Supplemental material

Table S1. Search strategy for MEDLINE database.

'arterial health' OR 'vascular function' OR 'cardiovascular disease' OR 'cardiovascular risk' OR 'endothelial function'	AND	'advanced glycation end products' OR 'AGE'	AND	'skin autofluorescence' OR 'SAF'	AND	'intima media thickness' OR 'IMT' OR 'pulse wave velocity' OR 'PWv'

Table S2. Characteristics of the studies included in the systematic review and meta-analysis.

	Age (years)		Sex (male/female)		BMI (kg/m²)		Total Cholesterol (mmol/L)		HDLc (mmol/L)		LDLc (mmol/L)		Triglycerides (mmol/L)	
	UHS	**HS**	**UHS**	**HS**	**UHS**	**HS**	**UHS**		**UHS**	**HS**	**UHS**	**HS**	**UHS**	**HS**
Araszkiewicz et al, 2015	23 (20-28)	-	49/28	-	23 (21-25)	-	5.3 (4.7-5.8)	-	1.9 (1.6-2.1)	-	2.9 (2.3-3.6)	-	0.9 (0.7-1.2)	-
Hollander et al, 2007	27 (20-34)	25 (21-32)	2/6	8/21	24 (22-28)	23 (21-26)	5.9 (5.2-7.7)	4.9 (4.2-5.4)	1.1 (1.0-1.3)	1.4 (1.3-1.8)	3.1 (1.6-1.7)	2.5 (2.1-3.0)	4.1 (3.1-7.1)	1.2 (0.9-1.6)
Blaauw et al, 2006	30.0±4.0	32.0±3.0	0/26	0/17	25.0±5.0	23.0±3.0	5.1±0.8	4.9±0.7	1.5±0.3	1.5±0.3	3.0±0.7	2.9±0.6	1.3±0.7	1.1±0.3
Llaurado et al, 2014	35.3±10.1	35.4±10.2	34/16	34/16	25.7±3.6	24.0±3.1	4.8±0.9	5.2±1.3	1.7 (1.2-1.9)	1.5 (1.2-1.9)	2.5 (2.1-3.1)	2.8 (2.3-3.6)	0.8 (0.6-1.0)	0.8 (0.6-1.2)
Osawa et al, 2017	37.4±12.4	34.7±12.4	34/71	15/8	23.0±3.0	20.6±2.6	4.8±0.8	4.7±0.6	1.7±0.3	1.6±0.3	2.7±0.7	2.7±0.6	0.8 (0.2-8.6)	0.7 (0.3-7.0)
De Leeuw et al, 2007	43.0±12.0	43.0±13.0	8/47	8/47	24.3±4.0	24.7±4.0	4.7±0.9	5.4±1.0	1.5±0.3	2.0±0.8	2.6±0.8	2.9±1.2	NA	NA
De Groot et al, 2015	18.0-80.0	18.0-80.0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
De Leeuw et al, 2010	51.0±11.0	56.0±14.0	12/12	17/4	25.0±3.0	26.0±5.0	5.0±0.8	4.9±0.7	1.5±0.3	1.4±0.4	3.3±0.8	3.0±0.8	NA	NA
Den Dekker et al, 2013	51.8±7.8 63.5±7.6	43.8±9.5	32/35 44/16	53/43	26.6 (23.8-29.8) 26.3 (24.2-29.5)	25.0 (23.1-27.7)	6.0 (4.9-6.7) 4.3 (3.9-5.4)	5.7 (4.7-6.7)	1.3 (1.0-1.6) 1.3 (1.1-1.4)	1.3 (1.1-1.7)	4.0 (3.3-4.5) 2.5 (2.1-3.2)	3.8 (2.9-4.7)	1.7 (1.1-2.7) 1.7 (1.1-2.1)	1.4 (0.9-2.1)
Dadoniene et al, 2015	52.64±11.2	52.6±7.7	6/41	6/41	24.3±4.6	26.1±4.5	5.8±1.5	6.2±1.1	1.4±0.4	1.6±0.3	3.7±1.3	4.1±1.0	1.5±0.7	1.1±0.5
Lutgers et al, 2010	55.0±10.0	-	27/32	-	24.9±2.50	-	5.9±0.9	-	1.6±0.4	-	4.3±1.0	-	1.2 (0.9-1.8)	-
Ueno et al, 2008	58.1±9.3	57.1±10.5	88/32	71/39	NA	NA	NA	NA	1.3±0.3	1.5±0.4	3.0±0.9	3.9±0.9	NA	NA

