (eg, inflammatory bowel disease, lactose malabsorption, celiac disease, obstructive bowel disease, etc); had severe thyroid disease; had a serious mental disorder; used any drug that can affect bowel movements (eg, prokinetics, antispasmodics, digestive stimulants, antidiarrheal agents, antibiotics, antihistamines, laxatives, etc); or smoked. <u>N total at baseline</u>: 43 Intervention: 23 Control: 20 <u>Important prognostic factors[2]</u>: *Age ± SD: 21,4 (2,1)* *I: 21,6 (1,8)* *C: 21,2 (2,4)* *Sex:* *I: 100% F* *C: 100% F*	minutes of relaxation training. Major topics included establishing a therapeutic relationship and setting a therapeutic goal (session 1), education on IBS related to CBT (session 2), training in cognitive restructuring (sessions 3-5), training in effective coping (sessions 6 and 7), and training in enhancing positive emotion (session 8).24 CBT was conducted in a group of 4-6 participants by the same psychotherapist. The control group received general information about IBS (eg, overview, cause, symptoms, treatments, and diet) and other usual care for 50 minutes during the first week.		Intervention: N 2 (9%) Control: N 3 (15%) Two participants from the CBT group and 3 from the control group withdrew from the study because of personal problems (n = 1), health problems (n = 1), and loss of contact (n = 3), resulting in 38 participants having completed the study.

		The CBT and control groups did not differ in any demographic factors or baseline measures of the study variables.			

Bijlage 4: Quality assessment of systematic reviews and RCT's

Calprotectin: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/n.a.	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
An, 2019	Yes	Yes	No (excluded studies not described)	Yes	n.a.	Yes	No (no distinction between primary and secondary care)	No (not mentioned)	Yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?
8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

FIT: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/n.a.	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
Westwood, 2017	Yes	Yes	No, excluded not.	Yes	Yes	Yes	Yes	No	Yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?
8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

FIT – Table of quality assessment for Diagnostic tests

The methodological quality of included studies was assessed using **Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2)** with four domains to assess risk of bias and three domains to assess the applicability of the study to the review question.

Study reference (first author, publication year)	Risk of bias – patient selection[1] (Yes/No/Unclear)	Risk of bias – index test[2] (Yes/No /Unclear)	Risk of bias – reference standard[3] (Yes/No /Unclear)	Risk of bias – flow and timing[4] (Yes/No /Unclear)	Applicability concerns – patient[5] (Yes/No /Unclear)	Applicability concerns – index test[6] (Yes/No /Unclear)	Applicability concerns – reference standard[7] (Yes/No /Unclear)
Nicholson, 2020	No	No	No	No	Yes (high % CRC)	No	No
Lue, 2020	No	No	No	No	No	No	No
Mowat, 2019	No	No	No	No	No	No	No
Juul, 2018	No	No	No	No	No	No	No
Hogberg, 2017	No	No	No	No	No	No	No
Elias, 2016	No	No	No	No	No	No	No

1. Could the selection of patients have introduced *bias*?
2. Was a consecutive or random sample of patients enrolled? / b. Was a case-control design avoided? / c. Did the study avoid inappropriate exclusions?
3. Could the conduct or interpretation of the index test have introduced *bias*?
4. Were the index test results interpreted without knowledge of the results of the reference standard? / b. If a threshold was used, was it pre-specified?
5. Could the reference standard, its conduct, or its interpretation have introduced *bias*?
6. Is the reference standard likely to correctly classify the target condition? / b. Were the reference standard results interpreted without knowledge of the results of the index test?
7. Could the patient flow have introduced *bias*?
8. Was there an appropriate interval between index test(s) and reference standard? / b. Did all patients receive a reference standard?
9. Did patients receive the same reference standard? / d. Were all patients included in the analysis?
10. Is there *concern* that the included patients do not match the review question?
11. Is there *concern* that the index test, its conduct, or interpretation differ from the review question?
12. Is there *concern* that the target condition as defined by the reference standard does not match the review question?

Diet – Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study First author, year	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/not applicable	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
Ford (2018)	Yes	Yes	No (but can be found in Moayyedi 2014)	No (but can be found in Moayyedi 2014)	Not applicable	Yes	Yes	No	No

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?
8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Diet – Psyllium fibre: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study First author, year	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/not applicable	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
Dionne, 2018	Yes	Yes	Yes	No (age, gender and other characteristics of participants in the included studies were not mentioned in the SR)	Not applicable	Yes	Yes	Yes	Yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?
8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Diet – Gluten free and low FODMAP – Risk of bias table for intervention studies (randomized controlled trials)

Study reference (first author, publication year)	Describe method of randomisation[1]	Bias due to inadequate concealment of allocation?[2] (unlikely/likely/unclear)	Bias due to inadequate blinding of participants to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to inadequate blinding of care providers to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to inadequate blinding of outcome assessors to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to selective outcome reporting on basis of the results?[4] (unlikely/likely/unclear)	Bias due to loss to follow-up?[5] (unlikely/likely/unclear)	Bias due to violation of intention to treat analysis?[6] (unlikely/likely/unclear)
Zahedi (2017)	participants were randomly allocated into two groups according to the pre-arranged balanced block randomization	Unlikely	Likely	Unclear (dieticians were not blinded)	unclear	unlikely	unlikely	unlikely
Eswaran (2017)	via computer generation in a 1:1 ratio	unlikely	Likely	unclear	unlikely	unlikely	Likely	unlikely
Harvie (2017)	Randomization of numbers was done online (http://www.random.org)	unlikely	Likely	Unclear	unclear	Unlikely	unclear	unlikely
Patcharatrakul (2019)	Not described	unclear	Likely	unclear (dieticians were not blinded)	Likely	unlikely	Unlikely	unlikely
Pederson (2014)	Random allocation software at a 1:1:1 based on http://mahmoodsaghaei.tripod.com/Softwares/randalloc.html	unlikely	Likely (unblinded)	Unclear	likely	unlikely	Likely	Unlikely

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules.

3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has “soft” (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Diet – Gluten free: Risk of bias table for intervention studies (randomized controlled trials)

Study reference (first author, publication year)	Describe method of randomisation[1]	Bias due to inadequate concealment of allocation?[2] (unlikely/likely/unclear)	Bias due to inadequate blinding of participants to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to inadequate blinding of care providers to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to inadequate blinding of outcome assessors to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to selective outcome reporting on basis of the results?[4] (unlikely/likely/unclear)	Bias due to loss to follow-up?[5] (unlikely/likely/unclear)	Bias due to violation of intention to treat analysis?[6] (unlikely/likely/unclear)
Biesiekierski, 2011	Patients were randomized according to a computer-generated list of random numbers held by an independent observer to either the gluten or the placebo treatment group	Unlikely (patients randomized according to computer-generated list)	Unlikely (patients were blinded to the study treatment, κ score of 0.24, low agreement between actual treatment and participant guessing)	Unlikely (investigators were blinded to study treatment)	Unlikely (investigators evaluating patients were blinded to study treatment)	unlikely	Likely (no statistical difference between both groups in patients that ended prematurely reported in terms of days but not on outcome measures)	unlikely
Zanwar, 2016	Patients were randomized by an independent observer according to a computer-generated list of random numbers. Both patients and investigators were blinded to the study treatment.	Unlikely (Patients were randomized by an independent observer according to a computer-generated list)	Unclear	Unclear	Likely (symptoms are very subjective. Patients that are included in the trial responded to the initial gluten free diet)	Unlikely	Likely (more loss to follow up in the gluten group)	unlikely
Shahbazkhani, 2015	The patients were randomized according to block randomization method held by an independent observer to either the gluten or the placebo treatment	Unlikely	Unclear	Unclear	Unclear (symptoms are very subjective. Patients that are included in the trial responded to the initial gluten free diet)	Unlikely	Unlikely	unlikely

	group. Both patients and investigators evaluating patients were blinded to the study treatment.							

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules.
3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has “soft” (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Probiotics: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/n.a.	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
Niu 2020	yes	yes	No, not excluded	yes	n.a.	yes	yes	yes	yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?
8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Probiotics: Risk of bias table for intervention studies (randomized controlled trials)

Study reference (first author, publication year)	Describe method of randomisation[1]	Bias due to inadequate concealment of allocation?[2] (unlikely/likely/ unclear)	Bias due to inadequate blinding of participants to treatment allocation?[3] (unlikely/likely/ unclear)	Bias due to inadequate blinding of care providers to treatment allocation?[3] (unlikely/likely/ unclear)	Bias due to inadequate blinding of outcome assessors to treatment allocation?[3] (unlikely/likely/ unclear)	Bias due to selective outcome reporting on basis of the results?[4] (unlikely/likely/ unclear)	Bias due to loss to follow-up?[5] (unlikely/likely/ unclear)	Bias due to violation of intention to treat analysis?[6] (unlikely/ likely/ unclear)
Gupta, 2021	by SAS random number generation method	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Skrzydlo, 2020	allocated according to a computer-generated blocked list with a block size of 2 to the synbiotic (patients receiving a synbiotic preparation) or placebo group. The block size was not disclosed to the investigators, and the allocation was blinded to both patients and investigators.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Likely ?
Shi, 2020	Patients were randomly divided into the probiotics group and control group by random number table	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Sadrin, 2020	The study was a double-blind trial. Neither investigators nor patients were aware of	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely

	product allocation until the end of the trial. The type of randomization was the block randomization method and it was stratified by care centres with participants randomly allocated (1:1 basis) to either probiotics or placebo. An 88-case randomisation arrangement was performed by an independent statistician according to the sequence generated with SAS® software (SAS® 8.2 software (SAS®, Cary, NC, USA)).							
Martoni, 2020	Block randomization (block size: 6) was performed using Stats Direct software (version 3.2), generating distinct alphanumeric codes.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Lewis, 2020	Eligible participants were assigned a randomization code from a list generated by www. randomization.com, and allocated to each intervention group in a	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely

	1:1:1 ratio.							
Kim, 2020	patients were randomized to receive either placebo or a multispecies probiotic mixture through a computer-generated table.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Gayathri, 2020	Method not reported Single blinded (part?)	Unclear	Unlikely	Likely	Likely	Unlikely	Unlikely	Unlikely
Barraza, 2020	Patients were randomized 1:1:1 using a computer-generated random list into 3 groups single blinded	Unlikely	Unlikely	Likely	Likely	Unlikely	Unlikely	Unlikely
Andresen, 2020	Randomly assigned in 1:1 ratio by computer-generated blocked randomisation list with a block size of four.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Stevenson, 2019	Method not stated	Unclear	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Oh, 2019	The random allocation sequence was conducted using a computer-generated, blocked randomization list independent of the research group and with a consealed block.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Madempudi, 2019	The randomization was done in 1:1 ratio and generated by statistical analysis system (SAS) version	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Likely	Likely

	9.4.							
Helo, 2019	“randomly received” no further explanation.	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	Unclear
Al-Jassim, 2019	“randomly assigned” no further information	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules.
3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has “soft” (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Peppermint oil: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study **First author, year**	**Appropriate and clearly focused question?** **Yes/no/unclear**	**Comprehensive and systematic literature search?** **Yes/no/unclear**	**Description of included and excluded studies?** **Yes/no/unclear**	**Description of relevant characteristics of included studies?** **Yes/no/unclear**	**Appropriate adjustment for potential confounders in observational studies?** **Yes/no/unclear/not applicable**	**Assessment of scientific quality of included studies?** **Yes/no/unclear**	**Enough similarities between studies to make combining them reasonable?** **Yes/no/unclear**	**Potential risk of publication bias taken into account?** **Yes/no/unclear**	**Potential conflicts of interest reported?** **Yes/no/unclear**
Alammar 2019	Yes	Yes	Yes	Unclear No definition of outcome measures reported	Not applicable	Yes	Unclear	Yes	Yes

Peppermint oil: Risk of bias table for intervention studies (randomized controlled trials)

Study reference (first author, publication year)	**Describe method of randomisation[1]**	**Bias due to inadequate concealment of allocation?[2]** **(unlikely/likely/ unclear)**	**Bias due to inadequate blinding of participants to treatment allocation?[3]** **(unlikely/likely/ unclear)**	**Bias due to inadequate blinding of care providers to treatment allocation?[3]** **(unlikely/likely/ unclear)**	**Bias due to inadequate blinding of outcome assessors to treatment allocation?[3]** **(unlikely/likely/ unclear)**	**Bias due to selective outcome reporting on basis of the results?[4]** **(unlikely/likely/ unclear)**	**Bias due to loss to follow-up?[5]** **(unlikely/likely/ unclear)**	**Bias due to violation of intention to treat analysis?[6]** **(unlikely/likely/ unclear)**
Weerts 2020	Randomization was done with ALEA (Abcoude, The Netherlands) Screening and Enrolment Application software using the minimization method, accounted for inclusion center, IBS subtypes (diarrhea, mixed, constipation, undefined), sex, and age	Unlikely	Unlikely *Blinding of the patients may not have been entirely successful due to the smell and taste of peppermint oil and other recognizable adverse events.*	Unlikely	Unlikely	Unlikely	Unclear *More patients receiving peppermint oil vs placebo discontinued treatment because of adverse events: 3 in the small-intestinal–release peppermint oil group (4.8%) and 5 in the ileocolonic-release peppermint oil group (7.9%), compared with 1 in the placebo group (1.6%).*	Unlikely *All analyses were based on the intention-to-treat (ITT) principle, with correction for the minimization variables of sex, inclusion center, IBS subtype, and age.*

Linaclotide -Table of quality assessment for systematic reviews of RCT's and observational studies

Study	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/n.a.	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
Atluri, 2014	Yes	Yes	No, not excluded	Yes	n.a.	Yes	Yes	Yes	Yes

Antidepressants: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study		**Ford, 2019**
Appropriate and clearly focused question?[1]	Yes/no/unclear	Yes
Comprehensive and systematic literature search?[2]	Yes/no/unclear	Yes
Description of included and excluded studies?[3]	Yes/no/unclear	No, not excluded
Description of relevant characteristics of included studies?[4]	Yes/no/unclear	Yes
Appropriate adjustment for potential confounders in observational studies?[5]	Yes/no/unclear/n.a.	n.a.
Assessment of scientific quality of included studies?[6]	Yes/no/unclear	Yes
Enough similarities between studies to make combining them reasonable?[7]	Yes/no/unclear	Yes
Potential risk of publication bias taken into account?[8]	Yes/no/unclear	Yes
Potential conflicts of interest reported?[9]	Yes/no/unclear	Yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?
8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Psychological therapies: Table of quality assessment for systematic reviews of RCT's and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and clearly focused question?[1] Yes/no/unclear	Comprehensive and systematic literature search?[2] Yes/no/unclear	Description of included and excluded studies?[3] Yes/no/unclear	Description of relevant characteristics of included studies?[4] Yes/no/unclear	Appropriate adjustment for potential confounders in observational studies?[5] Yes/no/unclear/n.a.	Assessment of scientific quality of included studies?[6] Yes/no/unclear	Enough similarities between studies to make combining them reasonable?[7] Yes/no/unclear	Potential risk of publication bias taken into account?[8] Yes/no/unclear	Potential conflicts of interest reported?[9] Yes/no/unclear
Billings, 2020	Yes	Yes	No, not excluded	Yes	n.a.	Yes	Yes	Yes	Yes
Ford, 2019	Yes	Yes	No, not excluded	Yes	n.a.	Yes	Yes	Yes	Yes
Li, 2014	Yes	Yes	No, not excluded	Yes	n.a.	Yes	Yes	Yes	Yes
Lee, 2014	Yes	Yes	No, not excluded	Yes	n.a.	Yes	Yes	Yes	Yes
Park, 2014	Yes	Yes	No, not excluded	Yes	n.a.	Yes	Yes	Yes	Yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined
2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCT's)
6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I^2)?

