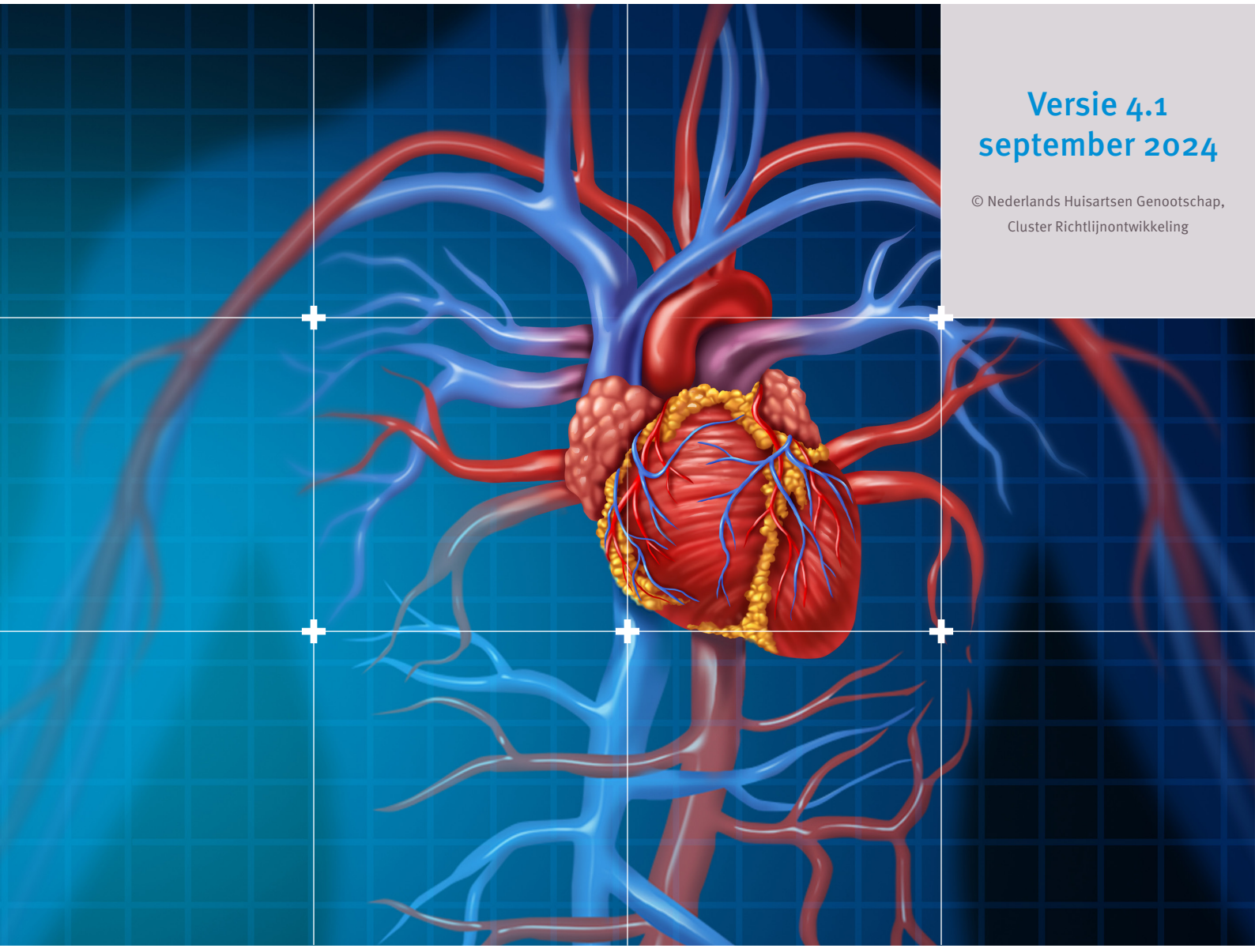
Totstandkoming en methoden

NHG-Standaard CVRM (M84)



Versie 4.1
september 2024

nhg
Nederlands
Huisartsen
Genootschap

Inhoudsopgave

1 Samenstelling werkgroep

De NHG-Standaard Cardiovasculair risicomanagement, die ook wordt uitgebracht als multidisciplinaire richtlijn Cardiovasculair risicomanagement (zie www.richtlijnendatabase.nl), is opgesteld door een multidisciplinaire werkgroep die naast huisartsen bestond uit vertegenwoordigers van diverse andere partijen. De richtlijnontwikkeling werd ondersteund door medewerkers van het Kennisinstituut van de Federatie van Medisch Specialisten en het Nederlands Huisartsen Genootschap.
De herziening vond plaats met behulp van een stuurgroep en per herziene module een aantal expertiseleden.

Stuurgroep

- Prof. dr. A.W. (Arno) Hoes (voorzitter), klinisch epidemioloog, werkzaam in het UMC Utrecht te Utrecht
- Prof. dr. Y.M. (Yvo) Smulders (vicevoorzitter), internist-vasculair geneeskundige, werkzaam in het Amsterdam UMC, locatie VUmc te Amsterdam, NIV
- Drs. N.J.P. (Klaas) Borst, internist ouderengeneeskunde, werkzaam in het Isala ziekenhuis te Zwolle, NIV
- Dr. F.A.L. (Frans) van der Horst, klinisch chemicus, werkzaam in het Reinier Medisch Diagnostisch Centrum te Delft, NVKC
- Dr. A.H. (AnHo) Liem, cardioloog niet praktiserend, NVVC
- Prof. dr. F.M.A.C. (Fabrice) Martens, cardioloog, werkzaam in het Amsterdam UMC te Amsterdam, NVVC
- Prof. F. (Francesco) Mattace-Raso, klinisch geriater, werkzaam in het Erasmus Medisch Centrum te Rotterdam, NVKG
- Prof. E.P. (Eric) Moll van Charante, huisarts niet praktiserend, huisarts-onderzoeker, werkzaam in het Amsterdam UMC, locatie AMC te Amsterdam, NHG
- L.A.C. (Sanne) Ruigrok MSc, beleidsadviseur, werkzaam bij Harteraad te Den Haag, Harteraad
- Prof. dr. B.K. (Birgitta) Velthuis, radioloog, werkzaam in het UMC Utrecht te Utrecht, NVvR
- Prof. dr. F.L.J. (Frank) Visseren, internist-vasculair geneeskundige, werkzaam in het UMC Utrecht te Utrecht, NIV
- Dr. Tj. (Tjerk) Wiersma, senior-wetenschappelijk medewerker, werkzaam bij het Nederlands Huisartsen Genootschap te Utrecht, NHG

Met ondersteuning van:

- Dr. W.M. Lijfering, senior adviseur, Kennisinstituut van de Federatie Medisch Specialisten (vanaf september 2023)
- Dr. B.H. (Bernardine) Stegeman, senior adviseur, Kennisinstituut van de Federatie Medisch Specialisten (tot augustus 2023).
- Dr. N.L. van der Zwaluw, senior adviseur, Kennisinstituut van de Federatie Medisch Specialisten (vanaf april 2023)

Betrokken expertiseleden

- Module 1.1 ‘Streefwaarden LDL-C bij behandeling met lipidenverlagende medicatie’ & Module 1.2 Dyslipidemie bij (kwetsbare) ouderen:
    - Drs. M. (Marco) Krukerink, huisarts, werkzaam in Huisartsenpraktijk Krukerink & De Wolde te Borne, NHG
    - Prof. F. (Francesco) Mattace-Raso, klinisch geriater, werkzaam in het Erasmus Medisch Centrum te Rotterdam, NVKG

    - Dr. J.E. (Jeanine) Roeters van Lennep, internist-vasculair geneeskundige, werkzaam in het Erasmus MC te Rotterdam, NIV
    - Dr. P. (Pernette) de Sauvage Nolting, cardioloog, werkzaam in Hartkliniek Rotterdam te Rotterdam, NVVC
    - Drs. J.J.S. (Judith) Tjin-A-Ton, kaderhuisarts hart- en vaatziekten, werkzaam in huisartsenpraktijk Frakking & Tjin-A-Ton te Amstelveen, NHG
    - Dr. M.E. (Janneke) Wittekoek, cardioloog, werkzaam bij Stichting Heartlife klinieken te Utrecht, NVVC
    - Prof. dr. Y.M. (Yvo) Smulders, internist-vasculair geneeskundige, werkzaam in het Amsterdam UMC, locatie VUmc te Amsterdam, NIV

- Module 2.1 Schatten van het risico op hart- en vaatziekten (en implicaties voor het aanbieden van behandeling) & Module 2.2 Coronaire kalkscore
    - Dr. M.L. (Louis) Handoko, cardioloog, werkzaam in het Amsterdam UMC, locatie VUmc te Amsterdam, NVVC
    - Dr. R.N. (Nils) Planken, radioloog, werkzaam in het Amsterdam UMC, locatie AMC te Amsterdam, NVvR
    - L.A.C. (Sanne) Ruigrok MSc, beleidsadviseur, werkzaam bij Harteraad te Den Haag, Harteraad
    - Drs. P. (Paul) Smits, kaderhuisarts hart- en vaatziekten, werkzaam bij De HOEDT-huisartsen te Zoetermeer, NHG
    - Prof. dr. F.L.J. (Frank) Visseren, internist-vasculair geneeskundige, werkzaam in het UMC Utrecht te Utrecht, NIV
    - Prof. dr. R. (Rozemarijn) Vliegenthart, radioloog, werkzaam in het Universitair Medisch Centrum Groningen te Groningen, NVvR
- Module 3.1 Wanneer moet een verhoogde bloeddruk medicamenteus behandeld worden? & Module 3.2 Streefwaarde bloeddruk bij (kwetsbare) ouderen & Module 3.3 Bloeddruk streefwaarde bij volwassenen & Module 3.4 Op welke manier moet een verhoogde bloeddruk behandeld worden?
    - Prof. Dr. B.J.H. (Bert-Jan) van den Born, internist-vasculair geneeskundige, werkzaam in het Amsterdam UMC, locatie AMC te Amsterdam, NIV
    - Dr. J. (Jaap) Deinum, internist-vasculair geneeskundige, Radboud UMC, Nijmegen, NIV
    - Dr. K. (Karen) Konings, kaderhuisarts hart- en vaatziekten, werkzaam in huisartsenpraktijk K. Konings te Maastricht, NHG
    - Drs. J.J.S. (Judith) Tjin-A-Ton, kaderhuisarts hart- en vaatziekten, werkzaam in huisartsenpraktijk Frakking & Tjin-A-Ton te Amstelveen, NHG
    - Dr. S.E. (Sarah) Vermeer, neuroloog, werkzaam in het Rijnstate Ziekenhuis te Arnhem, NVN
    - Dr. A.J. (Bart) Voogel, cardioloog, werkzaam in het Spaarne Gasthuis te Hoofddorp, NVVC
- Module 4 Andere voorspellers van het risico op hart- en vaatziekten
    - Dr. C. (Calin) Popa, reumatoloog, werkzaam in de Sint Maartenskliniek te Nijmegen, NVR
    - Dr. O.W.H. (Olivier) van der Heijden, gynaecoloog-perinatoloog, werkzaam in het Radboud UMC te Nijmegen, NVOG
    - Dr. K. (Karen) Konings, kaderhuisarts hart- en vaatziekten, werkzaam in huisartsenpraktijk K. Konings te Maastricht, NHG
    - Dr. A.H. (AnHo) Liem, cardioloog niet praktiserend, NVVC

- Module 5 Etnische achtergrond
    - Prof. E.P. (Eric) Moll van Charante, huisarts-onderzoeker, werkzaam in het Amsterdam UMC, locatie AMC te Amsterdam, NHG
    - Drs. P. (Paul) Smits, kaderhuisarts hart- en vaatziekten, werkzaam bij De HOEDT-huisartsen te Zoetermeer, NHG
    - Dr. M. (Melanie) Tan, internist-vasculair geneeskundige, werkzaam in het UMC Utrecht te Utrecht, NIV

2 Inleiding

2.1 Doel van de standaard

De multidisciplinaire richtlijn Cardiovasculair risicomanagement (CVRM) c.q. NHG-Standaard CVRM is een update van de richtlijn/standaard uit 2019 over dit onderwerp. Doel is het formuleren van een eenduidig beleid over CVRM dat gevolgd wordt door zowel huisartsen als medisch specialisten.

2.2 Gebruikers van de richtlijn

De richtlijn is primair ontwikkeld voor huisartsen, cardiologen en internisten.

2.3 Betrokkenheid beroeps- en patiëntenorganisaties

Bij de herziening van deze standaard waren verschillende wetenschappelijke verenigingen, beroepsorganisaties en patiëntenverenigingen betrokken.

2.4 Presentatie

De richtlijn kent een digitale modulaire presentatie met als doel toekomstige gedeeltelijke herzieningen te vereenvoudigen.

2.5 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.

2.6 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 en gedocumenteerd, en waar relevant in overleg met de patiënt, te doen.

Bij deze richtlijn hoort een *disclaimer.*

2.7 Belangenverstrengeling

Alle stuurgroep/werkgroepleden hebben een KNAW Code ter voorkoming van oneigenlijke beïnvloeding door belangenverstrengeling ingevuld. Zie **bijlage 1** voor een samenvattend overzicht.

2.8 Financiering

Het Nederlands Huisartsen Genootschap heeft de totstandkoming van deze richtlijn gefinancierd, met aanvullende financiering van ZonMw.

3 Methoden

Deze standaard is ontwikkeld volgens de *Handleiding Ontwikkelen van NHG-richtlijnen.* De verkorte versie hiervan is te vinden op *Totstandkoming NHG-Standaarden | NHG-Richtlijnen*.

3.1 Voorbereidingsfase

Knelpuntenanalyse en opstellen van uitgangsvragen
Tijdens de need-for-update fase inventariseerde het Kennisinstituut de geldigheid van de richtlijn. Naast de betrokken wetenschappelijke verenigingen en patiëntenorganisaties zijn hier ook andere stakeholders voor benaderd in juni 2021. Per onderdeel is aangegeven of deze geldig is, kan worden samengevoegd met een ander onderdeel, obsoleet is en kan vervallen of niet meer geldig is en moet worden herzien. Ook was er de mogelijkheid om nieuwe onderwerpen aan te dragen die aansluiten bij één (of meerdere) richtlijn(en). De onderdelen die door één of meerdere partijen werden aangekaart als 'niet geldig' zijn meegegaan in de prioriteringsfase. Voor de geprioriteerde onderwerpen zijn concept-uitgangsvragen herzien of opgesteld en definitief vastgesteld.

3.2 Ontwikkelingsfase

De werkwijze staat beschreven in de Verantwoording van de *MDR Cardiovasculair risicomanagement (CVRM).*

Patiëntenperspectief
Er werd aandacht besteed aan het patiëntenperspectief door afvaardiging van Harteraad in de clusterstuurgroep. De verkregen input is meegenomen bij het opstellen van de uitgangsvragen, de keuze voor de uitkomstmaten en bij het opstellen van de overwegingen. De concepttekst is ook voor commentaar voorgelegd aan Harteraad en de eventueel aangeleverde commentaren zijn bekeken en verwerkt. Op de NHG-publiekssite *Thuisarts.nl* staan teksten die ontleend zijn aan de standaard en bedoeld zijn als de patiëntversie van de standaard.

3.3 Commentaar- en autorisatiefase

Versie 4.1
De conceptrichtlijnmodule werd aan de betrokken (wetenschappelijke) verenigingen en (patiënt) organisaties voorgelegd ter commentaar. De commentaren werden verzameld en besproken met het cluster. Naar aanleiding van de commentaren werd de conceptrichtlijnmodule aangepast en definitief vastgesteld door het cluster. De definitieve richtlijnmodule werd aan de deelnemende (wetenschappelijke) verenigingen en (patiënt)organisaties voorgelegd voor autorisatie en door hen geautoriseerd dan wel geaccordeerd. De NHG Autorisatiecommissie (AC) heeft de standaard op 5 juni 2024 geautoriseerd.

3.4 Procedure voor herziening

Deze standaard wordt periodiek herzien. Uiterlijk in 2026 bepaalt het NHG of deze richtlijn nog actueel is. Zo nodig wordt een nieuwe werkgroep geïnstalleerd om de standaard te herzien. De geldigheid van deze standaard komt eerder te vervallen indien nieuwe ontwikkelingen aanleiding zijn om een herzieningstraject te starten.

3.5 Eerdere versies

Zie de eerdere versie van de *Totstandkoming en methoden* met nog actuele zoekstrategieën van de NHG-Standaard Cardiovasculair risicomanagement.

BIJLAGEN

Bijlage 1 Samenvattende tabel KNAW belangenverklaringen

De Code ter voorkoming van oneigenlijke beïnvloeding door belangenverstrengeling is gevolgd. Alle clusterleden hebben schriftelijk verklaard of zij in de laatste drie jaar directe financiële belangen (betrekking bij een commercieel bedrijf, persoonlijke financiële belangen, onderzoeksfinanciering) of indirecte belangen (persoonlijke relaties, reputatiemanagement) hebben gehad. Gedurende de ontwikkeling of herziening van een module worden wijzigingen in belangen aan de voorzitter doorgegeven. De belangenverklaring wordt opnieuw bevestigd tijdens de commentaarfase.
Een overzicht van de belangen van de clusterleden en het oordeel over het omgaan met eventuele belangen vindt u in onderstaande tabel. De ondertekende belangenverklaringen zijn op te vragen bij het secretariaat van het Kennisinstituut van de Federatie Medisch Specialisten.

Werkgroeplid	**Functie**	**Nevenfuncties**	**Gemelde belangen**	**Ondernomen restrictie**
Hoes (voorzitter)	Vice-voorzitter raad van bestuur / decaan, UMC Utrecht	- Lid redactieraad, European Journal of Heart Failure (onbezoldigd) - Lid redactieraad ESC Heart Failure (onbezoldigd) - Lid adviescommissie, Vereniging voor Epidemiologie (onbezoldigd) - Raad van toezicht, Dutch CardioVascular Association (onbezoldigd) - Lid Task Force Heart Failure guidelines European Society of Cardiology (onbezoldigd) - Lid raad van toezicht Netherlands Center for One Health (onbezoldigd) - Lid raad van commissarissen Utrecht Holdings (onbezoldigd - Lid Gezondheidsraad (tot 1-1-2022)	-	Geen
Smulders	- Hoogleraar Interne Geneeskunde - Opleider Interne Geneeskunde	- Lid Hoofdredactie Ned Tijdschr Geneeskunde – bezoldigd - Div beoordelingscommissies ZON-MW – vacatievergoeding - Bestuurslid Ned Internisten-Vereniging – vacatievergoeding - Lid en vice-voorzitter ESC richtlijn-commissie revisie cardiovasculaire preventierichtlijn, onbezoldigd - Jaarlijks vasculair update symposium, spreker, bezoldigd	-	Geen
Visseren	- Internist-vasculair geneeskundige - hoogleraar interne geneeskunde - epidemioloog	Voorzitter van de Task Force of the European Society of Cardiology for the 2021 European guidelines on cardiovascular disease prevention in clinical practice.	Mede-initiatiefnemer van de U-Prevent website voor gebruik van risico algoritmes in de klinische praktijk. De website is eigendom van ORTEC. Betrokkenheid bestaat uit wetenschappelijk advies.	Geen

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen restrictie
Borst	Internist ouderengeneeskunde en vasculaire geneeskunde	Lid Forum visitatorum (vacatievergoeding)	-	Geen
Mattace-Raso	- Hoogleraar Geriatrie Erasmus MC Rotterdam - Sectorhoofd Geriatrie	- Werkgroep Muziek tijdens perio operatief proces FMS - Lid Full Board European Society of Geriatric Medicine - Lid Academic Board European Society of Geriatric Medicine - Lid Special Interest Group Cardiovascular Disease of the Dutch Geriatrics Society - Lid Special Interest Group Cardiovascular Disease of the European Society of Geriatric Medicine - Lid Editorial Board wetschappelijk Journals 2011-2020: Hypertension 2020-today: BMC Geriatrics 2020-today: Panminerva Medica 2020-today: American Journal of Hypertension 2019-today: Aging Clinical and Experimental Research 2015-today: Clinical Interventions in Aging	-	Geen
Liem	Gepensioneerd cadioloog (eerder verbonden aan Franciscus gasthuis Rotterdam tot 31-12-2019)	- eerder lid richtlijnencommissie CVRM - eerder lid richtlijncommissie vetstofwisselingsstoornissen - lid Raad van Toezicht WCN (onbetaald)	2018-2021: vergoeding op uurbasis voor presentaties en adviesraden op het gebied van CVRM Lipiden, antithrombotica, anti-diabetica) en Hartfalen. Deelname aan vele trials vanuit WCN.	Geen, adviesraden zijn gestaakt gedurende het proces
Martens	Cardioloog Hoogleraar Preventieve Cardiologie	Namens de NVVC lid commissie nationale richtlijn CVRM 2019 (onkostenvergoeding) Namens de NVVC lid Werkgroep van het project NVVC – Visie op ESC-richtlijnen (onkostenvergoeding) Namens de NVVC voorzitter Werkgroep Geneesmiddelen Namens de DCVA voorzitter Commissie Preventie	Vergoeding voor presentaties op het gebied van CVRM (lipiden, antitrombotica en anti- diabetica), via bemiddeling bureau's zoals Medcon, Sam Health, Health Investments, Springer Healthcare, Breau Prevents etc.	Geen, adviesraden zijn gestaakt sinds lidmaatschap Stuurgroep CVRM
Wiersma	senior wetenschappelijk medewerker NHG	-	-	Geen

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen restrictie
Moll van Charante	Hoogleraar afdeling Huisartsgeneeskunde (0,5 fte) en afdeling Public & Occupational Health (0,5 fte) Amsterdam UMC. Leerstoel: CVRM in een multi-etnische populatie	- 2018-2020: werkgroeplid NHG-standaard Dementie - 2019-2020: werkgroep Zorgstandaard Dementie, in opdracht van het Ministerie van VWS en het Deltaplan Dementie (ontwikkeld i.s.m Movisie, Nivel, Pharos, Trimbos-instituut en Vilans) - 2019-2021: werkgroeplid interdisciplinaire medisch specialistische richtlijn 'Diagnostiek en behandeling van dementie'	Betrokken bij de ontwikkeling van een app voor zelfmanagement van risicofactoren voor hartvaatziekten en dementie. Het aandeel van resp. Vital Health Software en Philips Vital Health in deze studie is gefinancierd vanuit een Europese grant.	Geen
Velthuis	Radioloog	- Bestuurslid European Society of Cardiovascular Radiology (ESCR) tot 2022 - onbetaald. - Bestuurslid Nederlands Vasculair Forum (NVF) - onbetaald	Vergoedingen als spreker voor Nederlandse Vereniging voor Radiologie (NVvR). Philips research geld voor PhD onderzoeker vanaf 2023	Geen
Van der Horst	Laboratorium specialist klinische chemie en laboratoriumgeneeskunde	- RvA Auditor ISO 15189, betaald - NHG Labcodeplatform, onbetaald - NVKC-werkgroep Geneesmiddel-test interactie, onbetaald - NVKC-werkgroep Diagnostische richtlijnmodules KC SKMS project, onbetaald	-	Geen
Ruigrok	Beleidsadviseur	Geen	Geen	Geen

Expertisegroep

Clusterlid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen restrictie
Born, van den	Internist-vasculair geneeskundige,	- Voorzitter Nederlandse Hypertensie Vereniging, onbetaald - Voorzitter richtlijn Hypertensief Spoedgeval, vacatievergoeding	- Figaro/Fidelio studie, Bayer BV - behandeling van finerenone vs placebo bij patienten met hypertensie en CKD - Precision study, Idorsia Pharmaceuticals Ltd. - behandeling van aprocitentan bij patienten met therapieresistente hypertensie, - ATHENA project, Life Sciences Health TKI - thuismonitoring van de bloeddruk - CFD in renal artery stenosis, Nierstichting Nederland - waarde van computational fluid dynamics voor de optimalisatie van CT voor de identificatie van hemodynamisch relevante nierarteriestenose	Geen onderzoek betreft onderwerpen die niet in de herziene modules ter sprake komen.

Clusterlid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen restrictie
De Sauvage Nolting	Cardioloog	-	-	Geen
Deinum	Internist Radboud UMC Nijmegen	-	-	Geen
Handoko	Cardioloog	Medical Lectures Handoko: Als ZZP-er verzorg ik lezingen/presentaties en/of medisch strategisch advies op het gebied van de cardiologie (betaald).	Via Medical Lectures Handoko ontving/ontvang ik sprekersvergoeding / vergoeding voor advieswerk van Novartis, Boehringer Ingelheim, Daiichi Sankyo, Vifor Pharma, AstraZeneca, Bayer, MSD, Quin.	Geen
Heijden, van der	Gynaecoloog-perinatoloog	- Gemandateerde deelnemer namens NVOG in diverse multidisciplinaire richtlijncommissies, vacatievergoeding - Deelnemer NVOG-werkgroep Otterlo, maternale geneeskunde; onbetaald - NTOG (Nederlands Tijdschrift voor Obstetrie en Gynaecologie), deelredactie perinatologie; onbetaald	-	Geen
Konings	- Huisarts 0,8 fte - Kaderarts HVZ 0,2 fte	Aspirant Directie-lid regionale zorggroep ZIO, betaald	Schrijver van ECG-leerboek: ECG's beoordelen en begrijpen - De ECG 10+ methode – (royalties)	Geen
Krukerink	Huisarts	Podcastmaker, Huisartspodcast.nl gedeeltelijk betaald door vakblad H&W	-	Geen
Planken	Radioloog Amersterdam UMC, aandachtsgebied cardiovasculaire radiologie	- Bestuur cardiovasculaire sectie NVvR, onbetaald - SKMS-projectgroep coronair CTA, vergoeding - Werkgroep AP NVvR NVVC, vergoeding	- Consultancy services: Bayer, Hemolens - Speakers fee: Bayer, Kalcio Healthcare	Geen
Popa	Reumatoloog	- Bestuur Nederlands Vasculair Forum; onbetaald - Secretaris werkgroep Vasculair reumatologie, Nederlandse Vereniging voor Reumatologie (NVR); onbetaald - lid redactie Nederlands Tijdschrift voor Reumatologie; onbetaald	-	Geen

Clusterlid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen restrictie
Roeters van Lennep	Internist-vasculair geneeskundige	- voorzitter Nederlandse Vereniging voor internisten Vasculair Geneeskunde, onbetaald - voorzitter Horizoncommissie cardiovasculaire geneeskunde,ZIN, onbetaald - lid raad van Toezicht Heartlife klinieken, onbetaald - lid bestuur Nederlandse Vereniging voor Gender & Gezondheid, onbetaald - lid Executive committe European Atherosclerosis Society, onbetaald - lid Wetenschappelijke Advies Raad Hartstichting, onbetaald - lid Adviesraad Stichting LEEFH, onbetaald	Lokale PI bij verschillende internationale onderzoeken op het gebied van lipidenverlagende medicatie dat gefinancierd wordt door farmaceut.	Geen
Smits	Huisarts	- Kaderhuisarts hart- en vaatziekten - Coórdinator onderwijscommissie HartvaatHAG (vergoeding waarnemer 1/2 dag per week) - Bestuur HartvaatHAG (vacatie) - Onderwijs zorggroepen en huisartsinstituten (betaald) - Adviseur zorggroep Zoetermeer (betaald) - Projectleider zorginhoudelijke indicatoren ketenzorg InEen (betaald)	-	Geen
Tan	Internist-vasculair geneeskundige	-	-	Geen
Tjin-A-Ton	Huisarts - Huisartsenpraktijk Frakking & Tjin-A-Ton (40 uur)	- Bestuurslid Stichting Amstelland Zorg Huisartsen coöperatie Amstelland - Kaderhuisarts Hart & Vaatziekten (ZZP) -Betaald op uur-basis. - Commissie Maatschappij en kwaliteit, Hartstichting - onbetaald	-	Geen
Vermeer	Neuroloog Rijnstate	-	-	Geen

Clusterlid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen restrictie
Vliegenthart	Radioloog	- Voorzitter (tot okt 2023), sectie cardiovasculaire radiologie NVvR, onbetaald - Vice President (tot okt 2022), European Society of Cardiovascular Radiology, onbetaald - President (sinds okt 2022), European Society of Cardiovascular Radiology, onbetaald - Deputy Editor (sinds januari 2023), Radiology, honorarium - Associate Editor (tot eind 2022), European Journal of Radiology, honorarium - Associate Editor (tot eind 2022), Journal of Cardiovascular Computed Tomography, onbetaald - Lid, Strategic Advisory Board, Institute of Cardiometabolism and Nutrition, onbetaald	- Hartstichting, CVON subsidie: CONCRETE studie - CT kalkscore bij huisartspatiënten met pijn op de borst (PI) - Siemens Healthineers, Institutional research grants met betrekking op: ImaLife studie - Imaging in Lifelines (PI) - Lezingen over cardiothoracale beeldvorming waarvoor honorarium (Siemens Healthineers / Bayer Healthcare)	Geen
Voogel	Cardioloog Spaarne Gasthuis	- Lid ESC MCQ committee (onbetaald) - Lid visitatiecommissie NVVC (betaald) - Docent InHolland opleiding echocardiografie (betaald)	-	Geen
Wittekoek	- Cardioloog en CEO: Stichting HeartLife klinieken - Consultant: Hart voor Preventie BV	- Columnist/onbetaald/auteur meerdere boeken/royalties – betaald - Consultancy, webinars, nascholingen voor Pharma: onkosten en betaald - Raad van Toezicht Nederlands Slaapinstituut/betaald	-	Geen

Bijlage 2 Uitgangsvragen

Uitgangsvraag (PICO)	**Uitkomstmaten (O)**
Welke streefwaarden van LDL-C dienen te worden gehanteerd bij de behandeling met lipidenverlagende medicatie bij personen tot en met 70 jaar met een (zeer) hoog risico op hart- en vaatziekten?	Cruciaal: - hart- en vaatziekten - bijwerkingen Belangrijk: - mortaliteit door hart- en vaatziekten
Wat is de meerwaarde van de behandeling met lipidenverlagende middelen bij (kwetsbare) ouderen (> 70 jaar)?	Cruciaal: - hart- en vaatziekten - kwaliteit van leven - functioneren Belangrijk: - bijwerkingen - totale mortaliteit
Wat is de toegevoegde waarde van een coronaire kalkscore bij het reclassificeren van het risico op hart- en vaatziekten?	Cruciaal: - hart- en vaatziekten morbiditeit/mortaliteit - reclassificatie
Wanneer moet een verhoogde bloeddruk behandeld worden?	Cruciaal: - het risico op hart- en vaatziekten - bijwerkingen Belangrijk: - mortaliteit door hart- en vaatziekten - (acute) nierziekten
Welke bloeddrukstreefwaarde dient te worden gehanteerd bij de behandeling van hypertensie bij (kwetsbare) ouderen (> 70 jaar)?	Cruciaal: - hart- en vaatziekten - kwaliteit van leven - functioneren Belangrijk: - bijwerkingen - totale mortaliteit
Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk bij volwassenen (< 70 jaar)?	Cruciaal: - het risico op hart- en vaatziekten - bijwerkingen Belangrijk: - mortaliteit
Wat is de toegevoegde waarde van etnische achtergrond bij het reclassificeren van het risico op hart- en vaatziekten?	Cruciaal: - hart- en vaatziekten morbiditeit/mortaliteit - reclassificatie

Bijlage 3 Zoekstrategieën

Zoekverantwoording voor uitgangsvraag:

Welke streefwaarden van LDL-C dienen te worden gehanteerd bij de behandeling met lipidenverlagende medicatie bij personen tot en met 70 jaar met een (zeer) hoog risico op hart- en vaatziekten?