Ninomiya et al, 2018	59.3±12.8	-	65/75	-	27.3±5.5	-	NA	-	1.3±0.4	-	2.9±0.9	-	1.8±1.2	-
Ueno et al, 2011	59.9±10.1	-	127/85	-	21.4±2.8	-	NA	-	1.2±0.3	-	2.7±0.8	-	NA	-
Hangai et al, 2016	61.0±13.0	-	72/50	-	26.4±5.1	-	4.9±0.9	-	1.4±04	-	2.8±0.8	-	1.6±0.8	-
Osawa et al, 2018	61.1±12.3	40.3±7.8	107/86	11/13	27.7±5.95	20.9±2.9	5.0±1.2	5.1±0.9	1.3±0.4	1.8±0.4	2.8±1.1	3.0±0.6	1.5 (0.3-7.4)	0.7 (0.3-3.5)
Yoshioka, 2018	61.2±11.2	53.8±13.0	89/73	20/22	24.9±4.0	22.6±4.0	NA	NA	1.6±0.5	1.8±0.4	2.7±0.7	3.2±0.9	1.3±0.6	1.4±0.8
Tanaka et al, 2009	65.1±11.6	64.1±12.4	59/69	11/8	22.1±3.3	24.6±3.2	NA	NA	1.2±0.4	NA	2.2±0.7	NA	1.3±0.7	NA
Kimura et al, 2014	65.1±11.6	-	59/69	-	22.1±3.3	-	NA	-	1.2±0.4	-	2.1±0.7	-	1.2±0.7	-
Temma et al, 2015	66.6±9.2	-	38/23	-	25.5±4.6	-	4.8±0.9	-	1.3±0.3	-	2.8±0.8	-	1.7±0.8	-
Hofmann et al, 2013	68.7±10.2	-	52/0	-	27.8±4.0	-	NA	-	NA	-	NA	-	NA	-
McIntyre et al, 2011	73.5±8.0	72.8±9-0	126/158	545/878	NA	NA	4.0±0.8	4.9±1.2	NA	NA	NA	NA	NA	NA
McIntyre et al, 2013	74 (67-79)	-	680/1037	-	28.4 (25.6-31.8)	-	4.6 (3.9-5.5)	-	1.4 (1.1-1.7)	-	NA	-	NA	-
Igase et al, 2017	76.5±6.7	67.2±9.9	9/9	75/133	22.9±2.1	22.8±3.0	NA	NA	1.6±0.3	1.6±0.4	3.1±0.8	3.0±0.8	1.0±0.4	1.1±0.6
Watfa et al, 2012	-	49.1±10.4 77.5±8.4	-	29/26 26/35	-	27.2±5.5 25.3±4.5	-	2.1±0.5 1.8±0.5	-	0.6±0.1 0.5±0.2	-	1.4±0.4 1.3±0.4	-	1.2±1.0 1.0±0.6

Table S2. Characteristics of the studies included in the systematic review and meta-analysis. Cont.