8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Psychological therapies: Risk of bias table for intervention studies (randomized controlled trials)

Study reference (first author, publication year)	**Describe method of randomisation[1]**	**Bias due to inadequate concealment of allocation?[2]** (unlikely/likely/ unclear)	**Bias due to inadequate blinding of participants to treatment allocation?[3]** (unlikely/likely/ unclear)	**Bias due to inadequate blinding of care providers to treatment allocation?[3]** (unlikely/likely/ unclear)	**Bias due to inadequate blinding of outcome assessors to treatment allocation?[3]** (unlikely/likely/ unclear)	**Bias due to selective outcome reporting on basis of the results?[4]** (unlikely/likely/ unclear)	**Bias due to loss to follow-up?[5]** (unlikely/likely/ unclear)	**Bias due to violation of intention to treat analysis?[6]** (unlikely/likely/ unclear)
Lackner, 2018 and 2019	Simple randomization without constraints was performed using a centralized Web-based allocation scheme (1:1:1) overseen by a study coordinator without patient care responsibilities.	unlikely	likely	Unclear	unlikely	Unclear	likely	Likely (although the authors state it is not; they explain why they cannot use ITT analysis)
Everitt, 2019a-c	Randomisation was at the level of the individual, stratified by recruitment	unlikely	likely	likely	unlikely	Unclear	likely	unlikely

	centre, with randomly varying block sizes to ensure approximately equal group sizes. Randomisation was implemented via an independent web-based randomisation service at the UK-CRC registered King's Clinical Trials Unit.							
Peter, 2018	Unclear	Unclear	likely	likely	likely	Unclear	unlikely	unlikely
Jang, 2017	Participants were assigned randomly to the CBT or control group using a random number generator (https:// www.randomizer.org/).	unlikely	likely	unlikely	unlikely	unlikely	unlikely	Unclear

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules.
3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient

assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has “soft” (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Bijlage 5: Forest plots

Diet

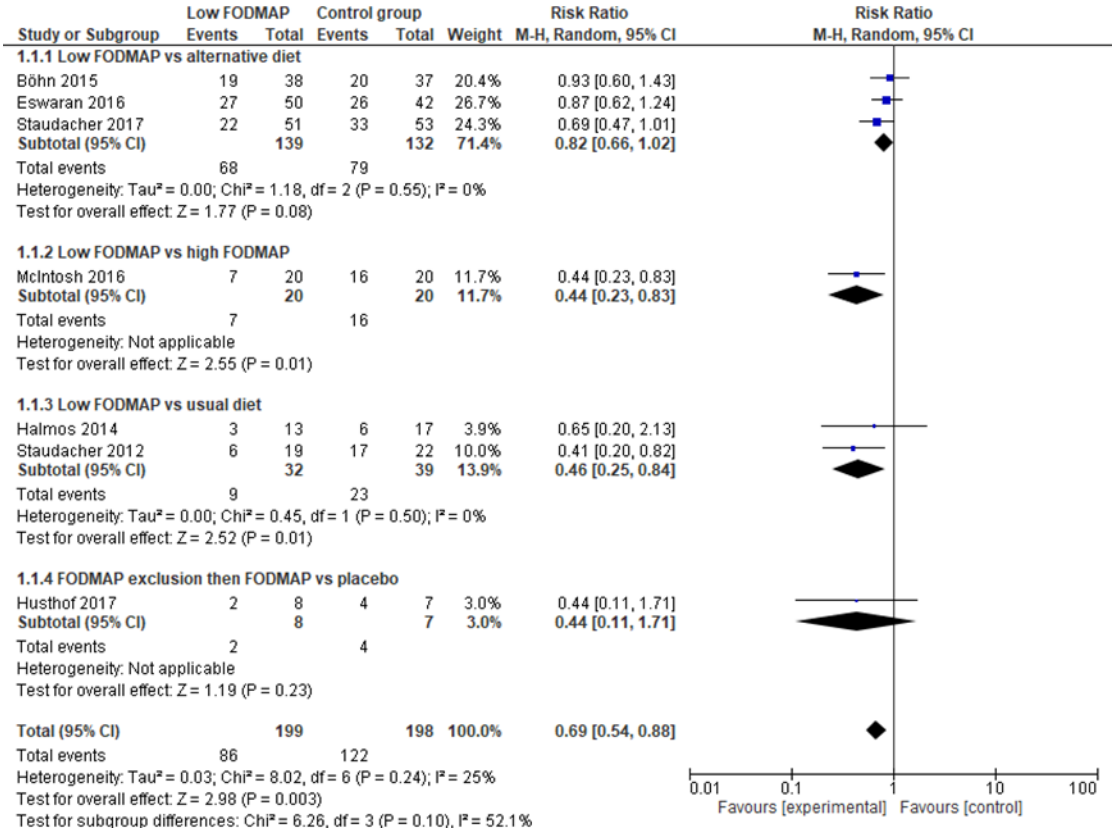


Figure 1: Low FODMAP diet and global improvement in IBS symptoms (data from Dionne 2018)

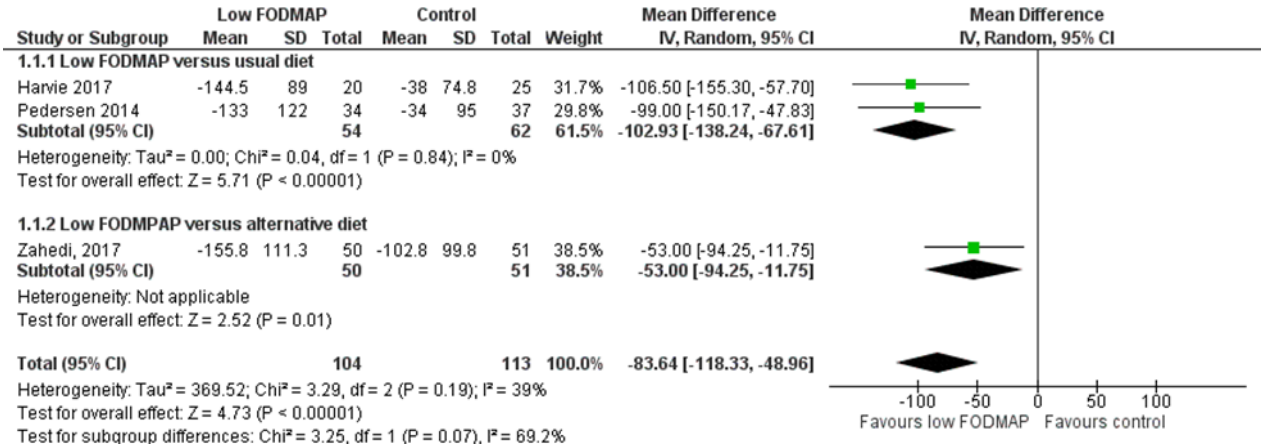
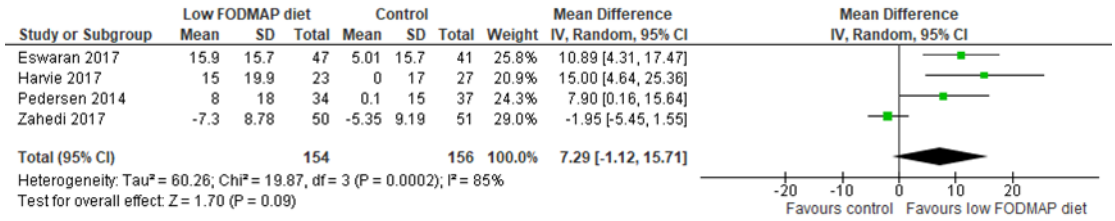


Figure 2: Low FODMAP diet of mean difference in IBS-SSS score



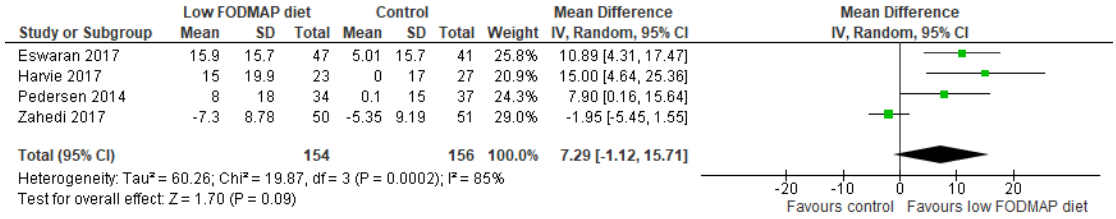


Figure 3: Low FODMAP diet, pooled mean difference IBS-QoL

Probiotics

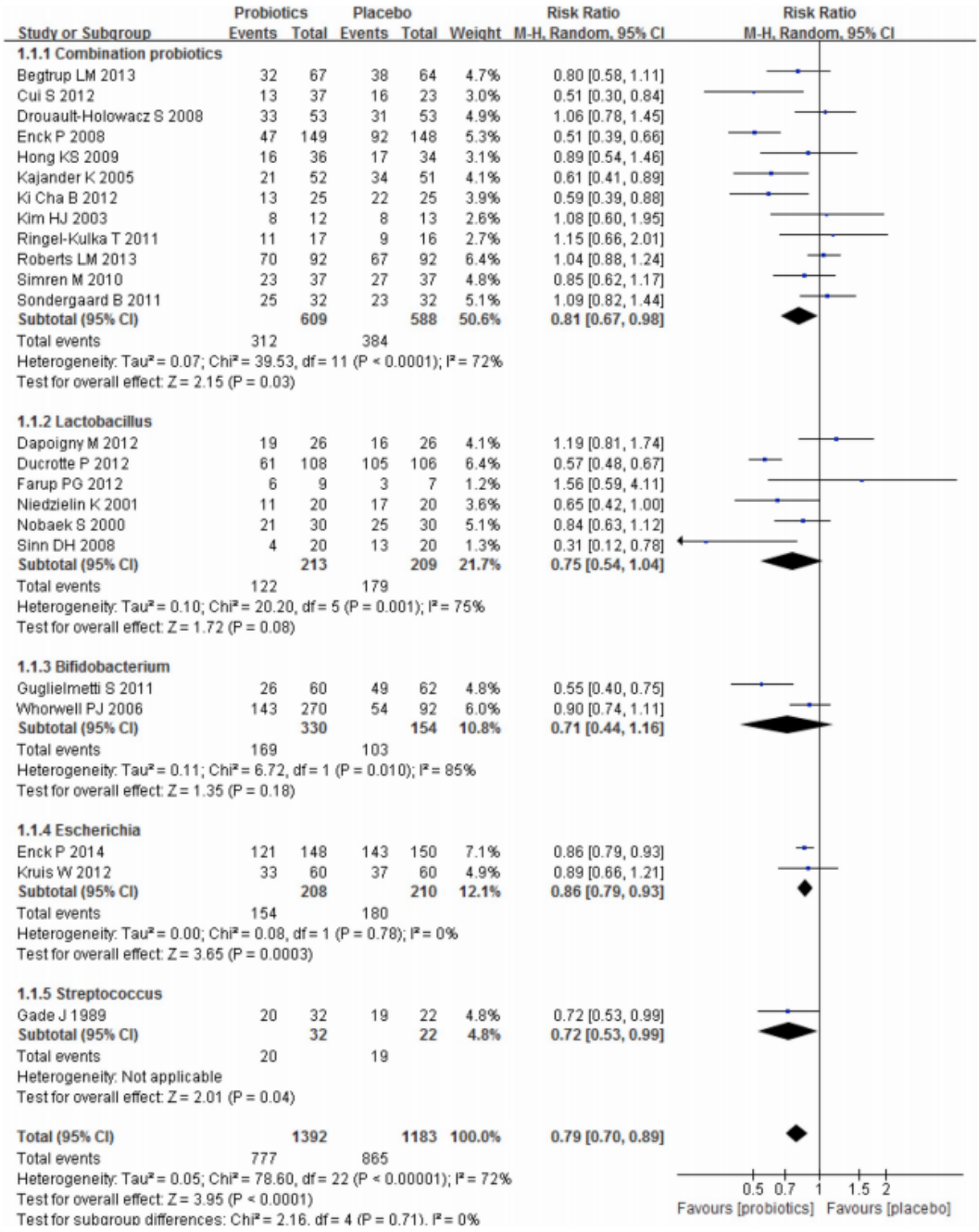


Fig. 2. Forest plot of comparison between probiotics and placebo in term of persistence of symptoms for IBS.

Figure 1. Meta-analysis from systematic review Niu (2020) probiotics and outcome 'persistence of symptoms'.

Figure from systematic review Niu (2020) probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

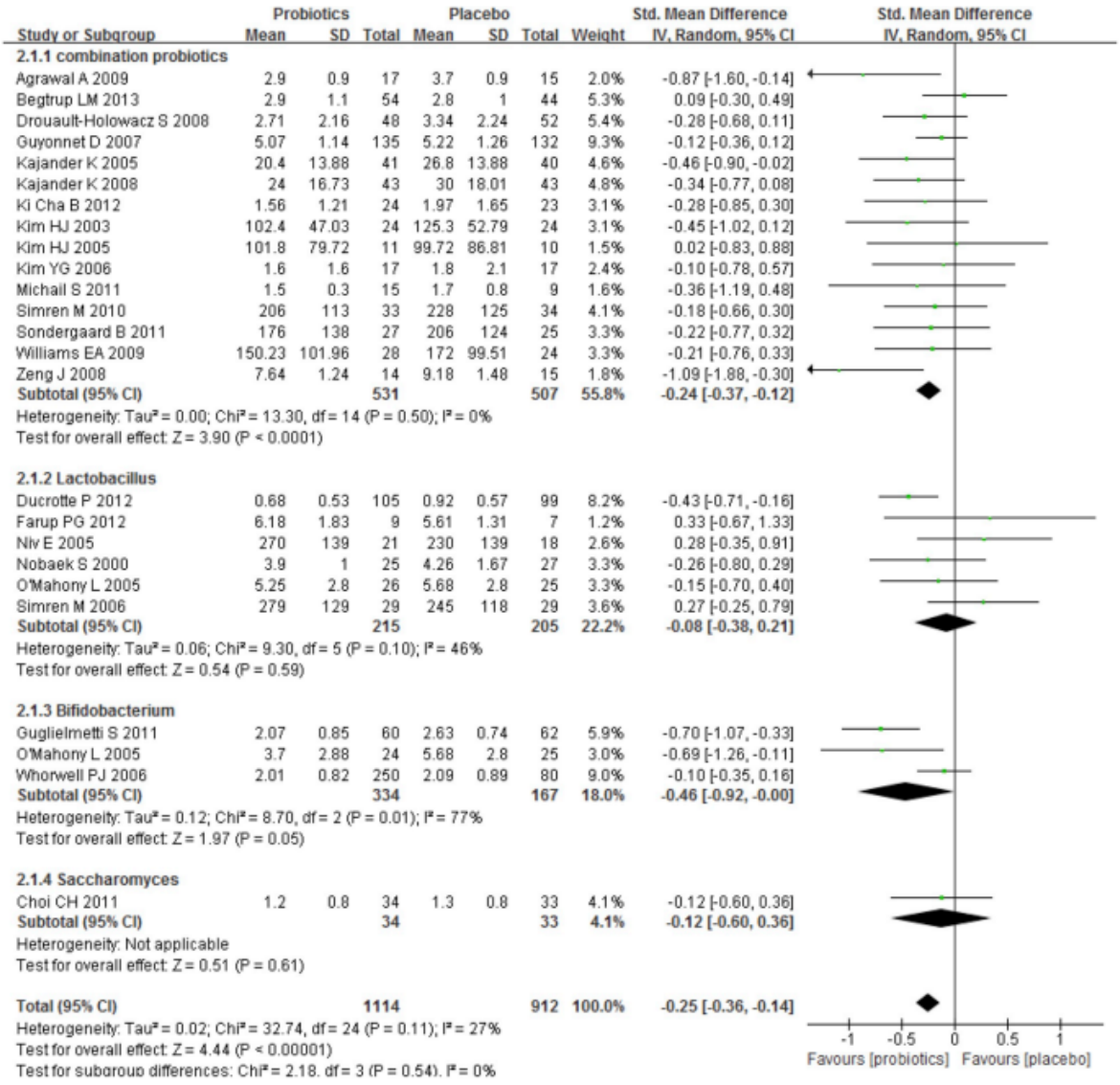
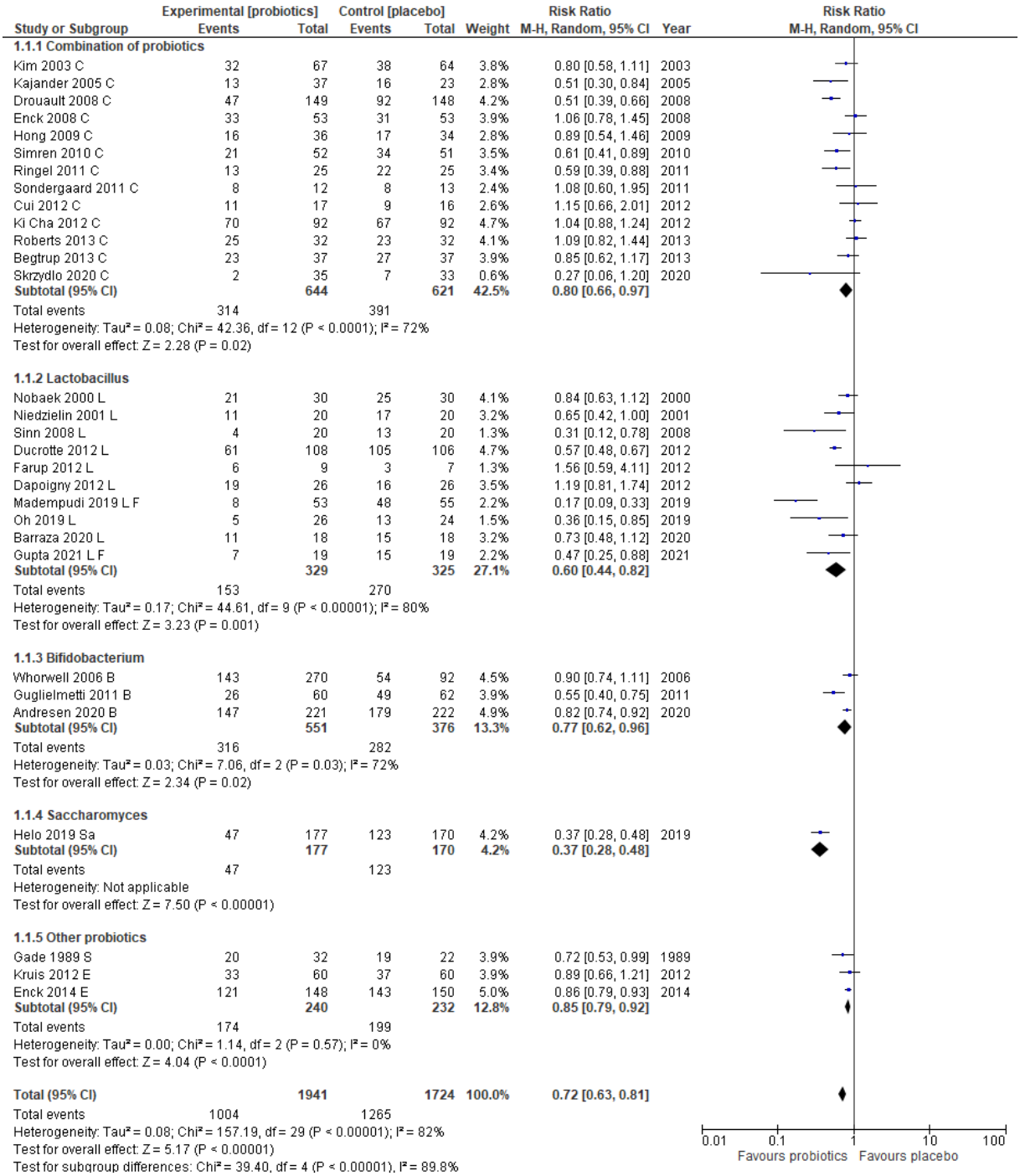
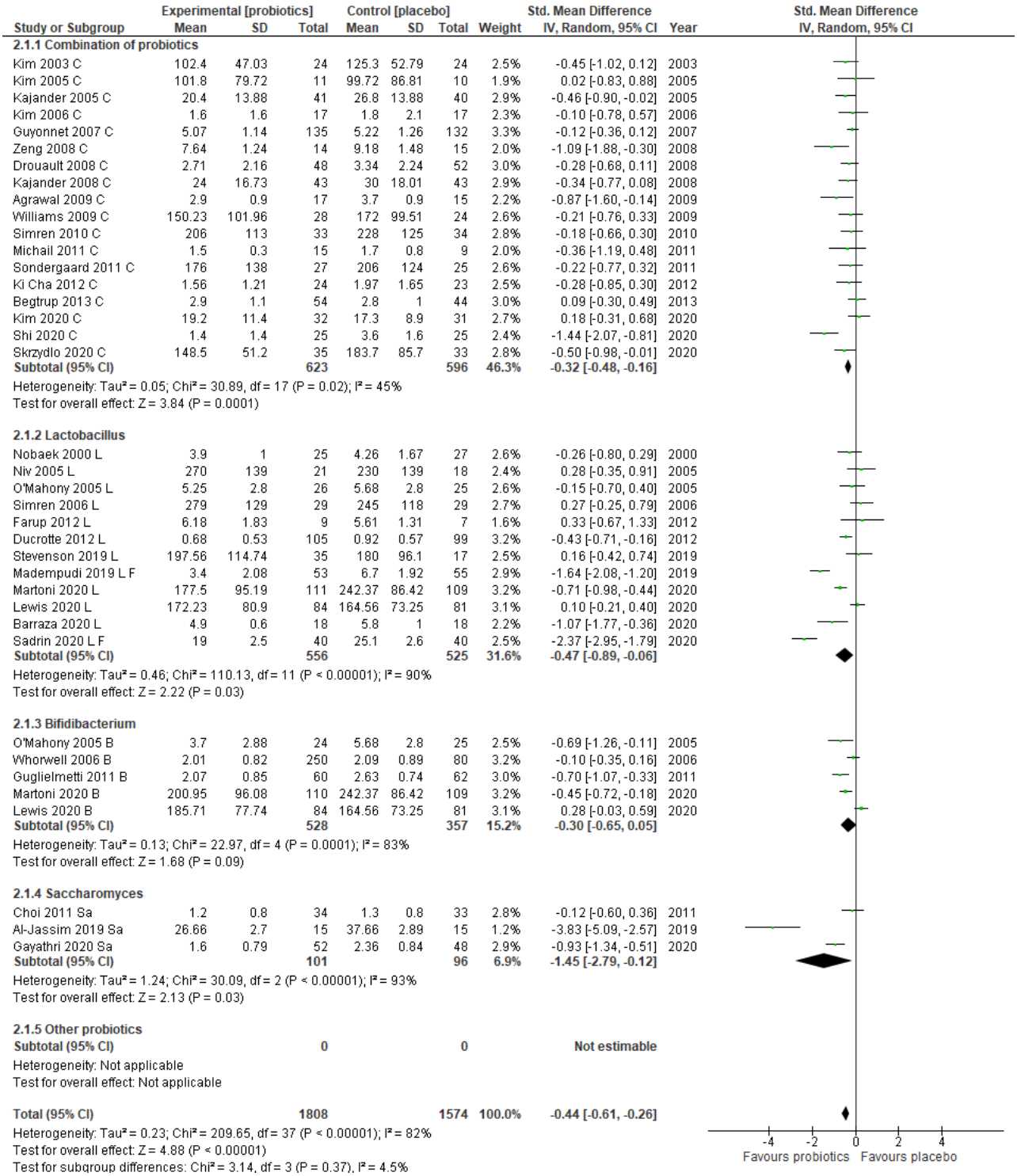