Uitgangsvraag: Welke streefwaarden van LDL-C dienen te worden gehanteerd bij de behandeling met lipidenverlagende medicatie bij personen met een (zeer) hoog risico op hart- en vaatziekten?	
Database(s): Medline, Embase	Datum: 26-06-2017, 16-12-2021
Periode: 2005-juni 2017, 2017-	Talen: E N , nvt. 16-12-2021
Toelichting: **16-12-2021** Er is een update uitgevoerd van de strategie van 2017. Daarbij is ervoor gekozen om de totale strategie specifieker op te zetten. Er is geen beperking toegepast op taal en tijd en er is gezocht vanaf 1-1-2017.	

26-6-2017

Database	Zoektermen	Totaal
Medline (OVID) 2005-juni 2017 Engels, Nederlands	1 exp *Cardiovascular Diseases/ or (cardiovascular disease* or CVD or vascular disease* or vascular event* or coronary heart disease or CHD).ti,ab,kf. (1961435) 6 *Cholesterol, LDL/ or ((LDL or low-density lipoprotein) adj3 (C or cholesterol)).ti,ab,kf. (53396) 7 (preventi* or statin* or control or therapy).ti,ab,kf. (4244147) 8 (dt or tu or pc).fs. (3562424) 9 exp Hydroxymethylglutaryl-CoA Reductase Inhibitors/ (35783) 10 (hmg coa reductase inhibitor* or statin* or Atorvastatin* or Lovastatin* or Meglutol* or Pravastatin* or Rosuvastatin* or Simvastatin*).ti,ab,kf. (49677) 11 Reference Values/ or target*.ti,ab,kf. or risk.ti. or mortality.ti,ab. or incidence.ti. or relation*.ti. or association.ti. or lipid-modifying.ti. or lipid level*.ti,ab. or reduction.ti,ab. or lowering.ti,ab. (3613106) 12 7 or 8 or 9 or 10 or 11 (8796660) 13 1 and 6 and 12 (20559) 14 limit 13 to (yr="2005 -Current" and (dutch or english)) (12440) 15 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy$).tw. or ((systematic* or literature) adj2 review$1).tw. or (systematic adj overview$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (331922) 16 14 and 15 (702) 26 remove duplicates from 16 (643) – 638 uniek Specifiekere search voor RCT's: 1 exp *Cardiovascular Diseases/ or (cardiovascular disease* or CVD or vascular disease* or vascular event* or coronary heart disease or CHD).ti,ab,kf. (2068780) 6 *Cholesterol, LDL/ or ((LDL or low-density lipoprotein) adj3 (C or cholesterol)).ti,ab,kf. (56376) 7 exp *Hydroxymethylglutaryl-CoA Reductase Inhibitors/ (26564) 8 (hmg coa reductase inhibitor* or statin* or Atorvastatin* or Lovastatin* or Meglutol* or Pravastatin* or Rosuvastatin* or Simvastatin*).ti,kf. (28632) 9 ("lipid lowering therapy" or "intensive lipid lowering").ti,ab,kf. (2823) 10 7 or 8 or 9 (35798) 11 1 and 6 and 10 (4402) 15 limit 11 to (yr="2009 -Current" and (dutch or english)) (2216) 16 randomized controlled trial.pt. or random*.ti. (567019) 17 15 and 16 (608) – 487 uniek	828 SR's (vanaf 2005, sensitieve search) 684 RCT's, vanaf 2009, specifieke search

Embase

16-12-2021

No.	Query	Results
#16	#14 NOT #13	686
#15	#9 AND #14	1
#14	#11 AND #12	900
#13	#10 AND #12	362
#12	#4 AND [1-1-2017]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	3465
#11	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1852245
#10	'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	733409
#9	a AND comparison AND of AND two AND ldl AND cholesterol AND targets AND after AND ischemic AND s troke AND p. AND amarenco, AND j.s. AND kim, AND labreuche, AND h. AND charles, AND j. AND abtan, AND y. AND béjot, AND l. AND cabrejo	1
#8	#4 AND #7	3
#7	#5 OR #6	3
#6	efficacy AND safety AND more AND intensive AND lowering AND ldl AND cholesterol AND a AND 'meta analysis' AND of AND data AND from AND 170 AND 000 AND participants AND 2010 AND baigent	2
#5	between AND achieved AND 'low density' AND lipoprotein AND levels AND major AND adverse AND cardiac AND events AND in AND patie nts AND with AND stable AND ischemic AND heart AND disease AND taking AND statin AND treatment	1
#4	#1 AND #2 AND #3	17720
#3	'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR 'hmg coa reductase inhibitor*':ti,ab OR statin*:ti,ab OR atorvastatin*:ti,ab OR lovastatin*:ti,ab OR meglutol*:ti,ab OR pravastatin*:ti,ab OR rosuvastatin*:ti,ab OR simvastatin*:ti,ab OR 'lipid modifying':ti OR 'lipid level*':ti,ab OR 'reference value'/exp OR 'reference value*':ti,ab,kw OR target*:ti,ab,kw	2613098

No.	Query	Results
#2	'cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,ab OR cvd:ti,ab OR 'vascular disease*':ti,ab OR 'vascular event*':ti,ab OR 'coronary heart disease':ti,ab OR chd:ti,ab	3228633
#1	'low density lipoprotein cholesterol'/exp/mj OR 'very low density lipoprotein cholesterol'/exp/mj OR (((ldl OR 'low-density lipoprotein*') NEAR/3 (c OR cholesterol)):ti,ab)	101123

26-6-2021

Embase (Elsevier)	'low density lipoprotein cholesterol'/exp/mj OR 'very low density lipoprotein cholesterol'/exp/mj OR ((ldl OR 'low-density lipoprotein*') NEAR/3 (c OR cholesterol)):ti,ab AND ('cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,ab OR cvd:ti,ab OR 'vascular disease*':ti,ab OR 'vascular event*':ti,ab OR 'coronary heart disease':ti,ab OR chd:ti,ab) AND (preventi*:ti,ab OR control:ti,ab OR therapy:ti,ab OR 'drug therapy':lnk OR prevention:lnk OR 'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR 'hmg coa reductase inhibitor*':ti,ab OR statin*:ti,ab OR atorvastatin*:ti,ab OR lovastatin*:ti,ab OR meglutol*:ti,ab OR pravastatin*:ti,ab OR rosuvastatin*:ti,ab OR simvastatin*:ti,ab OR target*:ti,ab OR risk:ti OR mortality:ti,ab OR incidence:ti OR relation*:ti OR association:ti OR 'lipid modifying':ti OR 'lipid level*':ti,ab OR reduction:ti,ab OR lowering:ti,ab OR 'reference value'/exp) AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2005-2017]/py NOT 'conference abstract':it AND ('meta analysis'/de OR cochrane:ab OR embase:ab OR psycinfo:ab OR cinahl:ab OR medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de) NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp) (622) – 190 uniek Specifiekere search voor RCT's: (('low density lipoprotein cholesterol'/exp/mj OR 'very low density lipoprotein cholesterol'/exp/mj OR (((ldl OR 'low-density lipoprotein*') NEAR/3 (c OR cholesterol)):ti,ab)) AND ('cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,ab OR cvd:ti,ab OR 'vascular disease*':ti,ab OR 'vascular event*':ti,ab OR 'coronary heart disease':ti,ab OR chd:ti,ab) AND ('hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR 'hmg coa reductase inhibitor*':ti OR statin*:ti OR atorvastatin*:ti OR lovastatin*:ti OR meglutol*:ti OR pravastatin*:ti OR rosuvastatin*:ti OR simvastatin*:ti OR target*:ti) OR 'lipid lowering therapy':ti,ab OR 'intensive lipid lowering':ti,ab) AND ((random*:ti OR 'randomized controlled trial'/exp) NOT 'conference abstract':it) AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2009-2017]/py (539) – 197 uniek

Ovid/Medline

16-12-2021

#	Searches	Results
9	5 and 7	769
8	5 and 6	242
7	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1337375
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	536192

	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	limit 4 to dt="20170101-20211231"	2983
4	1 and 2 and 3	10338
3	exp Hydroxymethylglutaryl-CoA Reductase Inhibitors/ or (hmg coa reductase inhibitor* or statin* or Atorvastatin* or Lovastatin* or Meglutol* or Pravastatin* or Rosuvastatin* or Simvastatin*).ti,ab,kf. or Reference Values/ or target*.ti,ab,kf. or reference value*.ti,ab,kf.	1985090
2	exp *Cardiovascular Diseases/ or (cardiovascular disease* or CVD or vascular disease* or vascular event* or coronary heart disease or CHD).ti,ab,kf.	2339571
1	*Cholesterol, LDL/ or ((LDL or low-density lipoprotein) adj3 (C or cholesterol)).ti,ab,kf.	67352

Zoekverantwoording voor uitgangsvraag:

Wat is de meerwaarde van de behandeling met lipidenverlagende middelen bij (kwetsbare) ouderen (> 70 jaar)?

Uitgangsvraag: Welke streefwaarde van LDL dient te worden gehanteerd bij de behandeling van patiënten met een verschillende mate van verhoogd risico op het hart- en vaatziekten?	
Database(s): Medline, Embase	Datum: 26-06-2017, 16-12-2021
Periode: 2005-juni 2017, 2017-	Talen: E N , nvt. 16-12-2021
Toelichting: 16-12-2021 Er is een update uitgevoerd van de strategie van 2017. Daarbij is ervoor gekozen om de totale strategie specifieker op te zetten. Er is geen beperking toegepast op taal en tijd en er is gezocht vanaf 1-1-2017.	

PICO1 (2017)

Database	Zoektermen	Totaal
Medline (OVID) 1946 – maart 2016	Dyslipidemias/ or Hydroxymethylglutaryl-CoA Reductase Inhibitors/ or exp Simvastatin/ or exp Pravastatin/ or exp Rosuvastatin Calcium/ or exp Lovastatin/ or exp Atorvastatin Calcium/ or statin*.ti OR simvastatin*.ab,ti OR pravastatin*.ab,ti OR rosuvastatin*.ab,ti OR lovastatin*.ab,ti OR fluvastatin*.ab,ti OR cerivastatin*.ab,ti OR pitavastatin*.ab,ti OR atorvastatin*.ab,ti AND exp *Aged/ or aged.ti. or exp *Frail Elderly/ or *"Aged, 80 and over"/ or exp *Aging/ or exp *Geriatric Assessment/ or (elderly or geriatric or 'community dwelling' or frail* or ag?ing or septuagenarian or octogenarian or nonagenarian or centenarian or 'old people' or eldest or oldest).ti limit to (dutch or english or german) *Gebruikte filters:* Systematische reviews: (meta-analysis/ or meta-analysis as topic/ or (meta adj analy$).tw. or ((systematic* or literature) adj2 review$1).tw. or (systematic adj overview$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or	618

	psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) RCTs: (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$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) Observationeel: Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy$.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/ (Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies) = 412	
Embase (Elsevier)	'statin (protein)'/exp/mj OR statin*:ti OR simvastatin*:ab,ti OR pravastatin*:ab,ti OR rosuvastatin*:ab,ti OR lovastatin*:ab,ti OR fluvastatin*:ab,ti OR cerivastatin*:ab,ti OR pitavastatin*:ab,ti OR atorvastatin*:ab,ti OR 'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj AND ((dutch)/lim OR (english)/lim OR (german)/lim) AND (embase)/lim AND ('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 AND ('aged'/exp/mj OR 'geriatric assessment'/exp/mj OR aged:ti OR elderly:ti OR geriatric:ti OR 'community dwelling':ti OR frail*:ti OR ageing:ti OR aging:ti OR septuagenarian:ti OR octogenarian:ti OR nonagenarian:ti OR centenarian:ti OR 'old people':ti OR eldest:ti OR oldest:ti) OR 'statin (protein)'/exp/mj OR statin*:ti OR simvastatin*:ab,ti OR pravastatin*:ab,ti OR rosuvastatin*:ab,ti OR lovastatin*:ab,ti OR fluvastatin*:ab,ti OR cerivastatin*:ab,ti OR pitavastatin*:ab,ti OR atorvastatin*:ab,ti OR 'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj AND ((dutch)/lim OR (english)/lim OR (german)/lim) AND (embase)/lim AND ('aged'/exp OR 'geriatric assessment'/exp OR aged:ti OR elderly:ab,ti OR geriatric:ab,ti OR 'community dwelling':ab,ti OR frail*:ab,ti OR ageing:ab,ti OR aging:ab,ti OR septuagenarian:ab,ti OR octogenarian:ab,ti OR nonagenarian:ab,ti OR centenarian:ab,ti OR 'old people':ab,ti OR eldest:ab,ti OR oldest:ab,ti) AND ((systematic NEAR/2 review*):ti OR 'meta analysis':ti OR cochrane:ta) OR 'statin (protein)'/exp/mj OR statin*:ti OR simvastatin*:ab,ti OR pravastatin*:ab,ti OR rosuvastatin*:ab,ti OR lovastatin*:ab,ti OR fluvastatin*:ab,ti OR cerivastatin*:ab,ti OR pitavastatin*:ab,ti OR atorvastatin*:ab,ti OR 'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj AND ((dutch)/lim OR (english)/lim OR (german)/lim) AND (embase)/lim AND ('clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR ('prospective study'/de NOT 'randomized controlled trial'/de) OR 'cohort analysis'/de OR (cohort NEAR/1 (study OR studies)):ab,ti OR (case:ab,ti AND (control NEAR/1 (study OR studies)):ab,ti) OR (follow:ab,ti AND (up NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)):ab,ti OR (epidemiologic NEAR/1 (study OR studies)):ab,ti OR ('cross sectional' NEAR/1 (study OR studies)):ab,ti) AND ('aged'/exp/mj OR 'geriatric assessment'/exp/mj OR aged:ti OR elderly:ti OR geriatric:ti OR 'community dwelling':ti OR frail*:ti OR ageing:ti OR aging:ti OR septuagenarian:ti OR octogenarian:ti OR nonagenarian:ti OR centenarian:ti OR 'old people':ti OR eldest:ti OR oldest:ti)	

	= 403	

PICO2 (2021)

Embase

16-12-2021

No.	Query	Results
#16	#14 NOT #13	686
#15	#9 AND #14	1
#14	#11 AND #12	900
#13	#10 AND #12	362
#12	#4 AND [1-1-2017]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	3465
#11	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1852245
#10	'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	733409
#9	a AND comparison AND of AND two AND ldl AND cholesterol AND targets AND after AND ischemic AN D stroke AND p. AND amarenco, AND j.s. AND kim, AND labreuche, AND h. AND charles, AND j. AND ab tan, AND y. AND béjot, AND l. AND cabrejo	1
#8	#4 AND #7	3
#7	#5 OR #6	3
#6	efficacy AND safety AND more AND intensive AND lowering AND ldl AND cholesterol AND a AND 'meta analysis' AND of AND data AND from AND 170 AND 000 AND participants AND 2010 AND baigent	2
#5	between AND achieved AND 'low density' AND lipoprotein AND levels AND major AND adverse AND cardiac AND events AND in AND pati ents AND with AND stable AND ischemic AND heart AND disease AND taking AND statin AND treatmen t	1
#4	#1 AND #2 AND #3	17720

No.	Query	Results
#3	'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR 'hmg coa reductase inhibitor*':ti,ab OR statin*:ti,ab OR atorvastatin*:ti,ab OR lovastatin*:ti,ab OR meglutol*:ti,ab OR pravastatin*:ti,ab OR rosuvastatin*:ti,ab OR simvastatin*:ti,ab OR 'lipid modifying':ti OR 'lipid level*':ti,ab OR 'reference value'/exp OR 'reference value*':ti,ab,kw OR target*:ti,ab,kw	2613098
#2	'cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,ab OR cvd:ti,ab OR 'vascular disease*':ti,ab OR 'vascular event*':ti,ab OR 'coronary heart disease':ti,ab OR chd:ti,ab	3228633
#1	'low density lipoprotein cholesterol'/exp/mj OR 'very low density lipoprotein cholesterol'/exp/mj OR (((ldl OR 'low-density lipoprotein*') NEAR/3 (c OR cholesterol)):ti,ab)	101123

26-6-2021

Embase (Elsevier)	'low density lipoprotein cholesterol'/exp/mj OR 'very low density lipoprotein cholesterol'/exp/mj OR ((ldl OR 'low-density lipoprotein*') NEAR/3 (c OR cholesterol)):ti,ab AND ('cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,ab OR cvd:ti,ab OR 'vascular disease*':ti,ab OR 'vascular event*':ti,ab OR 'coronary heart disease':ti,ab OR chd:ti,ab) AND (preventi*:ti,ab OR control:ti,ab OR therapy:ti,ab OR 'drug therapy':lnk OR prevention:lnk OR 'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR 'hmg coa reductase inhibitor*':ti,ab OR statin*:ti,ab OR atorvastatin*:ti,ab OR lovastatin*:ti,ab OR meglutol*:ti,ab OR pravastatin*:ti,ab OR rosuvastatin*:ti,ab OR simvastatin*:ti,ab OR target*:ti,ab OR risk:ti OR mortality:ti,ab OR incidence:ti OR relation*:ti OR association:ti OR 'lipid modifying':ti OR 'lipid level*':ti,ab OR reduction:ti,ab OR lowering:ti,ab OR 'reference value'/exp) AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2005-2017]/py NOT 'conference abstract':it AND ('meta analysis'/de OR cochrane:ab OR embase:ab OR psycinfo:ab OR cinahl:ab OR medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de) NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp) (622) – 190 uniek Specifiekere search voor RCT's: (('low density lipoprotein cholesterol'/exp/mj OR 'very low density lipoprotein cholesterol'/exp/mj OR (((ldl OR 'low-density lipoprotein*') NEAR/3 (c OR cholesterol)):ti,ab)) AND ('cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,ab OR cvd:ti,ab OR 'vascular disease*':ti,ab OR 'vascular event*':ti,ab OR 'coronary heart disease':ti,ab OR chd:ti,ab) AND ('hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR 'hmg coa reductase inhibitor*':ti OR statin*:ti OR atorvastatin*:ti OR lovastatin*:ti OR meglutol*:ti OR pravastatin*:ti OR rosuvastatin*:ti OR simvastatin*:ti OR target*:ti) OR 'lipid lowering therapy':ti,ab OR 'intensive lipid lowering':ti,ab) AND ((random*:ti OR 'randomized controlled trial'/exp) NOT 'conference abstract':it) AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2009-2017]/py (539) – 197 uniek

Zoekverantwoording voor uitgangsvraag:

Wat is de toegevoegde waarde van een coronaire kalkscore bij het reclassificeren van het risico op hart- en vaatziekten?

UPDATE – 2022 Algemene informatie

Richtlijn: Cluster CVRM	
Uitgangsvraag: Leidt toevoeging van de uitslag van een coronary artery calcium bepaling (CAC-score) aan het klassieke predictiemodel bij patiënten zonder HVZ tot een betere risicoschatting, bij voorkeur afgemeten aan klinisch relevante reclassificatie, voor wat betreft hun 10-jaars mortaliteit- en morbiditeit aan HVZ?	
Database(s): Ovid/Medline, Embase	Datum: 17-3-2022
Periode: mei 2017 -	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: Voor deze vraag is gezocht met de volgende elementen: Hart- en vaatziekten EN CAC score Vanwege het grote aantal referenties wordt gestart met de SR's en de RCT's	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 17-3-2022 met relevante zoektermen gezocht naar systematische reviews en RCT's over de vraag of toevoeging van de uitslag van een coronary artery calcium bepaling (CAC-score) aan het klassieke predictiemodel bij patiënten zonder HVZ tot een betere risicoschatting leidt, bij voorkeur afgemeten aan klinisch relevante reclassificatie, voor wat betreft hun 10-jaars mortaliteit- en morbiditeit aan HVZ. De literatuurzoekactie leverde 317 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	123	57	130
RCT's	170	88	187
Observationele studies			
Overig			
Totaal			317

Embase

No.	Query	Results
#18	#14 NOT #12 NOT #11 Prognostisch zonder limiet obs	1076
#17	#14 NOT #13 NOT #12 NOT #11 Prognostisch NOT OBS	99
#16	#13 NOT #12 NOT #11 OBS	1777
#15	#12 NOT #11 RCT	170
#14	#5 AND #10	1176
#13	#5 AND (#8 OR #9)	2002
#12	#5 AND #7	196
#11	#5 AND #6 SR	123
#10	'area under the curve'/exp OR 'brier score'/exp OR 'computer prediction'/exp OR 'c statistic'/exp OR 'c statistics'/exp OR 'integrated discrimination improvement'/exp OR 'net reclassification improvement'/exp OR 'net reclassification index'/exp OR 'prediction'/exp OR 'predictive model'/exp OR 'predictive modeling'/exp OR 'predictive validity'/exp OR 'predictive value'/exp OR 'regression analysis'/exp OR 'statistical model'/exp OR 'area under the curve':ti,ab,kw OR 'brier score*':ti,ab,kw OR 'c statistic*' OR 'computer prediction':ti,ab,kw OR 'decision curve	2838573

No.	Query	Results
	anal*':ti,ab,kw OR (('net reclassification' NEAR/2 (improvement OR index)):ti,ab,kw) OR (((predict* OR statistical*) NEAR/3 (model* OR validity OR value)):ti,ab,kw) OR 'proportional hazards model*':ti,ab,kw OR 'r square*':ti,ab,kw OR regression:ti,ab,kw OR predict*:ti OR multivariate:ti,ab,kw	
#9	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient * OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	12697718
#8	'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)	6767914
#7	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1839814
#6	'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	733409

No.	Query	Results
	(((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	
#5	#4 AND [1-5-2017]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	2583
#4	#2 AND #3	9462
#3	'cardiovascular disease'/exp OR 'cardiovascular risk'/exp OR 'cardiovascular disease*':ti,ab,kw OR cvd:ti,ab,kw OR 'vascular disease*':ti,ab,kw OR 'vascular event*':ti,ab,kw OR 'coronary heart disease':ti,ab,kw OR chd:ti,ab,kw OR 'cardiovascular risk*':ti,ab,kw	5012342
#2	'coronary artery calcium score'/exp OR 'cac score':ti,ab,kw OR ((coronary NEAR/3 calc* NEAR/3 scor*):ti,ab,kw)	10154

Ovid/Medline

#	Searches	Results
17	14 not 12 not 11 Prognostisch	628
16	13 not 12 not 11 OBS	802
15	12 not 11 RCT	88
14	9 and 10	685
13	(7 or 8) and 10	909
12	6 and 10	103
11	5 and 10 SR	57
10	4 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	1245
9	Area Under Curve/ or exp Forecasting/ or "Predictive Value of Tests"/ or exp Multivariate Analysis/ or exp Regression Analysis/ or exp Models, Statistical/ or area under the curve.ti,ab,kf. or brier score*.ti,ab,kf. or c statistic*.ti,ab,kf. or computer prediction.ti,ab,kf. or decision curve anal*.ti,ab,kf. or (net reclassification adj2 (improvement or index)).ti,ab,kf. or ((predict* or statistical*) adj3 (model* or validity or value)).ti,ab,kf. or proportional hazards model*.ti,ab,kf. or r square*.ti,ab,kf. or regression.ti,ab,kf. or predict*.ti. or multivariate.ti,ab,kf.	2163120
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/	5107766

	or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	
7	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.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/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	4095298
6	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1359441
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/))	553153
4	limit 3 to yr="2017 -Current"	1294
3	1 and 2	3366
2	(cac score or (coronary adj3 calc* adj3 scor*)).ti,ab,kf.	3825

1	exp Cardiovascular Diseases/ or exp Heart Disease Risk Factors/ or (cardiovascular disease* or CVD or vascular disease* or vascular event* or coronary heart disease or CHD or cardiovascular risk*).ti,ab,kf.	2728819

Database	Zoektermen	Totaal
Medline (PubMed) 2005-feb 2017 Engels, Nederlands	(CAC(tiab) OR coronary calcium score(tiab) OR calcium score(tiab) OR coronary artery calcium(tiab) OR coronary arterial calcium(tiab) OR coronary artery calcification(tiab) OR coronary arterial calcification(tiab) OR coronary calcification(tiab) OR coronary computed tomographic angiography(tiab) OR CCTA(tiab)) AND (cardiovascular diseases/epidemiology(mj) OR cardiovascular diseases/mortality(mj) OR CVD(tiab) OR cardiovascular disease(tiab) OR vascular disease(tiab) OR vascular event(tiab) OR coronary heart disease(tiab) OR CHD(tiab)) AND (predict*(tiab) OR reclassification(tiab) OR statistics as topic(mh) OR risk assessment(mh) OR risk factors(mh) OR risk(ti) OR mortality(tiab)) AND (meta-anal*(tiab) OR systematic(sb) OR random*(tiab) OR RCT(tiab) OR review(pt))	257

Zoekverantwoording voor uitgangsvraag:

Wanneer moet een verhoogde bloeddruk behandeld worden?

Algemene informatie

Richtlijn: CVRM	
Uitgangsvraag: Wanneer moet een verhoogde bloeddruk medicamenteus behandeld worden?	
Database(s): Embase	Datum:31-10-2022
Periode: 2016-	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: Voor deze vraag is gezocht met de volgende concepten: Cardiovascular disease AND blood pressure AND (cardiovascular risk OR risk factor OR risk assesment) Deze zoekstrategie is tot stand gekomen op basis van de indextermen van een aantal sleutelartikelen. Het aantal referenties dat wordt gevonden is groot, vandaar dat eerst wordt gestart met de systematische reviews van Embase, gericht op de Europese markt. Eventueel kan later Ovid/Medline worden toegevoegd. De selectie zal worden uitgevoerd met behulp van de AI-functie in Rayyan.	
Te gebruiken voor richtlijnen tekst: In de databases- Embase is op 31-10-2022 met relevante zoektermen gezocht vanaf 2016 naar systematische reviews over bloeddruk en het cardiovascular risico. De literatuurzoekactie leverde 1729 unieke treffers op.	

Zoekopbrengst

	EMBASE	OVID/MEDLINE	Ontdubbeld
SR's	1735		1729
RCT's			
Observationele studies			
Overig			
Totaal			

Zoekstrategie

Embase

No.	Query	Results
#35	#19 NOT #32 sleutelartikelen te oud (2000)	1
#34	#19 AND #32 sleutelartikelen gevonden	3
#33	#6 AND #32	1735
#32	#31 AND [1-1-2016]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	61657
#31	#28 AND #29 AND #30	127213
#30	'cardiovascular risk'/exp OR 'risk factor'/exp OR 'cardiovascular risk':ti,kw OR 'risk factor':ti,kw OR 'risk assessment'/exp	1954861
#29	'cardiovascular disease'/exp/mj OR 'cardiovascular disease*':ti,kw	3207832
#28	'hypertension'/exp/mj OR 'blood pressure'/exp/mj OR hypertens*:ti,kw OR 'blood pressure':ti,kw	603857
#27	'hypertension'/exp/mj OR 'blood pressure'/exp OR hypertens*:ti,ab,kw OR 'blood pressure':ti,ab,kw	1405056
#26	#2 AND #23 blood pressure regulation. Sleutelartikelen niet gevonden	0
#25	#1 AND #23	3
#24	#5 AND #19	1
#23	#19 NOT #20	3
#22	#19 AND #20	1
#21	#19 AND #20	1
#20	#10 OR #11 OR #12	4908
#19	#15 OR #16 OR #17 OR #18	4
#18	systolic AND diastolic AND blood AND pulse AND pressure, AND mean AND arterial AND pressure AND as AND predictors AND of AND cardiovascular AND disease AND risk AND in AND men AND sesso NOT effect:ti	1
#17	isolated AND systolic AND diastolic AND hypertension AND by AND the AND 2017 AND american AND college AND heart AND association AND guidelines AND risk AND of AND cardiovascular AND disease AND a AND large AND prospective AND cohort AND study AND li	1
#16	the AND total AND direct AND effects AND of AND systolic AND diastolic AND blood AND pressure AND on AND cardiovascular AND disease AND longevity AND using AND mendelian	1
#15	binary AND cutpoint AND the AND combined AND effect AND of AND systolic AND diastolic AND blood AND pressure AND on AND cardiovascular AND disease AND mortality AND a AND 'community based' AND cohort AND study	1
#14	#12 NOT #11 NOT #10	3341
#13	#11 NOT #10	1001
#12	#5 AND (#8 OR #9)	4594
#11	#5 AND #7	1296
#10	#5 AND #6	566
#9	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross	13567512

	over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#8	'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)	6767914
#7	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1839814
#6	'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	870867
#5	#4 AND [1-1-2016]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) Oorspronkelijke strategie. Sleutelartikelen worden niet gevonden	21386
#4	#1 AND #2 AND #3	35577
#3	'cardiovascular disease'/exp OR 'cardiovascular risk'/exp OR (((cardiovascular OR 'heart disease*') NEAR/3 risk*):ti,ab,kw)	5176138
#2	'blood pressure regulation'/exp OR 'reference value'/exp OR (('blood pressure' NEAR/3 (control OR baseline* OR standard* OR level* OR regulati* OR target* OR reference OR threshold)):ti,ab,kw) OR 160:ti,ab,kw OR 165:ti,ab,kw OR 170:ti,ab,kw OR 175:ti,ab,kw OR 180:ti,ab,kw	783595
#1	'hypertension'/exp/mj OR 'blood pressure'/exp OR hypertens*:ti,ab,kw OR 'blood pressure':ti,ab,kw	1405056

Zoekverantwoording voor uitgangsvraag:

Welke bloeddrukstreefwaarde dient te worden gehanteerd bij de behandeling van hypertensie bij (kwetsbare) ouderen (> 70 jaar)?