Fig. 3. Forest plot of comparison between probiotics and placebo in term of GSS or APS for IBS.

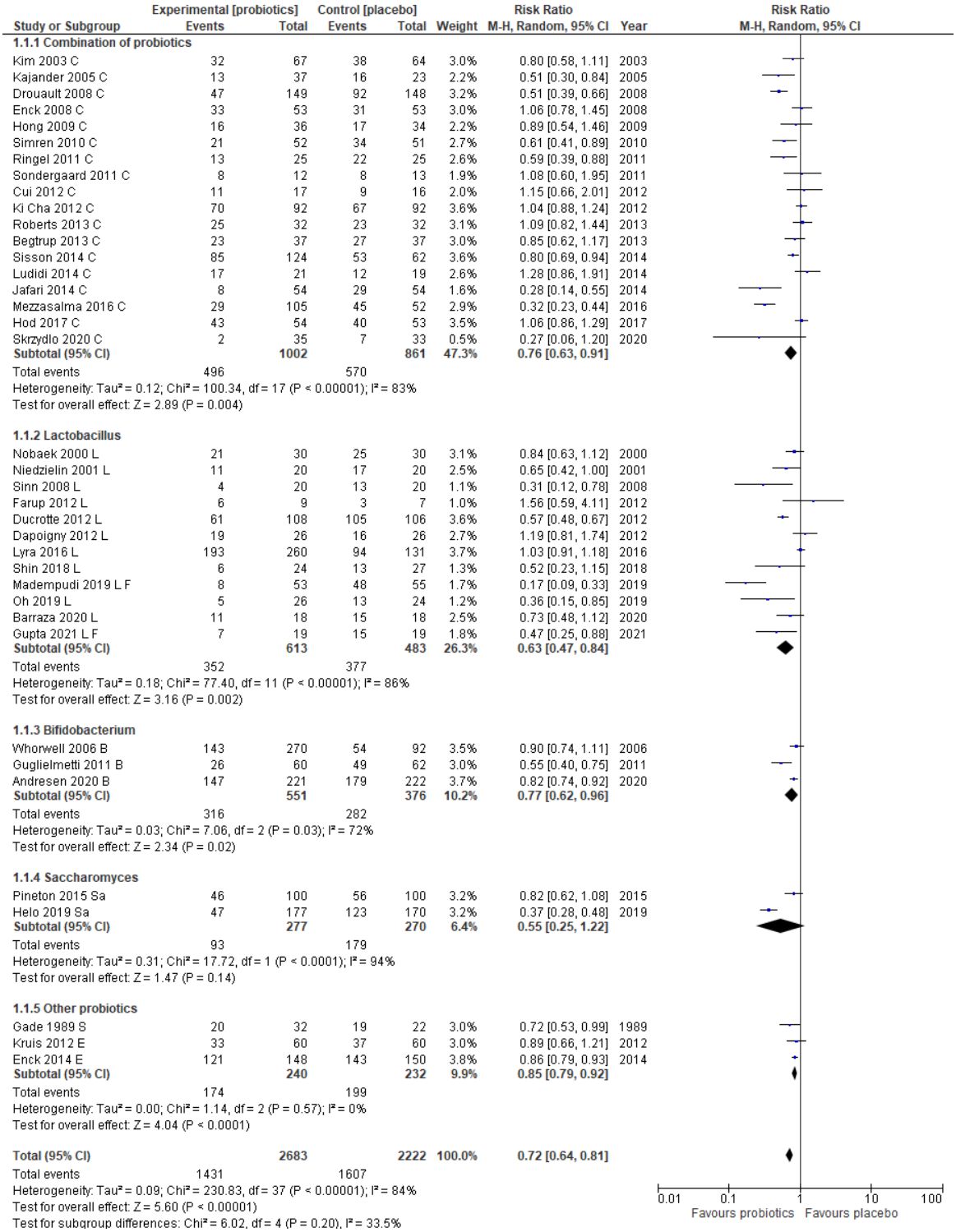
Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019): probiotics and outcome 'persistence of symptoms'.



Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019): probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

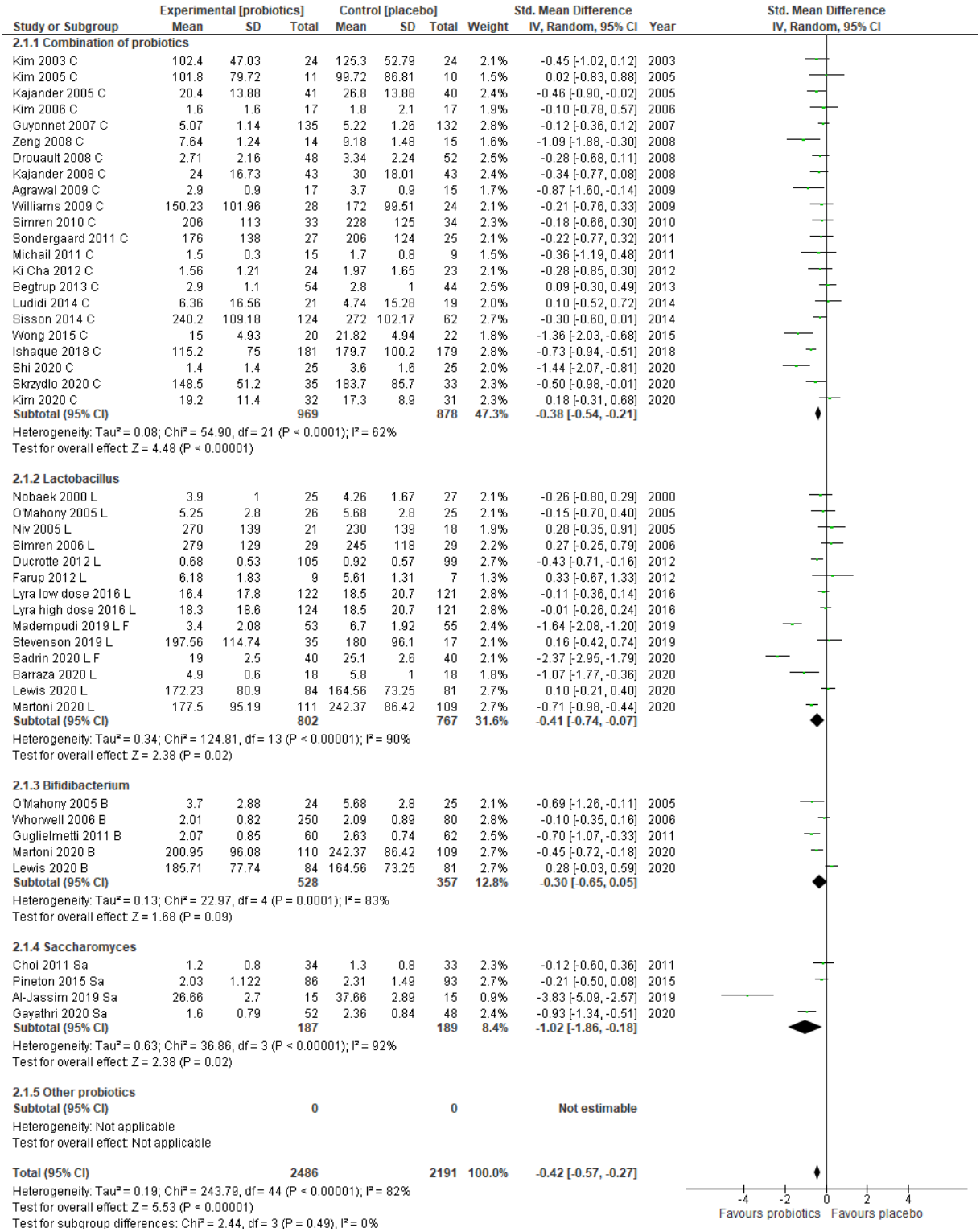


Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020): probiotics and outcome 'persistence of symptoms'.
[*RR was 0,79 (0,70-0,89), toen 0,72 (0,63-0,81), nu 0,72 (0,64-0,81)***]**



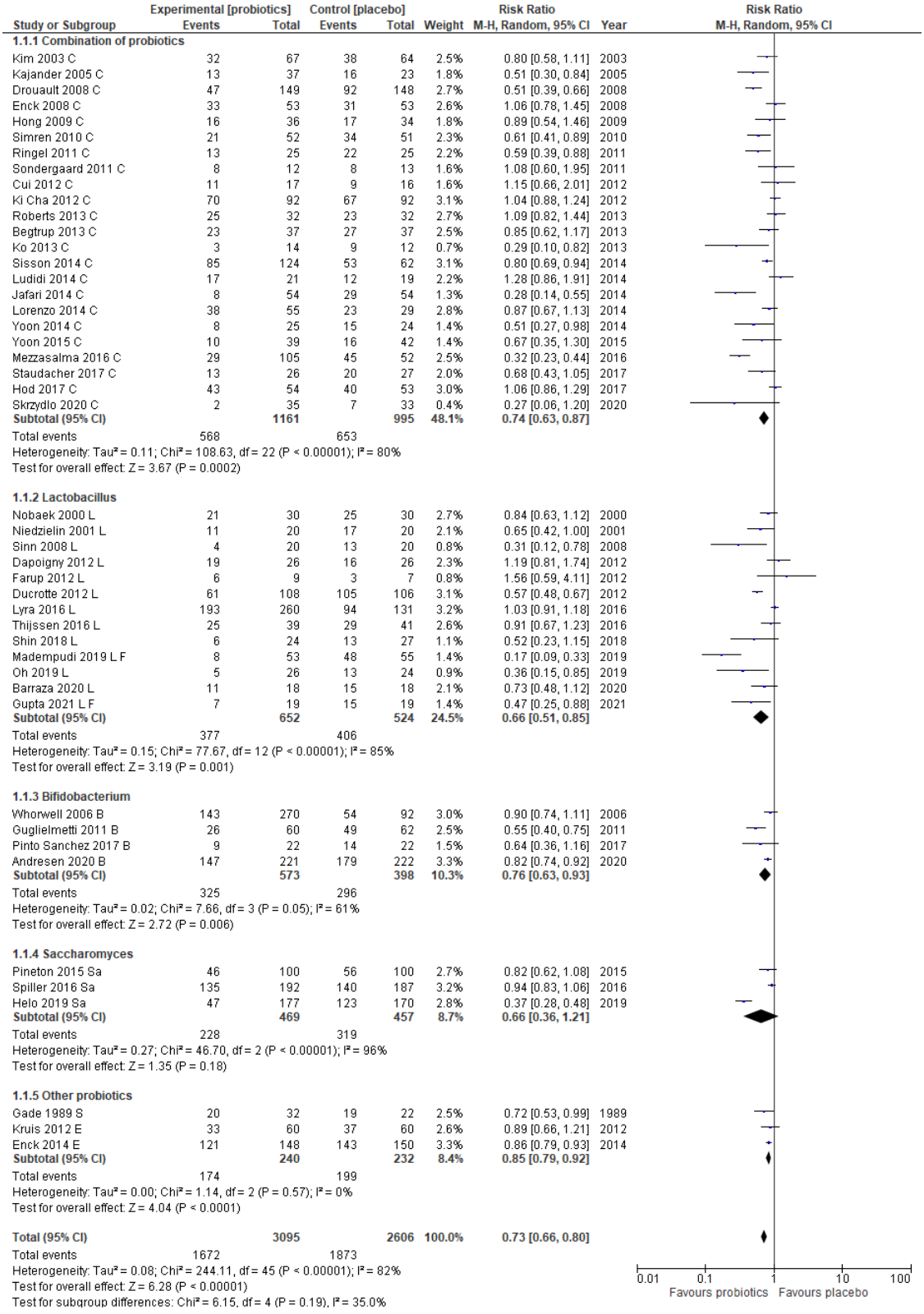
Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020): probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

[*SMD was -0,25, toen -0,44 (-0,61 – -0,26) is nu -0,42 (-0,57 – -0,27)***]**



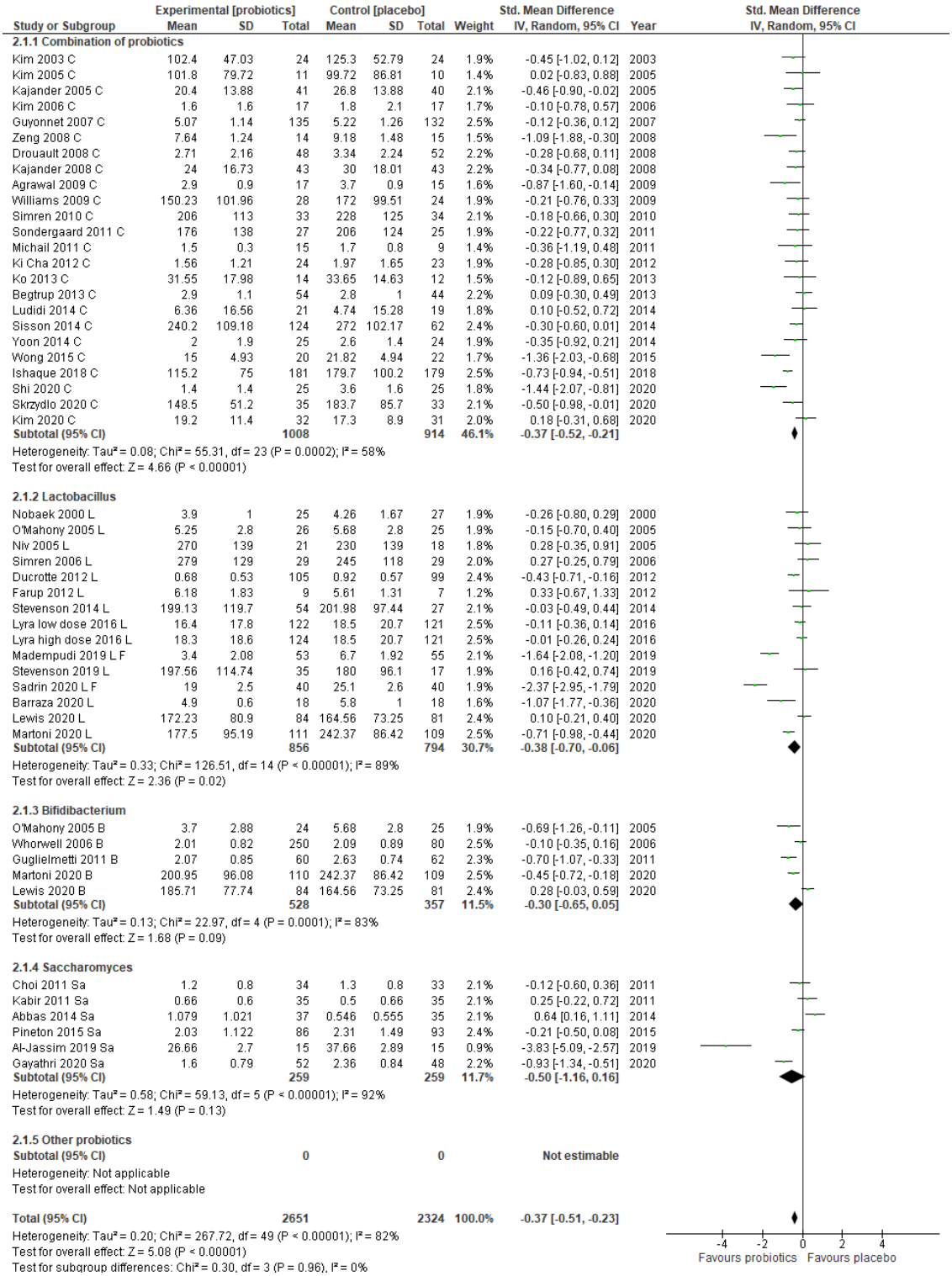
Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020) PLUS Ford (2018): probiotics and outcome 'persistence of symptoms'.

[*RR was 0,79 (0,70-0,89), toen 0,72 (0,63-0,81), daarna 0,72 (0,64-0,81) en nu 0,73 (0,66-0,89)***]** (*8 RCT's uit Ford toegevoegd*)



Forest plot with analysis of review Niu (2020) PLUS RCT's published after the search data of Niu (April 2019) PLUS Sun (2020) PLUS Ford (2018): probiotics and outcome 'general symptom score (GSS) or abdominal pain score (APS)'.

[*SMD was -0,25, toen -0,44 (-0,61 – -0,26) daarna -0,42 (-0,57 – -0,27) en nu -0,37 (-0,52 – -0,23)***]** (*5 RCT's uit Ford*)

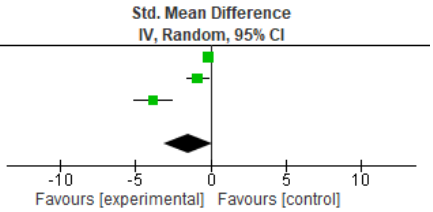


Analysis subtype IBS (C and D)

Forest plot IBS-C Outcome General symptom score or abdominal pain score

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Guyonnet 2007 C	5.07	1.14	135	5.22	1.26	132	36.2%	-0.12 [-0.36, 0.12]	2007
Agrawal 2009 C	2.9	0.9	17	3.7	0.9	15	34.0%	-0.87 [-1.60, -0.14]	2009
Al-Jassim 2019 Sa	26.66	2.7	15	37.66	2.89	15	29.9%	-3.83 [-5.09, -2.57]	2019
Total (95% CI)			**167**			**162**	**100.0%**	**-1.48 [-3.10, 0.14]**	

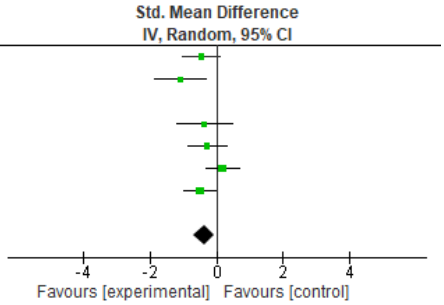
Heterogeneity: Tau² = 1.88; Chi² = 34.37, df = 2 (P < 0.00001); I² = 94%
Test for overall effect: Z = 1.79 (P = 0.07)



Forest plot IBS-D Outcome General symptom score or abdominal pain score

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Kim 2003 C	102.4	47.03	24	125.3	52.79	24	17.7%	-0.45 [-1.02, 0.12]	2003
Zeng 2008 C	7.64	1.24	14	9.18	1.48	15	11.7%	-1.09 [-1.88, -0.30]	2008
Ringel 2011 C	0	0	0	0	0	0		Not estimable	2011
Michail 2011 C	1.5	0.3	15	1.7	0.8	9	10.8%	-0.36 [-1.19, 0.48]	2011
Ki Cha 2012 C	1.56	1.21	24	1.97	1.65	23	17.7%	-0.28 [-0.85, 0.30]	2012
Kim 2020 C	19.2	11.4	32	17.3	8.9	31	20.8%	0.18 [-0.31, 0.68]	2020
Skrzydlo 2020 C	148.5	51.2	35	183.7	85.7	33	21.3%	-0.50 [-0.98, -0.01]	2020
Total (95% CI)			**144**			**135**	**100.0%**	**-0.36 [-0.68, -0.05]**	

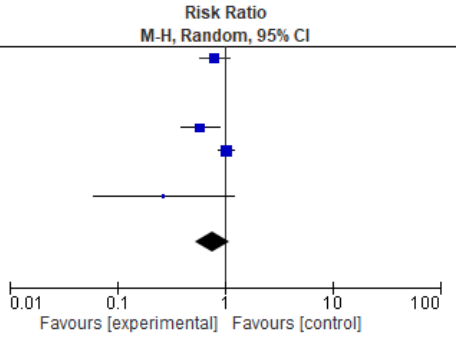
Heterogeneity: Tau² = 0.06; Chi² = 8.38, df = 5 (P = 0.14); I² = 40%
Test for overall effect: Z = 2.25 (P = 0.02)



Forest plot IBS-D Outcome Persistence of symptoms

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kim 2003 C	32	67	38	64	30.7%	0.80 [0.58, 1.11]	2003
Zeng 2008 C	0	0	0	0		Not estimable	2008
Michail 2011 C	0	0	0	0		Not estimable	2011
Ringel 2011 C	13	25	22	25	26.9%	0.59 [0.39, 0.88]	2011
Ki Cha 2012 C	70	92	67	92	37.3%	1.04 [0.88, 1.24]	2012
Kim 2020 C	0	0	0	0		Not estimable	2020
Skrzydlo 2020 C	2	35	7	33	5.0%	0.27 [0.06, 1.20]	2020
Total (95% CI)		**219**		**214**	**100.0%**	**0.77 [0.54, 1.11]**	
Total events	117		134				

Heterogeneity: Tau² = 0.08; Chi² = 10.86, df = 3 (P = 0.01); I² = 72%
Test for overall effect: Z = 1.41 (P = 0.16)



Peppermint oil

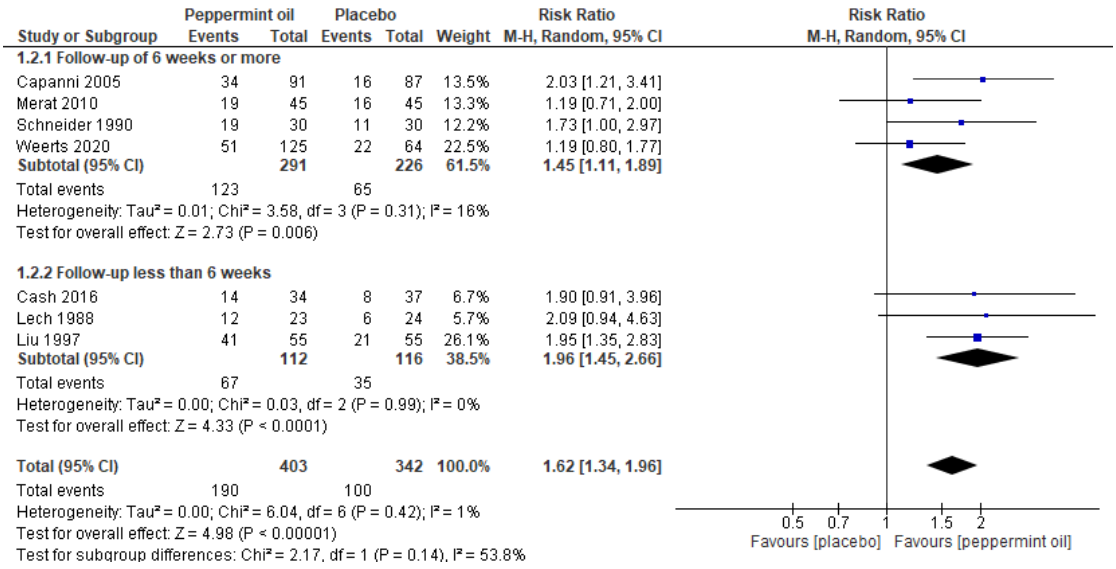


Figure 1. Forest plot of peppermint oil compared with placebo on abdominal pain.

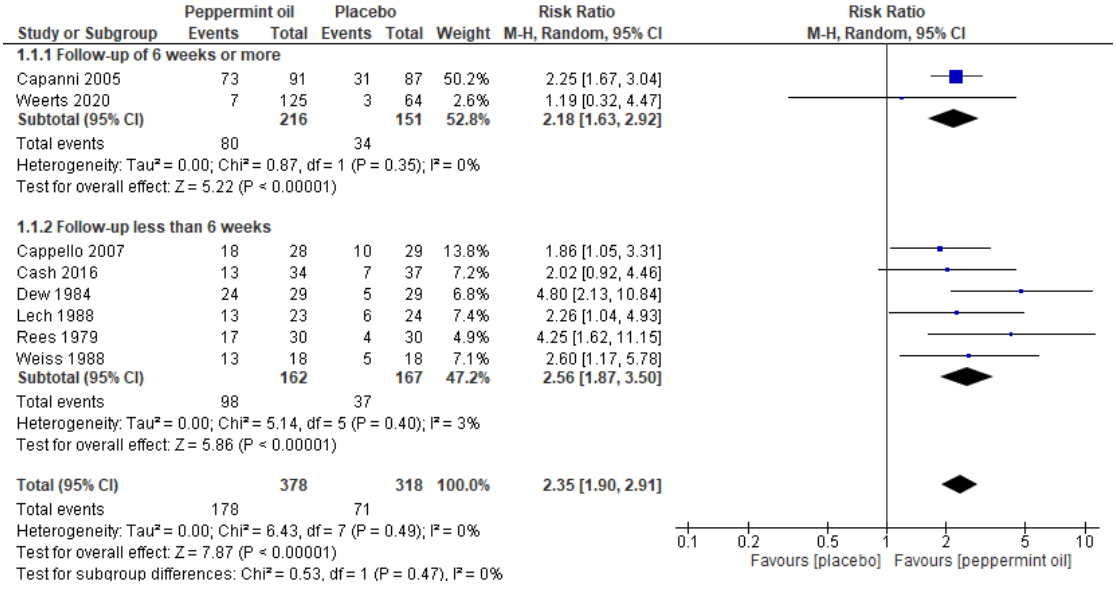


Figure 2. Forest plot of peppermint oil compared with placebo on global improvement.

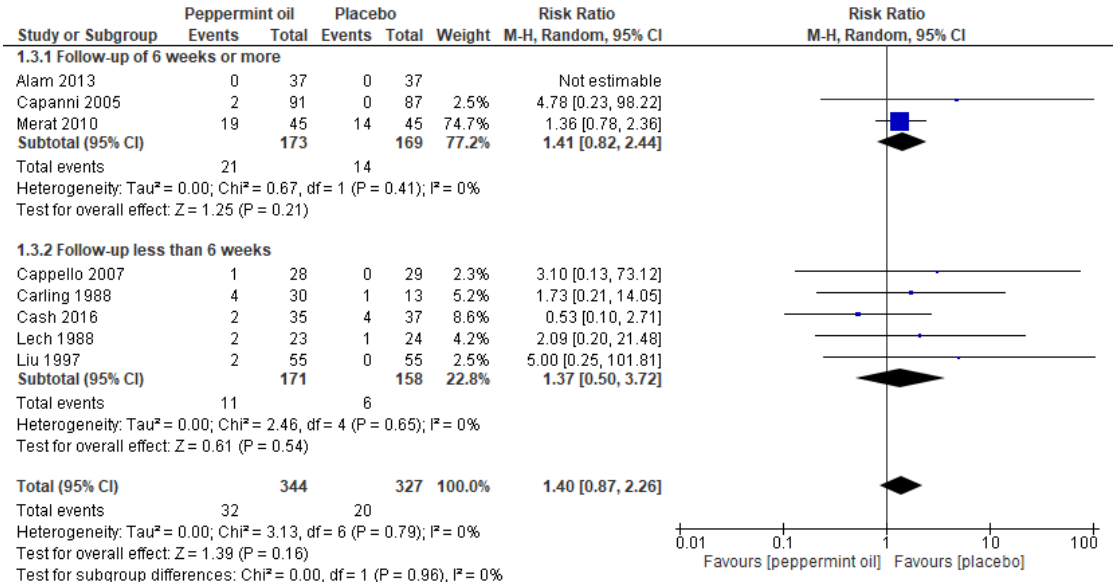


Figure 3. Forest plot of peppermint oil compared with placebo on adverse events.

Linaclotide

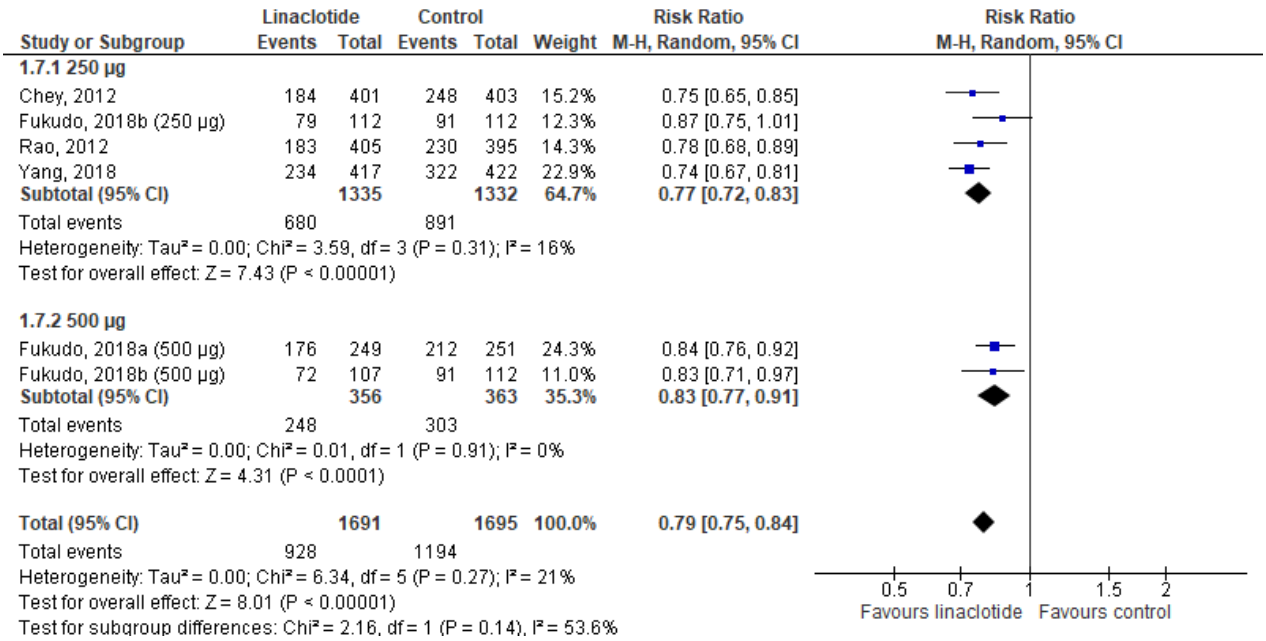


Figure 1. Forest plot of linaclotide compared with placebo showing clinically meaningful improvement in abdominal pain.

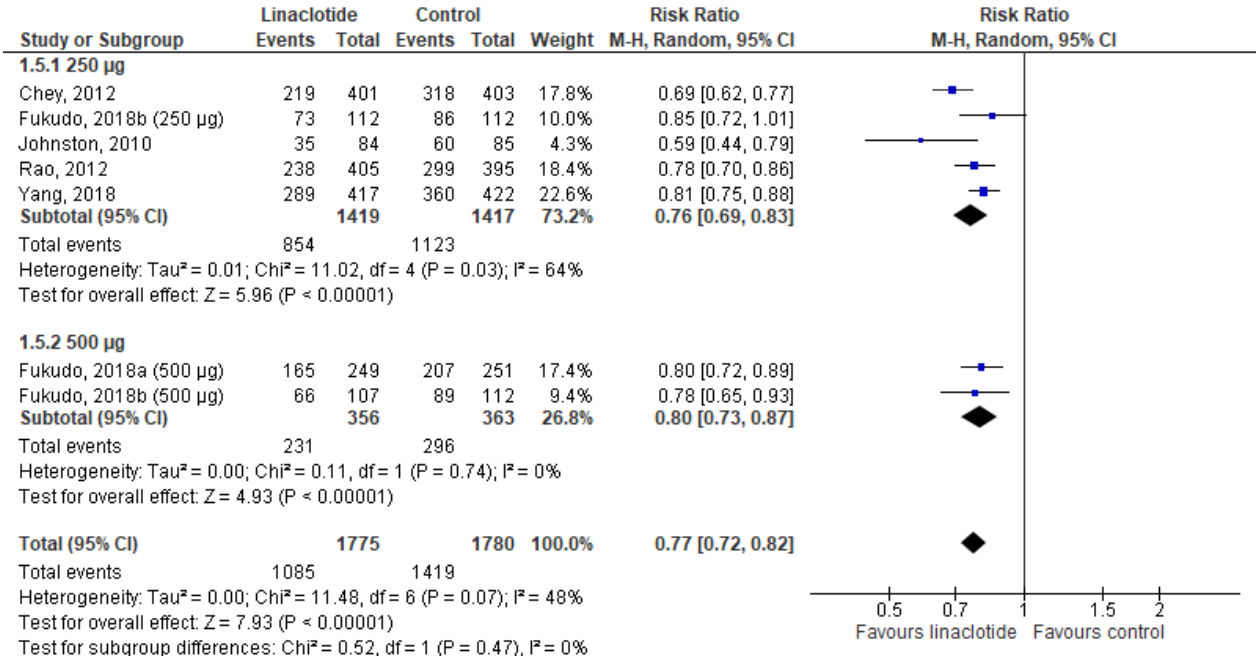


Figure 2: Forest plot of linaclotide compared with placebo showing failure to achieve global relief response (RevMan)