Database	Zoektermen		Totaal
Medline (OVID) 1948-apr. 2016 Engels	1	(exp Hypertension/ or hypertensi*.ti,ab. or 'blood pressure'.ti,ab. or hbp.ti,ab. or Blood Pressure/) and (Antihypertensive Agents/ or antihypertensi*.ti,ab.) (62711)	1491
	2	exp Aged/ or aged.ti. or exp Frail Elderly/ or "Aged, 80 and over"/ or exp Aging/ or exp Geriatric Assessment/ or (elderly or geriatric or 'community dwelling' or frail* or ag?ing or septuagenarian* or octogenarian* or nonagenarian* or centenarian* or 'old people' or eldest or oldest or "biological age").ti,ab. (2834312)	
	3	1 and 2 (19119)	
	4	limit 3 to english (16115)	
	15	*Reference Values/ or (target* or threshold or (reference adj2 value*)).ab. /freq=2 or (goal* or target* or (reference adj2 value*)).ti. or intensi*.ti,ab. or ((pressure or BP) adj3 goal*).ab. /freq=2 or (elderly or "very old" or "oldest old" or "80 years").ti. (1054271)	
	16	4 and 15 (2710)	
	17	(meta-analysis/ or meta-analysis as topic/ or (meta adj analy$).tw. or ((systematic* or literature) adj2 review$1).tw. or (systematic adj overview$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (275361)	
	18	16 and 17 (98)	
	19	(randomized controlled trial/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or randomized controlled trial.pt. or random*.ti,ab. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (991935)	
	20	16 and 19 (1044)	
	21	20 not 18 (978)	
Embase (Elsevier)	'aged'/exp/mj OR 'geriatric assessment'/exp/mj OR aged:ti OR elderly:ab,ti OR geriatric*:ab,ti OR 'community dwelling':ab,ti OR frail*:ab,ti OR ageing:ab,ti OR aging:ab,ti OR septuagenarian*:ab,ti OR octogenarian*:ab,ti OR nonagenarian*:ab,ti OR centenarian*:ab,ti OR 'old people':ab,ti OR eldest:ab,ti OR oldest:ab,ti OR 'biological age' OR (individual NEAR/2 (patient* OR participant*) NEAR/2 data*):ab,ti AND (english)/lim AND (embase)/lim AND ('hypertension'/exp/mj OR 'blood pressure'/exp/mj OR hypertensi*:ab,ti OR 'blood pressure':ab,ti OR hbp:ab,ti) AND ('antihypertensive agent'/exp/mj OR antihypertensi*:ab,ti) AND ('reference value'/exp OR goal*:ti OR target*:ti OR threshold:ti OR (reference NEAR/2 value*):ti OR intensi*:ab,ti OR elderly:ti OR 'very old':ti OR 'oldest old':ti OR '80 years':ti) 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp) AND ('randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it (77) 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR	

	metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp) (658)	

Algemene informatie

Richtlijn: Cluster CVRM	
Uitgangsvraag: UV 3.2 en 3.3. Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk?	
Database(s): Ovid/Medline, Embase	Datum: 29-3-2022
Periode: 2016-	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: In overleg met de adviseur wordt besloten om UV 3.2 (kwetsbare ouderen) en UV 3.3 te combineren omdat er voor ca. 80% overlap is. Onderstaande Cochrane reviews worden als uitgangspunt gebruikt en worden aangevuld met de meest recente RCT's vanaf 2016. Er wordt gezocht met de volgende elementen: Hypertensie EN streefwaarden EN cardiovasculair risico EN antihypertensieve therapie. Alle sleutelartikelen worden gevonden in de basisset. Uiteindelijk wordt 1 artikel uit 2011 gemist vanwege de tijdslimiet. **Cochrane reviews** Blood pressure targets in adults with hypertension Arguedas J.A.; Leiva V.; Wright J.M. Cochrane Database of Systematic Reviews (2020) 2020:12 Article Number: CD004349. Date of Publication: 17 Dec 2020 Blood pressure targets for the treatment of people with hypertension and cardiovascular disease Saiz L.C.; Gorricho J.; Garjón J.; Celaya M.C.; Erviti J.; Leache L. Cochrane Database of Systematic Reviews (2020) 2020:9 Article Number: CD010315. Date of Publication: 9 Sep 2020 Blood pressure targets for hypertension in older adults Garrison S.R.; Kolber M.R.; Korownyk C.S.; Mccracken R.K.; Heran B.S.; Allan G.M. Cochrane Database of Systematic Reviews (2017) 2017:8 Article Number: CD011575. Date of Publication: 8 Aug 2017	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 29-3-2022 met relevante zoektermen gezocht naar RCT's over de streefwaarden bij behandeling verhoogde bloeddruk. De literatuurzoekactie leverde 998 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's			
RCT's	640	601	998
Observationele studies			
Overig			
Totaal			**998**

Embase

No.	Query	Results
#22	#13 NOT #12 RCT	640
#21	#6 AND #20 sleutelartikelen gevonden	3
#20	#16 OR #17 OR #18 OR #19	4
#19	effects AND of AND blood AND pressure AND lowering AND on AND outcome AND incidence AND in AND hypertension AND thomopoulos AND 2016 NOT treatment:ti	1
#18	blood AND pressure AND lowering AND for AND prevention AND of AND cardiovascular AND disease AND death AND ettehad NOT european AND heart AND journal	1
#17	a AND randomized AND trial AND of AND intensive AND versus AND standard AND 'blood pressure' AND control. AND 2015 AND wright NOT final:ti	1
#16	the AND effects AND reduction AND of AND different AND 'pressure lowering' AND regimens AND on AND major AND cardiovascular AND events AND according AND to AND baseline AND blood AND pressure AND huxley AND 2011	1
#15	blood AND pressure AND targets AND for AND the AND treatment AND of AND people AND with AND hypertension AND cardiovascular AND disease AND saiz AND 2020	1
#14	#6 AND #11	2116
#13	#6 AND #8	821
#12	#6 AND #7	169
#11	#9 OR #10	14700940
#10	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw	12982450

No.	Query	Results
	OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR (((‘or' OR 'rr') NEAR/6 ci):ab)))	
#9	'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)	6974259
#8	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1891965
#7	'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	810492
#6	#5 AND [1-1-2016]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	2838
#5	#1 AND #2 AND #3 AND #4	11674
#4	'cardiovascular disease'/exp/mj AND ('prevention'/exp OR 'risk reduction'/exp OR prevent*:ti,ab,kw OR risk*:ti,kw) OR 'cardiovascular risk'/exp OR (((cardiovascular OR 'heart disease*') NEAR/3 risk*):ti,ab,kw)	741126
#3	'antihypertensive agent'/exp OR 'antihypertensive therapy'/exp OR antihypertensi*:ti,kw OR 'anti hypertensi*':ti,kw	837636
#2	'blood pressure regulation'/exp OR 'reference value'/exp OR (('blood pressure' NEAR/3 (control OR baseline* OR standard* OR level* OR regulati* OR target* OR reference OR threshold)):ti,ab,kw) OR 120:ti,ab,kw OR 130:ti,ab,kw OR 135:ti,ab,kw OR 140:ti,ab,kw OR 150:ti,ab,kw OR (((goal? OR intensive* OR strict* OR target* OR tight*) NEAR/4 (antihypertensive? OR hypertensive? OR bp OR dbp OR diastolic OR pressure? OR sbp OR systolic OR treat*)):ti,ab,kw)	1435670
#1	'hypertension'/exp OR 'blood pressure'/exp OR hypertens*:ti,ab,kw OR 'blood pressure':ti,ab,kw	1577203

Ovid/Medline

#	Searches	Results
11	9 not 10 RCT	601
10	(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/))	555509
9	7 and 8 RCT	773
8	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1362761
7	6 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	2625
6	limit 5 to yr="2016 -Current"	2719
5	1 and 2 and 3 and 4	9575
4	(exp Cardiovascular Diseases/ and (Primary Prevention/ or Secondary Prevention/ or Risk Reduction Behavior/ or prevent*.ti,ab,kf. or risk*.ti,ab,kf.)) or exp Heart Disease Risk Factors/ or ((cardiovascular or heart disease*) adj3 risk*).ti,ab,kf.	637071
3	exp Antihypertensive Agents/ or (antihypertensive or anti hypertensive).ti,ab,kf.	288685
2	Reference Values/ or (blood pressure adj3 (control or baseline* or standard* or level* or regulati* or target* or reference or threshold)).ti,ab,kf. or "120".ti,ab,kf. or "130".ti,ab,kf. or "135".ti,ab,kf. or "140".ti,ab,kf. or "150".ti,ab,kf. or ((goal? or intensive* or strict* or target* or tight*) adj4 (antihypertensive? or hypertensive? or bp or dbp or diastolic or pressure? or sbp or systolic or treat*)).ti,ab,kf.	1187049
1	exp Hypertension/ or exp Blood Pressure/ or hypertens*.ti,ab,kf. or blood pressure.ti,ab,kf.	848734

Zoekverantwoording voor uitgangsvraag:

Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk bij volwassenen (< 70 jaar)?

Algemene informatie

Richtlijn: Cluster CVRM	
Uitgangsvraag: UV 3.2 en 3.3. Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk?	
Database(s): Ovid/Medline, Embase	Datum: 29-3-2022
Periode: 2016-	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: In overleg met de adviseur wordt besloten om UV 3.2 (kwetsbare ouderen) en UV 3.3 te combineren omdat er voor ca. 80% overlap is. Onderstaande Cochrane reviews worden als uitgangspunt gebruikt en worden aangevuld met de meest recente RCT's vanaf 2016. Er wordt gezocht met de volgende elementen: Hypertensie EN streefwaarden EN cardiovasculair risico EN antihypertensieve therapie. Alle sleutelartikelen worden gevonden in de basisset. Uiteindelijk wordt 1 artikel uit 2011 gemist vanwege de tijdslimiet. **Cochrane reviews** Blood pressure targets in adults with hypertension Arguedas J.A.; Leiva V.; Wright J.M. Cochrane Database of Systematic Reviews (2020) 2020:12 Article Number: CD004349. Date of Publication: 17 Dec 2020 Blood pressure targets for the treatment of people with hypertension and cardiovascular disease Saiz L.C.; Gorricho J.; Garjón J.; Celaya M.C.; Erviti J.; Leache L. Cochrane Database of Systematic Reviews (2020) 2020:9 Article Number: CD010315. Date of Publication: 9 Sep 2020 Blood pressure targets for hypertension in older adults Garrison S.R.; Kolber M.R.; Korownyk C.S.; Mccracken R.K.; Heran B.S.; Allan G.M. Cochrane Database of Systematic Reviews (2017) 2017:8 Article Number: CD011575. Date of Publication: 8 Aug 2017
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 29-3-2022 met relevante zoektermen gezocht naar RCT's over de streefwaarden bij behandeling verhoogde bloeddruk. De literatuurzoekactie leverde 998 unieke treffers op.

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's			
RCT's	640	601	998
Observationele studies			
Overig			
Totaal			**998**

Embase

No.	Query	Results
#22	#13 NOT #12 RCT	640
#21	#6 AND #20 sleutelartikelen gevonden	3
#20	#16 OR #17 OR #18 OR #19	4

No.	Query	Results
#19	effects AND of AND blood AND pressure AND lowering AND on AND outcome AND incidence AND in AND hypertension AND thomopoulos AND 2016 NOT treatment:ti	1
#18	blood AND pressure AND lowering AND for AND prevention AND of AND cardiovascular AND disease AND death AND ettehad NOT european AND heart AND journal	1
#17	a AND randomized AND trial AND of AND intensive AND versus AND standard AND 'blood pressure' AND control. AND 2015 AND wright NOT final:ti	1
#16	the AND effects AND reduction AND of AND different AND 'pressure lowering' AND regimens AND on AND major AND cardiovascular AND events AND according AND to AND baseline AND blood AND pressure AND huxley AND 2011	1
#15	blood AND pressure AND targets AND for AND the AND treatment AND of AND people AND with AND hypertension AND cardiovascular AND disease AND saiz AND 2020	1
#14	#6 AND #11	2116
#13	#6 AND #8	821
#12	#6 AND #7	169
#11	#9 OR #10	14700940
#10	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	12982450
#9	'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	6974259

No.	Query	Results
	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)	
#8	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1891965
#7	'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	810492
#6	#5 AND [1-1-2016]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	2838
#5	#1 AND #2 AND #3 AND #4	11674
#4	'cardiovascular disease'/exp/mj AND ('prevention'/exp OR 'risk reduction'/exp OR prevent*:ti,ab,kw OR risk*:ti,kw) OR 'cardiovascular risk'/exp OR (((cardiovascular OR 'heart disease*') NEAR/3 risk*):ti,ab,kw)	741126
#3	'antihypertensive agent'/exp OR 'antihypertensive therapy'/exp OR antihypertensi*:ti,kw OR 'anti hypertensi*':ti,kw	837636
#2	'blood pressure regulation'/exp OR 'reference value'/exp OR (('blood pressure' NEAR/3 (control OR baseline* OR standard* OR level* OR regulati* OR target* OR reference OR threshold)):ti,ab,kw) OR 120:ti,ab,kw OR 130:ti,ab,kw OR 135:ti,ab,kw OR 140:ti,ab,kw OR 150:ti,ab,kw OR (((goal? OR intensive* OR strict* OR target* OR tight*) NEAR/4 (antihypertensive? OR hypertensive? OR bp OR dbp OR diastolic OR pressure? OR sbp OR systolic OR treat*)):ti,ab,kw)	1435670
#1	'hypertension'/exp OR 'blood pressure'/exp OR hypertens*:ti,ab,kw OR 'blood pressure':ti,ab,kw	1577203

Ovid/Medline

#	Searches	Results
11	9 not 10 RCT	601
10	(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/))	555509
9	7 and 8 RCT	773
8	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1362761
7	6 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	2625
6	limit 5 to yr="2016 -Current"	2719
5	1 and 2 and 3 and 4	9575
4	(exp Cardiovascular Diseases/ and (Primary Prevention/ or Secondary Prevention/ or Risk Reduction Behavior/ or prevent*.ti,ab,kf. or risk*.ti,ab,kf.)) or exp Heart Disease Risk Factors/ or ((cardiovascular or heart disease*) adj3 risk*).ti,ab,kf.	637071
3	exp Antihypertensive Agents/ or (antihypertensive or anti hypertensive).ti,ab,kf.	288685
2	Reference Values/ or (blood pressure adj3 (control or baseline* or standard* or level* or regulati* or target* or reference or threshold)).ti,ab,kf. or "120".ti,ab,kf. or "130".ti,ab,kf. or "135".ti,ab,kf. or "140".ti,ab,kf. or "150".ti,ab,kf. or ((goal? or intensive* or strict* or target* or tight*) adj4 (antihypertensive? or hypertensive? or bp or dbp or diastolic or pressure? or sbp or systolic or treat*)).ti,ab,kf.	1187049
1	exp Hypertension/ or exp Blood Pressure/ or hypertens*.ti,ab,kf. or blood pressure.ti,ab,kf.	848734

Zoekverantwoording voor uitgangsvraag:

Wat is de toegevoegde waarde van etnische achtergrond bij het reclassificeren van het risico op hart- en vaatziekten?

Algemene informatie

Richtlijn: Cluster CVRM	
Uitgangsvraag: UV5 Leidt toevoeging van etniciteit aan het predictiemodel op basis van alleen klassieke risicofactoren tot een betere risicoschatting bij patiënten zonder hart- en vaatziekten	
Database(s): Ovid/Medline, Embase	Datum: 8-3-2022
Periode: 2017-	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: Deze vraag is een update van die van 2017. Er is gezocht met de volgende elementen: (risico op) Hart- en vaatziekten EN etniciteit EN Nederland De oorspronkelijke zoekstrategie is uitgebreid en aangepast aan de Nederlandse situatie.	
Te gebruiken voor richtlijnen tekst: In de databases Embase en Ovid/Medline is op 8 maart 2022 met relevante zoektermen gezocht naar systematische reviews, observationele en prognostische en overige studies. De literatuurzoekactie leverde 138 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR's	11	7	12
Prognostische studies	5	10	118
Observationele studies	96	74	8
Overig	23	12	26
Totaal			138

Zoekstrategie

Embase

No.	Query	Results
#15	#5 NOT #7 NOT #12 NOT #11 Overige	23
#14	#7 NOT #12 NOT #11 Prognostisch	5
#13	#12 NOT #11 Observationeel	96
#12	#5 AND (#9 OR #10)	100
#11	#5 AND #8 SR	11
#10	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw	12930928

No.	Query	Results
	OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#9	'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)	6940671
#8	'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	804778
#7	#5 AND #6	206
#6	'area under the curve'/exp OR 'brier score'/exp OR 'computer prediction'/exp OR 'c statistic'/exp OR 'c statistics'/exp OR 'integrated discrimination improvement'/exp OR 'net reclassification improvement'/exp OR 'net reclassification index'/exp OR 'prediction'/exp OR 'predictive model'/exp OR 'predictive modeling'/exp OR 'predictive validity'/exp OR 'predictive value'/exp OR 'regression analysis'/exp OR 'statistical model'/exp OR 'area under the curve':ti,ab,kw OR 'brier score*':ti,ab,kw OR 'c statistic*' OR 'computer prediction':ti,ab,kw OR 'decision curve anal*':ti,ab,kw OR (('net reclassification' NEAR/2 (improvement OR index)):ti,ab,kw) OR (((predict* OR statistical*) NEAR/3 (model* OR validity OR value)):ti,ab,kw) OR 'proportional hazards model*':ti,ab,kw OR 'r square*':ti,ab,kw OR regression:ti,ab,kw OR predict*:ti OR multivariate:ti,ab,kw	2827713

No.	Query	Results
#5	#4 AND [1-1-2017]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	135
#4	#1 AND #2 AND #3	2018
#3	'netherlands'/exp OR netherlands:ti,ab,kw OR holland:ti,ab,kw OR dutch:ti,ab,kw,la	244808
#2	'afghan'/exp OR 'antillean'/exp OR 'african'/de OR 'east asian'/de OR 'chinese'/exp OR 'eastern european'/de OR 'indonesian'/exp OR 'iraqi'/exp OR 'japanese (people)'/exp OR 'moroccan'/exp OR 'polish citizen'/exp OR 'somali (people)'/exp OR 'southeast asian'/de OR 'syrian'/exp OR 'turk (people)'/exp OR 'surinamese'/exp OR 'multiracial person'/exp OR 'black person'/de OR 'migrant'/exp OR moroccan*:ti,ab,kw OR turk*:ti,ab,kw OR multiracial OR antillean*:ti,ab,kw OR african*:ti,ab,kw OR asian*:ti,ab,kw OR moluccan*:ti,ab,kw OR indonesian*:ti,ab,kw OR chinese*:ti,ab,kw OR 'east european*':ti,ab,kw OR 'eastern european*':ti,ab,kw OR iraqi:ti,ab,kw OR afghan*:ti,ab,kw OR syrian*:ti,ab,kw OR immigrant*:ti,ab,kw OR migrant*:ti,ab,kw	955362
#1	'cardiovascular disease'/exp OR 'cardiovascular risk'/exp OR 'cardiovascular disease*':ti,ab,kw OR cvd:ti,ab,kw OR 'vascular disease*':ti,ab,kw OR 'vascular event*':ti,ab,kw OR 'coronary heart disease':ti,ab,kw OR chd:ti,ab,kw OR 'cardiovascular risk*':ti,ab,kw	5003425

Ovid/Medline

#	Searches	Results
16	6 not 13 not 12 not 11 Overige	12
15	13 not 12 not 11 Prognostisch	10
14	12 not 11 Observationeel	74
13	6 and 9	48
12	6 and (8 or 10)	77
11	6 and 7 SR	7
10	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or	5100444

	followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	
9	Area Under Curve/ or exp Forecasting/ or "Predictive Value of Tests"/ or exp Multivariate Analysis/ or exp Regression Analysis/ or exp Models, Statistical/ or area under the curve.ti,ab,kf. or brier score*.ti,ab,kf. or c statistic*.ti,ab,kf. or computer prediction.ti,ab,kf. or decision curve anal*.ti,ab,kf. or (net reclassification adj2 (improvement or index)).ti,ab,kf. or ((predict* or statistical*) adj3 (model* or validity or value)).ti,ab,kf. or proportional hazards model*.ti,ab,kf. or r square*.ti,ab,kf. or regression.ti,ab,kf. or predict*.ti. or multivariate.ti,ab,kf.	2158677
8	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.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/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	4087194
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 models, animal/) not humans/))	551318
6	5 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/)	103
5	limit 4 to yr="2017 -Current"	105
4	1 and 2 and 3	340
3	afghanistan/ or Indonesia/ or Iraq/ or Japan/ or morocco/ or Poland/ or somalia/ or syria/ or Turkey/ or Ethnicity/ or Racial Groups/ or "Transients and Migrants"/ or Refugees/ or (moroccan* or turk* or multiracial or antillean* or african* or asian* or moluccan* or indonesian* or chinese* or east european* or eastern european* or iraqi or afghan* or syrian* or immigrant* or migrant*).ti,ab,kf.	954915
2	(dutch or holland or netherlands).ti,ab,kf,la.	145613
1	exp Cardiovascular Diseases/ or exp Heart Disease Risk Factors/ or (cardiovascular disease* or CVD or vascular disease* or vascular event* or coronary heart disease or CHD or cardiovascular risk*).ti,ab,kf.	2725153

Bijlage 4 Uitgesloten artikelen na full-tekst beoordeling

Exclusietabel voor uitgangsvraag:

Welke streefwaarden van LDL-C dienen te worden gehanteerd bij de behandeling met lipidenverlagende medicatie bij personen tot en met 70 jaar met een (zeer) hoog risico op hart- en vaatziekten?

Tabel update 2021

Referentie	Reden
Oyama K, Giugliano RP, Tang M, Bonaca MP, Saver JL, Murphy SA, et al. Effect of evolocumab on acute arterial events across all vascular territories: results from the FOURIER trial. European heart journal. 2021;42(47):4821-9.	FOURIER-trial. Data reeds geïncludeerd.
Jin S, Nie X, Li Y, Yuan J, Cui Y, Zhao L. Effect of More Intensive LDL-C-Lowering Therapy on Long-term Cardiovascular Outcomes in Early-Phase Acute Coronary Syndrome: A Systematic Review and Meta-analysis. Clinical therapeutics. 2021;43(7):e217-e29.	SR, geen van de geïncludeerde trials komt in aanmerking.
Elgendy IY, Elshazly MB. LDL-C-lowering therapies reduce major vascular events in patients aged > =75 y. Annals of internal medicine. 2021;174(4):JC38.	Commentaar op een trial
Deedwania P, Murphy SA, Scheen A, Badariene J, Pineda A, Lira o, et al. Efficacy and Safety of PCSK9 Inhibition With Evolocumab in Reducing Cardiovascular Events in Patients With Metabolic Syndrome Receiving Statin Therapy: Secondary Analysis From the FOURIER Randomized Clinical Trial. JAMA cardiology. 2021;6(2):139-47.	FOURIER-trial: analyse bij patiënten met het metabool syndroom
Amarenco P, Kim JS, Labreuche J, Charles H, Giroud M, Lee B-C, et al. Impact of Lower Versus Higher LDL Cholesterol Targets on Cardiovascular Events After Ischemic Stroke in Patients With Diabetes. Diabetes. 2021;70(8):1807-15.	TST-trial: Analyse naar subgroup diabetes. Echter, alle deelnemers hebben een stroke gehad.
Wiviott SD, Giugliano RP, Morrow DA, De Ferrari GM, Lewis BS, Huber K, et al. Effect of Evolocumab on Type and Size of Subsequent Myocardial Infarction: A Prespecified Analysis of the FOURIER Randomized Clinical Trial. JAMA cardiology. 2020;5(7):787-93.	FOURIER-trial: analyse naar de uitkomst MI subtype
Wang N, Fulcher J, Abeysuriya N, Park L, Kumar S, Di Tanna GL, et al. Intensive LDL cholesterol-lowering treatment beyond current recommendations for the prevention of major vascular events: a systematic review and meta-analysis of randomised trials including 327 037 participants. The Lancet Diabetes and Endocrinology. 2020;8(1):36-49.	SR naar de daling in LDL
Robinson JG, Jayanna MB, Bairey Merz CN, Stone NJ. Clinical implications of the log linear association between LDL-C lowering and cardiovascular risk reduction: Greatest benefits when LDL-C > 100 mg/dl. PloS one. 2020;15(10):e0240166.	Meta-analyse: daling in LDL
Ödesjö H, Björck S, Franzén S, Hjerpe P, Manhem K, Rosengren A, et al. Adherence to lipid-lowering guidelines for secondary prevention and potential reduction in CVD events in Swedish primary care: A cross-sectional study. BMJ Open. 2020;10(10).	Onderzoek naar adherentie en geen follow-up
Gencer B, Mach F, Murphy SA, De Ferrari GM, Huber K, Lewis BS, et al. Efficacy of Evolocumab on Cardiovascular Outcomes in Patients With Recent Myocardial Infarction: A Prespecified Secondary Analysis From the FOURIER Trial. JAMA cardiology. 2020;5(8):952-7.	FOURIER-trial: subgroepanalyse bij patiënten met MI

Alkhalil M. Effects of intensive lipid-lowering therapy on mortality after coronary bypass surgery: A meta-analysis of 7 randomised trials. Atherosclerosis. 2020;293:75-8.	SR bij patiënten die een CABG ondergingen
Vallejo-Vaz AJ, Ray KK, Ginsberg HN, Davidson MH, Eckel RH, Lee LV, et al. Associations between lower levels of low-density lipoprotein cholesterol and cardiovascular events in very high-risk patients: Pooled analysis of nine ODYSSEY trials of alirocumab versus control. Atherosclerosis. 2019;288:85-93.	Meta-analyse van ODYSSEY-trials en subgroepen comorbiditeiten (niet alleen vergelijking intensief versus minder-intensief of uitkomsten gerelateerd aan LDL-daling)
Steg PG, Szarek M, Bhatt DL, Bittner VA, Bregeault M-F, Dalby AJ, et al. Effect of Alirocumab on Mortality After Acute Coronary Syndromes. Circulation. 2019;140(2):103-12.	Duplicaat van publication ODYSSEY-OUTCOMES-trial
Rosenson RS, Hegele RA, Koenig W. Cholesterol-Lowering Agents. Circulation research. 2019;124(3):364-85.	Narratieve review
Ray KK, Colhoun HM, Szarek M, Baccara-Dinet M, Bhatt DL, Bittner VA, et al. Effects of alirocumab on cardiovascular and metabolic outcomes after acute coronary syndrome in patients with or without diabetes: a prespecified analysis of the ODYSSEY OUTCOMES randomised controlled trial. The lancet Diabetes & endocrinology. 2019;7(8):618-28.	Subgroepanalyse: diabetes (alle patiënten hadden HVZ)
Murphy SA, Pedersen TR, Gaciong ZA, Ceska R, Ezhov MV, Connolly DL, et al. Effect of the PCSK9 Inhibitor Evolocumab on Total Cardiovascular Events in Patients With Cardiovascular Disease: A Prespecified Analysis From the FOURIER Trial. JAMA cardiology. 2019;4(7):613-9.	Analyse FOURIER-trial van totaal aantal events
Lee J, Holbrook A. Pooled RCTs: Lowering LDL-C levels using statins reduces major vascular events in all age groups. Annals of internal medicine. 2019;170(12):JC65.	Commentaar op een meta-analyse
Jukema JW, Zijlstra LE, Bhatt DL, Bittner VA, Diaz R, Drexel H, et al. Effect of Alirocumab on Stroke in ODYSSEY OUTCOMES. Circulation. 2019;140(25):2054-62.	Analyse ODYSSEY OUTCOMES-trial naar effect op verschillende vormen van beroerte.
Dicembrini I, Giannini S, Ragghianti B, Mannucci E, Monami M. Effects of PCSK9 inhibitors on LDL cholesterol, cardiovascular morbidity and all-cause mortality: a systematic review and meta-analysis of randomized controlled trials. Journal of Endocrinological Investigation. 2019;42(9):1029-39.	SR: gezocht tot dec 2017 (recentere reviews beschikbaar)
Soran H, Adam S, Durrington PN. Optimising treatment of hyperlipidaemia: Quantitative evaluation of UK, USA and European guidelines taking account of both LDL cholesterol levels and cardiovascular disease risk. Atherosclerosis. 2018;278:135-42.	Onderzoek naar behandeling conform richtlijnen en het effect op LDL
Sabatine MS, Wiviott SD, Im K, Murphy SA, Giugliano RP. Efficacy and safety of further lowering of low-density lipoprotein cholesterol in patients starting with very low levels: A meta-analysis. JAMA Cardiology. 2018;3(9):823-8.	Onderzoek naar baseline LDL 1.8 en effect van verlaging
Navarese EP, Robinson JG, Kowalewski M, Kolodziejczak M, Andreotti F, Bliden K, et al. Association Between Baseline LDL-C Level and Total and Cardiovascular Mortality After LDL-C Lowering: A Systematic Review and Meta-analysis. JAMA. 2018;319(15):1566-79.	Meta-analyse: daling in LDL
Koskinas KC, Siontis GCM, Piccolo R, Mavridis D, Räber L, Mach F, et al. Effect of statins and non-statin LDL-lowering medications on cardiovascular outcomes in secondary prevention: A meta-analysis of randomized trials. European Heart Journal. 2018;39(14):1172-80.	SR: Trials hebben we reeds geïncudeerd in de module
Kaasenbrood L, Ray KK, Boekholdt SM, Smulders YM, LaRosa JC, Kastelein JJP, et al. Estimated individual lifetime benefit from PCSK9 inhibition in statin-treated patients with coronary artery disease. Heart (British Cardiac Society). 2018;104(20):1699-705.	Onderzoek naar het geschatte effect van PCSK9

Hong N, Lee YH, Tsujita K, Gonzalez JA, Kramer CM, Kovarnik T, et al. Comparison of the effects of ezetimibe-statin combination therapy on major adverse cardiovascular events in patients with and without diabetes: A meta-analysis. Endocrinology and Metabolism. 2018;33(2):219-27.	SR: Effect bij diabetes. Geen van de geïncludeerde trials voldoet aan de huidige selectiecriteria (geen vergelijking tussen intensief vs minder intensief, patiënten met HVZ en diabetes of geen primaire uitkomstmaat HVZ).
Soran H, Kwok S, Adam S, Ho JH, Durrington PN. Evidence for more intensive cholesterol lowering. Current Opinion in Lipidology. 2017;28(4):291-9.	Recentere reviews beschikbaar
He X, Liu T, Pan Y, Li X. Efficacy of LDL-C lowering therapy in patients with non-ST-segment elevation acute coronary syndrome: A meta-analysis. Chinese Journal of Evidence-Based Medicine. 2017;17(5):550-6.	Effect van therapie bij NSTE-ACS
Giugliano RP, Wiviott SD, Blazing MA, De Ferrari GM, Park J-G, Murphy SA, et al. Long-term Safety and Efficacy of Achieving Very Low Levels of Low-Density Lipoprotein Cholesterol : A Prespecified Analysis of the IMPROVE-IT Trial. JAMA cardiology. 2017;2(5):547-55.	Effect van lage LDL-C-waarden na behandeling
Giugliano RP, Keech A, Murphy SA, Huber K, Tokgozoglu SL, Lewis BS, et al. Clinical Efficacy and Safety of Evolocumab in High-Risk Patients Receiving a Statin: Secondary Analysis of Patients With Low LDL Cholesterol Levels and in Those Already Receiving a Maximal-Potency Statin in a Randomized Clinical Trial. JAMA cardiology. 2017;2(12):1385-91.	Onderzoek of een lager LDL-niveau zinvol is.
Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement fromthe European Atherosclerosis Society Consensus Panel. European Heart Journal. 2017;38(32):2459-72.	Causaliteit van LDL op ACS
Davies GM, Vyas A, Baxter CA. Economic evaluation of ezetimibe treatment in combination with statin therapy in the United States. Journal of Medical Economics. 2017;20(7):723-31.	Kosteneffectiviteit van ezetimibe en statine in Amerika
Anonymous. Ezetimibe + statin: insufficient benefit. Prescrire international. 2016;25(175):245-6.	Commentaar op een trial
Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, Mihaylova B, et al. Efficacy and safety of LDL-lowering therapy among men and women: Meta-analysis of individual data from 174 000 participants in 27 randomised trials. The Lancet. 2015;385(9976):1397-405.	Onderzoek naar man-vrouwverschil
Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, et al. Ezetimibe added to statin therapy after acute coronary syndromes. New England Journal of Medicine. 2015;372(25):2387-97.	Reeds geïncludeerd in de eerdere literatuuranalyse
Yan YL, Qiu B, Hu LJ, Jing XD, Liu YJ, Deng SB, et al. Efficacy and safety evaluation of intensive statin therapy in older patients with coronary heart disease: A systematic review and meta-analysis. European Journal of Clinical Pharmacology. 2013;69(12):2001-9.	SR: recentere reviews beschikbaar
Baigent C, Blackwell L, Emberson J, Holl, LE, Reith C, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: A meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet. 2010;376(9753):1670-81.	SR: recentere reviews beschikbaar

Tabel 2017

Auteur en jaartal	Redenen van exclusie
Soran, 2017	Gezocht in 1 database; zoekstrategie niet beschikbaar
Olsson, 2017	Narratieve review
Bahiru, 2017	Niet alleen cholesterolverlagende medicatie; vergeleken met placebo
Lafeber, 2017	RCT polypill versus usual care

Schmidt, 2017	Systematische review naar effectiviteit van PCSK9-antilichamen
Jena, 2016	Data uit een cohortstudie
Peng, 2016	Geen Risk of Bias beoordeling per studie (wel voor publicatie bias)
Webster, 2016	Geen systematische zoekactie
Cai, 2015	Associatie tussen genetische afwijking en HVZ
Cholesterol Treatment Trialists, 2015	Geen systematische zoekactie
Karlson, 2015	Geen systematische zoekactie; gesponsord door farmaceut
Preiss, 2015	RCT's vergeleken met placebo geïncludeerd
Thomopoulos, 2015	RCT's vergeleken met placebo geïncludeerd
Boekholdt, 2014	Gezocht in 1 database
Bruckert, 2014	Narratieve review
Gudzune, 2014	Systematische review van intensieve behandeling met lipidenverlagende medicatie versus minder intensief
Naci, 2014	Effectschatters niet gerapporteerd omdat het doel van review het onderzoeken van industry-sponsored bias was
Soran, 2014	Narratieve review
Karlson, 2013	Geen systematische zoekactie; gesponsord door farmaceut
Naci, 2013	Effectschatters niet gerapporteerd omdat het doel van review het onderzoeken van industry-sponsored bias was
Ribeiro, 2013	Geen uitkomst LDL-waarde
Ye, 2012	Uitkomst van interesse endotheel functie
Morrone, 2012	Niet systematisch gezocht
Cholesterol Treatment Trialists, 2012	Geen systematische zoekactie
McKinney, 2012	RCT's vergeleken met placebo geïncludeerd
Sniderman, 2011	Verschil tussen markers LDL, non-HDL en apoB
Chan, 2011	Systematische review van intensieve behandeling met statines versus minder intensief
Ramjee, 2011	Niet origineel; beschrijving van de CTT meta-analyse
Seehusen, 2011	Case report met review van literatuur

Exclusietabel voor uitgangsvraag:

Wat is de meerwaarde van de behandeling met lipidenverlagende middelen bij (kwetsbare) ouderen (> 70 jaar)?

PICO1

Tabel 2017

Auteur en jaartal	Redenen van exclusie
Review filter	
Thai, 2016	Focus op medicatie interacties
Lowe, 2015	Geen kwaliteitsbeoordeling; alleen gezocht in Medline; studies al in bovenstaande reviews
Iwere, 2015	Meerdere trials geïncludeerd met een populatie jonger dan 70 jaar. Trials met > 70 zijn reeds geïncludeerd in Savarese, 2013
Zoungas, 2014	Narratieve review
Savaraese, 2014	Erratum
Savarese, 2013	Recentere systematische review beschikbaar
Fulcher, 2013	Congres abstract
Chen, 2012	Patiënten met diabetes
Weatherley, 2011	Risicoschatting op basis van bestaande predictiemodellen
Mills, 2011	Intensivering van statine dosering
Kolovou, 2011	Narratieve review

Biffi, 2011	Alleen beroerte als uitkomst, geen RCT's geïncludeerd
Biffi, 2011	Merendeel observationele studies geïncludeerd
Berthold, 2011	Narratieve review
Lakhan, 2010	Merendeel observationele studies; onduidelijk leeftijd van patienten
Brugts, 2009	Merendeel RCT's patiënten jonger dan 70 jaar
Walker, 2008	Narratieve review
Afilalo, 2008	Patiënten jonger dan 70 jaar
Bonovas, 2007	Studie met 70-plussers reeds geincludeerd in Teng, 2015
Raffel, 2006	Narratieve review
Law, 2006	Alleen gezocht in Medline
Hey-Hadavi, 2006	Betreft de associatie tussen verschillende doseringen van atorvastatine
Dornbrook-Lavender, 2003	Geen zoekstrategie weergegeven; geen in- en exclusie gegevens; gemiddelde leeftijd niet weergegeven, veel waarschijnlijk onder de 70 gemiddeld. Sommige studies wel al geïncludeerd in recentere SR's
Birch, 2002	Alleen gezocht in Medline; Voldoet niet aan leeftijdscriterium
Mellies, 1993	1 onderzochte statine: pravastatin en relatief oud
RCT-filter	
Wu, 2015	Cohortstudie
Wilmot, 2015	Narratieve review
Schwartz, 2015	Narratieve review
Pilotto, 2015	Patiënten met DM; associatie tussen effectiviteit van statine en voorspelde mortaliteit risico
Pedro-botet, 2015	Narratieve review
Hamilton-Craig, 2015	Narratieve review
Sigurdsson, 2014	Editorial
Savarese, 2014	Editorial
Reiner, 2014	Narratieve review
Fontana, 2014	Verdeling van medicatie disutility
Drewes, 2014	PROSPER-trial analysis, gestratificeerd bij homocysteine niveaus
Stender, 2013	Geen vergelijkende groep
Stender, 2013	Vergelijking tussen twee statines in verschillende doseringen; geen placebo gegeven
Rizzo, 2013	Narratieve review
Lloyd, 2013	Studie (PROSPER) reeds geïncludeerd
Bhardwaj, 2013	Narratieve review
Sicras-Mainar, 2012	Cohortstudie
Schiattarellla, 2012	Narratieve review
Chokshi, 2012	Voorspellers voor het gebruik van een statine
Shao, 2011	Narratieve review
Szadkowska, 2010	Narratieve review
Gransbo, 2010	Cohortstudie
Fricker, 2009	Editorial
Shepherd, 2004	Editorial; beschrijving van een andere studie
Yaffe, 2002	Cohortstudie
Jackevicius, 2002	Cohortstudie
Houx, 2002	Baseline gegevens van reeds geïncludeerde studie (PROSPER)
Benner, 2002	Cohort studie
Ito, 2001	Vergelijking tussen verschillende doseringen
Chikamori, 2000	Observationele studie
Campeau, 1999	Geen relevante uitkomsten gerapporteerd
Miettinen, 1997	Patiënten waren maximaal 70 jaar oud
Lansberg, 1995	Geen vergelijking

Santinga, 1994	Geen relevante uitkomsten gerapporteerd
LaRosa, 1994	Geen relevante uitkomsten gerapporteerd

PICO2

Tabel update 2021

Referentie	Reden
Oyama K, Giugliano RP, Tang M, Bonaca MP, Saver JL, Murphy SA, et al. Effect of evolocumab on acute arterial events across all vascular territories : results from the FOURIER trial. European heart journal. 2021;42(47):4821-9.	FOURIER-trial. Onderzoek naar intensieve behandeling versus minder intensieve behandeling
Jin S, Nie X, Li Y, Yuan J, Cui Y, Zhao L. Effect of More Intensive LDL-C-Lowering Therapy on Long-term Cardiovascular Outcomes in Early-Phase Acute Coronary Syndrome: A Systematic Review and Meta-analysis. Clinical therapeutics. 2021;43(7):e217-e29.	SR, geen van de geïncludeerde trials komt in aanmerking.
Elgendy IY, Elshazly MB. LDL-C-lowering therapies reduce major vascular events in patients aged > =75 y. Annals of internal medicine. 2021;174(4):JC38.	Commentaar op een trial
Deedwania P, Murphy SA, Scheen A, Badariene J, Pineda A, Lira o, et al. Efficacy and Safety of PCSK9 Inhibition With Evolocumab in Reducing Cardiovascular Events in Patients With Metabolic Syndrome Receiving Statin Therapy: Secondary Analysis From the FOURIER Randomized Clinical Trial. JAMA cardiology. 2021;6(2):139-47.	FOURIER-trial: analyse bij patiënten met het metabool syndroom
Amarenco P, Kim JS, Labreuche J, Charles H, Giroud M, Lee B-C, et al. Impact of Lower Versus Higher LDL Cholesterol Targets on Cardiovascular Events After Ischemic Stroke in Patients With Diabetes. Diabetes. 2021;70(8):1807-15.	TST-trial: Analyse naar subgroep diabetes. Echter, alle deelnemers hebben een beroerte gehad.
Wiviott SD, Giugliano RP, Morrow DA, De Ferrari GM, Lewis BS, Huber K, et al. Effect of Evolocumab on Type and Size of Subsequent Myocardial Infarction: A Prespecified Analysis of the FOURIER Randomized Clinical Trial. JAMA cardiology. 2020;5(7):787-93.	FOURIER-trial: analyse naar de uitkomst MI subtype
Wang N, Fulcher J, Abeysuriya N, Park L, Kumar S, Di Tanna GL, et al. Intensive LDL cholesterol-lowering treatment beyond current recommendations for the prevention of major vascular events: a systematic review and meta-analysis of randomised trials including 327 037 participants. The Lancet Diabetes and Endocrinology. 2020;8(1):36-49.	SR naar de daling in LDL
Robinson JG, Jayanna MB, Bairey Merz CN, Stone NJ. Clinical implications of the log linear association between LDL-C lowering and cardiovascular risk reduction: Greatest benefits when LDL-C > 100 mg/dl. PloS one. 2020;15(10):e0240166.	Meta-analyse: daling in LDL
Ödesjö H, Björck S, Franzén S, Hjerpe P, Manhem K, Rosengren A, et al. Adherence to lipid-lowering guidelines for secondary prevention and potential reduction in CVD events in Swedish primary care: A cross-sectional study. BMJ Open. 2020;10(10).	Onderzoek naar adherentie en geen follow-up
Gencer B, Mach F, Murphy SA, De Ferrari GM, Huber K, Lewis BS, et al. Efficacy of Evolocumab on Cardiovascular Outcomes in Patients With Recent Myocardial Infarction: A Prespecified Secondary Analysis From the FOURIER Trial. JAMA cardiology. 2020;5(8):952-7.	FOURIER-trial: subgroepanalyse bij patiënten met MI
Alkhalil M. Effects of intensive lipid-lowering therapy on mortality after coronary bypass surgery: A meta-analysis of 7 randomised trials. Atherosclerosis. 2020;293:75-8.	SR bij patiënten die een CABG ondergingen
Vallejo-Vaz AJ, Ray KK, Ginsberg HN, Davidson MH, Eckel RH, Lee LV, et al. Associations between lower levels of low-density lipoprotein cholesterol and	Meta-analyse van ODYSSEY-trials en subgroepen comorbiditeiten (niet alleen vergelijking intensief versus minder-

cardiovascular events in very high-risk patients: Pooled analysis of nine ODYSSEY trials of alirocumab versus control. Atherosclerosis. 2019;288:85-93.	intensief of uitkomsten gerelateerd aan LDL-daling)
Steg PG, Szarek M, Bhatt DL, Bittner VA, Bregeault M-F, Dalby AJ, et al. Effect of Alirocumab on Mortality After Acute Coronary Syndromes. Circulation. 2019;140(2):103-12.	Duplicaat van publication ODESSEY-OUTCOMES-trial
Rosenson RS, Hegele RA, Koenig W. Cholesterol-Lowering Agents. Circulation research. 2019;124(3):364-85.	Narratieve review
Ray KK, Colhoun HM, Szarek M, Baccara-Dinet M, Bhatt DL, Bittner VA, et al. Effects of alirocumab on cardiovascular and metabolic outcomes after acute coronary syndrome in patients with or without diabetes: a prespecified analysis of the ODYSSEY OUTCOMES randomised controlled trial. The lancet Diabetes & endocrinology. 2019;7(8):618-28.	Subgroepanalyse: diabetes (alle patiënten hadden HVZ)
Murphy SA, Pedersen TR, Gaciong ZA, Ceska R, Ezhov MV, Connolly DL, et al. Effect of the PCSK9 Inhibitor Evolocumab on Total Cardiovascular Events in Patients With Cardiovascular Disease: A Prespecified Analysis From the FOURIER Trial. JAMA cardiology. 2019;4(7):613-9.	Analyse FOURIER-trial van totaal aantal events
Lee J, Holbrook A. Pooled RCTs: Lowering LDL-C levels using statins reduces major vascular events in all age groups. Annals of internal medicine. 2019;170(12):JC65.	Commentaar op een meta-analyse
Jukema JW, Zijlstra LE, Bhatt DL, Bittner VA, Diaz R, Drexel H, et al. Effect of Alirocumab on Stroke in ODYSSEY OUTCOMES. Circulation. 2019;140(25):2054-62.	Analyse ODESSEY OUTCOMES-trial naar effect op verschillende vormen van beroerte.
Dicembrini I, Giannini S, Ragghianti B, Mannucci E, Monami M. Effects of PCSK9 inhibitors on LDL cholesterol, cardiovascular morbidity and all-cause mortality: a systematic review and meta-analysis of randomized controlled trials. Journal of Endocrinological Investigation. 2019;42(9):1029-39.	SR: gezocht tot dec 2017 (recentere reviews beschikbaar)
Soran H, Adam S, Durrington PN. Optimising treatment of hyperlipidaemia: Quantitative evaluation of UK, USA and European guidelines taking account of both LDL cholesterol levels and cardiovascular disease risk. Atherosclerosis. 2018;278:135-42.	Onderzoek naar behandeling conform richtlijnen en het effect op LDL
Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, Edelberg JM, Goodman SG, Hanotin C, Harrington RA, Jukema JW, Lecorps G, Mahaffey KW, Moryusef A, Pordy R, Quintero K, Roe MT, Sasiela WJ, Tamby JF, Tricoci P, White HD, Zeiher AM; ODYSSEY OUTCOMES Committees and Investigators. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. N Engl J Med. 2018 Nov 29;379(22):2097-2107. doi: 10.1056/NEJMoa1801174. Epub 2018 Nov 7. PMID: 30403574.	Onderzoek naar intensieve behandeling versus minder intensieve behandeling
Sabatine MS, Wiviott SD, Im K, Murphy SA, Giugliano RP. Efficacy and safety of further lowering of low-density lipoprotein cholesterol in patients starting with very low levels: A meta-analysis. JAMA Cardiology. 2018;3(9):823-8.	Onderzoek naar baseline LDL 1,8 en effect van verlaging
Navarese EP, Robinson JG, Kowalewski M, Kolodziejczak M, Andreotti F, Bliden K, et al. Association Between Baseline LDL-C Level and Total and Cardiovascular Mortality After LDL-C Lowering: A Systematic Review and Meta-analysis. JAMA. 2018;319(15):1566-79.	Meta-analyse: daling in LDL
Koskinas KC, Siontis GCM, Piccolo R, Mavridis D, Räber L, Mach F, et al. Effect of statins and non-statin LDL-lowering medications on cardiovascular outcomes in secondary prevention: A meta-analysis of randomized trials. European Heart Journal. 2018;39(14):1172-80.	SR: Trials hebben we reeds geïncludeerd in de module
Kaasenbrood L, Ray KK, Boekholdt SM, Smulders YM, LaRosa JC, Kastelein JJP, et al. Estimated individual lifetime benefit from PCSK9 inhibition in statin-treated patients with coronary artery disease. Heart (British Cardiac Society). 2018;104(20):1699-705.	Onderzoek naar het geschatte effect van PCSK9

Hong N, Lee YH, Tsujita K, Gonzalez JA, Kramer CM, Kovarnik T, et al. Comparison of the effects of ezetimibe-statin combination therapy on major adverse cardiovascular events in patients with and without diabetes: A meta-analysis. Endocrinology and Metabolism. 2018;33(2):219-27.	SR: Effect bij diabetes. Geen van de geïncludeerde trials voldoet aan de huidige selectiecriteria (geen vergelijking tussen intensief versus minder intensief, patiënten met HVZ en diabetes of geen primaire uitkomstmaat HVZ).
Soran H, Kwok S, Adam S, Ho JH, Durrington PN. Evidence for more intensive cholesterol lowering. Current Opinion in Lipidology. 2017;28(4):291-9.	Recentere reviews beschikbaar
He X, Liu T, Pan Y, Li X. Efficacy of LDL-C lowering therapy in patients with non-ST-segment elevation acute coronary syndrome: A meta-analysis. Chinese Journal of Evidence-Based Medicine. 2017;17(5):550-6.	Effect van therapie bij NSTE-ACS
Giugliano RP, Wiviott SD, Blazing MA, De Ferrari GM, Park J-G, Murphy SA, et al. Long-term Safety and Efficacy of Achieving Very Low Levels of Low-Density Lipoprotein Cholesterol : A Prespecified Analysis of the IMPROVE-IT Trial. JAMA cardiology. 2017;2(5):547-55.	Effect van lage LDL-C-waarden na behandeling
Giugliano RP, Keech A, Murphy SA, Huber K, Tokgozoglu SL, Lewis BS, et al. Clinical Efficacy and Safety of Evolocumab in High-Risk Patients Receiving a Statin: Secondary Analysis of Patients With Low LDL Cholesterol Levels and in Those Already Receiving a Maximal-Potency Statin in a Randomized Clinical Trial. JAMA cardiology. 2017;2(12):1385-91.	Onderzoek of een lager LDL-niveau zinvol is.
Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement fromthe European Atherosclerosis Society Consensus Panel. European Heart Journal. 2017;38(32):2459-72.	Causaliteit van LDL op ACS
Davies GM, Vyas A, Baxter CA. Economic evaluation of ezetimibe treatment in combination with statin therapy in the United States. Journal of Medical Economics. 2017;20(7):723-31.	Kosteneffectiviteit van ezetimib en statine in Amerika
Anonymous. Ezetimibe + statin: insufficient benefit. Prescrire international. 2016;25(175):245-6.	Commentaar op een trial
Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L, Mihaylova B, et al. Efficacy and safety of LDL-lowering therapy among men and women: Meta-analysis of individual data from 174 000 participants in 27 randomised trials. The Lancet. 2015;385(9976):1397-405.	Onderzoek naar man-vrouwverschil
Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, et al. Ezetimibe added to statin therapy after acute coronary syndromes. New England Journal of Medicine. 2015;372(25):2387-97.	Reeds geïncludeerd in de eerdere literatuuranalyse
Yan YL, Qiu B, Hu LJ, Jing XD, Liu YJ, Deng SB, et al. Efficacy and safety evaluation of intensive statin therapy in older patients with coronary heart disease: A systematic review and meta-analysis. European Journal of Clinical Pharmacology. 2013;69(12):2001-9.	SR: recentere reviews beschikbaar
Baigent C, Blackwell L, Emberson J, Holl, LE, Reith C, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: A meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet. 2010;376(9753):1670-81.	SR: recentere reviews beschikbaar

Exclusietabel voor uitgangsvraag:

Wat is de toegevoegde waarde van een coronaire kalkscore bij het reclassificeren van het risico op hart- en vaatziekten?

Tabel 2017

Redenen van exclusie	Auteur en jaartal
Exclusie. Narrative review.	Sathiyakumar V, Blumenthal RS, Nasir K, Martin SS. Addressing Knowledge Gaps in the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: a Review of Recent Coronary Artery Calcium Literature. Current atherosclerosis reports. 2017;19(2):7
Exclusie. Narrative review.	Osawa K, Nakanishi R, Budoff MJ. Is there a role for coronary artery calcification scoring in primary prevention of cerebrovascular disease? Atherosclerosis. 2017;0
Exclusie. Narrative review.	Osawa K, Nakanishi R, Budoff M. Coronary Artery Calcification. Glob Heart. 2016;11(3):287-93
Exclusie. Narrative review.	Kianoush S, Rifai MA, Cainzos-Achirica M, Umapathi P, Graham G, Blumenthal RS, et al. An Update on the Utility of Coronary Artery Calcium Scoring for Coronary Heart Disease and Cardiovascular Disease Risk Prediction. Current atherosclerosis reports. 2016;18(3):13
Exclusie. Alleen laag risico vrouwen	Kavousi M, Desai CS, Ayers C, Blumenthal RS, Budoff MJ, Mahabadi AA, et al. Prevalence and Prognostic Implications of Coronary Artery Calcification in Low-Risk Women: A Meta-analysis. Jama. 2016;316(20):2126-34
Exclusie. Narrative review, alleen MESA study.	Blaha MJ, Yeboah J, Rifai MA, Liu K, Kronmal R, Greenland P. Providing Evidence for Subclinical CVD in Risk Assessment. Glob Heart. 2016;11(3):275-85
Exclusie. Narrative review.	Bambrick P, Tan WS, Mulcahy R, Pope GA, Cooke J. Vascular risk assessment in older adults without a history of cardiovascular disease. Experimental gerontology. 2016;79:37-45
Exclusie. Narrative review.	Zeb I, Budoff M. Coronary artery calcium screening: does it perform better than other cardiovascular risk stratification tools? International journal of molecular sciences. 2015;16(3):6606-20
Exclusie. Vergelijking CAC met MPI (myocardial perfusion imaging).	Yuoness SA, Goha AM, Romsa JG, Akincioglu C, Warrington JC, Datta S, et al. Very high coronary artery calcium score with normal myocardial perfusion SPECT imaging is associated with a moderate incidence of severe coronary artery disease. Eur J Nucl Med Mol Imaging. 2015;42(10):1542-50
Exclusie. Narrative review.	Weber LA, Cheezum MK, Reese JM, Lane AB, Haley RD, Lutz MW, et al. Cardiovascular Imaging for the Primary Prevention of Atherosclerotic Cardiovascular Disease Events. Curr Cardiovasc Imaging Rep. 2015;8(9):36
Exclusie. Narrative review.	Thomas DM, Divakaran S, Villines TC, Nasir K, Shah NR, Slim AM, et al. Management of Coronary Artery Calcium and Coronary CTA Findings. Curr Cardiovasc Imaging Rep. 2015;8(6):18
Exclusie. SR voor CRP en CAC met search tot Aug 2015. Alleen AUCs, geen reclassificatie.	Qureshi WT, Rana JS, Yeboah J, Nasir UB, Al-Mallah MH. Risk Stratification for Primary Prevention of Coronary Artery Disease: Roles of C-Reactive Protein and Coronary Artery Calcium. Current cardiology reports. 2015;17(12):110
Inclusie. Dallas Heart Study, met meta-analyse van NRI's, zoekdatum Dec 2014.	Paixao AR, Ayers CR, Sabbagh AE, Sanghavi M, Berry JD, Rohatgi A, et al. Coronary Artery Calcium Improves Risk Classification in Younger Populations. JACC Cardiovascular imaging. 2015;8(11):1285-93
Exclusie. Narrative review.	Manson JE, Bassuk SS. Biomarkers of cardiovascular disease risk in women. Metabolism: clinical and experimental. 2015;64(3):S33-9
Exclusie. Narrative review en study design Koreaanse studie.	Lee JH, B OH, Han D, Park HE, Choi SY, Sung J, et al. Reassessing the Usefulness of Coronary Artery Calcium Score among Varying Racial and Ethnic Groups by Geographic Locations: Relevance of the Korea Initiatives on Coronary Artery Calcification Registry. Journal of cardiovascular ultrasound. 2015;23(4):195-203
Exclusie. Narrative review.	Joshi PH, Nasir K. Discordance between Risk Factors and Coronary Artery Calcium: Implications for Guiding Treatment Strategies in Primary Prevention Settings. Progress in cardiovascular diseases. 2015;58(1):10-8
Exclusie. Narrative review.	Degrell P, Sorbets E, Feldman LJ, Steg PG, Ducrocq G. Screening for coronary artery disease in asymptomatic individuals: Why and how? Arch Cardiovasc Dis. 2015;108(12):675-82

Exclusie. Narrative review.	Wallace ML, Ricco JA, Barrett B. Screening strategies for cardiovascular disease in asymptomatic adults. Primary care. 2014;41(2):371-97
Exclusie. Narrative review.	Blaha MJ, Silverman MG, Budoff MJ. Is there a role for coronary artery calcium scoring for management of asymptomatic patients at risk for coronary artery disease?: Clinical risk scores are not sufficient to define primary prevention treatment strategies among asymptomatic patients. Circulation Cardiovascular imaging. 2014;7(2):398-408; discussion
Niet voltekst beoordeeld.	Anthony D, George P, Eaton CB. Cardiac risk factors: noninvasive testing to detect coronary heart disease. FP Essent. 2014;421:21-7
Exclusie. Narrative review.	Akhabue E, Thiboutot J, Cheng JW, Vittorio TJ, Christodoulidis G, Grady KM, et al. New and emerging risk factors for coronary heart disease. The American journal of the medical sciences. 2014;347(2):151-8
Exclusie. Narrative review.	Wachira JK, Stys TP. Cardiovascular disease and bridging the diagnostic gap. South Dakota medicine : the journal of the South Dakota State Medical Association. 2013;66(9):366-9
Exclusie. Narrative review.	Wierzbicki AS. New directions in cardiovascular risk assessment: the role of secondary risk stratification markers. International journal of clinical practice. 2012;66(7):622-30
Exclusie. SR, alleen PubMed, geen zoek- en selectieverantwoording.	Vliegenthart R, Morris PB. Computed tomography coronary artery calcium scoring: review of evidence base and cost-effectiveness in cardiovascular risk prediction. Journal of thoracic imaging. 2012;27(5):296-303
Exclusie. Narrative review.	Shah NR, Coulter SA. An evidence-based guide for coronary calcium scoring in asymptomatic patients without coronary heart disease. Texas Heart Institute journal / from the Texas Heart Institute of St Luke's Episcopal Hospital, Texas Children's Hospital. 2012;39(2):240-2
Exclusie. Narrative review.	Sekikawa A, Curb JD, Edmundowicz D, Okamura T, Choo J, Fujiyoshi A, et al. Coronary artery calcification by computed tomography in epidemiologic research and cardiovascular disease prevention. Journal of epidemiology / Japan Epidemiological Association. 2012;22(3):188-98
Exclusie. Wel SR, maar composite intervention (div. 'atherosclerosis screening' methods)	Rodondi N, Auer R, Sulzer VdB, Ghali WA, Cornuz J. Atherosclerosis screening by noninvasive imaging for cardiovascular prevention: a systematic review. Journal of general internal medicine. 2012;27(2):220-31
Inclusie. SR tot 7-9-2011, golden hit (en recenter dan de andere Peters 2011)	Peters SA, Ruijter HMd, Bots ML, Moons KG. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. Heart (British Cardiac Society). 2012;98(3):177-84
Exclusie. SR tot 1-2-2011, golden hit, maar andere Peters 2011 is recenter	Peters SA, Bakker M, Ruijter HMd, Bots ML. Added value of CAC in risk stratification for cardiovascular events: a systematic review. European journal of clinical investigation. 2012;42(1):110-6
Exclusie. Narrative review. Wel mooie summary Table 1 (tot en met 2010)	Nasir K, Clouse M. Role of nonenhanced multidetector CT coronary artery calcium testing in asymptomatic and symptomatic individuals. Radiology. 2012;264(3):637-49
Exclusie. Narrative review.	Erbel R, Budoff M. Improvement of cardiovascular risk prediction using coronary imaging: subclinical atherosclerosis: the memory of lifetime risk factor exposure. European heart journal. 2012;33(10):1201-13
Exclusie. Narrative review.	Budoff MJ. Screening for Ischemic Heart Disease with Cardiac CT: Current Recommendations. Scientifica. 2012;2012:812046
Exclusie. Narrative review.	Wilson SR, Lin FY, Min JK. Role of coronary artery calcium score and coronary CT angiography in the diagnosis and risk stratification of individuals with suspected coronary artery disease. Current cardiology reports. 2011;13(4):271-9
Niet verkrijgbaar.	Mehra S, Movahed H, Movahed A. Coronary artery calcium scoring. Reviews in cardiovascular medicine. 2011;12(2):e94-e103
Exclusie. Narrative review.	Hecht HS. Coronary artery calcium: utilization for primary prevention of CHD. Current cardiology reports. 2011;13(6):465-74

Exclusie. Narrative review, verslag van guideline-revision.	Budoff MJ, Malpeso JM. Is coronary artery calcium the key to assessment of cardiovascular risk in asymptomatic adults? Journal of cardiovascular computed tomography. 2011;5(1):12-5
Exclusie. Narrative review.	Sharma RK, Sharma RK, Voelker DJ, Singh VN, Pahuja D, Nash T, et al. Cardiac risk stratification: role of the coronary calcium score. Vascular health and risk management. 2010;6:603-11
Exclusie. Narrative review.	Patel AA, Budoff MJ. Screening for heart disease: C-reactive protein versus coronary artery calcium. Expert review of cardiovascular therapy. 2010;8(1):125-31
Exclusie. Narrative review.	Orringer CE. The absence of coronary calcium: clinical and therapeutic implications for the clinical lipidologist. Journal of clinical lipidology. 2010;4(6):472-7
Exclusie; wel een SR; geen definitie van CAC + versus CAC -; geen reclassificatie	Rennenberg RJ, Kessels AG, Schurgers LJ, Engelshoven JMv, Leeuw PWd, Kroon AA. Vascular calcifications as a marker of increased cardiovascular risk: a meta-analysis. Vascular health and risk management. 2009;5(1):185-97
Niet voltekst beoordeeld.	Pessana F, Armentano R, Chironi G, Megnien JL, Mousseaux E, Simon A. Subclinical atherosclerosis modeling: Integration of coronary artery calcium score to Framingham equation. Conference proceedings : Annual International Conference of the IEEE Engineering in Medicine and Biology Society IEEE Engineering in Medicine and Biology Society Annual Conference. 2009;2009:5348-51
Exclusie; SR uit 2009, alleen MEDLINE. Recentere SR beschikbaar (Peters 2012)	Helfand M, Buckley DI, Freeman M, Fu R, Rogers K, Fleming C, et al. Emerging risk factors for coronary heart disease: a summary of systematic reviews conducted for the U.S. Preventive Services Task Force. Annals of internal medicine. 2009;151(7):496-507
Exclusie. Clinical guideline	Using nontraditional risk factors in coronary heart disease risk assessment: U.S. Preventive Services Task Force recommendation statement. Annals of internal medicine. 2009;151(7):474-82
Exclusie. Narrative review.	Raggi P, Shaw LJ. Epidemiologic guidance with coronary artery calcium scoring. Current cardiology reports. 2008;10(1):60-6
Exclusie. Narrative review.	Raggi P, Khan A, Arepali C, Stillman AE. Coronary artery calcium scoring in the age of CT angiography: what is its role? Current atherosclerosis reports. 2008;10(5):438-43
Exclusie. Narrative review.	Elkeles R. Computed tomography imaging, coronary calcium and atherosclerosis. Expert review of cardiovascular therapy. 2008;6(8):1083-93
	Budoff MJ, Gul KM. Expert review on coronary calcium. Vascular health and risk management. 2008;4(2):315-24
Exclusie. Narrative review; wel poging SR, geen zoekverantwoording.	Simon A, Chironi G, Levenson J. Comparative performance of subclinical atherosclerosis tests in predicting coronary heart disease in asymptomatic individuals. European heart journal. 2007;28(24):2967-71
Exclusie. Wel SR, maar alleen over betekenis CAC-score zero.	Shareghi S, Ahmadi N, Young E, Gopal A, Liu ST, Budoff MJ. Prognostic significance of zero coronary calcium scores on cardiac computed tomography. Journal of cardiovascular computed tomography. 2007;1(3):155-9
Exclusie. Wel SR, maar over CAC-score bij mannen versus. vrouwen.	Bellasi A, Lacey C, Taylor AJ, Raggi P, Wilson PW, Budoff MJ, et al. Comparison of prognostic usefulness of coronary artery calcium in men versus women (results from a meta- and pooled analysis estimating all-cause mortality and coronary heart disease death or myocardial infarction). The American journal of cardiology. 2007;100(3):409-14
Exclusie. SR, geen reclassificatie.	Ardehali R, Nasir K, Kolandaivelu A, Budoff MJ, Blumenthal RS. Screening patients for subclinical atherosclerosis with non-contrast cardiac CT. Atherosclerosis. 2007;192(2):235-42
Exclusie. SR, geen reclassificatie.	Waugh N, Black C, Walker S, McIntyre L, Cummins E, Hillis G. The effectiveness and cost-effectiveness of computed tomography screening for coronary artery disease: systematic review. Health technology assessment (Winchester, England). 2006;10(39):iii-iv, ix-x, 1-41
Exclusie. Narrative review.	Thompson JB, Rivera JJ, Blumenthal RS, Danyi P. Primary prevention for patients with intermediate Framingham risk scores. Current cardiology reports. 2006;8(4):261-6
Exclusie. Narrative review.	Simon A, Chironi G, Levenson J. Performance of subclinical arterial disease detection as a screening test for coronary heart disease. Hypertension. 2006;48(3):392-6