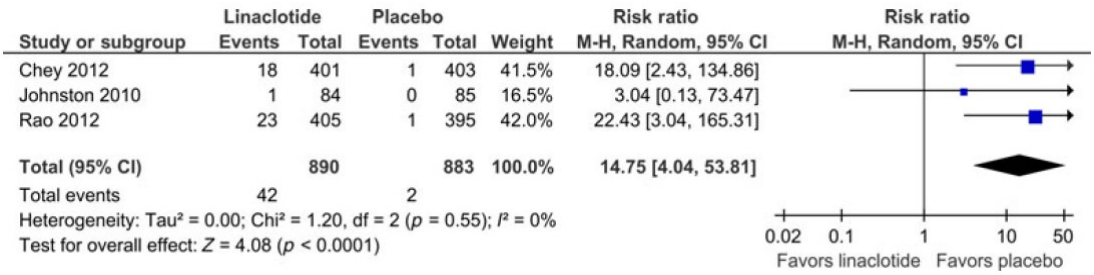


Figure 3. Forest plot of linaclotide compared with placebo showing incidence of diarrhea necessitating discontinuation of treatment. (Atluri, 2014)

Antidepressants
Forest-plots, based on Ford

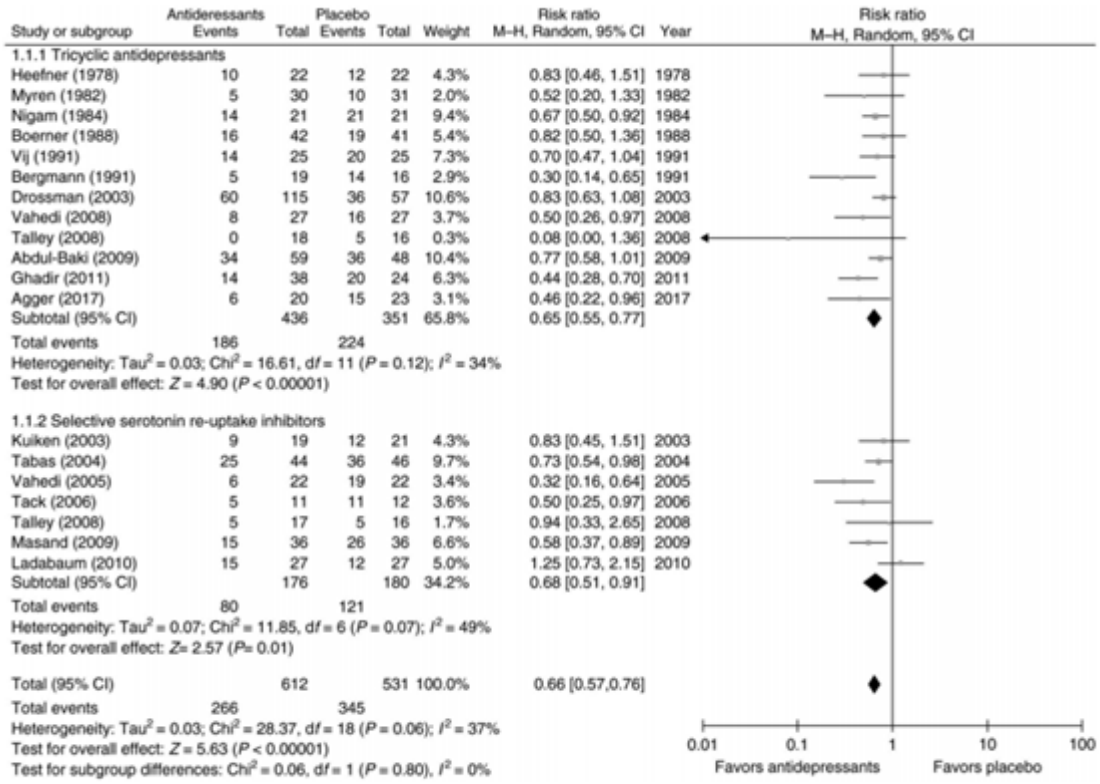


Fig. 2 Forest plot of randomized controlled trials of antidepressants versus placebo in irritable bowel syndrome

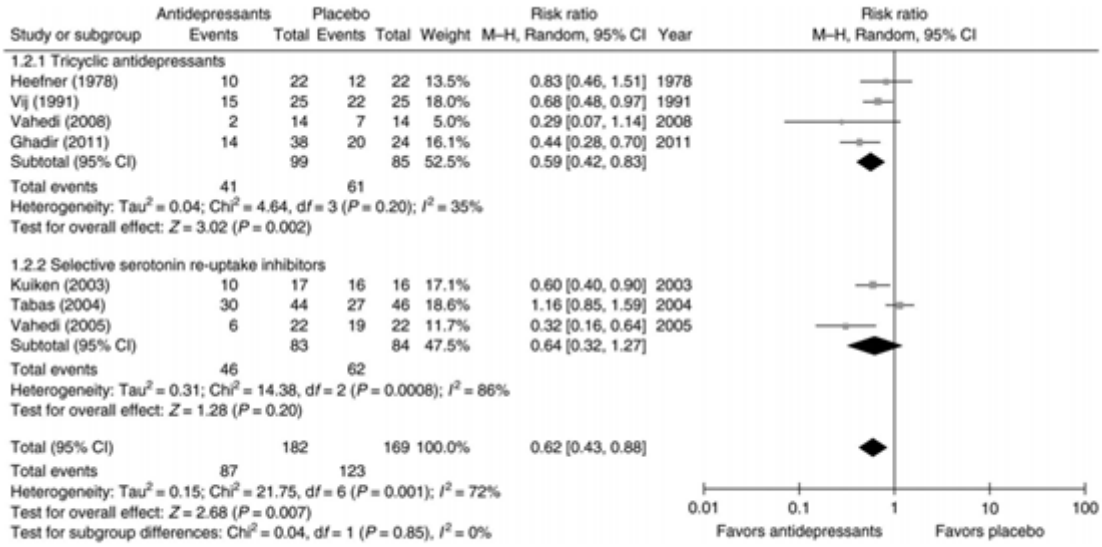


Fig. 3 Forest plot of randomized controlled trials of antidepressants versus placebo in terms of effect on abdominal pain in irritable bowel syndrome

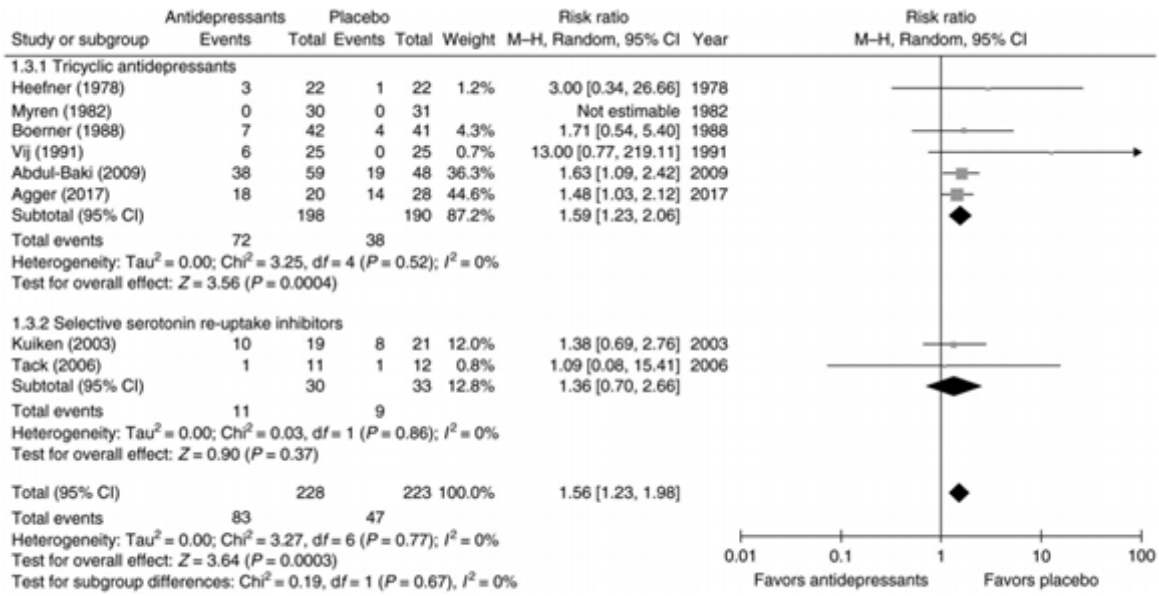
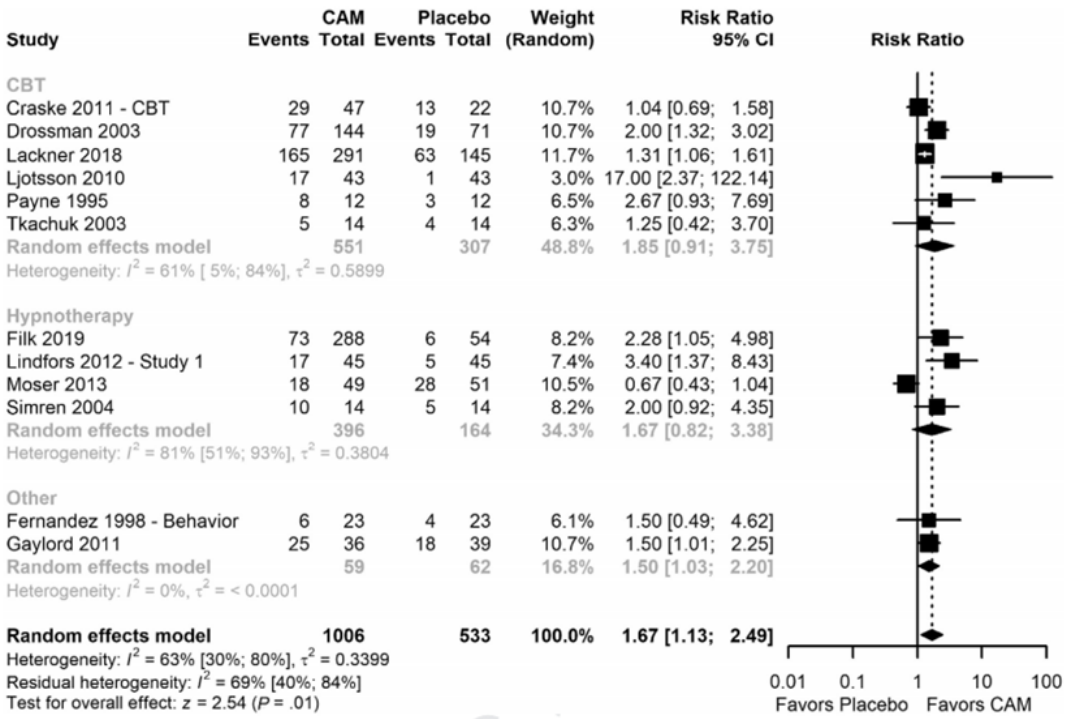


Fig. 4 Forest plot of adverse events in randomized controlled trials of antidepressants versus placebo in irritable bowel syndrome

Psychological therapies



Supplementary Figure 10. Forest plot of studies of mind-body based therapy vs placebo or sham with effect on overall response by intervention (between-group *P* value = .87). CAM, complementary and alternative medicine; CBT, cognitive behavioral therapy; CI, confidence interval.

Figure from systematic review Billings (2020) mind-body therapy (cognitive behavioural therapy and hypnotherapy) and outcome 'overall response'.

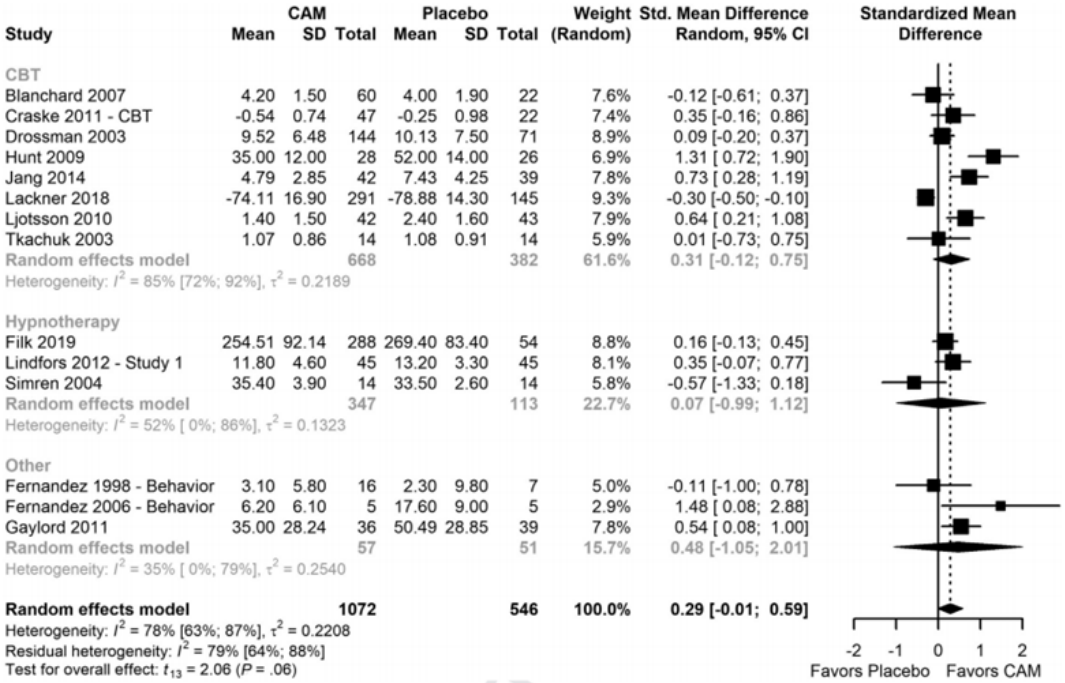


Figure 3. Forest plot of studies of mind-body based therapy vs placebo or sham with effect on abdominal pain by intervention. CAM, complementary and alternative medicine; CBT, cognitive behavioral therapy.

Figure from systematic review Billings (2020) mind-body therapy (cognitive behavioural therapy and hypnotherapy) and outcome 'effect on abdominal pain'.

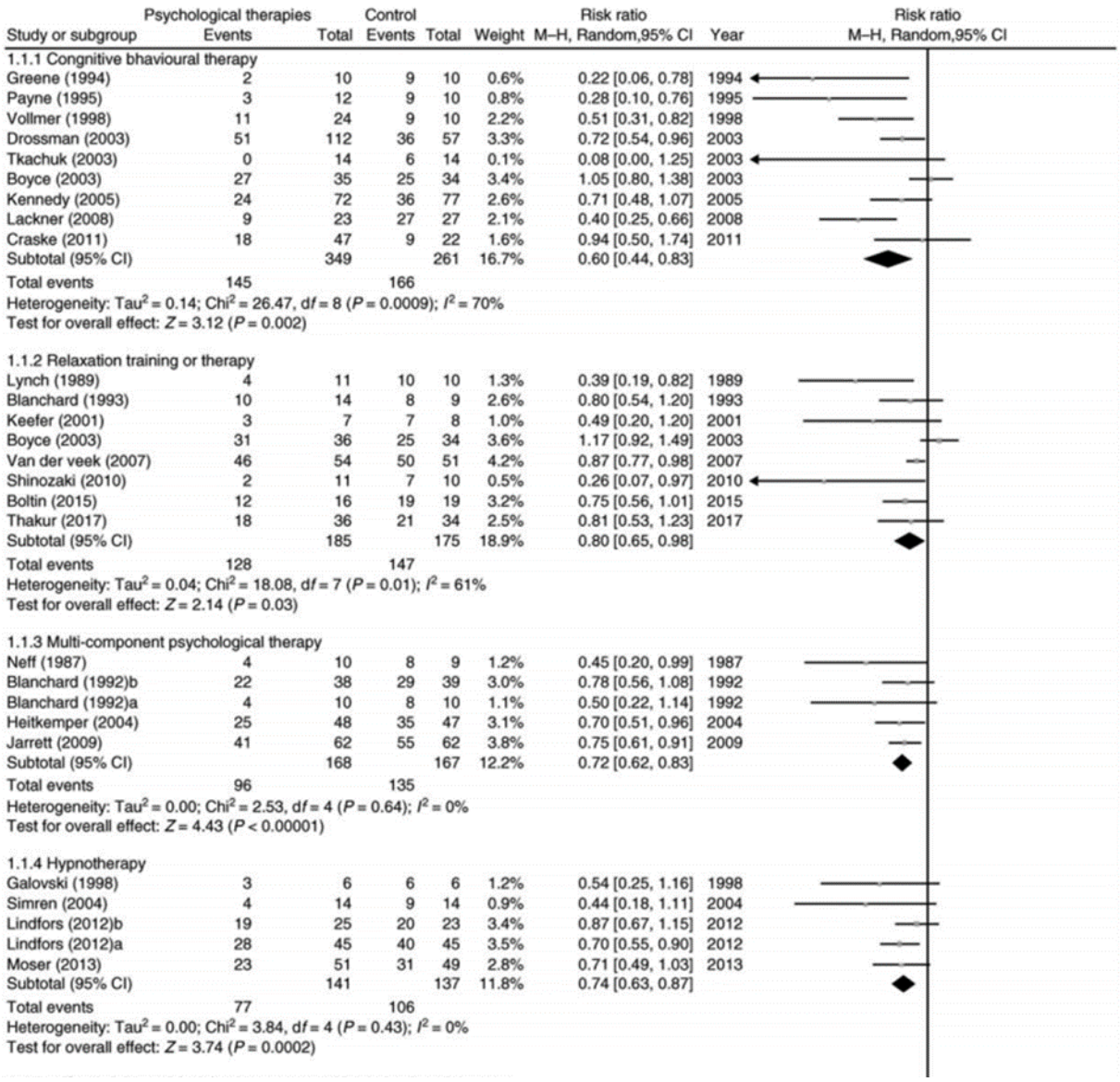
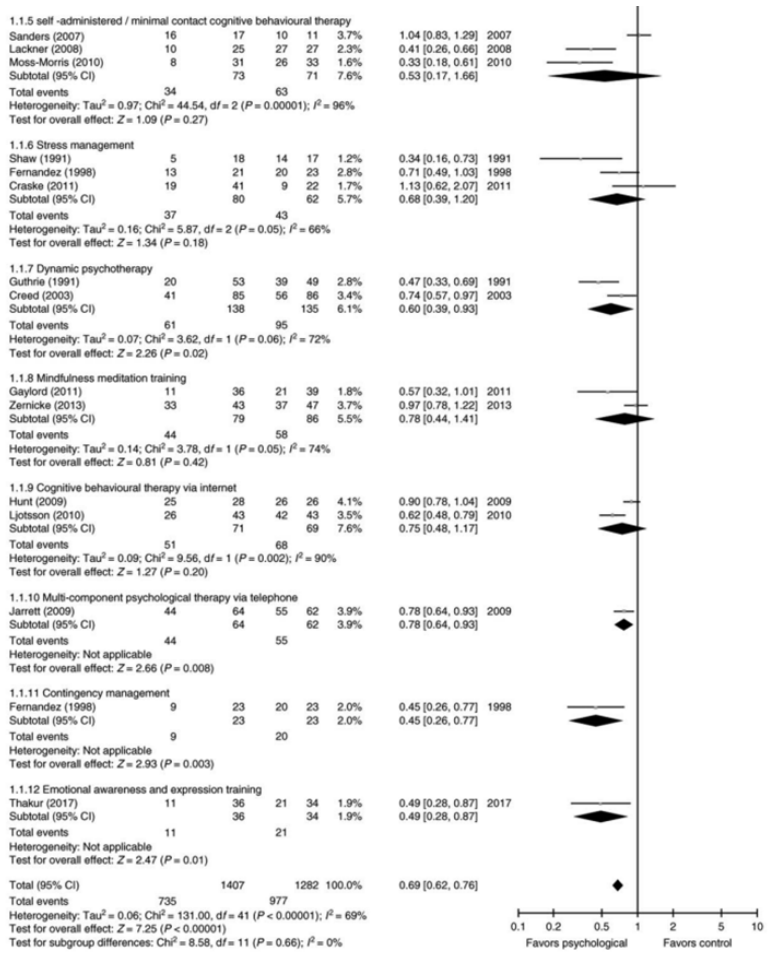


Figure from systematic review Ford (2019) Cognitive behavioural therapy, relaxation therapy, hypnotherapy and outcome 'no improvement in IBS symptoms'.



omized controlled trials of psychological therapies versus control in irritable bowel syndrome

Figure from systematic review Ford (2019) Cognitive behavioural therapy, relaxation therapy, hypnotherapy and outcome 'no improvement in IBS symptoms'.