Exclusie. Narrative review.	Thompson BH, Stanford W. Update on using coronary calcium screening by computed tomography to measure risk for coronary heart disease. The international journal of cardiovascular imaging. 2005;21(1):39-53
Exclusie. Narrative review.	Raggi P, Ferramosca E, Bellasi A, Ratti C. Coronary artery calcium screening: implications for clinical practice. Future cardiology. 2005;1(2):215-23
Exclusie. Narrative review.	Raggi P, Berman DS. Computed tomography coronary calcium screening and myocardial perfusion imaging. Journal of nuclear cardiology: official publication of the American Society of Nuclear Cardiology. 2005;12(1):96-103

Update-2022

Reference	Reason for exclusion
Muhlestein JB, Knowlton KU, Le VT, Lappe DL, May HT, Min DB, et al. Coronary Artery Calcium Versus Pooled Cohort Equations Score for Primary Prevention Guidance: Randomized Feasibility Trial. JACC: Cardiovascular Imaging. 2022.	CAUGHT-CAD-trial: Comparison CAC-score (without risk prediction) versus risk prediction
Venkataraman P, Kawakami H, Huynh Q, Mitchell G, Nicholls SJ, Stanton T, et al. Cost-Effectiveness of Coronary Artery Calcium Scoring in People With a Family History of Coronary Disease. JACC: Cardiovascular Imaging. 2021;14(6):1206-17.	CAUGHT-CAD-trial: Comparison CAC-score (without risk prediction) versus risk prediction & Outcome: cost effectiveness
Venkataraman P, Huynh Q, Nicholls SJ, Stanton T, Watts GF, Marwick TH. Impact of a coronary artery calcium-guided statin treatment protocol on cardiovascular risk at 12 months: Results from a pragmatic, randomised controlled trial. Atherosclerosis. 2021;334:57-65.	CAUGHT-CAD-trial: Comparison CAC-score (without risk prediction) versus risk prediction
Shafter AM, Shaikh K, Johanis A, Budoff MJ. De-risking primary prevention: role of imaging. Therapeutic Advances in Cardiovascular Disease. 2021;15.	Narrative review on existing risk estimations tools
Östgren CJ, Söderberg S, Festin K, Angerås O, Bergström G, Blomberg A, et al. Systematic Coronary Risk Evaluation estimated risk and prevalent subclinical atherosclerosis in coronary and carotid arteries: A population-based cohort analysis from the Swedish Cardiopulmonary Bioimage Study. European journal of preventive cardiology. 2021;28(3):250-9.	Cross-sectional analysis
Jacobsen AP, Al Rifai M, Arps K, Whelton SP, Budoff MJ, Nasir K, et al. A cohort study and meta-analysis of isolated diastolic hypertension: Searching for a threshold to guide treatment. European Heart Journal. 2021;42(21):2119-29.	Association between isolated diastolic hypertension and CVD
Gendarme S, Goussault H, Assié JB, Taleb C, Chouaïd C, Landre T. Impact on all-cause and cardiovascular mortality rates of coronary artery calcifications detected during organized, low-dose, computed-tomography screening for lung cancer: Systematic literature review and meta-analysis. Cancers. 2021;13(7).	Population: participants for lung cancer screening
Gallone G, Elia E, Bruno F, Angelini F, Franchin L, Bocchino PP, et al. Impact of lipid-lowering therapies on cardiovascular outcomes according to coronary artery calcium score. A systematic review and meta-analysis. Revista Espanola de Cardiologia. 2021.	SR: association CAC and CVD, no NRI
Cainzos-Achirica M, Bittencourt MS, Osei AD, Haque W, Bhatt DL, Blumenthal RS, et al. Coronary Artery Calcium to Improve the Efficiency of Randomized Controlled Trials in Primary Cardiovascular Prevention. JACC: Cardiovascular Imaging. 2021;14(5):1005-16.	NNS reported, no NRI. Data on costs, etc. from the US.
Bergström G, Persson M, Adiels M, Björnson E, Bonander C, Ahlström H, et al. Prevalence of Subclinical Coronary Artery Atherosclerosis in the General Population. Circulation. 2021:916-29.	Association between CAC-score and atherosclerosis
Azcui Aparicio RE, Ball J, Yiallourou S, Venkataraman P, Marwick T, Carrington MJ. Imaging-guided evaluation of subclinical atherosclerosis to enhance cardiovascular risk prediction in asymptomatic low-to-intermediate risk individuals: A systematic review. Preventive Medicine. 2021;153.	SR with reported NRI; included cohorts already included.

Ajufo E, Ayers CR, Vigen R, Joshi PH, Rohatgi A, de Lemos JA, et al. Value of coronary artery calcium scanning in association with the net benefit of aspirin in primary prevention of atherosclerotic cardiovascular disease. JAMA Cardiology. 2021;6(2):179-87.	Use of aspirin and the balance between bleeding events and risk of CVD
Abuzaid A, Saad M, Addoumieh A, Ha LD, Elbadawi A, Mahmoud AN, et al. Coronary artery calcium score and risk of cardiovascular events without established coronary artery disease: A systemic review and meta-analysis. Coronary Artery Disease. 2021:317-28.	Association CAC and CVD, no NRI
Van Der Aalst CM, Denissen SJAM, Vonder M, Gratama JWC, Adriaansen HJ, Kuijpers D, et al. Screening for cardiovascular disease risk using traditional risk factor assessment or coronary artery calcium scoring: The ROBINSCA trial. European Heart Journal Cardiovascular Imaging. 2020;21(11):1216-24.	Comparison between SCORE and CAC-scoring. CAC-scoring was without SCORE-calculation.
Orringer CE, Maki KC. HOPE for Rational Statin Allocation for Primary Prevention: A Coronary Artery Calcium Picture Is Worth 1000 Words. Mayo Clinic Proceedings. 2020;95(8):1740-9.	Narrative review
O'Neill D, Stone NJ, Forman DE. Primary Prevention Statins in Older Adults: Personalized Care for a Heterogeneous Population. Journal of the American Geriatrics Society. 2020;68(3):467-73.	Research among the elderly
Lo-Kioeng-Shioe MS, Rijlaarsdam-Hermsen D, van Domburg RT, Hadamitzky M, Lima JAC, Hoeks SE, et al. Prognostic value of coronary artery calcium score in symptomatic individuals: A meta-analysis of 34,000 subjects. International Journal of Cardiology. 2020;299:56-62.	Association CAC and CVD, no NRI
Liu S, Zheng X, Xu J, Wang X, Zhang Y, Lv B, et al. Predictive value of coronary artery calcium score in cardiovascular disease. Frontiers in Bioscience - Elite. 2020;12(1):113-25.	Association CAC and CVD, no NRI
Lindholt JS, Frystyk J, Hallas J, Rasmussen LM, Diederichsen ACP. Feasibility study of advanced cardiovascular screening in middle-aged patients with diabetes. Clinical Epidemiology. 2020;12:447-55.	Population: patients with diabetes
Lai R, Ju J, Lin Q, Xu H. Coronary Artery Calcification Under Statin Therapy and Its Effect on Cardiovascular Outcomes: A Systematic Review and Meta-Analysis. Frontiers in Cardiovascular Medicine. 2020;7.	Comparison between treated and untreated
Han D, Kolli KK, Gransar H, Lee JH, Choi SY, Chun EJ, et al. Machine learning based risk prediction model for asymptomatic individuals who underwent coronary artery calcium score: Comparison with traditional risk prediction approaches. Journal of Cardiovascular Computed Tomography. 2020;14(2):168-76.	Comparison between machine learning and routine check-up data
García-Ortiz L, Barreiro-Perez M, Merchan-Gómez S, Ignacio Recio-Rodriguez J, Sánchez-Aguadero N, Alonso-Dominguez R, et al. Prevalence of coronary atherosclerosis and reclassification of cardiovascular risk in Spanish population by coronary computed tomography angiography: EVA study. European Journal of Clinical Investigation. 2020;50(9).	Cross-sectional study, no follow-up available.
Elshazly MB, Abdellatif A, Dargham SR, Rifai MA, Quispe R, Cainzos-Achirica M, et al. Role of Coronary Artery and Thoracic Aortic Calcium as Risk Modifiers to Guide Antihypertensive Therapy in Stage 1 Hypertension (From the Multiethnic Study of Atherosclerosis). American Journal of Cardiology. 2020;126:45-55.	Population: participants with stage 1 hypertension, no risk estimation or NRI
de Ronde MWJ, Khoshiwal A, Planken RN, Boekholdt SM, Biemond M, Budoff MJ, et al. A pooled-analysis of age and sex based coronary artery calcium scores percentiles. Journal of Cardiovascular Computed Tomography. 2020;14(5):414-20.	Percentiles of CAC-score, no NRI
Commandeur F, Slomka PJ, Goeller M, Chen X, Cadet S, Razipour A, et al. Machine learning to predict the long-term risk of myocardial infarction and cardiac death based on clinical risk, coronary calcium, and epicardial adipose tissue: a prospective study. Cardiovascular research. 2020;116(14):2216-25.	Research into machine learning and prediction of CVD

Cainzos-Achirica M, Miedema MD, McEvoy JW, Al Rifai M, Greenland P, Dardari Z, et al. Coronary Artery Calcium for Personalized Allocation of Aspirin in Primary Prevention of Cardiovascular Disease in 2019: The MESA Study (Multi-Ethnic Study of Atherosclerosis). Circulation. 2020;141(19):1541-53.	No association reported with CVD or NRI reported
Wilson PWF, Polonsky TS, Miedema MD, Khera A, Kosinski AS, Kuvin JT. Systematic Review for the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2019;73(24):3210-27.	SR on cholesterol treatment
Shaikh K, Nakanishi R, Kim N, Budoff MJ. Coronary artery calcification and ethnicity. Journal of Cardiovascular Computed Tomography. 2019;13(6):353-9.	Association between CAC and ethnicity in the US
Rosenblit PD. Extreme Atherosclerotic Cardiovascular Disease (ASCVD) Risk Recognition. Current Diabetes Reports. 2019;19(8).	Narrative review on the need for an extreme risk category
Robinson JG. Lipid management beyond the guidelines. Progress in Cardiovascular Diseases. 2019;62(5):384-9.	Narrative review
Lindholt JS, Rasmussen LM, Søgaard R, Lambrechtsen J, Steffensen FH, Frost L, et al. Baseline findings of the population-based, randomized, multifaceted Danish cardiovascular screening trial (DANCAVAS) of men aged 65–74 years. British Journal of Surgery. 2019;106(7):862-71	No follow-up data available (yet)
Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139(25):e1046-e81.	Guideline
Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139(25):e1082-e143.	Duplicate reference
Denissen SJAM, van der Aalst CM, Vonder M, Oudkerk M, de Koning HJ. Impact of a cardiovascular disease risk screening result on preventive behaviour in asymptomatic participants of the ROBINSCA trial. European Journal of Preventive Cardiology. 2019;26(12):1313-22.	Research into impact of risk screening strategies on patient behavior.
Chicherina EN, Lobanova NY. Role of coronary artery calcium scores in the diagnosis of subclinical coronary artery atherosclerosis in patients with cardiovascular risk factors. Profilakticheskaya Meditsina. 2019;22(3):101-6.	Article written in Russian
Budoff M, Backlund J-YC, Bluemke DA, Polak J, Bebu I, Schade D, et al. The Association of Coronary Artery Calcification With Subsequent Incidence of Cardiovascular Disease in Type 1 Diabetes: The DCCT/EDIC Trials. JACC Cardiovascular imaging. 2019;12(7):1341-9.	Association CAC and CVD, no NRI
Vonder M, van der Aalst CM, Vliegenthart R, van Ooijen PMA, Kuijpers D, Gratama JW, et al. Coronary Artery Calcium Imaging in the ROBINSCA Trial: Rationale, Design, and Technical Background. Academic Radiology. 2018;25(1):118-28.	Trial protocol
Raggi P. Atherosclerosis imaging to refine cardiovascular risk assessment in diabetic patients: Computed tomography and positron emission tomography applications. Atherosclerosis. 2018;271:77-83.	Narrative review
Pham T, Fujiyoshi A, Arima H, Tanaka-Mizuno S, Hisamatsu T, Kadowaki S, et al. Association of coronary artery calcification with estimated coronary heart disease risk from prediction models in a community-based sample of Japanese men: The shiga epidemiological study of subclinical atherosclerosis (SESSA). Journal of Atherosclerosis and Thrombosis. 2018;25(6):477-89.	Association between CAC score and risk of CVD in Japanese men

Pang CL, Pilkington N, Wei Y, Peters J, Roobottom C, Hyde C. A methodology review on the incremental prognostic value of computed tomography biomarkers in addition to Framingham risk score in predicting cardiovascular disease: The use of association, discrimination and reclassification. BMC Cardiovascular Disorders. 2018;18(1).	Methodology SR into reported NRI and how Framingham Risk score was calculated.
Mortensen MB, Falk E, Li D, Nasir K, Blaha MJ, Sandfort V, et al. Statin Trials, Cardiovascular Events, and Coronary Artery Calcification: Implications for a Trial-Based Approach to Statin Therapy in MESA. JACC: Cardiovascular Imaging. 2018;11(2):221-30.	Tool risk classification-based trial inclusion criteria
Lin JS, Evans CV, Johnson E, Redmond N, Coppola EL, Smith N. Nontraditional risk factors in cardiovascular disease risk assessment: Updated evidence report and systematic review for the US preventive services task force. JAMA - Journal of the American Medical Association. 2018;320(3):281-97.	No meta-analysis, multiple publication of one cohort was included.
Lin JS, Evans CV, Johnson E, Redmond N, Burda BU, Coppola EL, et al. 2018.	Duplicate reference
Grønhøj MH, Gerke O, Mickley H, Steffensen FH, Lambrechtsen J, Sand NPR, et al. External validity of a cardiovascular screening including a coronary artery calcium examination in middle-aged individuals from the general population. European Journal of Preventive Cardiology. 2018;25(11):1156-66.	Research into participants and non-participants of a screening program.
Fan L, Fan K. Lung cancer screening CT-based coronary artery calcification in predicting cardiovascular events: A systematic review and meta-analysis. Medicine (United States). 2018;97(20).	Participants from a lung screening program
Braber TL, Reitsma JB, Mosterd A, Willemink MJ, Prakken NHJ, Halle M, et al. Cardiac imaging to detect coronary artery disease in athletes aged 35 years and older. A scoping review. Scandinavian journal of medicine & science in sports. 2018;28(3):1036-47.	Research into CAC imaging in sport persons
Ady Wirawan IM, Griffiths RF, Larsen PD. Cardiovascular Tests for Risk Assessment in Asymptomatic Adults and Implications for Pilots. Aerospace medicine and human performance. 2018;89(7):648-56.	No meta-analysis
Kvist TV, Lindholt JS, Rasmussen LM, Sogaard R, Lambrechtsen J, Steffensen FH, et al. The DanCavas Pilot Study of Multifaceted Screening for Subclinical Cardiovascular Disease in Men and Women Aged 65-74 Years. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2017;53(1):123-31.	Feasibility of a screening program
Gupta A, Lau E, Varshney R, Hulten EA, Cheezum M, Bittencourt MS, et al. The Identification of Calcified Coronary Plaque Is Associated With Initiation and Continuation of Pharmacological and Lifestyle Preventive Therapies: A Systematic Review and Meta-Analysis. JACC: Cardiovascular Imaging. 2017;10(8):833-42.	Association between nonzero CAC score and initiation of preventative therapy
Chaikriangkrai K, Jhun HY, Palamaner Subash Shantha G, Bin Abdulhak A, Sigurdsson G, Nabi F, et al. Coronary artery calcium score as a predictor for incident stroke: Systematic review and meta-analysis. International journal of cardiology. 2017;236:473-7.	Association CAC and Stroke, no NRI
Ambale-Venkatesh B, Yang X, Wu CO, Liu K, Gregory Hundley W, McClelland R, et al. Cardiovascular Event Prediction by Machine Learning: The Multi-Ethnic Study of Atherosclerosis. Circulation Research. 2017;121(9):1092-101.	Research into machine learning
Agarwal V, Shaw LJ, Berman D, Nasir K, Rozanski A, Blankstein R. Implications of Recent Clinical Trials in Cardiovascular Imaging on Primary Prevention Therapies. Current Cardiovascular Risk Reports. 2017;11(7).	Narrative review
Budoff MJ, Raggi P, Beller GA, Berman DS, Druz RS, Malik S, et al. Noninvasive Cardiovascular Risk Assessment of the Asymptomatic Diabetic Patient: The Imaging Council of the American College of Cardiology. JACC: Cardiovascular Imaging. 2016;9(2):176-92.	Narrative review
Ronan G. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart	How to detect IHD, not how to estimate risk of CVD

disease: A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology. Journal of Nuclear Cardiology. 2014;21(1):192-220.	
Mamudu HM, Paul TK, Veeranki SP, Budoff M. The effects of coronary artery calcium screening on behavioral modification, risk perception, and medication adherence among asymptomatic adults: A systematic review. Atherosclerosis. 2014;236(2):338-50.	CAC on medical adherence
Hulten E, Villines TC, Cheezum MK, Berman DS, Dunning A, Achenbach S, et al. Calcium score, coronary artery disease extent and severity, and clinical outcomes among low Framingham risk patients with low vs high lifetime risk: Results from the CONFIRM registry. Journal of Nuclear Cardiology. 2014;21(1):29-37.	Young asymptomatic population included
Criqui MH, Denenberg JO, McClelland RL, Allison MA, Ix JH, Guerci A, et al. Abdominal aortic calcium, coronary artery calcium, and cardiovascular morbidity and mortality in the multi-ethnic study of atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology. 2014;34(7):1574-9.	Research into the association of abdominal aortic calcium (AAC) with incident cardiovascular disease (CVD) independent of coronary artery calcium (CAC).
Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, et al. ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. European Heart Journal. 2013;34(39):3035-87.	ESC-guideline

Exclusietabel voor uitgangsvraag:

Wanneer moet een verhoogde bloeddruk behandeld worden?

Deelvraag 1

Referentie	**Reden voor exclusie**
Wang J, Liu J, Teng H, Zhang Y, Dong X, Chen W, et al. Blood pressure categories defined by the 2017 ACC/AHA guideline and all-cause mortality: a national cohort study in China and meta-analysis. Journal of Human Hypertension. 2022;36(1):95-105.	Geen resultaten gerapporteerd voor een bloeddruk boven 160 mmHg.
Lee JY, Hong JH, Lee S, An S, Shin A, Park SK. Binary cutpoint and the combined effect of systolic and diastolic blood pressure on cardiovascular disease mortality: A community-based cohort study. PLoS ONE. 2022;17(6).	Geen resultaten gerapporteerd voor een bloeddruk boven 160 mmHg.
Li FR, He Y, Yang HL, Liu HM, Zhou R, Chen GC, et al. Isolated systolic and diastolic hypertension by the 2017 American College of Cardiology/American Heart Association guidelines and risk of cardiovascular disease: a large prospective cohort study. Journal. 2021;39(8):1594-601.	Geen resultaten gerapporteerd voor een bloeddruk boven 160 mmHg.
Chan II, Kwok MK, Schooling CM. The total and direct effects of systolic and diastolic blood pressure on cardiovascular disease and longevity using Mendelian randomisation. Scientific reports. 2021;11(1):21799.	Geen resultaten gerapporteerd voor een bloeddruk boven 160 mmHg.
Abdi H, Amouzegar A, Tohidi M, Azizi F, Hadaegh F. Blood pressure and hypertension: Findings from 20 years of the tehran lipid and glucose study (TLGS). International Journal of Endocrinology and Metabolism. 2018;16.	Geen resultaten gerapporteerd voor een bloeddruk boven 160 mmHg.
Rådholm K, Festin K, Falk M, Midlöv P, Mölstad S, Östgren CJ. Blood pressure and all-cause mortality: A prospective study of nursing home residents. Age and Ageing. 2016;45(6):826-32.	Studie uitgevoerd bij ouderen met reverse causation en selectiebias als probleem. Resultaten zijn niet te interpreteren.
Sesso HD, Stampfer MJ, Rosner B, Hennekens CH, Gaziano JM, Manson JE, et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. 2000;36(5):801-7.	Geen resultaten gerapporteerd voor een bloeddruk boven 160 mmHg.

Exclusietabel voor uitgangsvraag:

Welke bloeddrukstreefwaarde dient te worden gehanteerd bij de behandeling van hypertensie bij (kwetsbare) ouderen (> 70 jaar)?

Tabel 2016

Auteur en jaartal	Redenen van exclusie
Review filter	
Parsons, 2016	Gemiddelde leeftijd van 65 jaar of ouder; effect van behandeling op beroerte
Peters, 2014	Type antihypertensiva
Goeres, 2014	Geen meta-analyse; leeftijd niet allen boven 70 jaar; geen RoB beoordeling
Sundstrom, 2014	Data gestratificeerd op risico en niet op leeftijd.
Ahola, 2012	Observationele studie met data van twee databases en jonger dan 70 jaar; geen subgroepanalyse
Schall, 2011	Geen evidence-tabel beschikbaar; geen bekende tool gebruikt voor Risk of Bias beoordeling, alleen benoemd items worden bekeken. Echter, er wordt in de tekst geen oordeel over gegeven.
Bejan-Angoulvant, 2010	Niet systematisch gezocht, onduidelijk ook tot wanneer trials zijn geïncludeerd
Musini, 2009	Leeftijdsgrens 60 jaar of ouder
Bulpitt, 2003	Resultaten van een pilot van de HYVET-studie, die reeds is geïncludeerd
Messerli, 2001	Alleen gezocht in Medline en tot juni 1999
Gueyffier, 1999	Geïncludeerd studies zijn ook geïncludeerd door Schall, 2011
Pearce, 1995	Recentere reviews komen in aanmerking
RCT-filter	
Omboni, 2015	Vergelijking tussen twee type antihypertensiva
Moonen, 2015	Stoppen met antihypertensiva
Tinetti, 2014	Observationele studie met data over hart- en vaatziekten en mortaliteit gerapporteerd (data reeds beschikbaar uit RCT's)
Beckett, 2014	Trial reeds geïncludeerd, rapportage van niet relevant subgroepanalyse
Zanchetti, 2014	Studieprotocol
Williamson, 2014	Patiënten met diabetes en jonger dan 70 jaar
Vagholkar, 2014	Geen relevante uitkomstmaten gerapporteerd
Tinetti, 2014	Geen relevante uitkomstmaten
Reboldi, 2014	Totale mortaliteit en hart- en vaatziekten in 1 uitkomstmaat gerapporteerd; gemiddelde leeftijd voor drie van vier groepen onder 70 jaar
Mohebi, 2014	Gemiddelde leeftijd onder 70 jaar en geen subgroepanalyse beschikbaar; observationele studies, geen propensity score analyse
Margolis, 2014	Patiënten met diabetes en jonger dan 70 jaar
Peters, 2013	Trial reeds geïncludeerd; geen relevante uitkomstmaat
Zhang, 2013	Geen relevante uitkomstmaten
White, 2013	Studieprotocol
Weir, 2013	Geen relevante uitkomstmaten
Beckett, 2012	Open label extensie van een trial, met als vergelijking vroeg starten versus laat starten
Zhang, 2011	Subgroepanalyse: 65 > of 65 ≤
Group, 2010	Patiënten met diabetes en jonger dan 70 jaar
Bangalore, 2010	Patiënten die een statine krijgen
Aronow, 2009	Letter to editor/ reactie van auteur
Verdecchia, 2009	Alleen subgroep analyse beschikbaar; reeds volledige artikel kunnen includeren
Tardif, 2008	Geen relevante uitkomstmaten
Rakugi, 2008	Narratieve review
Ogiharam, 2008	Vergelijking tussen twee anithypertensiva
Flack, 2008	Geen vergelijkende groep
Ferguson, 2008	Geen relevante uitkomstmaten

Patel, 2007	Patiënten met diabetes
Kintscher, 2007	Vergelijking tussen verschillende antihypertensiva
Kabakci, 2007	Risicofactoren voor hart- en vaatziekten
Fagard, 2007	Relevante data reeds geïncludeerd
Eijkelkamp, 2007	Geen relevante uitkomstmaten
Agostini, 2007	Intensiteit van behandeling gedefinieerd aan de hand van de hoeveelheid klassen van antihypertensiva werden gebruikt
Roumie, 2006	Geen relevante uitkomstmaten
Perkovic, 2006	Geen relevante uitkomstmaten
Group, 2005	Studieprotocol
Gard, 2004	Narratieve review
Ferrari, 2004	Geen relevante uitkomstmaten
Lithell, 2004	Meerderheid van placebogroep kreeg add-on antihypertensiva binnen vier maanden na het starten van de trial
Degl'Innoncenti, 2004	Meerderheid van placebogroep kreeg add-on antihypertensiva binnen vier maanden na het starten van de trial
Mancia, 2003	Vergelijking tussen verschillende antihypertensiva
Jungmann, 2003	Narratieve review
Jonsson, 2003	Geen relevante uitkomstmaten gerapporteerd (kosteneffectiviteit in zweden)
Lithell, 2003	Meerderheid van placebogroep kreeg add-on antihypertensiva binnen vier maanden na het starten van de trial
Camisasca, 2002	Uitvoering van een richtlijn
Hansson, 2001	Narratieve review
Emeriau, 2001	Vergelijking tussen medicamenten
Wassertheil-Smoller, 2000	Associatie tussen BMI, hypertensie en mortaliteit
Wang, 2000	Effectschatter met betrouwbaarheidsinterval niet te extraheren (wordt alleen in een grafiek weergegeven)
Trenkwalder, 2000	Narratieve review
Perry, 2000	Subgroepanalyse niet beschikbaar
Ogihara, 2000	Geen originele beschrijving van een studie
Lindholm, 2000	Vergelijking tussen verschillende
Lassila, 2000	Follow-up na een trial
Bulpitt, 2000	Vergelijking van medicamenten bij hoge diastolische bloeddruk
Brown, 2000	Vergelijking tussen antihypertensiva
Fagard, 1999	Originele studie geïncludeerd.
Alli, 1999	SBP en SBP als voorspellers van mortaliteit
Berlowitz, 1998	Ontwikkeling van een soort predictie model over behandeling van hypertensie
Zeng, 1998	Effect van medicatie op syncope
Winther, 1998	Patiënten met cognitieve stoornissen en zonder hypertensie
Whelton, 1998	Patiënten reeds op medicatie en vervolgens het effect van gewichtsverlies en beperkte zout inname
Staessen, 1998	Originele studie geïncludeerd.
Savage, 1998	Ontwikkeling van diabetes tijdens RCT
Pahor, 1998	Patiënten met hypertensie en nierfalen
Kostis, 1998	Over het stoppen van medicatie
Hansson, 1993	Narratieve review
Aagaard, 1984	Narratieve review
Welzel, 1982	Narratieve review

Tabel 2022

Reference	Reason
Signorini L, Zaza G, Gambaro G. The challenge of early glomerular filtration rate decline in response to antihypertensive treatment and chronic kidney disease outcomes. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association. 2022;37(2):222-9.	Narrative review
Marcum ZA, Cohen JB, Zhang C, Derington CG, Greene TH, Ghazi L, et al. Association of Antihypertensives That Stimulate vs Inhibit Types 2 and 4 Angiotensin II Receptors with Cognitive Impairment. JAMA Network Open. 2022;5(1):E2145319.	Comparison between types of medication, not target for BP
Wright CB, Auchus AP, Lerner A, Ambrosius WT, Ay H, Bates JT, et al. Effect of Intensive Versus Standard Blood Pressure Control on Stroke Subtypes. Hypertension (Dallas, Tex : 1979). 2021;77(4):1391-8.	Focus on stroke subtypes
Olsen E, Holzhauer B, Julius S, Kjeldsen SE, Larstorp ACK, Mancia G, et al. Cardiovascular outcomes at recommended blood pressure targets in middle-aged and elderly patients with type 2 diabetes mellitus and hypertension. Blood Pressure. 2021;30(2):82-9.	VALUE comparison of medication, not targets: Observational analysis of targets in diabetics
Olsen E, Holzhauer B, Julius S, Kjeldsen SE, Larstorp ACK, Mancia G, et al. Cardiovascular outcomes at recommended blood pressure targets in middle-aged and elderly patients with type 2 diabetes mellitus compared to all middle-aged and elderly hypertensive study patients with high cardiovascular risk. Blood pressure. 2021;30(2):90-7.	VALUE comparison of medication, not targets: Observational analysis of target in adults with a high risk of CVD
Lee JY, Han SH. Blood pressure control in patients with chronic kidney disease. The Korean journal of internal medicine. 2021;36(4):780-94.	Narrative review
Ku E, Sarnak MJ, Toto R, McCulloch CE, Lin F, Smogorzewski M, et al. Effect of Blood Pressure Control on Long-Term Risk of End-Stage Renal Disease and Death Among Subgroups of Patients With Chronic Kidney Disease. Journal of the American Heart Association. 2019;8(16):e012749.	Target to MAP
Plante TB, Juraschek SP, Miller ER, 3rd, Appel LJ, Cushman M, Littenberg B. Comparison of Frequency of Atherosclerotic Cardiovascular and Safety Events With Systolic Blood Pressure <120mm Hg Versus 135-139mm Hg in a Systolic Blood Pressure Intervention Trial Primary Prevention Subgroup. The American journal of cardiology. 2018;122(7):1185-90.	Analysis in patients without CVD -> observational data SPRINT already included
Ó Hartaigh B, Szymonifka J, Okin PM. Achieving target SBP for lowering the risk of major adverse cardiovascular events in persons with diabetes mellitus. Journal of Hypertension. 2018;36(1):101-9	Achieved SBP in diabetes patients
Berlowitz DR, Foy CG, Kazis LE, Bolin LP, Conroy MB, Fitzpatrick P, et al. Effect of intensive blood-pressure treatment on patient-reported outcomes. New England Journal of Medicine. 2017;377(8):733-44.	Data from MIND already included.
Mant J, McManus RJ, Roalfe A, Fletcher K, Taylor CJ, Martin U, et al. Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention after Stroke-Blood Pressure) randomised controlled trial. BMJ (Online). 2016;352.	PAST-BP, patients with a stroke, follow-up too short
Shi S, Gouskova N, Najafzadeh M, Wei L-J, Kim DH. Intensive versus standard blood pressure control in type 2 diabetes: a restricted mean survival time analysis of a randomised controlled trial. BMJ open. 2021;11(9):e050335.	ACCORD-trial participants with CVD included (~33%)
Pajewski NM, Berlowitz DR, Bress AP, Callahan KE, Cheung AK, Fine LJ, et al. Intensive vs Standard Blood Pressure Control in Adults 80 Years or Older: A Secondary Analysis of the Systolic Blood Pressure Intervention Trial. Journal of the American Geriatrics Society. 2020;68(3):496-504.	Subgroup analysis of > 80 years. (all participants between 75 and 80 were excluded making up to 55% of participants older than 75 years)
Gitsels LA, Kulinskaya E, Bakbergenuly I, Steel N. Optimal SBP targets in routine clinical care. Journal of hypertension. 2019;37(4):837-43.	Analysis and comparison of SPRINT and THIN (data from the UK), with THIN being observational data

Aggarwal R, Petrie B, Bala W, Chiu N. Mortality Outcomes With Intensive Blood Pressure Targets in Chronic Kidney Disease Patients. Hypertension (Dallas, Tex : 1979). 2019;73(6):1275-82.	4 trial analysis of participants with CKD of which two trials are separately included and two excluded
Brouwer TF, Vehmeijer JT, Kalkman DN, Berger WR, Van Den Born BJH, Peters RJ, et al. Intensive blood pressure lowering in patients with and patients without type 2 diabetes: A pooled analysis from two randomized trials. Diabetes Care. 2018;41(6):1142-8.	T2DM and BP targets -> ACCORD included participants with CVD and diabetes
Beddhu S, Greene T, Boucher R, Cushman WC, Wei G, Stoddard G, et al. Intensive systolic blood pressure control and incident chronic kidney disease in people with and without diabetes mellitus: secondary analyses of two randomised controlled trials. The Lancet Diabetes and Endocrinology. 2018;6(7):555-63.	CKD and SBP targets -> ACCORD included participants with CVD and diabetes
Buckley LF, Dixon DL, Wohlford GFt, Wijesinghe DS, Baker WL, Van Tassell BW. Intensive Versus Standard Blood Pressure Control in SPRINT-Eligible Participants of ACCORD-BP. Diabetes care. 2017;40(12):1733-8.	Participants with DM2 and SBP -> ACCORD included participants with CVD and diabetes
Bath PM, Scutt P, Blackburn DJ, Ankolekar S, Krishnan K, Ballard C, et al. Intensive versus Guideline Blood Pressure and Lipid Lowering in Patients with Previous Stroke: Main results from the pilot prevention of Decline in Cognition after Stroke trial' (PODCAST) randomised controlled trial. PLoS ONE. 2017;12(1).	Inclusion criteria for BP was 125-175 mmHg
Odden MC, McClure LA, Sawaya BP, White CL, Peralta CA, Field TS, et al. Achieved Blood Pressure and Outcomes in the Secondary Prevention of Small Subcortical Strokes Trial. Hypertension (Dallas, Tex : 1979). 2016;67(1):63-9.	Participants with stroke and association with achieved SBP

Exclusietabel voor uitgangsvraag:

Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk bij volwassenen (< 70 jaar)?

Reference	Reason
Signorini L, Zaza G, Gambaro G. The challenge of early glomerular filtration rate decline in response to antihypertensive treatment and chronic kidney disease outcomes. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association. 2022;37(2):222-9.	Narrative review
Marcum ZA, Cohen JB, Zhang C, Derington CG, Greene TH, Ghazi L, et al. Association of Antihypertensives That Stimulate vs Inhibit Types 2 and 4 Angiotensin II Receptors with Cognitive Impairment. JAMA Network Open. 2022;5(1):E2145319.	Comparison between types of medication, not target for BP
Wright CB, Auchus AP, Lerner A, Ambrosius WT, Ay H, Bates JT, et al. Effect of Intensive Versus Standard Blood Pressure Control on Stroke Subtypes. Hypertension (Dallas, Tex : 1979). 2021;77(4):1391-8.	Focus on stroke subtypes
Olsen E, Holzhauer B, Julius S, Kjeldsen SE, Larstorp ACK, Mancia G, et al. Cardiovascular outcomes at recommended blood pressure targets in middle-aged and elderly patients with type 2 diabetes mellitus and hypertension. Blood Pressure. 2021;30(2):82-9.	VALUE comparison of medication, not targets: Observational analysis of targets in diabetics
Olsen E, Holzhauer B, Julius S, Kjeldsen SE, Larstorp ACK, Mancia G, et al. Cardiovascular outcomes at recommended blood pressure targets in middle-aged and elderly patients with type 2 diabetes mellitus compared to all middle-aged and elderly hypertensive study patients with high cardiovascular risk. Blood pressure. 2021;30(2):90-7.	VALUE comparison of medication, not targets: Observational analysis of target in adults with a high risk of CVD
Lee JY, Han SH. Blood pressure control in patients with chronic kidney disease. The Korean journal of internal medicine. 2021;36(4):780-94.	Narrative review
Ku E, Sarnak MJ, Toto R, McCulloch CE, Lin F, Smogorzewski M, et al. Effect of Blood Pressure Control on Long-Term Risk of End-Stage Renal Disease and Death Among	Target to MAP

Subgroups of Patients With Chronic Kidney Disease. Journal of the American Heart Association. 2019;8(16):e012749.	
Plante TB, Juraschek SP, Miller ER, 3rd, Appel LJ, Cushman M, Littenberg B. Comparison of Frequency of Atherosclerotic Cardiovascular and Safety Events With Systolic Blood Pressure <120mm Hg Versus 135-139mm Hg in a Systolic Blood Pressure Intervention Trial Primary Prevention Subgroup. The American journal of cardiology. 2018;122(7):1185-90.	Analysis in patients without CVD -> observational data SPRINT already included
Ó Hartaigh B, Szymonifka J, Okin PM. Achieving target SBP for lowering the risk of major adverse cardiovascular events in persons with diabetes mellitus. Journal of Hypertension. 2018;36(1):101-9	Achieved SBP in diabetes patients
Berlowitz DR, Foy CG, Kazis LE, Bolin LP, Conroy MB, Fitzpatrick P, et al. Effect of intensive blood-pressure treatment on patient-reported outcomes. New England Journal of Medicine. 2017;377(8):733-44.	Data from MIND already included.
Mant J, McManus RJ, Roalfe A, Fletcher K, Taylor CJ, Martin U, et al. Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention after Stroke-Blood Pressure) randomised controlled trial. BMJ (Online). 2016;352.	PAST-BP, patients with a stroke, follow-up too short
Shi S, Gouskova N, Najafzadeh M, Wei L-J, Kim DH. Intensive versus standard blood pressure control in type 2 diabetes: a restricted mean survival time analysis of a randomised controlled trial. BMJ open. 2021;11(9):e050335.	ACCORD-trial participants with CVD included (~33%)
Pajewski NM, Berlowitz DR, Bress AP, Callahan KE, Cheung AK, Fine LJ, et al. Intensive vs Standard Blood Pressure Control in Adults 80 Years or Older: A Secondary Analysis of the Systolic Blood Pressure Intervention Trial. Journal of the American Geriatrics Society. 2020;68(3):496-504.	Subgroup analysis of > 80 years. (all participants between 75 and 80 were excluded making up to 55% of participants older than 75 years)
Gitsels LA, Kulinskaya E, Bakbergenuly I, Steel N. Optimal SBP targets in routine clinical care. Journal of hypertension. 2019;37(4):837-43.	Analysis and comparison of SPRINT and THIN (data from the UK), with THIN being observational data
Aggarwal R, Petrie B, Bala W, Chiu N. Mortality Outcomes With Intensive Blood Pressure Targets in Chronic Kidney Disease Patients. Hypertension (Dallas, Tex : 1979). 2019;73(6):1275-82.	4 trial analysis of participants with CKD of which two trials are separately included and two excluded
Brouwer TF, Vehmeijer JT, Kalkman DN, Berger WR, Van Den Born BJH, Peters RJ, et al. Intensive blood pressure lowering in patients with and patients without type 2 diabetes: A pooled analysis from two randomized trials. Diabetes Care. 2018;41(6):1142-8.	T2DM and BP targets -> ACCORD included participants with CVD and diabetes
Beddhu S, Greene T, Boucher R, Cushman WC, Wei G, Stoddard G, et al. Intensive systolic blood pressure control and incident chronic kidney disease in people with and without diabetes mellitus: secondary analyses of two randomised controlled trials. The Lancet Diabetes and Endocrinology. 2018;6(7):555-63.	CKD and SBP targets -> ACCORD included participants with CVD and diabetes
Buckley LF, Dixon DL, Wohlford GFt, Wijesinghe DS, Baker WL, Van Tassell BW. Intensive Versus Standard Blood Pressure Control in SPRINT-Eligible Participants of ACCORD-BP. Diabetes care. 2017;40(12):1733-8.	Participants with DM2 and SBP -> ACCORD included participants with CVD and diabetes
Bath PM, Scutt P, Blackburn DJ, Ankolekar S, Krishnan K, Ballard C, et al. Intensive versus Guideline Blood Pressure and Lipid Lowering in Patients with Previous Stroke: Main results from the pilot prevention of Decline in Cognition after Stroke trial' (PODCAST) randomised controlled trial. PLoS ONE. 2017;12(1).	Inclusion criteria for BP was 125-175 mmHg
Odden MC, McClure LA, Sawaya BP, White CL, Peralta CA, Field TS, et al. Achieved Blood Pressure and Outcomes in the Secondary Prevention of Small Subcortical Strokes Trial. Hypertension (Dallas, Tex : 1979). 2016;67(1):63-9.	Participants with stroke and association with achieved SBP

Exclusietabel voor uitgangsvraag:

Wat is de toegevoegde waarde van etnische achtergrond bij het reclassificeren van het risico op hart- en vaatziekten?

Reference	Reason for exclusion
Perini W, Snijder MB, Agyemang C, Peters RJ, Kunst AE, van Valkengoed IG. Eligibility for cardiovascular risk screening among different ethnic groups: The HELIUS study. European journal of preventive cardiology. 2020;27(11):1204-11. PubMed PMID: rayyan-279650075.	Research into a threshold for blood pressure treatment for different ethnic groups.
Perini W, Snijder MB, Peters RJG, Stronks K, Kunst AE. Increased cardiovascular disease risk in international migrants is independent of residence duration or cultural orientation: the HELIUS study. Journal of epidemiology and community health. 2018;72(9):825-31. PubMed PMID: rayyan-279650122.	Association between the risk of cardiovascular disease and residence duration in the Netherlands.
Perini W, Snijder MB, Peters RJG, Kunst AE. Ethnic disparities in estimated cardiovascular disease risk in Amsterdam, the Netherlands: The HELIUS study. Netherlands Heart Journal. 2018;26(5):252-62. PubMed PMID: rayyan-279650077.	Difference in average SCORE by ethnic groups, but not linked to cardiovascular disease.

Bijlage 5 Samenvatting onderzoekskarakteristieken

Onderzoekskarakteristieken voor uitgangsvraag:
Welke streefwaarden van LDL-C dienen te worden gehanteerd bij de behandeling met lipidenverlagende medicatie bij personen tot en met 70 jaar met een (zeer) hoog risico op hart- en vaatziekten?

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Schmidt, 2017 (individual study characteristics deduced from Schmidt, 2017) PS., study characteristics and results are extracted from the SR (unless stated otherwise)	SR and meta-analysis of RCTs *Literature search up to May 2016* **D**: FOURIER **S**: SPIRE 1/2 <u>Study design</u>: All were RCTs <u>Setting</u>: For all: outpatient care <u>Source of funding:</u> All RCTs were funded by pharmaceutical companies.	Inclusion criteria SR: • Parallel-group and factorial RCTs with follow-up of at least 24 weeks • Included adults 18 years of age or older, with or without a prior history of CVD • Randomised to a PCSK9 inhibitor or to placebo, statin, ezetimib of combination of these. Exclusion criteria SR: • Cluster RCTs, cross-over trails and non-randomised studies *20 studies included, of which five studies were only published as conference abstracts. These studies were excluded. A further 13 were excluded as the primary endpoint was not cardiovascular disease.* <u>Important patient characteristics at baseline</u>: <u>N, mean age</u> **D**: 27564 patients, 63 (SD 9) yrs **S**: 27438 patients, 63 (SD 9) yrs <u>Sex</u>: **D**: 75% Male **S**: 70% Male	**D**: Evolocumab **S**: Bococizumab Background therapy: **D**: Statin therapy **S**: Statins and/or ezetimib	**D**: Placebo **S**: Placebo	<u>End-point of follow-up</u>: **D**: 157 weeks **S**: 143 weeks <u>For how many participants were no complete outcome data available?</u> (intervention/control) **D**: Unclear **S**: Unclear	<u>Outcome measure-1</u> Defined as LDL Results on LDL levels were deduced from the individual trial publications <u>Outcome measure-2</u> Defined as CVD Results on CVD were deduced from the individual trial publications <u>Outcome measure-3</u> Defined as mortality due to CVD Results on mortality due to CVD were deduced from the individual trial publications <u>Outcome measure-4</u> Defined as adverse events Results on adverse events were deduced from the individual trial publications	**S**: Many participants were lost to follow-up due to antidrug antibody response

		<u>History of CVD:</u> **D**: 27564 (100%) **S**: 23198 (85%) <u>Participants with FH:</u> **D**: NA **S**: 1072 (4%)					
Nuβbaumer, 2016 (individual study characteristics deduced from Nusbaumer, 2016) PS., study characteristics and results are extracted from the SR (unless stated otherwise)	See the full article for all relevant information https://www-ncbi-nlm-nih-gov.eur.idm.oclc.org/pubmed/27412989						

Chan, 2011 (individual study characteristics deduced from Chan, 2011) PS., study characteristics and results are extracted from the SR (unless stated otherwise)	SR and meta-analysis of RCTs *Literature search up to April 2009* **A**: De Lemos, 2004 **B**: Cannon, 2004 **C**: Pedersen, 2005 **E**: LaRosa, 2005 <u>Study design</u>: RCT (parallel) <u>Setting and Country</u>: Not reported <u>Source of funding:</u> Not reported for included studies; unclear what kind of funding the review received.	Inclusion criteria SR: • At least one of the aims was to lower lipid levels • Lipid lowering was intensive and that the target LDL-C was in the vicinity of <2.1 mmol/l • Minimum follow-up period of 12 months post-intervention • Study population considered to be at high risk of vascular events • Data of the individual components of composite secondary end-points were available *7 studies included of which 3 were excluded as the primary endpoint was not cardiovascular disease* <u>Important patient characteristics at baseline</u>: <u>N, mean age</u> **A**: 4497 patients, 61 yrs **B**: 4162, 58 yrs **C**: 8888, 62 yrs **E**: 10001, 61 yrs <u>*Sex:*</u> Not reported Criteria: **A**: Post acute coronary syndrome **B**: Post acute coronary syndrome **C**: Previous MI **E**: Clinically evident CHD, LDL<3.4	**A**: Simvastatin 40 mg, 1m/80 mg **B**: Atorvastatin 80 mg **C**: Atorvastatin 80 mg **E**: Atorvastatin 80 mg	**A**: placebo, 4 m/ simvastatin 20 mg **B**: Pravastatin 40 mg **C**: Simvastatin 20 mg **E**: Atorvastatin 10 mg	<u>End-point of follow-up</u>: **A**: 0.5 to 2 years, median 2.0 years **B**: 1.5 to 3 years, mean 2 years **C**: 4.0 to 5.9 years, median 4.8 years **E**: Median 4.9 years <u>For how many participants were no complete outcome data available?</u> (intervention/control) Not reported	<u>Outcome measure-1</u> Defined as LDL-concentration, percent change from baseline (%) (mean LDL level during treatment (mmol/l) **A**: I: -41.03 (1.71) C: -27.18 (2.10) **B**: I: -41.61 (1.60) C: -10.22 (2.46) **C:** I: -34.08 (2.07) C: -17.83 (2.58) **E**: I: -20.72 (1.99) C: 3.16 (2.61) <u>Outcome measure-2</u> Defined as major coronary events*, odds ratio (95%CI) **A**: 0.88 (0.75 to 1.03) **B**: 0.86 (0.74 to 0.99) **C**: 0.77 (0.70 to 0.85) **E**: 0.79 (0.68 to 0.91) <u>Outcome measure-3</u> Defined as cardiovascular/coronary heart disease deaths, odds ratio (9%CI) **A**: 0.74 (0.55 to 0.99) **B**: 0.78 (0.45 to 1.35) **C**: 0.98 (0.80 to 1.22) **E**: 0.79 (0.61 to 1.03) <u>Outcome measure-4</u> Defined as treatment discontinuation due to side effects, odds ratios (95%CI) **A**: 1.19 (0.75 to 1.88) **B**: 0.89 (0.78 to 1.01) **C**: 2.43 (2.04 to 2.91) **E**: 1.39 (1.18 to 1.64)	* Definition of major cardiovascular events was not only an event of CVD, but also deaths. Authors' conclusions: In those at high risk of cardiovascular events, intensive lipid lowering with statins to LDL-C level <2.1 mmol/l significantly reduces risk of stroke, major coronary events and CVD or CHD deaths compared to LDL-C level ≥2.1 mmol/l. Remarks: • All included trials included patients with CVD.

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison / control (C) [3]	Follow-up	Outcome measures and effect size [4]	Comments
PICO 1 Cholesterol target							
Amarenco, 2020 (TST trial)	Type of study: RCT Setting and country: France Funding and conflicts of interest: Industry (unrestricted grants)	Inclusion criteria: • 18 years or older • Had an ischemic stroke <3 months previously • Modified Rankin scale of 0 to 3 after stroke N total at baseline: Intervention: 1081 (analysed 1073) Control: 1077 (analysed 1075) Important prognostic factors[2]: Age ± SD: I: 67 (11) C: 67 (11) Sex: I: 68% M C: 69% M LDL-c at baseline (mean): I: 3.5 mmol/L C: 3.5 mmol/L Groups comparable at baseline? Yes	LDL cholesterol target of 1.8 mmol/L by use of any type and any dose of statin. 3 weeks after randomization, statin dose was adjusted or other lipid-lowering agents including ezetimibe were added to achieve the assigned LDL cholesterol target.	LDL cholesterol target of 2.4 mmol/L by use of any type and any dose of statin. 3 weeks after randomization, statin dose was adjusted or other lipid-lowering agents including ezetimibe were added to achieve the assigned LDL cholesterol target.	Length of follow-up: Median 5.3 years Loss-to-follow-up: Intervention: N = 295 (27%) Reasons (lost to follow-up (62); no signed consent (8); withdrawn consent (121); serious adverse event (2); investigator's decisions (102)) Control: N = 271 (25%) Reasons (lost to follow-up (49); no signed consent (2); withdrawn consent (108); serious adverse event (3); investigator's decisions (109)) Incomplete outcome data: Intervention: N = 8 (0.7%) Reasons (no signed consent) Control:	Outcome measure-1 Defined as major cardiovascular events* (primary outcome) I: 103 (10%) C: 139 (13%) HR: 0.74 (0.57-0.95), adjusted for entry event (stroke or TIA), time since entry event, sex and age at baseline; HR based on Cox model with competing risk (Finn and Gray model) Outcome measure-2 Defined is myocardial infarction or urgent coronary revascularisation I: 18 (2%) C: 27 (3%) HR: 0.66 (0.37-1.20) Outcome measure-3 Adverse event defined as intracranial hemorrhage I: 13 (1.2%) C: 11 (1.0%) HR: 1.17 (0.53-2.62)	*The primary end point was a composite of adjudicated nonfatal cerebral infarction or stroke of undetermined source, nonfatal myocardial infarction, hospitalization for unstable angina followed by urgent coronary artery revascularization, TIA requiring urgent carotid revascularization, or cardiovascular death including unexplained sudden death.

					N = 2 (0.2%) Reasons (no signed consent)		
PICO 2 Intensive cholesterol treatment							
Schwartz, 2018 (ODYSSEY OUTCOMES trial)	Type of study: RCT Setting and country: Multicentre, worldwide Funding and conflicts of interest: Industry	<u>Inclusion criteria</u> • 40 years of age or older • hospitalized with an acute coronary syndrome (myocardial infarction or unstable angina) 1 to 12 months before randomization • LDL cholesterol level of at least 70 mg per deciliter (1.8 mmol per liter), a non−high-density lipoprotein (HDL) cholesterol level of at least 100 mg per deciliter, or an apolipoprotein B level of at least 80 mg per deciliter. <u>N total at baseline</u>: Intervention: 9462 Control: 9462 <u>Important prognostic factors</u>[2]: Age ± SD: I: 58 (9) C: 58 (9) Sex: I: 75% M C: 75% M LDL-c at baseline (mean): I: 2.4 mmol/L C: 2.4 mmol/L	Alirocumab • Subcutaneous injection every two weeks • Background therapy: statins	Matching placebo • Background therapy: statins	<u>Length of follow-up</u>: Median 2.8 years <u>Loss-to-follow-up</u>: Intervention: N = 37 (0%) Reasons (patient did not want to continue (n=23); lost to follow-up (n=9); other reasons (n=5)) Control: N = 49 (1%) Reasons (patient did not want to continue (n=25); lost to follow-up (n=14); other reasons (n=10)) <u>Incomplete outcome data</u>: Every patient included in efficacy analysis	<u>Outcome measure-1</u> Defined as major cardiovascular events* (primary outcome) I: 903 (10%) C: 1052 (11%) HR 0.85 (0.78 to 0.93) <u>Outcome measure-2</u> Defined as death from cardiovascular causes I: 240 (3%) C: 271 (3%) HR 0.88 (0.74 to 1.05) <u>Outcome measure-3</u> Defined as serious adverse event I: 2202 (23%) C: 2350 (25%) HR not presented	* composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization

		Groups comparable at baseline? Yes					

Onderzoekskarakteristieken voor uitgangsvraag:

Wat is de meerwaarde van de behandeling met lipidenverlagende middelen bij (kwetsbare) ouderen (> 70 jaar)?

PICO1

Ouderen zonder hart- en vaatziekten

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/ control (C)	Follow-up	Outcome measures and effect size	Comments
Elderly without cardiovascular diseases							
Teng, 2015	SR and meta-analyses of RCT's and subgroups of RCTs *Literature search up to August 2014* **A**: ALLHAT, 2002 **B**: Collier, 2011 **C**: Bruckert, 2003 **D**: Glynn, 2010 **E**: Stephard, 2002 <u>Study design</u>: RCT <u>Setting and Country</u>: **A**: US, Puerto Rico, US Virgin Islands and Canada **B**: UK, Sweden, Norway, Denmark, Finland, Ireland **C**: France, Italy, Spain,	Inclusion criteria SR: • Trials in Human and published in English • Participants ≥65 years. If participants <65 years, inclusion when stratified results for patients > 65 years were reported. • Participants without established cardiovascular disease • Comparison between statin and usual care/placebo • Outcomes included major adverse cardiovascular events, all-cause mortality, elevation in hepatic transaminases, elevation in creatine kinase, myalgia, myopathy, rhabdomyolysis, serious adverse events, tolerability, incidence of new-onset diabetes and/or cognitive impairment. Exclusion criteria SR: • None. *8 studies included, of which 5 had a study sample with a age > 70 years* <u>Important patient characteristics at baseline</u>:	**A**: Pravastatin, 40 mg/day **B**: Atorvastatin, 10mg/day **C**: Fluvastatin XL, 80 mg/day **D**: Rosuvastatin, 20 mg/day **E**: Pravastatin, 40 mg/day	**A**: placebo or usual care **B**: placebo or usual care **C**: placebo or usual care **D**: placebo or usual care **E**: placebo or usual care	<u>End-point of follow-up</u>: Mean follow-up: **A**: 4.8 years **B**: 3.3 years **C**: 1 years **D**: 1.9 years **E**: 3.2 years <u>For how many participants were no complete outcome data available?</u> (intervention/control) **A:** Not reported (low Risk of Bias) **B**: Not reported (low Risk of Bias) **C**: Not reported (low Risk of Bias) **D**: Not reported (low Risk of Bias) **E**: Not reported (low Risk of Bias)	1. <u>Quality of life</u> Not reported 2. <u>Cognitive function</u> Not reported 3. <u>Adverse events</u> Defined as myalgia **A**: Not reported **B**: RR 0.82 (95%CI: 0.58;1.15) **C**: RR 0.11 (95%CI: 0.01;2.12) **D**: RR 1.31 (95%CI: 0.29;5.83) **E**: RR 1.15 (95%CI: 0.71;1.84) Defined as new onset diabetes **A**: Not reported **B**: RR 0.9 (95%CI: 0.64;1.26) **C**: Not reported **D**: RR 1.25 (95%CI: 0.91;1.73) **E**: Not reported Defined as serious adverse events **A**: RR 0.88 (95%CI: 0.45;1.73) **B**: RR 0.96 (95%CI: 0.87;1.06) **C**: RR 2.05 (95%CI: 0.19;22.54) **D**: RR 1.04 (95%CI: 0.94;1.15) **E**: RR 1.01 (95%CI: 0.96;1.06) 4. <u>Mortality</u> Defined as all-cause mortality **A**: RR 1.01 (95%CI: 0.91;1.13) **B**: RR 0.97 (95%CI: 0.77;1.22) **C**: RR 1.02 (95%CI: 0.06; 16.35) **D**: 0.79 (95%CI: 0.62;1.02) **E**: 0.98 (95%CI: 0.88;1.04) 5. <u>CVD events</u> Defined as major adverse cardiovascular events (myocardial infarction, stroke, coronary revascularization, cardiac sudden death, angina) **A**: RR 0.96 (95%CI: 0.89;1.05)	Neil, 2006, Collins, 2003, Nakaya, 2011 were excluded because the age of the study sample was <70 years. Of the original 8 RCTs included, 2 focussed on elderly, six trials comprised subgroups. Teng, 2015 judged the overall quality of evidence (8 RCTs) as moderate. A was open labelled, B, C, D and E were sponsored by the industry.

	Belgium and Israel **D**: North America, South America, Europe and Africa **E**: Scotland, Ireland and The Netherlands <u>Source of funding:</u> Systematic review: Not sponsored **A**: not sponsored by industry **B**: Sponsored by industry **C**: Sponsored by industry **D**: Sponsored by industry **E**: Sponsored by industry	<u>N, mean age</u> **A**: 5809 patients, 72 yrs **B**: 4445 patients, 71 yrs **C**: 1229 patients, 75.5 yrs **D:** 5695 patients, 74 yrs **E:** 3239 patients, 75 yrs <u>*Sex:*</u> **A**: 52.2% Male **B**: 81.4% Male **C**: 25.1% Male **D:** 48.4% Male **E:** 41.5% Male *Diabetes:* **A**: 38.3% **B**: 100% **C**: 7% **D:** 0% **E:** 12.2% *Hypertension* **A**: 100% **B**: 26.7% **C**: 55.9% **D:** 65.6% **E:** 71.6% Groups comparable at baseline? Unclear				**B**: RR 0.82 (95%CI: 0.73;0.93) **C**: Not reported **D**: 0.62 (95%CI: 0.46;0.82) **E**: 0.94 (95%CI: 0.78;1.14) Defined as myocardial infarction **A**: RR 0.81 (95%CI: 0.67;0.99) **B**: RR 0.63 (95%CI: 0.45;0.89) **C**: Not reported **D**: 0.68 (95%CI: 0.45;1.02) **E**: 0.91 (95%CI: 0.72;1.14) Defined as stroke **A**: RR 0.98 (95%CI: 0.79;1.20) **B**: RR 0.80 (95%CI: 0.58;1.11) **C**: Not reported **D**: Not reported **E**: 1.03 (95%CI: 0.73;1.45)	

Ouderen met hart- en vaatziekten – PICO1

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/ control (C)	Follow-up	Outcome measures and effect size	Comments
Elderly with cardiovascular diseases							
Shepherd, 2002 Trompet, 2010	Type of study: RCT Setting: multicenter Country: Scotland, Ireland and The Netherlands Source of funding: Industry sponsored	<u>Inclusion criteria</u>: • Aged between 70-82 years • Pre-existing vascular disease or raised risk of such disease because of smoking, hypertention, or diabetes • Total plasma cholesterol between 4.0-9.0 mmol/L • Triglyceride concentratie <6.0 mmol/L	Pravastatin 40mg/day	Placebo	<u>Length of follow-up</u>: Shepherd, 2002: 3.2 years (range 2.8 to 4.0 years) Trompet, 2010: mean 42 months (range 36 to 48 months) <u>Loss-to-follow-up</u>:	1. <u>Quality of life</u> Not reported 2. <u>Cognitive function</u> Determined using the Mini-Mental State Examination (MMSE). Analyses were adjusted for age, educational status, country and when appropriate for sex and version of the test. Four tests were included: 1. Attention (Executive functioning, Stroop-Colour-Word-test) Est 0.36 (95%CI=-0.02;0.74)	408 patients of the entire cohort (primary and secondary prevention), 277 control patients and 131 patients from the intervention group used non-study statin therapy. Here, we report only the results of the subgroup analyses that

		• Usage of > 75% and <120% of placebo medication during 4-week single-blind placebo lead-in period. Exclusion criteria: • Poor cognitive function (mini mental state examination score <24) N total at baseline: Intervention: 1306 Control:1259 Important prognostic factors: Data only reported for the complete cohort (primary and secondary prevention combined) Groups comparable at baseline? Unknown			Not specified for patients with previous vascular disease. Incomplete outcome data: Likely all patients analysed.	2. Processing Speed (Executive functioning, Letter-Digit Coding Test) Est -0.02 (95%CI=-0.08;0.09) 3. Immediate recal (Memory, 15-Picture Learning test) Est 0.002 (95%CI=-0.03;0.04) 4. Delayed recal (Memory, 15-Picture Learning test) Est 0.04 (95%CI=-0.01;0.09) 3. Adverse events Not reported separately for subgroup of patients with previous vascular disease. 4. Mortality (all-cause and CVD) Not reported separately for subgroup of patients with previous vascular disease. 5. CVD events Defined as definite or suspect death from coronary heart disease, non-fatal myocardial infarction, and fatal or non-fatal stroke I: 227 (17,4%) C: 273 (21.7%) HR 0.78 (95%CI=0.66;0.93)	included patients with stable angina, intermittend claudication, stroke, transient ischeamic attack, myocardial infarction, arterial surgery or amputation for vascular disease more than 6 months before study entry.

PICO2:

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison / control (C) [3]	Follow-up	Outcome measures and effect size [4]	Comments
PICO 2 Cholesterol target							
Amarenco, 2020 (TST trial), focus on subgroup aged > 75 years	Type of study: RCT Setting and country: France Funding and conflicts of interest: Industry (unrestricted grants)	Inclusion criteria: • 18 years or older • Had an ischemic stroke <3 months previously • Modified Rankin scale of 0 to 3 after stroke N total at baseline: Intervention: 1081 (analysed 1073), 259 > 75 years Control: 1077 (analysed 1075), 268 > 75 years Important prognostic factors[2]: Age ± SD: I: 67 (11) C: 67 (11) Sex: I: 68% M C: 69% M LDL-c at baseline (mean): I: 3.5 mmol/L C: 3.5 mmol/L Groups comparable at baseline? Yes	LDL cholesterol target of 1.8 mmol/L by use of any type and any dose of statin. 3 weeks after randomization, statin dose was adjusted or other lipid-lowering agents including ezetimibe were added to achieve the assigned LDL cholesterol target.	LDL cholesterol target of 2.4 mmol/L by use of any type and any dose of statin. 3 weeks after randomization, statin dose was adjusted or other lipid-lowering agents including ezetimibe were added to achieve the assigned LDL cholesterol target.	Length of follow-up: Median 5.3 years Loss-to-follow-up: Intervention: N = 295 (27%) Reasons (lost to follow-up (62); no signed consent (8); withdrawn consent (121); serious adverse event (2); investigator's decisions (102)) Control: N = 271 (25%) Reasons (lost to follow-up (49); no signed consent (2); withdrawn consent (108); serious adverse event (3); investigator's decisions (109)) Incomplete outcome data: Intervention: N = 8 (0.7%) Reasons (no signed consent)	Outcome measure-1 Defined as major cardiovascular events* (primary outcome) I: 103 (10%) C: 139 (13%) HR: 0.74 (0.57-0.95), adjusted for entry event (stroke or TIA), time since entry event, sex and age at baseline; HR based on Cox model with competing risk (Finn and Gray model) Outcome measure-2 Defined as myocardial infarction or urgent coronary revascularisation or mortality No data reported for the subgroup. Outcome measure-3 Defined as adverse events, quality of life or daily living. No data reported.	*The primary end point was a composite of adjudicated nonfatal cerebral infarction or stroke of undetermined source, nonfatal myocardial infarction, hospitalization for unstable angina followed by urgent coronary artery revascularization, TIA requiring urgent carotid revascularization, or cardiovascular death including unexplained sudden death.