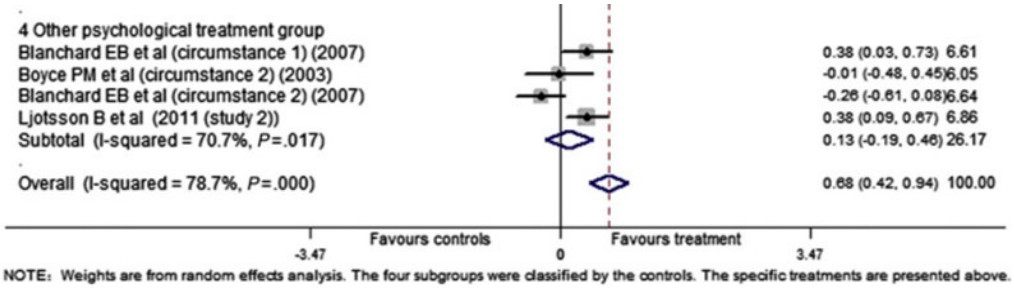


Fig. 2. Effect size estimates for the efficacy of CBT compared to controls in IBS symptom improvement at post-treatment.

Figure from systematic review Li (2014) other psychological treatments and outcome 'IBS symptom improvement' (post treatment).

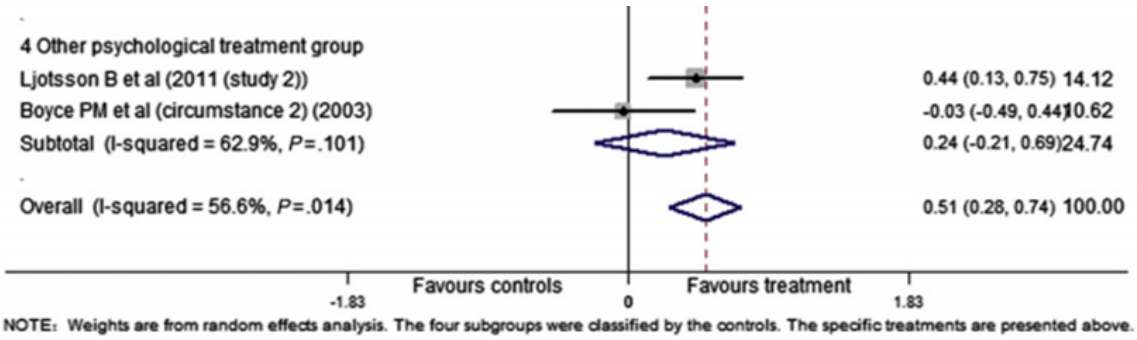


Fig. 3. Effect size estimates for the efficacy of CBT compared to controls in IBS symptom improvement at short-term follow-up.

Figure from systematic review Li (2014) other psychological treatments and outcome 'IBS symptom improvement' (at short-term follow-up).

Fig. 4. Effect size estimates for the efficacy of CBT compared to controls in improvement of IBS QOL.

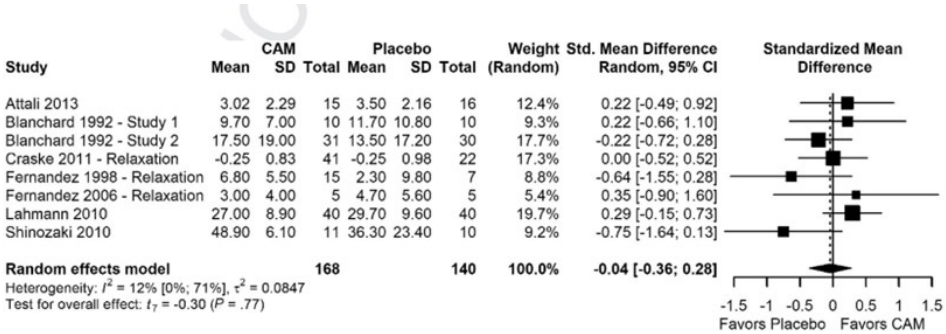
Figure from systematic review Li (2014) other psychological treatments and outcome 'improvement of IBS QOL'.

Table 2. Change in Overall Gastrointestinal Symptom Score

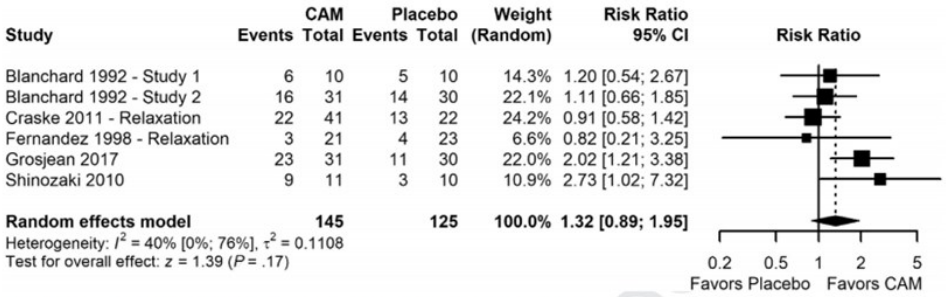
Author (yr)	Outcome measurement	3 months		*P*-value	12 months		*P*-value
		Intervention (SD)	Control (SD)		Intervention (SD)	Control (SD)	
Galovski et al[21] (1998)	CPSR[a]	-0.55 (0.53)	0.32 (0.49)	0.00047	NA	NA	NA
Roberts et al[23] (2006)	Full symptom score	-13.00 (10.50)	-4.5 (13.90)	0.008	-9.10 (14.00)	-6.40 (14.70)	0.440
Lindfors et al[20] (2012) study 1	GI-symptom questionnaire	-4.50 (8.60)	-0.80 (7.30)	< 0.05	NA	NA	NA
Lindfors et al[20] (2012) study 2	GSRS-IBS	-0.43 (0.90)	-0.10 (1.00)	0.220	NA	NA	NA

[a]CPSR was measured at right after end of treatment.
SD, standard deviation; CPSR, composite primary symptom reduction; NA, not allowed; GSRS, gastrointestinal symptom rating scale; IBS, irritable bowel syndrome.

Figure from systematic review Lee (2014) other psychological treatments and outcome 'Quality Of Life'.



Supplementary Figure 2. Forest plot of studies of body-based therapy vs placebo or sham with effect on abdominal pain. CAM, complementary and alternative medicine; CI, confidence interval; SD, standard deviation.



Supplementary Figure 3. Forest plot of studies of body-based therapy vs placebo or sham with effect on overall response. CAM, complementary and alternative medicine; CI, confidence interval.

Figure from systematic review Billings (2020) body-based therapy (relaxation therapy) and outcome 'effect on abdominal pain' and 'overall response'.

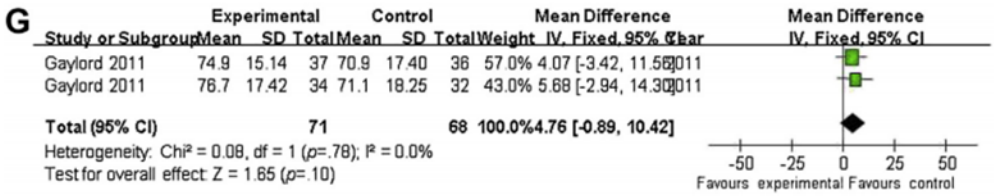


Figure 3. (*continued*).

Figure 3. Comparing outcomes of relaxation therapy versus control: (A) Improved irritable bowel syndrome (IBS) symptom. (B) Total IBS symptom severity score. (C) Abdominal pain frequency in IBS symptom severity score. (D) Dissatisfaction with bowel habit in IBS symptom severity score. (E) Bloating in IBS symptom severity score. (F) Anxiety. (G) Quality of life. *Note.* CI = confidence interval; IV = inverse variance.

Figure from systematic review Park (2014) relaxation therapy and outcome 'quality of life'.

Bijlage 6: Gevolgen van diagnostische testeigenschappen

Calprotectin Table Patient relevant consequences

Outcome	Consequences for medical system	Consequences for patient	Weight (for decision-making)
True positive	*A positive calprotectin test points at an organic disease and more tests/ examination will be done (colonoscopy).*	*Confirmation of complaints, maybe agitation about a serious illness and follow up tests.*	7 – crucial
False positive	*Organic diseases will be excluded during the test that will follow (colonoscopy).*	*Unnecessary worrying about a serious illness and follow up tests (tests are not needed and not without risks).* *Higher costs.*	7 – crucial
True negative	*An organic disease is excluded correctly. No follow up tests.*	*Reassurance of patient. No referral, no follow up tests, no waiting time. Maybe some worrying if patient do not trust the result of the test.* *Low costs.*	7 – crucial
False negative	*An organic disease is excluded while it is present. No follow up tests. Delayed diagnose.*	*False reassurance of patient, wrong or no therapy, maybe less benefit because of delayed therapy.*	7 – crucial
Test	*Faeces for calprotectin test can be obtained by patient him/herself.*	*Faeces for testing calprotectin is easy to obtain, not difficult for patient.*	7 – crucial
	Colonoscopy: is additional examination.	*Experiencing a colonoscopy is not pleasant and is risky (lesion or perforation of colon, bleeding).*	
Resources	*Costs of testing calprotectin are low (+/- €50) compared to alternative (colonoscopy; +/- €600).* *Colonoscopy: visit of hospital or diagnostic centre.*	*Obtaining faeces for testing calprotecin can be done at home.* *Colonoscopy will be done in a hospital or diagnostic centre. The patient must travel to a location.*	7 – crucial

FIT Patient relevant consequences

Outcome	Consequences for medical system	Consequences for patient	Weight (for decision-making)
True positive	*A positive FIT points at an organic disease and more tests/ examination will be done (colonoscopy).*	*Confirmation of complaints, maybe agitation about a serious illness and follow up tests.*	7 – crucial
False positive	*Organic diseases will be excluded during the test that will follow (colonoscopy).*	*Unnecessary worrying about a serious illness and follow up tests (tests are not needed and not without risks).* *Higher costs.*	7 – crucial
True negative	*An organic disease is excluded correctly. No follow up tests.*	*Reassurance of patient. No referral, no follow up tests, no waiting time. Maybe some worrying if patient do not trust the result of the test.* *Low costs.*	7 – crucial
False negative	*An organic disease is excluded while it is present. No follow up tests. Delayed diagnose.*	*False reassurance of patient, wrong or no therapy, maybe less benefit because of delayed therapy.*	7 – crucial
Test	*Faeces for FIT can be obtained by patient him/herself.*	*Faeces for FIT is easy to obtain, not difficult for patient.*	7 – crucial
	Colonoscopy: is additional examination.	*Experiencing a colonoscopy is not pleasant and is risky (lesion or perforation of colon, bleeding).*	
Resources	*Costs of FIT are low (+/- €8) compared to alternative (colonoscopy; +/- €600).* *Colonoscopy: visit of hospital or diagnostic centre.*	*Obtaining faeces for FIT can be done at home.* *Colonoscopy will be done in a hospital or diagnostic centre. The patient must travel to a location.*	7 – crucial

Bijlage 7: Zoekstrategieën

Calprotectin

Richtlijn: prikkebare darm syndroom	
Uitgangsvraag: diagnostische waarde calprotectin	
Database(s): Ovid/Medline, Embase	Datum: 08-12-2020
Periode: 2010	Talen: nvt
Literatuurspecialist: Carla Sloof (NHG)	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gezocht met de elementen gastrointestinal symptoms (P), calprotectin (I) en diagnostische kenmerken(O) De calprotectinetest toont geen IBS aan maar sluit andere aandoeningen uit. In overleg is daarom gekozen voor zoeken naar de patiënt die zich presenteert met (niet acute) buikpijn In plaats van zoeken naar IBS. Ook als IBS niet genoemd wordt is het uitsluiten van IBD/kanker bij patiënten met buikpijn/gastro-intestinale klachten relevante informatie voor de richtlijn IBS. Gezien de diagnostische vraag is gezocht met het filter voor SR's en het observationele filter (niet naar RCT's) Het sleutelartikel van Otten valt vanwege het datumfilter buiten de resultaten. De overige 3 sleutelartikelen bevinden zich in de set SR's en observationeel.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	30	15	31
RCT's	-	-	-
Observationele studies	139	114	166
Overig	-	-	-
Totaal	169	129	197

Zoekstrategie

Embase

No.	Query	Results
#12	#11 NOT #10 *(overige studietypes)*	**139**
#11	#2 AND #9	144
#10	#1 AND #9 *(systematic reviews)*	**30**
#9	#7 AND [1-1-2010]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	281
#8	#3 AND #7	4
#7	#4 AND #5 AND #6	841
#6	'diagnosis'/exp OR 'sensitivity and specificity'/exp OR 'predictive value'/exp OR 'diagnostic use'/exp OR diagnos*:ti,kw OR sensitivity:ab,ti,kw OR	8488543

	specificity:ab,ti,kw OR 'predictive value':ab,ti,kw OR ppv:ab,ti,kw OR npv:ab,ti,kw OR 'diagnostic accurac*':ab,ti,kw	
#5	'calgranulin'/exp OR 'calprotectin test kit'/exp OR 'l1 antigen*':ab,ti,kw OR calprotectin*:ab,ti,kw OR calgranulin*:ab,ti,kw OR 'fecal cp':ab,ti,kw OR 'faecal cp':ab,ti,kw	10371
#4	'lower abdominal pain'/exp OR 'abdominal pain'/mj OR (((functional OR chronic* OR 'non acute') NEAR/1 (gastro* OR colon* OR bowel OR intestin*) NEAR/2 symptom*):ti,ab,kw) OR (((gastro* OR intestin* OR colon* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,kw) OR 'abdominal pain':ti,ab,kw OR 'abdomen pain':ti,ab,kw OR 'abdominal complaint*':ti,ab,kw OR ((discriminat*:ab,ti,kw OR distinguish*:ab,ti,kw OR differentiat*:ab,ti,kw OR 'differential diagnos*':ab,ti,kw) AND (ibs:ab,ti,kw OR irritable:ab,ti,kw OR functional:ab,ti,kw OR spastic:ab,ti,kw))	272330
#3	31680263 AND an:au OR (31464777 AND petryszyn) OR (22407858 AND kok:au) OR (18597588 AND otten:au)	4
#2	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	6233676
#1	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	687126

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to December 04, 2020

Search Strategy:

#	Searches	Results
1	abdominal pain/ or 'abdominal pain'.ti,ab,kf. or 'abdomen pain'.ti,ab,kf. or 'abdominal complaint*'.ti,ab,kf. or ((functional or chronic* or 'non acute') adj2 (gastro* or colon* or bowel or intestin*) adj3 symptom*).ti,ab,kf. or ((gastro* or intestin* or colon* or colorectal) adj2 (dis* or symptom*)).ti,kf. or ((discriminat* or distinguish* or differentiat* or differential-diagnos*) and (IBS or irritable or functional or spastic)).ti,ab,kf.	192483
2	exp Leukocyte L1 Antigen Complex/ or 'l1 antigen*'.ti,ab,kf. or calprotectin*.ti,ab,kf. or calgranulin*.ti,ab,kf. or 'fecal cp'.ti,ab,kf. or 'faecal cp'.ti,ab,kf.	5594
3	exp "Sensitivity and Specificity"/ or exp diagnosis/ or diagnosis.fs. or "diagnostic use".fs. or diagnos*.ti,kf. or sensitivity.ti,ab,kf. or specificity.ti,ab,kf. or "predictive value".ti,ab,kf. or PPV.ti,ab,kf. or NPV.ti,ab,kf. or (diagnostic adj1 accurac*).ti,ab,kf.	10405143
4	1 and 2 and 3	288
5	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature")	466230

	adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	
6	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	3584426
7	4 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	274
8	limit 7 to yr="2010 -Current"	222
9	8 and 5 *(systematic reviews)*	**15**
10	8 and 6	118
11	10 not 9 *(overige studietypes)*	**114**