					Control: N = 2 (0.2%) Reasons (no signed consent)		

Onderzoekskarakteristieken voor uitgangsvraag:

Wat is de toegevoegde waarde van een coronaire kalkscore bij het reclassificeren van het risico op hart- en vaatziekten?

Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Peters 2011 PS. Individuele studiekarakteristieken en resultaten zijn geëxtraheerd uit de SR, tenzij anders aangegeven	SR van cohort studies *Literatuur search op 7 sept 2011* **A**: Polonsky, 2010 **B**: Erbel, 2010 **C**: Elias-Smale, 2010 **D:** Mohlenkamp, 2011 <u>Study design</u>: SR <u>Setting and Country</u>: Nederland (SR) **A**: USA **B**: Duitsland **C**: Nederland **D:** Duitsland <u>Source of funding:</u> Niet commercieel (deze SR); niet gerapporteerd per studie	Inclusiecriteria SR: - Studies naar de toegevoegde waarde van de CAC-score wanneer toegevoegd aan een model met traditionele risicofactoren - Uitkomstmaten: fatale and non-fatale CV-events - Domein: patiënten zonder symptomatische HVZ en zonder DM Exclusiecriteria SR: - Geen reclassificatie-maat gerapporteerd (toevoeging WdR) <u>Belangrijkste baseline karakteristieken van</u>	Interventie (toegevoegd aan risicopredictiemodel op basis van traditionele RF): **A**: mean CACS **B**: ln (CACS +1) **C**: ln (CACS+1) **D**: Sum CACS	Controle: risicopredictie op basis van traditionele RF. Definitie intermediair risico: **A**: 3-10% AR; 5-jaars **B**: 10 tot 20% en 6 to 20% AR; 5 jaars **C**: 10 tot 20% AR; 10-jaars **D**: 3-10% AR; 5-jaars	<u>Follow-up (Jaren)</u>: **A**: 6 jr **B:** 5 jr **C**: 9 jr **D**: 5 jr <u>Incomplete data</u> Niet gerapporteerd <u>Event-rate:</u> **A**: 3.6% **B: 2.3%** **C**: 6.7% **D**: 2.2%	<u>Uitkomstmaten</u> **A**: fatale en niet-fatale coronaire hartziekten **B**: fatale en niet-fatale coronaire hartziekten **C:** fatale en niet-fatale coronaire hartziekten **D:** fatale en niet-fatale hart- en vaatziekten (CVD) <u>Effectmaten</u> **- Net Reclassification Index (BI) in %** **A**: -overall 25 (16 to 34) -intermediate 55 (41 to 69) **B***: intermediate risk 10-20%:* -overall 22 -intermediate 22 *intermediate risk 6-20%:* -overall 20 (6 to 33) -intermediate 31 **C**: -overall 14 (4 to 24) **D**: -overall 25 **- Δ C-statistic** **A**: 0.76 → 0.81 : 0.05 **B:** 0.68 → 0.75: 0.07 **C**: 0.72 → 0.76: 0.04 **D**: 0.72 → 0.76: 0.04	Author's conclusion: 'The evidence for added value for CAC is considerable'. 'Although current guidelines on the use of imaging for asymptomatic atherosclerosis contain conflicting recommendations, the majority of guidelines point towards the usefulness of CAC in risk prediction for the development of cardiovascular events, especially in individuals that are classified at intermediate risk.' 'The present SR also showed that intermediate risk individuals may benefit most from additional assessment using CAC.' Personal remarks on study quality, conclusions, and other issues (potentially) relevant to the research question: - enige heterogeniteit van deze 4 studies met betrekking tot populatie, follow-up duur, definitie risico categorieën, CAC

		individuele studies: N, leeftijd (gemiddeld in Jaren) **A**: 5868; 42 **B**: 4129; 59 **C**: 2028; 70 **D:** 1934; 57 *Geslacht:* **A**: 46% man **B**: 47% man **C**: 43% man **D:** 31% man					drempelwaarden, eindpunten en opgenomen risicofactoren in het traditionele model; AMSTAR 5/11 Level of evidence: GRADE (per comparison and outcome measure) including reasons for down/upgrading. Uitkomst NRI: Laag, 1 level downgrading op basis van onderzoeksopzet en matig-lage AMSTAR score; 1 level downgrading o.b.v te weinig informatie over publicatiebias
Paixao 2015 PS. Individuele studiekarakteristieken en resultaten zijn geëxtraheerd uit de SR, tenzij anders aangegeven	Meta-analyse NRI *Literatuur search tot en met 31 december 2014.* **A**: Polonsky, 2010 (MESA) **B**: Erbel, 2010 (HNR) **C**: Elias-Smale, 2010 (Rotterdam) **D:** Paixao, 2015 (DHS) Study design: Random-effects meta-analyse Setting and Country: Nederland (SR) **A**: USA **B**: Duitsland **C**: Nederland **D:** USA Source of funding:	Inclusiecriteria SR: - Studies naar de toegevoegde waarde van de CAC-score wanneer toegevoegd aan een model met traditionele risicofactoren - Studies die een NRI rapporteerden Belangrijkste baseline karakteristieken van individuele studies: N, leeftijd (gemiddeld in Jaren) **A**: 5868; 42 **B**: 4129; 59 **C**: 2028; 70 **D:** 2084; 44 *Geslacht:*	Interventie (toegevoegd aan risicopredictiemodel op basis van traditionele RF): **A**: mean CACS **B**: ln(CACS +1) **C**: ln(CACS+1) **D**: ln(CACS+1)	Controle: risicopredictie op basis van traditionele RF. Definitie intermediair risico: **A**: 3 tot 10% AR; 5-jaars **B**: 10 tot 20% en 6 tot-20% AR; 5 jaars **C**: 10 tot 20% AR; 10-jaars **D**: 6 tot 20% AR; 10-jaars	Follow-up (Jaren): **A**: 6 jr **B:** 5 jr **C**: 9 jr **D**: 9 jr Incomplete data Niet gerapporteerd Event-rate: **A**: 3.6% **B: 2.3%** **C**: 6.7% **D**: 2.7% (57/2084)	Uitkomstmaten **A**: fatale en niet-fatale coronaire hartziekten **B**: fatale en niet-fatale coronaire hartziekten **C:** fatale en niet-fatale coronaire hartziekten **D:** fatale en niet-fatale coronaire hartziekten Effectmaten **- Net Reclassification Index (BI) in %** **A**: -overall 25 (16 to 34) -intermediate 55 (41 tot 69) **B:** intermediate risk 10 tot 20% -overall 22 -intermediate 22 intermediate risk 6 tot 20% -overall 20 (6 tot 33) -intermediate 31 **C**: -overall 14 (4 tot 24) **D**: -overall 21 (4 tot 38) - **Pooled $NRI_{overall}$ A-D** 20.2% (BI 14.6 – 25.8); (I^2 0%; p=0.451) **- Δ C-statistic** **A**: 0.76 → 0.81 : 0.05 **B:** 0.68 → 0.75 : 0.07 **C**: 0.72 → 0.76 : 0.04	Author's conclusion: 'In a young multi-ethnic cohort, the addition of CAC to a model composed of traditional CHD risk factors significantly improved discrimination and risk classification' Personal remarks on study quality, conclusions, and other issues (potentially) relevant to the research question: - alleen coronaire hartziekten, iets verschillende definities uitkomstmaat; I^2 underpowered?, AMSTAR 2/11 score (= zeer laag) Level of evidence: GRADE (per comparison and outcome measure) including reasons for down/upgrading. Uitkomst NRI: Laag, 1 level downgrading op basis

	Niet commercieel (deze SR); niet gerapporteerd per studie	**A**: 46% man **B**: 47% man **C**: 43% man **D:** 44% man				**D**: 0.86 → 0.89 : 0.03	van onderzoeksopzet en matig-lage AMSTAR score; 1 level downgrading o.b.v te weinig informatie over publicatiebias

Onderzoekskarakteristieken voor uitgangsvraag:
Wanneer moet een verhoogde bloeddruk behandeld worden?

Evidence table for systematic review of RCTs and observational studies (intervention studies)
Research question 2: What are the benefits or harms of blood pressure lowering medication in persons without cardiovascular disease and increased blood pressure (≥ 160 mmHg)?

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
The Blood Pressure Lowering Treatment Trialists' Collaboration, 2021 PS., study characteristics and results are not extracted from the SR (unless stated otherwise). For details, we refer to the publication.	SR and meta-analysis of RCTs *Literature search up to Sept, 2019* Total of 48 trials were included, of 22 trials were drug classes comparison which were not considered. <u>Study design</u>: RCT <u>Setting and Country</u>: trials were from around the world. <u>Source of funding and conflicts of interest:</u> Not reported for the included trials. Meta-analysis was supported by	Inclusion criteria SR: trials that randomly assigned participants to pharmacological blood pressure-lowering medications versus placebo or other classes of blood pressure-lowering medications, or between more versus less intensive treatment regimens, which had at least 1000 persons-years of follow-up in each randomly allocated group. Exclusion criteria SR: Trials that only included participants with heart failure or short-term interventions in participants with acute myocardial infarction or other acute settings *48 studies included* <u>Important patient characteristics at baseline</u>:	See publication For this research question, only data on medication versus placebo or intensive versus less intensive treatment were included.	See publication For this research question, only data on medication versus placebo or intensive versus less intensive treatment were included.	<u>End-point of follow-up</u>: See publication <u>For how many participants were no complete outcome data available?</u> (intervention/control) See publication	<u>Outcome measure-1</u> Defined as all-cause mortality among participants with no prior CVD at baseline Effect measure: HR per 5 mmHg reduction in SBP [95% CI]: 160 to 169 mmHg: 1.03 (0.85-1.24) ≥170 mmHg: 0.88 (0.74 to 1.05) Defined as cardiovascular mortality among participants with no prior CVD at baseline Effect measure: HR per 5 mmHg reduction in SBP [95% CI]: 160 to 169 mmHg: 1.11 (0.85-1.45) ≥170 mmHg: 0.89 (0.68-1.16) <u>Outcome measure-2</u> Defined as major cardiovascular events (a composite of fatal or non-fatal stroke, fatal or non-fatal myocardial infarction or ischaemic heart disease, or heart failure causing death or requiring admission to hospital). Effect measure: HR per 5 mmHg reduction in SBP [95% CI]:	One author reported received personal fees from pharmaceutical companies.

	non-commercial grants	*See publication* N, mean age *See publication* *Sex:* *See publication*				160 to 169 mmHg: 0.93 (0.80-1.09) ≥170 mmHg: 0.84 (0.72-0.98) Outcome measure-3 Defined as acute cardiovascular events No data reported Outcome measure-4 Defined as (acute) renal disease No data reported Outcome measure-4 Defined as adverse events No data reported	

Onderzoekskarakteristieken voor uitgangsvraag:

Welke bloeddrukstreefwaarde dient te worden gehanteerd bij de behandeling van hypertensie bij (kwetsbare) ouderen (> 70 jaar)?

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison/ control (C)	Follow-up	Outcome measures and effect size	Comments
Comparison: Antihypertensive versus placebo							
Beckett, 2008 Additional data from Peters, 2008	Type of study: RCT (parallel) Setting: 195 centers Country: 13 countries across Western and Eastern Europe, China, Australasia, and North Africa Source of funding: Non-commercial	Inclusion criteria: • 80 years or older • Persistent hypertension (a sustained systolic hypertension of 160 mmHg) Exclusion criteria: • Contraindication to use the trial medications • Accelerated hypertension • Secondary hypertension • Hemorrhagic stroke in the previous 6 months • Heart failure requiring	Indapamide (sustained release, 1.5 mg) The angiotensin-converting-enzyme inhibitor perindopril (2 or 4 mg), or matching placebo, was added if necessary to achieve the target blood pressure of 150/80 mmHg.	Matching placebo	Length of follow-up: Mean 2.1 years (range 0 to 6.5) Loss-to-follow-up: Intervention: N = 847 (44%) Reasons: 196 died; 282 declined to participate; 4 were withdrawn by investigator; 27 had protocol withdrawal event	1. Quality of life Not reported 2. Functional status Cognition, measured with the MMSE*, mean change from baseline I: 0.7 points (SD 4.0) C: -1.1 points (SD 3.9) P=0.08 Dementia, n I: 126 C: 137	Data on cognition was reported in the publication by Peters, 2008. *Data was available in 1687 under active treatment versus 1649 under placebo.

		treatment with antihypertensive medication • Serum creatinine level greater than 150 µmol per liter • Serum potassium level of less than 3.5 mmol per liter or more than 5.5 mmol per liter • Gout • Diagnosis of clinical dementia • Requirement of nursing care N total at baseline: Intervention: 1933 Control: 1912 Important prognostic factors[2]: Age ± SD: I: 83 (3) C: 83 (3) Sex: I: 39% M C: 40% M Groups comparable at baseline? Yes			and no open follow-up; 164 were at centers closed by data monitoring committee; 168 for other administrative reasons; 6 lost to follow-up Control: N = 896 (47%) Reasons: 235 died; 266 declined to participate; 5 were withdrawn by investigator; 42 had protocol withdrawal event and no open follow-up; 166 were at centers closed by data monitoring committee; 171 for other administrative reasons; 11 lost to follow-up Incomplete outcome data: Intervention:	HR 0.86 (95%CI: 0.67-1.09) 3. Adverse events Number of serious adverse events, n (%) I: 358 (19) C: 448 (23) P=0.001 4. Mortality Measured as all-cause mortality or death due to a cardiovascular event, n (rate per 1000 patient years) *Total mortality, hazard ratio* I: 196 (47) C: 235 (60) HR 0.79 (95%CI 0.65-0.95) *Death due to cardiovascular event, hazard ratio* I: 99 (24) C: 121 (31) HR 0.77 (95%CI 0.60-1.01) 5. CVD Measured as all cardiovascular events, n (rate per 1000 patient years)	

					N = 847 (44%) Reasons: 196 died; 282 declined to participate; 4 were withdrawn by investigator; 27 had protocol withdrawal event and no open follow-up; 164 were at centers closed by data monitoring committee; 168 for other administrative reasons; 6 lost to follow-up Control: N = 896 (47%) Reasons: 235 died; 266 declined to participate; 5 were withdrawn by investigator; 42 had protocol withdrawal event and no open follow-up; 166 were at centers closed by data monitorin	I: 138 (34) C: 193 (51) HR 0.66 (95%CI 0.53-0.82) 6. <u>Blood pressure</u> Blood pressure was measured annual, mean change from baseline in BP (SD) in mmHg *At two years, seated* I: SBP 29.5 (15.4); DBP 12.9 (9.5) C: SBP 14.5 (18.5); DBP 6.8 (10.5)	

					g committee; 171 for other administrative reasons; 11 lost to follow-up		
Staessen, 1998	Type of study: RCT (parallel) Setting: Patients with isolated systolic hypertension Country: Belgium, Belorussia, Bulgaria, Croatia, Estonia, Finland, France, Germany, Greece, Ireland, Israel, Italy, Lithuania, Netherlands, Poland, Portugal, Romania, Russian Federation, Slovakia, Slovenia, Spain, United Kingdom Source of funding: Industry	Inclusion criteria: • 60 years or older • During run-in placebo phase, seated systolic blood pressure between 160 and 219 mmHg and diastolic blood pressure below 95 mmHg • Standing systolic blood pressure of 140 mmHg of more • Consented to be enrolled • Long-term follow-up was possible Exclusion criteria: • Systolic hypertension secondary to a disorder that needed specific medical or surgical treatment • Retinal haemorrhage or papilledema • Congestive heart failure • Dissecting aortic aneurysm • Serum creatinine at presentation of 180 µmol/ L or more	Antihypertensive treatment – Nitrendipine (10-40 mg/d) If necessary, the calcium channel blocker was combined with or replaced by enalapril maleate (5-20 mg/d) or hydrochlorothiazide (12.5-25 mg/d) or both drugs. The study medications were stepwise titrated and combined to reduce sitting systolic blood pressure by 20 mmHg or more to less than 150 mmHg.	Control group – matching placebo	Length of follow-up: Median follow-up of 2.0 years (range 1 to 97 months) Loss-to-follow-up: Intervention: N = 660 (28%) Reasons: 123 died; 174 supervised open follow-up; 242 unsupervised open follow-up; 121 unavailable for follow-up Control: N = 780 (34%) Reasons: 137 died; 295 supervised open follow-up; 232 unsupervised open follow-up; 116 unavailable for follow-up	1. Quality of life Not reported 2. Functional status Not reported 3. Adverse events Not reported 4. Mortality Measured as all-cause mortality or death due to a cardiovascular event, n (rate per 1000 patient years) *Total mortality, hazard ratio* I: 123 (20.5) C: 137 (24) HR 0.86 (95%CI 0.67-1.10) *Death due to cardiovascular event, hazard ratio* I: 59 (9.8) C: 77 (13.5) HR 0.73 (95%CI 0.52-1.03) 5. CVD	

		• History of severe nosebleeds, stroke, myocardial infarction in the year before the study • Dementia or substance abuse • Any condition prohibiting a sitting or standing position • Severe concomitant cardiovascular or noncardiovascular disease N total at baseline: Intervention: 2398 Control: 2297 Important prognostic factors[2]: Age ± SD: 70.2 (6.7) Sex: 33% M Groups comparable at baseline? Cannot be judged			Incomplete outcome data: Intervention: N = 660 (28%) Reasons: 123 died; 174 supervised open follow-up; 242 unsupervised open follow-up; 121 unavailable for follow-up Control: N = 780 (34%) Reasons: 137 died; 295 supervised open follow-up; 232 unsupervised open follow-up; 116 unavailable for follow-up	Measured as all cardiovascular events, n (rate per 1000 patient years) I: 137 (23.3) C: 186 (33.9) HR 0.69 (95%CI 0.55-0.86) 6. Blood pressure Blood pressure was measured every three months, mean change from baseline in BP (SD) in mmHg *At median follow-up, seated* I: SBP 23 (16); DBP 7 (8) C: SBP 13 (17); DBP 2 (8) Mean difference SBP: 10.1 (95CI: 8.8-11.4) Mean difference DBP: 4.5 (95%CI: 3.9-5.1)	
Comparison: intensive treatment versus standard treatment							
Wei, 2013	Type of study: RCT (parallel) Setting: Hypertensive patients	Inclusion criteria: • Older than 70 years • SBP ≥ 150 mmHg and /or DBP ≥ mmHg, measured	Intensive treatment (blood pressure target ≤ 140/90 mmHg)	Standard treatment (blood pressure target ≤ 150/90 mmHg)	Length of follow-up: 4 years Loss-to-follow-up: Intervention:	1. Quality of life Not reported 2. Functional status	Patients were examined on at least two separate occasions, and BP was measured on the right upper

	Country: China Source of funding: Not stated	twice on different days OR diagnosed with hypertension and currently receiving antihypertensive treatment. <u>Exclusion criteria</u>: • Secondary hypertension • Valvular heart disease • Chronic kidney dysfunction • Previous myocardial infarction • Stroke in the past six months <u>N total at baseline</u>: Intervention: 363 Control: 361 <u>Important prognostic factors</u>[2]: Age ± SD: I: 76 (5) C: 76 (5) Sex: I: 67% M C: 66% M Groups comparable at baseline? Yes			N = 2 (0.6%) Reasons: 1 consent withdrawal; 1 lost to follow-up Control: N = 7 (2%) Reasons: 5 consent withdrawal; 2 lost to follow-up <u>Incomplete outcome data</u>: Intervention: N = 2 (0.6%) Reasons: 1 consent withdrawal; 1 lost to follow-up Control: N = 7 (2%) Reasons: 5 consent withdrawal; 2 lost to follow-up	Not reported 3. <u>Adverse events</u> Not reported 4. <u>Mortality</u> Measured as all-cause mortality or death due to a cardiovascular event, n (%) *Total mortality, risk ratio* I: 51 (14) C: 87 (24) RR 0.63 (95%CI 0.46-0.87) *Death due to cardiovascular event, risk ratio* I: 25 (7) C: 50 (14) RR 0.53 (95%CI 0.33-0.84) 5. <u>CVD</u> Measured as all cardiovascular events, n (%) I: 40 (11) C: 67 (19) RR 0.63 (95%CI 0.44-0.92) 6. <u>Blood pressure</u> Blood pressure was measured every six months,	arm at least twice per visit by the auscultatory method using a sphygmomanometer with the patients in the sitting position after 5 to 10 minutes of rest. If measured values differed by > 4 mmHg, recalibration was required. BP measurements were performed at 8 AM to 11 AM and averaged for each visit. BP was monitored after enrollment, which was measured in the fourth week, the third month, the sixth month, and every 6 months thereafter. By the end of the study, all patients were followed-up an average of 10 times.

						mean BP (SD) in mmHg I: SBP 135.7 (9.0); DBP 76.2 (6.1) C: SBP 149.7 (11.0); DBP 82.1 (7.5) Mean difference SBP 14; DBP 6, p<0.01)	
Ogihara, 2010	Type of study: RCT (parallel) Setting: Elderly with isolated systolic hypertension Country: Japan Source of funding: Non-commercial	Inclusion criteria: • Aged between 70 and 84 years • Isolated systolic hypertension (systolic BP > 160 mmHg and diastolic BP <90 mmHg) N total at baseline: Intervention: 1627 (1545 described) Control: 1633 (1534 described) Important prognostic factors[2]: Age ± SD: I: 76 (4) C: 76 (4) Sex: I: 38% M C: 37% M Groups comparable at baseline? Yes	Strict control group Valsartan, 40 to 80 mg once daily, was administrated as the first-step therapy. If the target BP in each group was not achieved within 1 to 2 months, the dose of valsartan was increased ≤ 160 mg, and/or other antihypertensive agents except other angiotensin II type 1 receptor blockers were added, for example, low-dose diuretics, Ca antagonists, and so on to maintain the target BP.	Moderate control group	Length of follow-up: Mean 2.85 years Loss-to-follow-up: Intervention: N = 82 (5%) Reasons: 42 withdrew consent; 40 no follow-up just after randomization Control: N = 99 (6%) Reasons: 45 withdrew consent; 54 no follow-up just after randomization Incomplete outcome data: Intervention: N = 82 (5%) Reasons: 42	1. Quality of life Not reported 2. Functional status Not reported 3. Adverse events Measured as the rates of serious adverse events, percentage I: 5.6% C: 5.2% P=0.61 4. Mortality Measured as all-cause mortality or death due to a cardiovascular event, n (%) *Total mortality, hazard ratio* I: 24 (2) C: 30 (2) HR 0.78 (95%CI 0.46-1.33), adjusted for sex, age,	About 50% in each group were already taking antihypertensive drugs.

					withdrew consent; 40 no follow-up just after randomization Control: N = 99 (6%) Reasons: 45 withdrew consent; 54 no follow-up just after randomization	BMI, smoking, dyslipidaemia, diabetes mellitus, and antihypertensive agents used before enrolment. *Death due to cardiovascular event, hazard ratio* I: 11 (1) C: 11 (1) HR 0.97 (95%CI 0.42-2.25), adjusted for sex, age, BMI, smoking, dyslipidaemia, diabetes mellitus, and antihypertensive agents used before enrolment. 5. <u>CVD</u> Not reported 6. <u>Blood pressure</u> Blood pressure at the end of 36 months, mean BP (SD) in mmHg I: SBP 136.6 (13.3); DBP 74.2 (8.8) C: SBP 142.0 (12.5); DBP 76.5 (8.9) Mean difference	

						SBP 5.6; DBP 1.7, p<0.001)	
The SPRINT research group, 2015 Additional data from SPRINT-MIND	Type of study: RCT (parallel) Setting: Patients at increased risk of CVD Country: United States of America Source of funding: Non-commercial	<u>Inclusion criteria</u>: • Age at least 50 years • Systolic BP of 130 to 180 mmHg • Increased risk of CVD* <u>Exclusion criteria</u>: • Diabetes mellitus • Prior stroke • Dementia <u>N total at baseline</u>: Intervention: 4678 (1317 older than 74 yrs) Control: 4683 (1319 older than 74 yrs) <u>Important prognostic factors</u>[2]: Age ± SD: I: 79 (4) C: 79 (4) Sex: Not stated for the subgroup Groups comparable at baseline?	Intensive treatment (blood-pressure target less than 120 mmHg)	Standard treatment (blood-pressure target less than 140 mmHg)	<u>Length of follow-up</u>: Median follow-up: 3.26 (not stated for the subgroup) <u>Loss-to-follow-up</u>: Not stated for the subgroup <u>Incomplete outcome data</u>: Not stated for the subgroup	1. <u>Quality of life</u> Not reported 2. <u>Functional status</u> Probable dementia, ascertained via MoCA, learning and memory and processing speed. I: 95 (17.8 cases per 1000 Person-Years) C: 116 (22.0 cases per Person-Years) HR 0.88 (0.66-1.16) 3. <u>Adverse events</u> Measured as the rates of serious adverse events**, n (%) I: 640 (49) C: 638 (48) HR 1.00, p=0.93 4. <u>Mortality</u> Measured as all-cause mortality or death due to a cardiovascular event, n (%)	*Increased cardiovascular risk was defined by one or more of the following: clinical or subclinical cardiovascular disease other than stroke; chronic kidney disease, excluding polycystic kidney disease, with an estimated glomerular filtration rate (eGFR) of 20 to less than 60 ml per minute per 1.73 m2 of body surface area, calculated with the use of the four variable Modification of Diet in Renal Disease equation; a 10-year risk of cardiovascular disease of 15% or greater on the basis of the Framingham risk score; or an age of 75 years or older. **In both groups, injurious falls was among the most frequent serious adverse events. Among patients under intensive treatment also frequent was

						Total mortality, hazard ratio I: 73 (6) C: 106 (8) HR 0.68 (95%CI 0.50-0.92), stratified according to clinic *Death due to cardiovascular event, hazard ratio* I: 11 (1) C: 11 (1) HR 0.97 (95%CI 0.42-2.25), adjusted for sex, age, BMI, smoking, dyslipidaemia, diabetes mellitus, and antihypertensive agents used before enrolment. 5. <u>CVD</u> Measured as composite outcome: myocardial infarction, acute coronary syndrome, stroke, acute decompensated heart failure, or death from cardiovascular causes, n (%) I: 101 (8) C: 144 (11)	acute kidney injury or acute renal failure.

						HR 0.67 (0.51-0.86) I: 108 (8) C: 158 (12) HR 0.65 (0.50-0.85) 6. Blood pressure Not stated for the subgroup	
Zhang, 2021	Type of study: RCT Setting and country: Multiple clinical centers across China Funding and conflicts of interest: Non-commercial. The companies that donated the drugs and devices had no role in the design of the trial or in the analysis of the data.	Inclusion criteria: • Aged 60 to 80 years • Hypertension (SBP of 140 to 190 mmHg during 3 screening visits or taking antihypertensive medication Exclusion criteria: • Patients with a history of ischemic or hemorrhagic stroke N total at baseline: Intervention: 4243 (of which 1023 are 70-80 years) Control: 4268 (of which 1032 are 70-80 years) Important prognostic factors[2]: age ± SD: I: 66 (SD 5) C: 66 (SD 5) Sex: I: 47% M C:46 % M SBP: I: 146 (17)	Target SBP 110 to 130 mmHg The patients were provided with antihypertensive drugs, including olmesartan (an angiotensin-receptor blocker), amlodipine (a calcium-channel blocker), and hydrochlorothiazide (a diuretic).	Target SBP 130 to 150 mmHg The patients were provided with antihypertensive drugs, including olmesartan (an angiotensin-receptor blocker), amlodipine (a calcium-channel blocker), and hydrochlorothiazide (a diuretic).	Length of follow-up: 48 months Loss-to-follow-up: Intervention: N 126 (3.0%) Reasons (102 lost-to-follow-up; 24 discontinued interventions) Control: N 166 (3.9%) Reasons (132 lost-to-follow-up; 34 discontinued interventions) Incomplete outcome data: Intervention: N 102 (2.4%) Reasons (not stated other than lost-to-follow-up)	Outcome measure-1: Defined as cardiovascular disease* 70-80 years I: 49 (4.7%) C: 66 (6.4%) HR 0.73 (95%CI 0.50 to 1.05), adjusted for clinical center Outcome measure-2: Defined as mortality Not stated for subgroup Outcome measure-3: Defined as adverse events Not stated for subgroup	* The primary outcome was a composite of stroke (ischemic or hemorrhagic), acute coronary syndrome (acute myocardial infarction and hospitalization for unstable angina), acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes.

		C: 146 (17)			Control: N 132 (3.1%) Reasons (not stated other than lost-to-follow-up)		

Onderzoekskarakteristieken voor uitgangsvraag:

Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk bij volwassenen (< 70 jaar)?

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Zhang, 2021	Type of study: RCT Setting and country: Multiple clinical centers across China Funding and conflicts of interest: Non-commercial. The companies that donated the drugs and devices had no role in the design of the trial or	Inclusion criteria: • Aged 60 to 80 years • Hypertension (SBP of 140 to 190 mmHg during 3 screening visits or taking antihypertensive medication Exclusion criteria: • Patients with a history of ischemic or hemorrhagic stroke N total at baseline: Intervention: 4243 (of which 1023 are 70-80 years) Control: 4268 (of which 1032 are 70-80 years) Important prognostic factors[2]: age ± SD: I: 66 (SD 5) C: 66 (SD 5) Sex: I: 47% M C:46 % M SBP: I: 146 (17) C: 146 (17)	Target SBP 110 to 130 mmHg The patients were provided with antihypertensive drugs, including olmesartan (an angiotensin-receptor blocker), amlodipine (a calcium-channel blocker), and hydrochlorothiazide (a diuretic).	Target SBP 130 to 150 mmHg The patients were provided with antihypertensive drugs, including olmesartan (an angiotensin-receptor blocker), amlodipine (a calcium-channel blocker), and hydrochlorothiazide (a diuretic).	Length of follow-up: 48 months Loss-to-follow-up: Intervention: N 126 (3.0%) Reasons (102 lost-to-follow-up; 24 discontinued interventions) Control: N 166 (3.9%) Reasons (132 lost-to-follow-up; 34 discontinued interventions) Incomplete outcome data: Intervention: N 102 (2.4%) Reasons (not stated other than lost-to-follow-up) Control: N 132 (3.1%) Reasons (not stated other than lost-to-follow-up)	Outcome measure-1: Defined as cardiovascular disease* I: 147 (3.5%) C: 196 (4.6%) HR 0.74 (95%CI 0.60 to 0.92), adjusted for clinical center 70-80 years I: 49 (4.7%) C: 66 (6.4%) HR 0.73 (95%CI 0.50 to 1.05), adjusted for clinical center Outcome measure-2: Defined as mortality Any cause I: 67 (1.6%) C: 64 (1.5%) HR 1.11 (95%CI 0.78 to 1.56), adjusted for clinical center Cardiovascular I: 18 (0.4%) C: 25 (0.6%) HR 0.72 (95%CI 0.39 to 1.32), adjusted for clinical center	* The primary outcome was a composite of stroke (ischemic or hemorrhagic), acute coronary syndrome (acute myocardial infarction and hospitalization for unstable angina), acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes.

	in the analysis of the data.					Outcome measure-3: Defined as adverse events Hypotension (SBP < 110 mmHg or DBP < 50 mmHg) I: 146 (3.4%) C: 113 (2.6%) HR 1.31 (95%CI 1.02 to 1.68), adjusted for clinical center Dizziness I: 45 (1.1%) C: 49 (1.1%) HR 0.92 (95%CI 0.61 to 1.39), adjusted for clinical center Syncope I: 6 (0.1%) C: 2 (<0.1%) Too few numbers for HR.	
SPRINT, 2021 (final report)	Type of study: RCT (parallel) Setting: Patients at increased risk of CVD Country: United States of America Source of funding: Non-commercial	Inclusion criteria: • Age at least 50 years • Systolic BP of 130 to 180 mmHg • Increased risk of CVD* Exclusion criteria: • Diabetes mellitus • Prior stroke • Dementia N total at baseline: Intervention: 4678 (1317 older than 74 yrs) Control: 4683 (1319 older than 74 yrs) Important prognostic factors[2]: Age ± SD: I: 67 (9) C: 67 (10) Sex: I: 36% F C: 35% F	Intensive treatment (blood-pressure target less than 120 mmHg)	Standard treatment (blood-pressure target less than 140 mmHg)	Length of follow-up: Median follow-up: 3.33 years Loss-to-follow-up: Intervention: N 489 (10.5%) Reasons (111 lost-to-follow-up; 224 discontinued interventions; 154 withdrew consent) Control: N 497 (10.6%) Reasons (134 lost-to-follow-up; 242 discontinued interventions; 121 withdrew consent) Incomplete outcome data:	Outcome measure-1: Defined as cardiovascular disease*** I: 264 (5.6%) C: 354 (7.6%) HR 0.73 (95%CI 0.63 to 0.86), adjusted for clinical site Outcome measure-2: Defined as mortality Any cause I: 163 (%) C: 215 (%) HR 0.75 (95%CI 0.61 to 0.92), adjusted for clinical site Cardiovascular I: 41 (%) C: 71 (%) HR 0.58 (95%CI 0.39 to 0.84), adjusted for clinical site Outcome measure-3: Defined as adverse events	*Increased cardiovascular risk was defined by one or more of the following: clinical or subclinical cardiovascular disease other than stroke; chronic kidney disease, excluding polycystic kidney disease, with an estimated glomerular filtration rate (eGFR) of 20 to less than 60 ml per minute per 1.73 m2 of body surface area, calculated with the use of the four variable Modification of Diet in Renal Disease equation; a 10-year risk of cardiovascular disease of 15% or greater on the basis of the Framingham risk score; or an age of 75 years or older.

					Intervention: N 111 (2.4%) Reasons (not stated other than lost-to-follow-up) Control: N 134 (2.9%) Reasons (not stated other than lost-to-follow-up)	Hypotension (SBP < 110 mmHg or DBP < 50 mmHg) I: 99 (2.1%) C: 58 (1.2%) HR 1.71 (95%CI 1.24 to 2.38) Dizziness Not reported Syncope I: 97 (2.1%) C: 73 (1.6%) HR 1.33 (95%CI 0.98 to 1.81)	**In both groups, injurious falls was among the most frequent serious adverse events. Among patients under intensive treatment also frequent was acute kidney injury or acute renal failure. ***The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome not resulting in infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes
SPS3, 2013	Type of study: RCT Setting and country: multinational, North America, Latin America, and Spain Funding and conflicts of interest: Non-commercial	Inclusion criteria: • aged 30 years or older; • were normotensive or hypertensive; • had had a recent (within 180 days), symptomatic, MRI-confirmed lacunar stroke; • were without surgically amenable ipsilateral carotid artery stenosis or high-risk cardioembolic sources. Exclusion criteria: • disabling stroke (modified Rankin score of 4 or higher); • previous intracranial haemorrhage from non-traumatic causes; • cortical ischaemic stroke. N total at baseline: Intervention: 1501 Control: 1519	Target < 130 mmHg	Target 130-149 mmHg	Length of follow-up: Mean 3.7 years Loss-to-follow-up: N 90 (3%) Reasons (not described, nor per group) Incomplete outcome data: N 465 (15%) Reasons (withdrawn consent (n=242), site closure (n=151), physician request (n=12), and other reasons (n=60); not separated per group)	Outcome measure-1: Defined as major vascular event* I: 160 (2.9%) C: 188 (3.5%) HR 0.84 (95%CI 0.68 to 1.04) Outcome measure-2: Defined as mortality Any cause I: 106 (1.8%) C: 101 (1.7%) HR 1.03 (95%CI 0.79 to 1.35) Vascular death I: 36 (0.6%) C: 41 (0.7%) HR 0.86 (95%CI 0.55 to 1.35) Outcome measure-3: Defined as adverse events Hypotension Not reported	* One classified as both intracerebral and other, and one as both intracerebral and subdural or epidural.

		Important prognostic factors[2]: age ± SD: I: 63 (11) C: 63 (11) Sex: I: 61% M C: 65% M SBP, mmHg I: 142 (19) C: 144 (19)				Dizziness when standing up I: 324 (22%) C: 304 (21%) OR 1.10 (95%CI 0.92 to 1.31) Syncope I: 11 (0.2%) C: 5 (0.1%) Too few numbers to calculate HR	
Verdecchia, 2009 (Cardio-Sis trial)	Type of study: RCT Setting and country: 44 centres in Italy Funding and conflicts of interest: Commercial	Inclusion criteria: • aged 55 years or older • Systolic blood pressure of 150 mm Hg or higher, who had been receiving antihypertensive treatment for at least 12 weeks. • at least one additional risk factor**. Exclusion criteria: with a fasting glucose of 7.0 mmol/L or higher and those with a history of diabetes, because existing evidence6–9 lends supports to intensive lowering of diastolic blood pressure in such patients and because present guidelines recommend tight blood-pressure control in patients with diabetes.3–5 Other exclusion criteria were any disease reducing life expectancy, renal dysfunction (serum creatinine > 176.8 µmol/L), clinically relevant hepatic or haematological disorders, valvular	Tight control, target <130 mmHg	Usual control, target <140 mmHg	Length of follow-up: Median 2.0 years Loss-to-follow-up: Intervention: N 0 (0%) Control: N 1 (0.2%) Reasons (not described) Incomplete outcome data: Intervention: N 43 (7.7%) Reasons (not described) Control: N 35 (6.3%) Reasons (not described)	Outcome measure-1: Defined as cardiovascular disease* I: 27 (4.8%) C: 52 (9.4%) HR 0.50 (95%CI 0.31 to 0.79) Outcome measure-2: Defined as mortality from any cause I: 4 (0.7%) C: 5 (0.9%) Numbers are too few to calculate HR Outcome measure-3: Defined as adverse events Hypotensive symptoms I: 5 (0.9%) C: 2 (0.4%) Dizziness I: 2 (0.4%) C: 4 (0.7%) Syncope Not reported	* Death from any cause, MI, stroke, TIA, atrial fibrillation, admission for heart failure, angina, or coronary revascularisation ** Additional risk factor may be: • cigarette smoking, • total cholesterol ≥5.2 mmol/L, • HDL cholesterol <1.0 mmol/L, • LDL cholesterol ≥3.4 mmol/L, • Family history of premature cardiovascular disease in first degree relative [<65 years in women and <55 years in men], • previous transient ischaemic attack or stroke, • established coronary or peripheral arterial disease).

		heart disease, disorders confusing the electrocardiographic diagnosis of left ventricular hypertrophy (complete right or left bundle block, Wolff -Parkinson-White syndrome, previous Q-wave myocardial infarction, and paced heart rhythm), atrial fi brillation, and substance misuse. <u>N total at baseline</u>: Intervention: 558 Control: 553 <u>Important prognostic factors</u>[2]: age ± SD: I: 67 (7) C: 67 (7) Sex: I: 59% F C: 59% F SBP, mmHg I: 163.3 (11.1) C: 163.3 (11.3)					

Onderzoekskarakteristieken voor uitgangsvraag:

Wat is de toegevoegde waarde van etnische achtergrond bij het reclassificeren van het risico op hart- en vaatziekten?

Study reference	Study characteristics	Patient characteristics	Prognostic factor(s)	Follow-up	Outcome measures and effect size	Comments
Gijsberts, 2015	Type of study: participant meta-analysis Setting: 15 population based cohorts worldwide	Inclusion criteria: • Cohorts with available baseline data on age, sex, blood pressure, cholesterol fractions, smoking status, use of antihypertensive medication, diabetes mellitus and CIMT-measurements, follow-up information on	Ethnicity: • White as reference group • Black • Asian • Hispanic	Mean follow-up: 9.1 yr (range 3.8 to 13.1 yr) For how many participants were no complete	<u>Cardiovascular events</u> 10-yr event rate • White: 8.1% • Black: 9.2% • Asian: 6.7% • Hispanic: 7.8% • Total: 8.2%	

	Countries: USA, Germany, Japan, UK, Canada, NLD, Finland, Sweden, Norway Source of funding: Non-commercial (Netherlands Organisation for Health Research and Development)	occurrence of cardiovascular events • individuals to whom the Framingham criteria are applicable Exclusion criteria: • Cohorts without information about ethnicity if it was reasonable to assume that > 95% of the participants belonged to one race/ethnic group N=60.211 individual records Mean age: 59 yr Sex: 51% M / 49% F 46,788 Whites (78%) 7,200 Blacks (12%) 3,816 Asians (6%) 2,407 Hispanics (4%)		outcome data available? Incomplete data on mean common CIMT, cardiovascular risk factors, and (time to) CV events, approximately 12% of total values, were imputed	HR (95% CI) **Age** • White 1.89 (1.86 to 1.93) reference • Black: 1.52 (1.44 to 1.60), P<0.05 • Asian: 1.75 (1.49 to 2.01) • Hispanic: 1.69 (1.48 to 1.90) **Total cholesterol** • White 1.09 (1.07 to 1.12) reference • Black: 1.20 (1.13 to 1.26), P<0.05 • Asian: 0.95 (0.78 to 1.13) • Hispanic: 1.15 (0.96 to 1.34)	
Drawz, 2012	Type of study: cohort study Setting: 19.811 subjects of ALLHAT cohort Countries: USA Source of funding: Non-commercial funding. ALLHAT investigators received financial support by industry.	Inclusion criteria: • Age ≥55 yr • Hypertension with ≥1 additional risk factor for CHD Exclusion criteria: • Age > 74 • Missing baseline data for HDL, or both cLDL and total cholesterol • History of CHD (assessed with questionnaire) N=19.811 Mean age: 64 yr Sex: 51% M / 49% F 8108 Whites (61%) 5099 Blacks (39%)	Ethnicity: • White • Black	5-yr follow-up For how many participants were no complete outcome data available? Not reported	<u>Coronary heart disease (CHD), 5-yr*</u> *Net Reclassification Improvement* Non-black, men: 1.3% (P=0.54) Non-black, women: -5.5% (P=0.11) Black, men: -4.1% (P=0.46) Black, women: 4.4% (P=0.31)	*NRI of model included CKD and race compared to basic model without these variables

Bijlage 6 Risk of bias-tabellen

Risk of Bias-tabel voor uitgangsvraag:

Welke streefwaarden van LDL-C dienen te worden gehanteerd bij de behandeling met lipidenverlagende medicatie bij personen tot en met 70 jaar met een (zeer) hoog risico op hart- en vaatziekten?

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**
Schmidt, 2017	Yes	Yes	Yes	Yes	Not applicable	Yes	Yes	Yes	Yes
Nuβbaumer, 2016	Yes	Yes	Yes	Yes	Not applicable	Yes	Yes	No	Yes
Chan, 2011	Yes	Yes	Yes	Yes	Not applicable	Yes	Yes	Yes	Unclear

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?** Definitely yes Probably yes Probably no Definitely no	**Was the allocation adequately concealed?** Definitely yes Probably yes Probably no Definitely no	**Blinding: Was knowledge of the allocated interventions adequately prevented?** **Were patients blinded?** **Were healthcare providers blinded?** **Were data collectors blinded?** **Were outcome assessors blinded?** **Were data analysts blinded?** Definitely yes Probably yes Probably no	**Was loss to follow-up (missing outcome data) infrequent?** Definitely yes Probably yes Probably no Definitely no	**Are reports of the study free of selective outcome reporting?** Definitely yes Probably yes Probably no Definitely no	**Was the study apparently free of other problems that could put it at a risk of bias?** Definitely yes Probably yes Probably no Definitely no	**Overall risk of bias If applicable/necessary, per outcome measure** **LOW** **Some concerns** **HIGH**

			Definitely no				
Amarenco, 2020 (TST trial)	Definitely yes Reason: From study protocol: "Randomization list has been created by the biostatistician of the clinical research unit of the Bichat Stroke Center, using SAS software version 9.1."	Definitely yes Reason: Computerized system with login was used.	**Probably no** Reason: Outcome assessors were blinded. However, due to the nature of the intervention, health providers were not blinded. It was unclear if participants were blinded.	**Definitely no** Reason: 25% and 27% in the intervention and control group, respectively, were lost to follow-up. Reasons were similar between groups. Participants were censored at last available follow-up.	Definitely yes Reason: Protocol was published and the trial was registered as well. Outcomes were reported as described in protocol.	Definitely yes Reason: Industry provided an unrestricted grant and were not involved in the trial, data collection or analysis.	**LOW** (major cardiovascular events and myocardial infarction or urgent coronary revascularisation) Reason: Due to the nature of the intervention and control, not being blinded most likely did not result in bias. Because participants lost to follow-up were censored (non-informative censoring), and reasons for lost to follow-up were similar, this most likely did not result in bias.
Schwartz, 2018 (ODYSSEY OUTCOMES trial)	Probably yes Reason: Although not specifically stated, a call was used to assign treatment. Randomization was done stratified by country.	No information Reason: No information is provided on allocation concealment.	Probably yes Reason: Patients, healthcare providers, and outcome assessors were blinded.	Definitely yes Reason: Number of participants lost tot follow-up was less than 1%.	Definitely yes Reason: Trial was registered and study protocol was published with list of outcomes reported.	**Definitely no** Reason: Sponsor (industry) was involved in data collection, etc. Employees were authors.	**Some concerns**

Risk of bias-tabel voor uitgangsvraag:

Wat is de meerwaarde van de behandeling met lipidenverlagende middelen bij (kwetsbare) ouderen (> 70 jaar)?

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?**	**Was the allocation adequately concealed?**	**Blinding: Was knowledge of the allocated interventions adequately prevented?** **Were patients blinded?**	**Was loss to follow-up (missing outcome data) infrequent?**	**Are reports of the study free of selective outcome reporting?**	**Was the study apparently free of other problems that could put it at a risk of bias?**	**Overall risk of bias** **If applicable/necessary, per outcome measure**

	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	**Were healthcare providers blinded?** **Were data collectors blinded?** **Were outcome assessors blinded?** **Were data analysts blinded?** Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	**LOW** **Some concerns** **HIGH**
Amarenco, 2020 (TST trial)	Definitely yes Reason: From study protocol: "Randomization list has been created by the biostatistician of the clinical research unit of the Bichat Stroke Center, using SAS software version 9.1."	Definitely yes Reason: Computerized system with login was used.	**Probably no** Reason: Outcome assessors were blinded. However, due to the nature of the intervention, health providers were not blinded. It was unclear if participants were blinded.	**Definitely no** Reason: 25% and 27% in the interventio n and control group, respectivel y, were lost to follow-up. Reasons were similar between groups. Participants were censored at last available follow-up.	Definitely yes Reason: Protocol was published and the trial was registered as well. Outcomes were reported as described in protocol.	Definitely yes Reason: Industry provided an unrestricte d grant and were not involved in the trial, data collection or analysis.	**LOW** (major cardiovascular events) Reason: Due to the nature of the intervention and control, not being blinded most likely did not result in bias. Because participants lost to follow-up were censored (non-informative censoring), and reasons for lost to follow-up were similar, this most likely did not result in bias.

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/ notapplicable	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
Teng, 2015	Yes	No	No	No, some of the data could not be retrieved	Not appliciable	Yes	Yes	No	yes

Study reference (first author, publication year)	Describe method of randomisation[1]	Bias due to inadequate concealment of allocation? (unlikely/likely /unclear)	Bias due to inadequate blinding of participants to treatment allocation? (unlikely/likely /unclear)	Bias due to inadequate blinding of care providers to treatment allocation? (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? (unlikely/likely /unclear)	Bias due to loss to follow-up? (unlikely/likely /unclear)	Bias due to violation of intention to treat analysis? (unlikely/likely /unclear)
Shepherd, 2002 Trompet, 2015	"Sequence was generated with a computerised pseudorandom number generator and consisted of balanced blocks of size four"	Unlikely	Unlikely	unlikely	unlikely	Unlikely	Unclear	Unlikely

Risk of bias-tabel voor uitgangsvraag:

Wanneer moet een verhoogde bloeddruk behandeld worden?

Table of quality assessment for systematic reviews of RCTs 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
The Blood Pressure Lowering Treatment Trialists' Collaboration, 2021	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes

Risk of bias-tabel voor uitgangsvraag:

Welke bloeddrukstreefwaarde dient te worden gehanteerd bij de behandeling van hypertensie bij (kwetsbare) ouderen (> 70 jaar)?

Study reference (first author, publication year)	Describe method of randomisation	Bias due to inadequate concealment of allocation? (unlikely/likely/unclear)	Bias due to inadequate blinding of participants to treatment allocation? (unlikely/likely/unclear)	Bias due to inadequate blinding of care providers to treatment allocation? (unlikely/likely/unclear)	Bias due to inadequate blinding of outcome assessors to treatment allocation? (unlikely/likely/unclear)	Bias due to selective outcome reporting on basis of the results? (unlikely/likely/unclear)	Bias due to loss to follow-up? (unlikely/likely/unclear)	Bias due to violation of intention to treat analysis? (unlikely/likely/unclear)
Antihypertensive versus placebo								
Beckett, 2008 (HYVET)	"Randomization was stratified according to age and sex; permuted blocks of 4 and 6 of any 10 patients were used to ensure roughly equal assignment to each of the two groups within	Unclear. Not stated.	Unlikely. Matching placebo was given	Likely. Investigators were allowed to adjust the study medication according the blood pressure target.	Unlikely. "All events that were possible end points were reviewed by an independent committee, unaware of the group assignment, using predefined definitions from the protocol."	Unclear. Trial was registered retrospectively; although outcomes stated were reported.	Likely. Reasons for lost to follow-up were similar; however, total number was large and almost 50% in each group.	Unlikely. "The primary analysis was performed according to the intention-to-treat principle."

	large centers."							
Steassen, 1998	"Eligible patients were prospectively stratified by center, sex, and previous cardiovascular complications and thereafter randomized to double-blind treatment with active medication or placebo by means of a computerized random function."	Unclear. Not stated.	Unlikely. Matching placebo was given.	Unclear. Not stated.	Unlikely. The End Point Committee, which was unaware of the patients' treatment, (…)."	Unclear. Not stated whether the trial was registered.	Unclear. More participants withdrew from double-blind treatment in the control group; however, reasons are not stated.	Unlikely. "The analysis by intention to treat included all end points occurring during double-blind and open follow-up, regardless of whether the patients were taking the treatment to which they had been randomized."
Intensive versus standard blood pressure control								
The SPRINT research group, 2015	"Randomization was stratified according to clinical site."	Unclear. Not stated.	Likely. "Participants and study personnel were aware of the study-group assignments, (…)."	Likely. "Participants and study personnel were aware of the study-group assignments, (…)."	Unlikely. "Participants and study personnel were aware of the study-group assignments, but outcome adjudicators were not."	Unlikely. Trial registered prospectively with reported outcome stated in publication	Unclear. Not stated for the subgroup.	Unlikely. "(…) with the use of the intention-to-treat approach for all randomly assigned participants; (…)"
Wei, 2013	"(…) were randomly assigned to either intensive antihypertensive treatment or standard treatment by using a computer-generated	Unclear. Not stated	Likely. Participants were not blinded	Likely. Care providers could not be blinded.	Unlikely. "(…), endpoints were evaluated by the members of the Endpoint Evaluation Committee, who were blinded to the treatment assignments and the time course of BP."	Unclear. It was not reported whether the trial was registered.	Unlikely. Although reasons for lost to follow-up were not clear, numbers were very small (<3%).	Unlikely. "An intention-to-treat analysis was performed to ensure that all study participants were followed until the conclusion of the study, irrespective of whether the participant

	table of random numbers. ”							was still receiving or complying with the treatment.”
Ogihara, 2010	“(…), the patients were randomly assigned by the VALISH data center according to the following factors: sex, age (<75 or ≥75 years), systolic BP (<175 or ≥175 mmHg), antihypertensive therapy, and institution (weighting coefficient: 2).	Unclear. Not stated	Likely. Participants were not blinded	Likely. Care providers could not be blinded.	Unlikely. “End points and adverse events were blindly evaluated according to the prospective, randomized, open-label, blinded end point design by the endpoint committee and the safety committee, respectively.”	Unclear. It was not reported whether the trial was registered.	Unclear. Reasons for withdrawal were not stated.	Unlikely. “All of the registered study patients assigned to treatment were analysed on an intention-to-treat basis.”

Research question:

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?**	**Was the allocation adequately concealed?**	**Blinding: Was knowledge of the allocated interventions adequately prevented?** **Were patients blinded?** **Were healthcare providers blinded?** **Were data collectors blinded?**	**Was loss to follow-up (missing outcome data) infrequent?**	**Are reports of the study free of selective outcome reporting?**	**Was the study apparently free of other problems that could put it at a risk of bias?**	**Overall risk of bias** **If applicable/necessary, per outcome measure**
	Definitely yes	Definitely yes		Definitely yes			**LOW**

	Probably yes Probably no Definitely no	Probably yes Probably no Definitely no	**Were outcome assessors blinded?** **Were data analysts blinded?** Definitely yes Probably yes Probably no Definitely no	Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	**Some concerns HIGH**
Zhang, 2021	Definitely yes Reason: "Randomization was performed with the use of a central computerized randomization program on a Web-based interface, with stratification according to clinical center."	No information Reason: No stated in article, supplementary appendix or trial register.	**Definitely no** Reason: "Investigators and patients were aware of the trial-group assignments. […] Members of the adjudication committee were unaware of the trial-group assignments."	Definitely yes Reason: In both groups less than 4% did not complete assigned treatment with similar reasons.	Probably yes Reason: of the 12 outcomes reported in trial register, 9 were reported in the article. It seems likely the other outcomes will be reported in other articles.	Definitely yes Reason: The companies that donated the drugs and devices had no role in the design of the trial or in the analysis of the data.	Low Reason: Although the participants and researcher were not blinded, the outcomes were determined by committee masked to treatment assignment.

Risk of bias-tabel voor uitgangsvraag:

Welke streefwaarden dienen te worden gehanteerd bij behandeling van verhoogde bloeddruk bij volwassenen (< 70 jaar)?

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?**	**Was the allocation adequately concealed?**	**Blinding: Was knowledge of the allocated interventions adequately prevented?** **Were patients blinded?** **Were healthcare providers blinded?** **Were data collectors blinded?** **Were outcome assessors blinded?**	**Was loss to follow-up (missing outcome data) infrequent?**	**Are reports of the study free of selective outcome reporting?**	**Was the study apparently free of other problems that could put it at a risk of bias?**	**Overall risk of bias** **If applicable/necessary, per outcome measure**

	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	**Were data analysts blinded?** Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	**LOW** **Some concerns** **HIGH**
Zhang, 2021	Definitely yes Reason: "Randomization was performed with the use of a central computerized randomization program on a Web-based interface, with stratification according to clinical center."	No information Reason: No stated in article, supplementary appendix or trial register.	**Definitely no** Reason: "Investigators and patients were aware of the trial-group assignments. […] Members of the adjudication committee were unaware of the trial-group assignments."	Definitely yes Reason: In both groups less than 4% did not complete assigned treatment with similar reasons.	Probably yes Reason: of the 12 outcomes reported in trial register, 9 were reported in the article. It seems likely the other outcomes will be reported in other articles.	Definitely yes Reason: The companies that donated the drugs and devices had no role in the design of the trial or in the analysis of the data.	Low Reason: Although the participants and researchers were not blinded, the outcomes were determined by a committee masked to treatment assignment.
SPRINT, 2021	Probably yes Reason: "Randomization was stratified according to clinical site."	No information Reason: No stated in article, supplementary appendix or trial register.	**Definitely no** Reason: "Participants and study personnel were aware of the study-group assignments, but outcome adjudicators were not."	Definitely yes Reason: In both groups, about 10% were lost to follow-up, with similar reasons.	Definitely yes Reason: All outcomes were reported.	**Definitely no** Reason: Trial was stopped early.	**Some concerns** Reason: The trial was stopped early.
SPS3, 2013	Definitely yes Reason: "The schedule was computer generated with a permuted-block design (variable block size)."	Probably yes Reason: No detail information provided, but: "Upon patients' eligibility being established, study coordinators randomized patients via their data entry systems."	**Definitely no** Reason: Treatment was open label. Endpoints were determined by independent, masked committee.	Probably yes Reason: 3% were lost to follow-up. However, no reasons were given, or separately reported per group.	Probably yes Reason: Trial was registered, and primary outcomes were reported. Secondary outcome, cognitive function, was not reported.	Definitely yes Reason: -	Low Reason: Although the participants and researchers were not blinded, the outcomes were determined by committee masked to treatment assignment.

Cardio-Sis, 2009	**Definitely no** Reason: "After stratification by centre, we used a computerised random function […]. Randomisation was done with a fully computerised system, with the group assignment concealed and blocks of four patients per site."	**Definitely no** Reason: "After all steps were completed successfully, a randomisation code was provided by the system and patients were assigned in an open manner to one of the two groups."	**Definitely no** Reason: Only endpoint committee was blinded. "An endpoint committee, unaware of the randomisation code, adjudicated all incident clinical events […]."	Definitely yes Reason: Only one patient in the control group was lost to follow-up.	**Probably no** Reason: Trial was registered in year of end of inclusion, but only stated the primary outcome. Not all outcomes were reported.	Probably yes Reason: The study received funding from pharmaceutical companies. However, there are no indication of influence of the funding body (Sponsor was not involved in paper, etc.).	**HIGH** Reason: Randomization and allocation concealment was not adequate. Also, not all outcomes were reported.

Risk of bias-tabel voor uitgangsvraag:

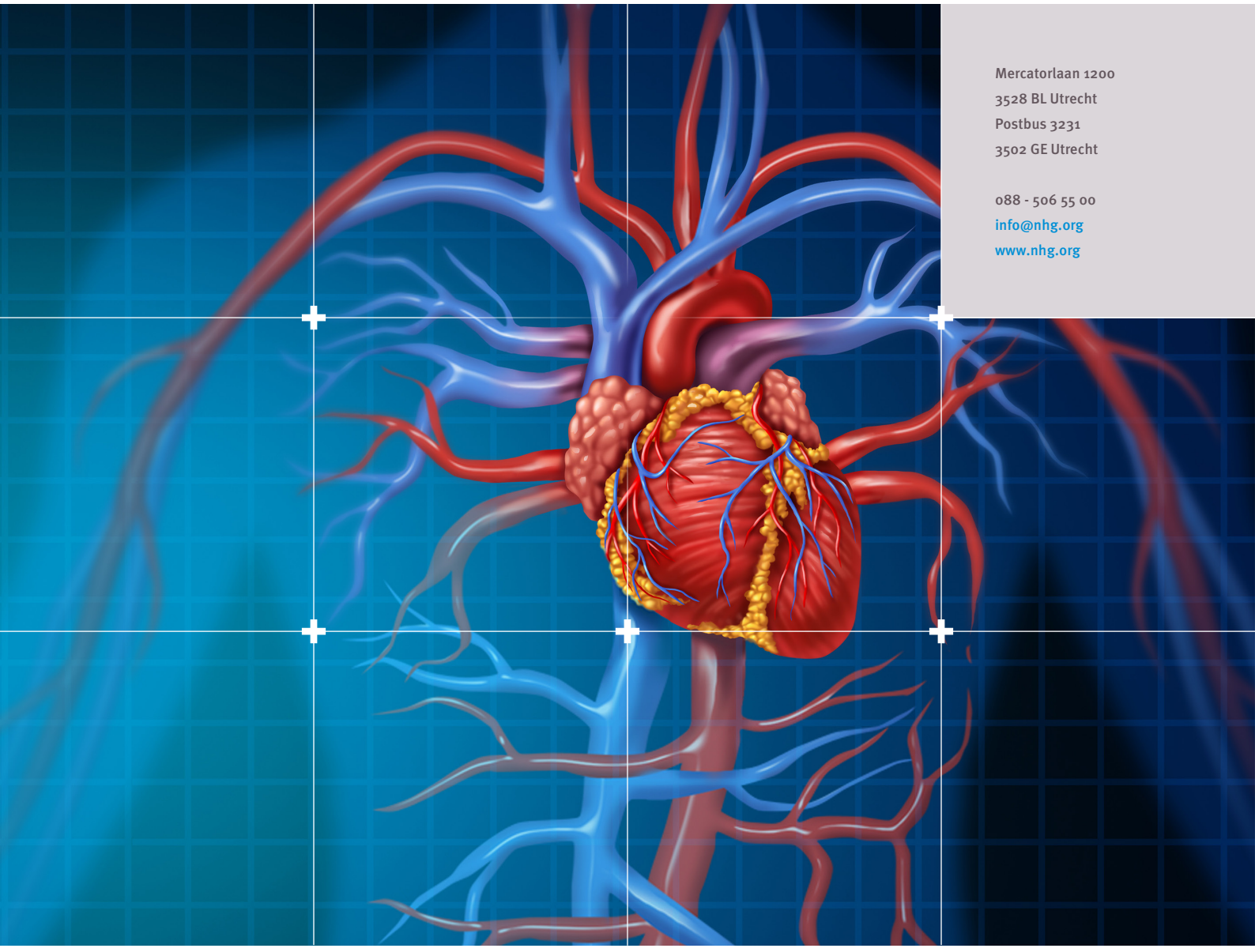
Wat is de toegevoegde waarde van etnische achtergrond bij het reclassificeren van het risico op hart- en vaatziekten?

Table of quality assessment – prognostic studies

Study reference (first author, year of publication)	**Was there a representative and well-defined sample of patients at a similar point in the course of the disease?** (yes/no/unclear)	**Was follow-up sufficiently long and complete?** (yes/no/unclear)	**Was the outcome of interest defined and adequately measured?** (yes/no/unclear)	**Was the prognostic factor of interest defined and adequately measured?** (yes/no/unclear)	**Was loss to follow-up / incomplete outcome data described and acceptable?** (yes/no/unclear)	**Was there statistical adjustment for all important prognostic factors?** (yes/no/unclear)	**Level of evidence**
Gijsberts, 2015	Yes	Yes	Unclear	Unclear	Yes	Yes	A2
Drawz, 2012	Yes	No (5 yr follow-up)	Yes	No (self-reported and Hispanic eligible in both black or non-black)	No (not described)	Yes	B

NHG-Standaard CVRM (M84)

NHG-Behandelrichtlijn Stoppen met roken



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