FIT

Richtlijn: prikkebare darm syndroom	
Uitgangsvraag: diagnostische waarde FIT (fecal immunochemistry test)	
Database(s): Ovid/Medline, Embase	Datum: 10-12-2020
Periode: 2010	Talen: nvt
Literatuurspecialist: Carla Sloof (NHG)	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gezocht met de elementen gastrointestinal symptoms (P), FIT (I) en diagnostische kenmerken(O) De FIT toont geen IBS aan maar sluit andere aandoeningen uit. In overleg is daarom gekozen voor zoeken naar de patiënt die zich presenteert met (niet acute) buikpijn in plaats van zoeken naar IBS. Ook als IBS niet genoemd wordt is het uitsluiten van IBD/kanker bij patiënten met buikpijn/gastro-intestinale klachten relevante informatie voor de richtlijn IBS. Gezien de diagnostische vraag is gezocht met het filter voor SR's en het observationele filter (niet naar RCT's)	

Zoekopbrengst

	EMBASE	OVID/MEDLINE	Ontdubbeld
SR's	6	5	8
RCT's	-	-	
Observationele studies	86	37	92
Overig	-	-	
Totaal	92	42	100

Zoekstrategie

Embase

No.	Query	Results
#10	#9 NOT #8	**86**
#9	#7 AND #2	89
#8	#7 AND #1	**6**
#7	#6 AND [1-1-2010]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	176
#6	#3 AND #4 AND #5	419
#5	'diagnosis'/exp OR 'sensitivity and specificity'/exp OR 'predictive value'/exp OR 'diagnostic use'/exp OR diagnos*:ti,kw OR sensitivity:ab,ti,kw OR specificity:ab,ti,kw OR 'predictive value':ab,ti,kw OR ppv:ab,ti,kw OR npv:ab,ti,kw OR 'diagnostic accurac*':ab,ti,kw	8494161
#4	'occult blood test'/exp OR 'fecal immunochemical testing'/exp OR (((fecal OR faecal) NEAR/2 immuno* NEAR/2 test*):ab,ti,kw) OR 'occult blood test*':ab,ti,kw	9643
#3	'lower abdominal pain'/exp OR 'abdominal pain'/mj OR (((functional OR chronic* OR 'non acute') NEAR/1 (gastro* OR colon* OR bowel OR intestin*) NEAR/2 symptom*):ti,ab,kw) OR (((gastro* OR intestin* OR colon* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,kw) OR 'abdominal pain':ti,ab,kw OR 'abdomen pain':ti,ab,kw OR 'abdominal complaint*':ti,ab,kw OR ((discriminat*:ab,ti,kw OR distinguish*:ab,ti,kw OR differentiat*:ab,ti,kw OR 'differential diagnos*':ab,ti,kw) AND (ibs:ab,ti,kw OR irritable:ab,ti,kw OR functional:ab,ti,kw OR spastic:ab,ti,kw))	272544
#2	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	6240718
#1	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR	688381

	((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	

https://www-elsevier-com.saz.idm.oclc.org/**Ovid/Medline**

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to December 08, 2020

Search Strategy:

#	Searches	Results
1	abdominal pain/ or 'abdominal pain'.ti,ab,kf. or 'abdomen pain'.ti,ab,kf. or 'abdominal complaint*'.ti,ab,kf. or ((functional or chronic* or 'non acute') adj2 (gastro* or colon* or bowel or intestin*) adj3 symptom*).ti,ab,kf. or ((gastro* or intestin* or colon* or colorectal) adj2 (dis* or symptom*)).ti,kf. or ((discriminat* or distinguish* or differentiat* or differential-diagnos*) and (IBS or irritable or functional or spastic)).ti,ab,kf.	192793
2	exp occult blood/ or ((fecal or faecal) adj2 immuno* adj2 test*).ti,ab,kf. or 'occult blood test*'.ti,ab,kf.	7737
3	exp "Sensitivity and Specificity"/ or exp diagnosis/ or diagnosis.fs. or "diagnostic use".fs. or diagnos*.ti,kf. or sensitivity.ti,ab,kf. or specificity.ti,ab,kf. or "predictive value".ti,ab,kf. or PPV.ti,ab,kf. or NPV.ti,ab,kf. or (diagnostic adj1 accurac*).ti,ab,kf.	10407533
4	1 and 2 and 3	210
5	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	467589
6	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	3589452
7	4 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	203
8	limit 7 to yr="2010 -Current"	90
9	8 and 5	**5**
10	8 and 6	37
11	10 not 9	**37**

Endoscopy

Richtlijn: PDS	
Uitgangsvraag: Helpt het uitvoeren van een endoscopie (als aanvulling op anamnese en lichamelijk onderzoek) bij het onderscheid maken tussen patiënten met organische aandoeningen (zoals IBD, maligniteiten) en functionele buikklachten (PDS).	
Database(s): Ovid/Medline, Embase	Datum: 24-11-2020
Periode: 2000	Talen: nvt
Literatuurspecialist: Ingeborg van Dusseldorp	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gezocht met de volgende elementen: prikkelbaredarmsyndroom (P) en colonoscopie (I) Daarnaast is gekozen voor het studiedesign Diagnostiek, sensitiviteit en specificiteit en SR en RCT. Alle sleutelartikelen worden gevonden	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 24-11-2020 met relevante zoektermen gezocht naar systematische reviews, RCT's en diagnostische studies (sensitiviteit en specificiteit) over het uitvoeren van een endoscopie bij het bepalen van onderscheid tussen patiënten met organische aandoeningen en functionele buikklachten (PD). De literatuurzoekactie leverde 1.263 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	56	61	109
Diagnostisch	367	607	884
RCT's	137	163	270
Overig			
Totaal			1263

Zoekstrategie

Embase

No.	Query	Results
#12	#10 NOT #9 NOT #8 = RCT's	137
#11	#9 NOT #8 = Diagnostisch	367
#10	#4 AND #7	221

No.	Query	Results
#9	#4 AND #6	395
#8	#4 AND #5 = SR	56
#7	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	2482943
#6	'sensitivity and specificity'/de OR sensitiv*:ab,ti OR specific*:ab,ti OR predict*:ab,ti OR 'roc curve':ab,ti OR 'receiver operator':ab,ti OR 'receiver operators':ab,ti OR likelihood:ab,ti OR 'diagnostic error'/exp OR 'diagnostic accuracy'/exp OR 'diagnostic test accuracy study'/exp OR 'inter observer':ab,ti OR 'intra observer':ab,ti OR interobserver:ab,ti OR intraobserver:ab,ti OR validity:ab,ti OR kappa:ab,ti OR reliability:ab,ti OR reproducibility:ab,ti OR ((test NEAR/2 're-test'):ab,ti) OR ((test NEAR/2 'retest'):ab,ti) OR 'reproducibility'/exp OR accuracy:ab,ti OR 'differential diagnosis'/exp OR 'validation study'/de OR 'measurement precision'/exp OR 'diagnostic value'/exp OR 'reliability'/exp OR 'diagnostic yield':ti,ab,kw	8289902
#5	('meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT ('conference abstract'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it)	525066
#4	#3 AND [1-1-2000]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	1033
#3	#1 AND #2	2099
#2	'colonoscopy'/exp OR colonoscop*:ti,ab,kw	91453

No.	Query	Results
#1	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR intestin* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'abdominal pain'/mj OR 'lower abdominal pain'/mj OR 'abdominal pain':ti,kw OR 'abdomen pain':ti,kw OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw	47944

Ovid/Medline

#	Searches	Results
13	11 not 10 not 9	163
12	10 not 9	607
11	5 and 7	261
10	5 and 8	629
9	5 and 6	61
8	(exp Sensitivity/ and Specificity/) or (Sensitiv* or Specific*).ti,ab. or (predict* or ROC-curve or receiver-operator*).ti,ab. or (likelihood or LR*).ti,ab. or exp Diagnostic Errors/ or (inter-observer or intra-observer or interobserver or intraobserver or validity or kappa or reliability).ti,ab. or reproducibility.ti,ab. or (test adj2 (re-test or retest)).ti,ab. or "Reproducibility of Results"/ or accuracy.ti,ab. or Diagnosis, Differential/ or Validation Studies.pt.	6633299
7	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2051429
6	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	464337
5	limit 4 to yr="2000 -Current"	1711
4	3 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	2104
3	1 and 2	2207
2	exp colonoscopy/ or colonscop*.ti,ab,kf.	30618

1	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or functional colonic disease*.ti,ab,kf. or mucomembraneous colitis.ti,ab,kf. or mucous colitis.ti,ab,kf. or ibs.ti,ab,kf. or ((functional or organic) adj1 (gastro* or colon* or bowel) adj2 (dis* or symptom*)).ti,ab,kf. or ((gastro* or intestin* or colon* or colorectal) adj2 (dis* or symptom*)).ti,kf. or abdominal pain.ti,ab,kf. or abdomen pain.ti,ab,kf. or abdominal complaint*.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf. or (ibsc or ibsd or ibsm).ti,ab,kf.	109550

Diet

Richtlijn: PDS	
Uitgangsvraag: Uv4 Is een FODMAP, vezelarm of matig laag-vezel, NICE-PDS (McKenzie) of glutenvrij dieet, aan te bevelen bij patiënten?	
Database(s): Ovid/Medline, Embase	Datum: 24-11-2020
Periode: 2000-	Talen: nvt
Literatuurspecialist: Ingeborg van Dusseldorp	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Er is met de volgende elementen gezocht: Prikkelbaredarmsyndroom (P) en FODMAP, psyllium, glutenvrij, low fiber (I) Voor deze vraag zijn de elementen psyllium en dietary fiber aan het zoekformulier toegevoegd. Omdat in de Mesh database geen passende trefwoorden aanwezig zijn voor FODMAP en low fiber diet is gekozen om de top term Diet therapy mee te nemen. Het volgende artikel: Am J Gastroenterol. 2013 May;108(5):718-27. doi: 10.1038/ajg.2013.63. Epub 2013 Apr 2. Fiber and functional gastrointestinal disorders Shanti Eswaran 1 , Jane Muir, William D Chey PMID: 23545709 DOI: 10.1038/ajg.2013.63 wordt niet gevonden omdat het een beschrijvend artikel is. Alle overige sleutelartikelen worden wel gevonden	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 24-11-2020 met relevante zoektermen gezocht naar systematische reviews en RCT's over de vraag of FODMAP, vezelarm of matig laag-vezel, glutenvrij dieet of psyllium is aan te bevelen. De literatuurzoekactie leverde 802 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	180	135	247
RCT's	376	330	555
Observationele studies			
Overig			
Totaal			802

Zoekstrategie

Embase

No.	Query	Results
#9	#8 NOT #7	376
#8	#5 AND #6	485
#7	#4 AND #6	180
#6	#3 AND [1-1-2000]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	1132
#5	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	2480251
#4	('meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT ('conference abstract'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it)	525224
#3	#1 AND #2	1989
#2	'low fiber diet'/exp OR 'dietary fiber'/exp OR 'low fodmap diet'/exp OR 'ispagula'/exp OR 'gluten free diet'/exp OR 'roughage poor diet*':ti,ab,kw OR (((low OR poor OR limited OR restricted) NEAR/2 ('fiber diet*' OR 'fibre diet*')):ti,ab,kw) OR fodmap:ti,ab,kw OR 'gluten free diet*':ti,ab,kw OR 'glutenfree diet*':ti,ab,kw OR 'agiocur':ti,ab,kw OR 'arcolax':ti,ab,kw OR 'betajel':ti,ab,kw OR 'fybogel':ti,ab,kw OR 'iso gel':ti,ab,kw OR 'isogel':ti,ab,kw OR 'ispaghul*':ti,ab,kw OR 'isphagul*':ti,ab,kw OR 'konsyl':ti,ab,kw OR 'metamucil':ti,ab,kw OR 'mucilax':ti,ab,kw	36856

No.	Query	Results
	OR 'mucilose':ti,ab,kw OR 'mucofalk':ti,ab,kw OR 'plantaginis semen':ti,ab,kw OR 'plantaglucide':ti,ab,kw OR 'plantago ovata extract':ti,ab,kw OR 'plantago seed':ti,ab,kw OR 'psyllium':ti,ab,kw OR 'regulan':ti,ab,kw OR 'transilane':ti,ab,kw OR 'vi siblin':ti,ab,kw OR 'volcolon':ti,ab,kw	
#1	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR intestin* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'abdominal pain'/mj OR 'lower abdominal pain'/mj OR 'abdominal pain':ti,kw OR 'abdomen pain':ti,kw OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw	47944

Ovid/Medline

#	Searches	Results
20	from 18 keep 1-330	330
19	from 16 keep 1-135	135
18	17 not 16	330
17	9 and 15	416
16	8 and 15	135
15	limit 14 to yr="2000 -Current"	1201
14	3 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	1533
13	10 or 11	446
12	11 not 10	317
11	7 and 9	402
10	7 and 8	129
9	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2051429
8	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp	464337

	models, animal/) not humans/))	
7	limit 6 to yr="2000 -Current"	1126
6	5 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	1362
5	1 and 4	1485
4	exp dietary fiber/ or exp psyllium/ or exp diet, gluten free/ or roughage poor diet*.ti,ab,kf. or ((low or poor or limited or restricted) adj2 (fiber diet* or fibre diet*)).ti,ab,kf. or fodmap.ti,ab,kf. or gluten free diet*.ti,ab,kf. or glutenfree diet*.ti,ab,kf. or agiocur.ti,ab,kf. or arcolax.ti,ab,kf. or betajel.ti,ab,kf. or fybogel.ti,ab,kf. or iso gel.ti,ab,kf. or isogel.ti,ab,kf. or ispaghul*.ti,ab,kf. or isphagul*.ti,ab,kf. or konsyl.ti,ab,kf. or metamucil.ti,ab,kf. or mucilax.ti,ab,kf. or mucilose.ti,ab,kf. or mucofalk.ti,ab,kf. or plantaginis semen.ti,ab,kf. or plantaglucide.ti,ab,kf. or plantago ovata extract.ti,ab,kf. or plantago seed.ti,ab,kf. or psyllium.ti,ab,kf. or regulan.ti,ab,kf. or transilane.ti,ab,kf. or vi siblin.ti,ab,kf. or volcolon.ti,ab,kf. or "low fermentable oligosaccharide disaccharide monosaccharide and polyol diet".ti,ab,kf.	26828
3	1 and 2	1664
2	diet therapy/ or exp dietary fiber/ or exp psyllium/ or exp diet, gluten free/ or roughage poor diet*.ti,ab,kf. or ((low or poor or limited or restricted) adj2 (fiber diet* or fibre diet*)).ti,ab,kf. or fodmap.ti,ab,kf. or gluten free diet*.ti,ab,kf. or glutenfree diet*.ti,ab,kf. or agiocur.ti,ab,kf. or arcolax.ti,ab,kf. or betajel.ti,ab,kf. or fybogel.ti,ab,kf. or iso gel.ti,ab,kf. or isogel.ti,ab,kf. or ispaghul*.ti,ab,kf. or isphagul*.ti,ab,kf. or konsyl.ti,ab,kf. or metamucil.ti,ab,kf. or mucilax.ti,ab,kf. or mucilose.ti,ab,kf. or mucofalk.ti,ab,kf. or plantaginis semen.ti,ab,kf. or plantaglucide.ti,ab,kf. or plantago ovata extract.ti,ab,kf. or plantago seed.ti,ab,kf. or psyllium.ti,ab,kf. or regulan.ti,ab,kf. or transilane.ti,ab,kf. or vi siblin.ti,ab,kf. or volcolon.ti,ab,kf. or "low fermentable oligosaccharide disaccharide monosaccharide and polyol diet".ti,ab,kf.	37266
1	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or functional colonic disease*.ti,ab,kf. or mucomembraneous colitis.ti,ab,kf. or mucous colitis.ti,ab,kf. or ibs.ti,ab,kf. or ((functional or organic) adj1 (gastro* or colon* or bowel) adj2 (dis* or symptom*)).ti,ab,kf. or ((gastro* or intestin* or colon* or colorectal) adj2 (dis* or symptom*)).ti,kf. or abdominal pain.ti,ab,kf. or abdomen pain.ti,ab,kf. or abdominal complaint*.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf. or (ibsc or ibsd or ibsm).ti,ab,kf.	109550

Peppermint oil

Richtlijn: PDS	
Uitgangsvraag: Is pepermuntolie effectief bij patiënten met PDS ?	
Database(s): Ovid/Medline, Embase	Datum: 24-11-2020
Periode: 2000-	Talen: nvt
Literatuurspecialist: Ingeborg van Dusseldorp	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is met de volgende elementen gezocht: prikkelbaredarmsyndroom (P) en perpermuntolie (I) Het artikel van Black. Peppermint Oil in Irritable Bowel Syndrome. Gastroenterology 2020;159:395–405 is bibliografisch onjuist. Het betreft een brief en is slechts 1 pagina. Om	

deze reden wordt het niet gevonden. Het artikel van Weerts. Efficacy and safety of peppermintoil in a randomized, double-blind trail in patients with irritable bowel syndrome. Gastroenterology. 2020.158.123-136, wordt wel aangetroffen in het resultaat.
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 24-11-2020 met relevante zoektermen gezocht naar systematische reviews en RCT's over de vraag of pepermuntolie effectief is bij patiënten met PDS. De literatuurzoekactie leverde 230 unieke treffers op.

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	92	29	95
RCT's	111	43	125
Observationele studies			
Overig			
Totaal			230

Zoekstrategie

Embase

No.	Query	Results
#9	#8 NOT #7	111
#8	#5 AND #6	170
#7	#4 AND #6	92
#6	#3 AND [1-1-2000]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	299
#5	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	2480251
#4	('meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection	525224

No.	Query	Results
	criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT ('conference abstract'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it)	
#3	#1 AND #2	438
#2	'peppermint oil'/exp OR 'colpermin':ti,ab,kw OR (((menth* OR peppermint OR mint*) NEAR/2 (oil OR oleum)):ti,ab,kw)	1962
#1	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR intestin* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'abdominal pain'/mj OR 'lower abdominal pain'/mj OR 'abdominal pain':ti,kw OR 'abdomen pain':ti,kw OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw	47944

Ovid/Medline

#	Searches	Results
14	from 12 keep 1-43	43
13	from 10 keep 1-29	29
12	11 not 10	43
11	8 and 9	64
10	7 and 9	29
9	5 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	109
8	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2051429
7	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp	464337

	models, animal/) not humans/))	
6	limit 5 to yr="2000 -Current"	103
5	1 and 3	117
4	2 and 3	117
3	(Plant Oils/ and Mentha piperita/) or colpermin.ti,ab,kf. or ((menth* or peppermint or mint*) adj2 (oil or oleum)).ti,ab,kf.	721
2	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or 'functional colonic disease*'.ti,ab,kf. or 'mucomembraneous colitis'.ti,ab,kf. or 'mucous colitis'.ti,ab,kf. or ibs.ti,ab,kf. or (functional adj1 (gastro* or colon* or bowel) adj2 (dis* or symptom*)).ti,ab,kf. or 'abdominal pain'.ti,kf. or 'abdomen pain'.ti,kf. or 'abdominal complaint*'.ti,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf.	42571
1	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or 'functional colonic disease*'.ti,ab,kf. or 'mucomembraneous colitis'.ti,ab,kf. or 'mucous colitis'.ti,ab,kf. or ibs.ti,ab,kf. or (functional adj1 (gastro* or colon* or bowel or intestin* or colorectal) adj2 (dis* or symptom*)).ti,ab,kf. or 'abdominal pain'.ti,ab,kf. or 'abdomen pain'.ti,ab,kf. or 'abdominal complaint*'.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf.	84124

Linaclotide

Richtlijn: PDS	
Uitgangsvraag: UV6 Is linaclotide (vergeleken met placebo) aan te bevelen bij (therapieresistente) PDS-C-patiënten (reguliere behandeling al gehad)?	
Database(s): Ovid/Medline, Embase	Datum: 24-11-2020
Periode: 2000-	Talen: nvt
Literatuurspecialist: Ingeborg van Dusseldorp	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gewerkt met de volgende thema's: Prikkelbaredarmsyndroom (P) en Linaclotide (I) Alle sleutelartikelen zijn gevonden.	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 24-11-2020 met relevante zoektermen gezocht naar systematische reviews en RCT's over het effect van linaclotide bij PDS-C patiënten De literatuurzoekactie leverde 226 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	68	34	74
RCT's	130	65	152
Observationele studies			
Overig			

Totaal			226

Zoekstrategie

Embase

No.	Query	Results
#33	#32 NOT #31 **= RCT**	**130**
#32	#28 AND #30	**163**
#31	#28 AND #29 **= SR**	**68**
#30	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	**2482943**
#29	('meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT ('conference abstract'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it)	**526329**
#28	#27 AND [1-1-2000]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	**329**
#27	#25 AND #26	**626**
#26	'linaclotide'/exp OR 'constella':ti,ab,kw OR 'linaclotide':ti,ab,kw OR 'linzess':ti,ab,kw OR 'md 1100':ti,ab,kw OR 'md1100':ti,ab,kw OR 'mm 416775':ti,ab,kw OR 'mm416775':ti,ab,kw	**1029**
#25	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw	**48038**

No.	Query	Results
	OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR colorectal* OR intestin*) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'abdominal pain'/mj OR 'lower abdominal pain'/mj OR 'abdominal pain':ti,kw OR 'abdomen pain':ti,kw OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw OR ibsc:ti,ab,kw OR ibsd:ti,ab,kw OR ibsm:ti,ab,kw	

Ovid/Medline

#	Searches	Results
12	from 10 keep 1-65	65
11	from 8 keep 1-34	34
10	9 not 8 **= RCT**	65
9	5 and	89
8	5 and 6 **= SR**	34
7	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2051429
6	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	464337
5	limit 4 to yr="2000 -Current"	171
4	3 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	171
3	1 and 2	189
2	(Linaclotide or constella or linaclotide or linzess or md 1100 or md1100 or mm 416775 or mm416775).ti,ab,kf.	289
1	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or functional colonic disease*.ti,ab,kf. or mucomembraneous colitis.ti,ab,kf. or mucous colitis.ti,ab,kf. or ibs.ti,ab,kf. or ((functional or organic) adj1 (gastro* or colon* or bowel) adj2 (dis* or symptom*)).ti,ab,kf. or ((gastro* or intestin* or colon* or colorectal) adj2 (dis* or symptom*)).ti,kf. or abdominal pain.ti,ab,kf. or abdomen pain.ti,ab,kf. or abdominal complaint*.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf. or (ibsc or ibsd or ibsm).ti,ab,kf.	109550

Antidepressants

Richtlijn: prikkebare darm syndroom	
Uitgangsvraag: antidepressiva	
Database(s): Ovid/Medline, Embase	Datum: 26-11-2020
Periode: 2010-	Talen: nvt
Literatuurspecialist: Carla Sloof (NHG)	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gezocht met de elementen IBS / gastrointestinal symptoms (P) en antidepressiva (I) Omdat de uitgangsvraag focust op TCA en SSRI, zijn die termen sensitief gezocht, en de overige/algemenere antidepressiva-termen ter aanvulling specifieker in titel of als major trefwoord. Het sleutelartikel van Drossman valt uit de resultaten vanwege het toepassen van de methodologische filters. Overige sleutelartikelen worden gevonden.	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 26-11-2020 met relevante zoektermen gezocht naar systematische reviews en RCT's over de vraag of TCA's/SSRI's effectief zijn bij patiënten met PDS. De literatuurzoekactie leverde 330 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	121	43	128
RCT's	180	60	202
Observationele studies	Nvt	Nvt	Nvt
Overig	nvt	nvt	Nvt
Totaal	301	103	330

Zoekstrategie

Embase

No.	Query	Results
#10	#7 OR #8	301
#9	**#8 NOT #7**	**180**
#8	#6 AND #2	242
#7	**#6 AND #1**	**121**
#6	#5 AND [1-1-2010]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	591
#5	#3 AND #4	1717
#4	'central nervous system agents'/mj OR 'antidepressant agent'/mj OR 'serotonin uptake inhibitor'/exp OR 'tricyclic antidepressant agent'/exp OR 'serotonin uptake inhibit*':ab,ti,kw OR 'serontonin reuptake inhibit*':ab,ti,kw OR ssri:ab,ti,kw OR	348750

	citalopram:ab,ti OR escitalopram:ab,ti OR fluoxetin*:ab,ti OR fluvoxamin*:ab,ti OR paroxetin*:ab,ti OR sertralin*:ab,ti OR 'tricyclic antidepress*':ab,ti,kw OR tca:ab,ti,kw OR amitriptylin*:ab,ti,kw OR imipramin*:ab,ti,kw OR nortriptylin*:ab,ti,kw OR antidepress*:ti,kw OR ((('gut brain' OR 'brain gut' OR central) NEAR/2 (modulat* OR neuromodulat*)):ab,ti,kw)	
#3	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR intestin* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'functional abdominal pain'/mj OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw	31917
#2	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	2484818
#1	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	684864

Ovid/Medline

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to November 25, 2020

Search Strategy:

#	Searches	Results
1	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or 'functional colonic disease*'.ti,ab,kf. or 'mucomembraneous colitis'.ti,ab,kf. or 'mucous colitis'.ti,ab,kf. or ibs.ti,ab,kf. or (functional adj1 (gastro* or colon* or bowel or intestin* or colorectal) adj2 (dis* or symptom*)).ti,ab,kf. or 'abdominal pain'.ti,ab,kf. or 'abdomen pain'.ti,ab,kf. or 'abdominal complaint*'.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf.	84138
2	*central nervous system agents/ or *antidepressant agent/ or exp serotonin uptake inhibitors/ or exp antidepressive agents, tricyclic/ or 'serotonin uptake inhibit*'.ti,ab,kf. or 'serontonin reuptake inhibit*'.ti,ab,kf. or ssri.ti,ab,kf. or citalopram.ti,ab,kf. or escitalopram.ti,ab,kf. or fluoxetin*.ti,ab,kf. or fluvoxamin*.ti,ab,kf. or paroxetin*.ti,ab,kf. or sertralin*.ti,ab,kf. or 'tricyclic antidepress*'.ti,ab,kf. or tca.ti,ab,kf. or amitriptylin*.ti,ab,kf. or imipramin*.ti,ab,kf. or nortriptylin*.ti,ab,kf. or antidepress*.ti,kf. or (('gut brain' or 'brain gut' or central) adj2 (modulat* or neuromodulat*)).ti,ab,kf.	110694
3	1 and 2	598
4	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or	464582

	literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	
5	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2052197
6	3 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	529
7	limit 6 to yr="2010 -Current"	244
8	**7 and 4**	**43**
9	7 and 5	92
10	**9 not 8**	**60**

Psychological therapies

Richtlijn: prikkebare darm syndroom	
Uitgangsvraag: psychologische therapieen	
Database(s): Ovid/Medline, Embase	Datum: 26-11-2020
Periode: 2010-	Talen: nvt
Literatuurspecialist: Carla Sloof (NHG)	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gezocht met de elementen IBS / gastrointestinal symptoms (P) en psychotherapie (I)	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 26-11-2020 met relevante zoektermen gezocht naar systematische reviews en RCT's over de vraag of TCA's/SSRI's effectief zijn bij patiënten met PDS. De literatuurzoekactie leverde 376 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	101	109	134
RCT's	167	193	242
Observationele studies	*Nvt*	*Nvt*	*Nvt*

Overig	*Nvt*	*nvt*	*Nvt*
Totaal	268	302	**376**

Zoekstrategie

Embase

No.	Query	Results
#10	#7 OR #8	268
#9	**#8 NOT #7**	**167**
#8	#6 AND #2	223
#7	**#6 AND #1**	**101**
#6	#5 AND [1-1-2010]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	494
#5	#3 AND #4	1717
#4	'psychotherapy'/exp/mj OR 'psychological therapy'/exp OR 'psychological intervention'/exp OR 'hypnotherapy'/exp OR psychotherap*:ab,ti,kw OR cbt:ab,ti,kw OR hypnotherap*:ab,ti,kw OR (((psychologic* OR 'cognitive behav*' OR relaxat* OR hypno*) NEAR/3 (therap* OR intervention* OR training)):ab,ti,kw)	202199
#3	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR intestin* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'functional abdominal pain'/mj OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw	31917
#2	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	2484818
#1	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	684864

Ovid/Medline

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to November 25, 2020

Search Strategy:

#	Searches	Results
1	exp irritable bowel syndrome/ or abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or 'functional colonic disease*'.ti,ab,kf. or 'mucomembraneous colitis'.ti,ab,kf. or 'mucous colitis'.ti,ab,kf. or ibs.ti,ab,kf. or	84138

	(functional adj1 (gastro* or colon* or bowel or intestin* or colorectal) adj2 (dis* or symptom*)).ti,ab,kf. or 'abdominal pain'.ti,ab,kf. or 'abdomen pain'.ti,ab,kf. or 'abdominal complaint*'.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf.	
2	exp psychotherapy/ or exp mind-body therapies/ or psychotherap*.ti,ab,kf. or cbt.ti,ab,kf. or hypnotherap*.ti,ab,kf. or ((psychologic* or 'cognitive behav*' or relaxat* or hypno*) adj3 (therap* or intervention* or training)).ti,ab,kf.	245764
3	1 and 2	1333
4	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	464582
5	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2052197
6	3 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	1250
7	limit 6 to yr="2010 -Current"	622
8	**7 and 4**	**109**
9	7 and 5	267
10	**9 not 8**	**193**

Probiotics

Richtlijn: prikkelbare darm syndroom	
Uitgangsvraag: probiotica	
Database(s): Ovid/Medline, Embase	Datum: 16-02-2021
Periode: 2010-	Talen: nvt
Literatuurspecialist: Carla Sloof (NHG)	
BMI zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting en opmerkingen: Voor deze vraag is gezocht met de elementen IBS / gastrointestinal symptoms (P) en probiotica (I)	

Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 16-02-2021 met relevante zoektermen gezocht naar systematische reviews en RCT's over de vraag of probiotica effectief zijn bij patiënten met PDS. De literatuurzoekactie leverde 582 unieke treffers op.

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	174	146	202
RCT's	293	273	380
Observationele studies	Nvt	Nvt	Nvt
Overig	nvt	nvt	Nvt
Totaal	467	419	**582**

Zoekstrategie

Embase

No.	Query	Results
#10	#7 OR #8	467
#9	**#8 NOT #7**	**293**
#8	#6 AND #2	391
#7	**#6 AND #1**	**174**
#6	#5 AND [1-1-2010]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	856
#5	#3 AND #4	1726
#4	'probiotic agent'/exp/mj OR probiotic*:ab,ti,kw OR 'pro biotic':ab,ti,kw OR (((supplement* OR diet* OR treat* OR therap*) NEAR/3 ('gut microbio*' OR lactobacill* OR bifido*)):ab,ti,kw)	40860
#3	'irritable colon'/exp/mj OR (((unstable OR irritable OR spastic) NEAR/2 (colon OR bowel OR colitis)):ti,ab,kw) OR 'functional colonic disease*':ti,ab,kw OR 'mucomembraneous colitis':ti,ab,kw OR 'mucous colitis':ti,ab,kw OR ibs:ti,ab,kw OR ((functional NEAR/1 (gastro* OR colon* OR bowel OR intestin* OR colorectal) NEAR/2 (dis* OR symptom*)):ti,ab,kw) OR 'functional abdominal pain'/mj OR 'abdominal complaint*':ti,kw OR fbd:ti,kw OR fbds:ti,kw	32460
#2	('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	2523115
#1	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab	706451

	OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	

Ovid/Medline

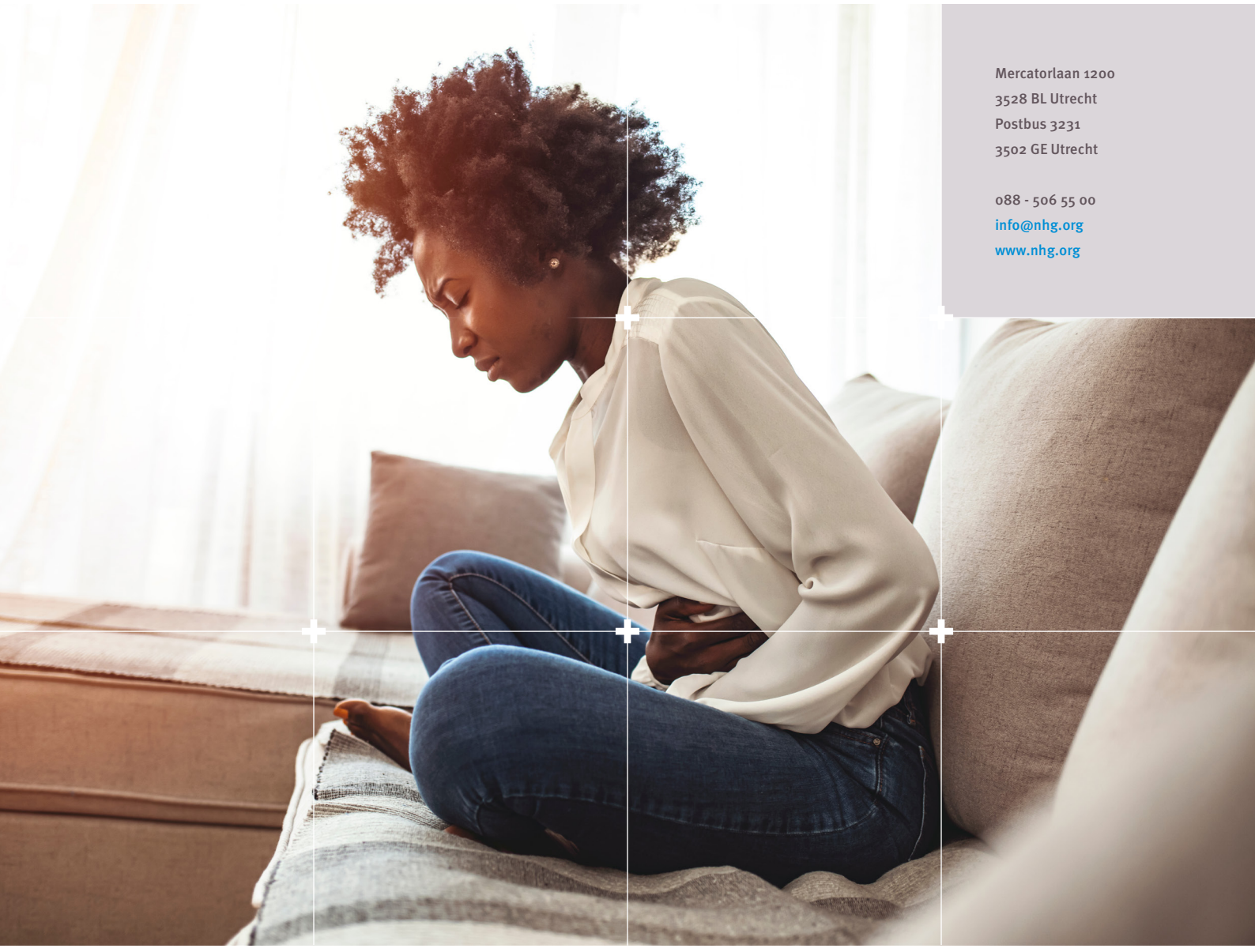
Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to February 15, 2021

Search Strategy:

#	Searches	Results
1	exp irritable bowel syndrome/ or *abdominal pain/ or ((unstable or irritable or spastic) adj2 (colon or bowel or colitis)).ti,ab,kf. or 'functional colonic disease*'.ti,ab,kf. or 'mucomembraneous colitis'.ti,ab,kf. or 'mucous colitis'.ti,ab,kf. or ibs.ti,ab,kf. or (functional adj1 (gastro* or colon* or bowel or intestin* or colorectal) adj2 (dis* or symptom*)).ti,ab,kf. or 'abdominal pain'.ti,kf. or 'abdomen pain'.ti,kf. or 'abdominal complaint*'.ti,ab,kf. or fbd.ti,ab,kf. or fbds.ti,ab,kf.	33260
2	exp probiotics/ or probiotic*.ti,ab,kf. or pro-biotic.ti,ab,kf. or ((supplement* or diet* or treat* or therap*) adj3 (gut-microbio* or lactobacill* or bifido*)).ti,ab,kf.	32993
3	1 and 2	1221
4	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	483136
5	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	2091905
6	3 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	1118
7	limit 6 to yr="2010 -Current"	844
8	**7 and 4**	**146**
9	7 and 5	367
10	**9 not 8**	**273**

Verantwoording/Totstandkoming

Richtlijn Prikkelbaredarmsyndroom



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