	SBP (mmHg)		DBP (mmHg)		HbA1c (%)		PWv (m/s)		C-IMT (mm)		SAF (AU)		Smoke	
	UHS	HS	UHS	HS	SSUHS	HS	UHS	SS	UHS	SS	UHS	SS	UHS	SS
Araszkiewicz et al, 2015	115.2±28.2	-	66.8±16.8	-	8.3 (7.2-8.8)	-	-	-	0.6 (0.5-0.7)	-	2.2 (1.9-2.6)	-	25	-
Hollander et al, 2007	NA	NA	NA	NA	4.8 (4.6-5.0)	4.9 (4.6-5.0)	-	-	0.5 (0.48-0.59)	0.6 (0.58-0.62)	1.7 (1.6-1.8)	1.6 (1.3-1.8)	2	1
Blaauw et al, 2006	128.0±10.0	115.0±9.0	81.0±9.0	68.0±8.0	NA	NA	-	-	0.64 ± 0.07	0.63 ± 0.09	NA	NA	11	5
Llaurado et al, 2014	125.0±12.2	120.6±10.4	72.9±8.3	70.8±8.4	7.5 (6.8-8.7)	5.3 (5.2-5.5)	6.8 (6.0-7.9)	6.1 (5.5-6.7)	-	-	2.1 (1.8-2.3)	1.7 (1.6-2.1)	24	16
Osawa et al, 2017	117.0±14.0	114.0±7.0	69.7±9.2	68.9±5.9	7.7±1.4	5.1±0.2	13.2±2.5	12.3±1.6	1.1±0.5	0.8±0.2	2.1±0.5	1.9±0.3	35	2
De Leeuw et al, 2007	128.0±17.0	125.0±18.0	80.0±9.0	78.0±10.0	NA	NA	-	-	NA	NA	1.5±0.5	1.3±0.4	14	2
De Groot et al, 2015	NA	NA	NA	NA	NA	NA	-	-	0.7 (0.5-1.7)	0.7 (0.4-1.5)	2.6 (1.3-4.7)	2.1 (1.3-3.8)	NA	NA
De Leeuw et al, 2010	120.0±11.0	127.0±20.0	74.0±8.0	70.0±9.0	5.4±0.4	5.4±0.6	-	-	0.72 (0.62-0.81)	0.67 (0.59-0.79)	1.5±0.5	1.3±0.4	14	2
Den Dekker et al, 2013	136 (128-146) 139 (127-164)	130 (120-140)	82 (75-90) 80 (75-85)	80 (73-90)	NA	NA	-	-	NA	NA	2.1 (1.8-2.5) 2.7 (2.2-3.3)	1.9 (1.7-2.1)	50 55	65
Dadoniene et al, 2015	NA	NA	NA	NA	NA	NA	7.5±1.7	7.5±1.3	-	-	2.2±0.5	1.9±0.5	NA	NA
Lutgers et al, 2010	130.0±20.0	-	82.0±12.0	-	5.3±0.4	-	-	-	0.8±0.2	-	1.6±0.4	-	NA	-
Ueno et al, 2008	149.0±15.0	129.0±21.0	79.0±7.0	73.0±10.0	NA	NA	17.9±4.5	14.2±2.3	-	-	1.8±0.7	1.3±0.5	33	60
Ninomiya et al, 2018	123.0±17.4	-	72.5±12.6	-	8.9±1.7	-	17.0±4.0	-	1.8±0.8	-	2.5±0.5	-	55	-

Ueno et al, 2011	149.0±17.0	-	-	-	NA	-	NA	-	0.8±0.2	-	1.8±0.7	-	45	-
Hangai et al, 2016	131.7±17.7	-	75.1±12.0	-	8.6±2.3	-	15.7±3.1	-	1.6±0.7	-	2.42±0.4	-	60	-
Osawa et al, 2018	124.6±17.2	113.9±9.9	73.2±12.1	69.3±9.0	8.9±1.7	5.3±0.3	17.2±4.6	12.8±1.4	1.9±0.8	0.9±0.5	2.6±0.5	1.9±0.3	98	4
Yoshioka, 2018	132.0±11.0	122.0±11.0	81.0±9.0	81.0±11.0	7.2±0.8	5.4±0.3	-	-	1.6±0.7	1.1±0.2	2.5±0.5	2.2±0.3	44	11
Tanaka et al, 2009	NA	NA	NA	NA	NA	NA	-	-	0.9 ± 0.4	NA	2.4±0.7	1.3±0.4	NA	NA
Kimura et al, 2014	-	-	-	-	NA	-	-	-	0.9±0.4	-	2.4±0.7	-	NA	-
Temma et al, 2015	130.7±15.5	-	70.9±9.3	-	7.0±0.8	-	-	-	1.6±0.8	-	2.5±0.5	-	NA	.
Hofmann et al, 2013	139.0±21.0	-	73.0±12.0	-	6.3±0.7	-	NA	.	-	-	NA	-	28	-
McIntyre et al, 2011	NA	NA	69.0±10.0	74.0±11.0	NA	NA	10.4±2.0	9.8±2.0	-	-	3.0±0.7	2.7±0.6	NA	NA
McIntyre et al, 2013	134.0±18.0	-	73.0±11.0	-	NA	-	9.9±2.0	-	-	-	2.7 (2.3-3.1)		929	-
Igase et al, 2017	124.4±13.3	123.7±14.9	NA	NA	5.9±0.8	5.8±0.6	17.7±3.2	15.8±2.8	-	-	2.6±0.6	2.1±0.4	2	8
Watfa et al, 2012	-	130.9±16.3 141.3±22.4	-	80.1±9.2 77.4±12.2	-	NA	-	7.5±1.9 11.8±4.2	-	-	-	2.1±0.5 2.8±0.6	-	61 43

Data are shown as mean ± SD or interquartile range; AU: arbitrary units; BMI: body max index; C-IMT: carotid intima-media thickness; DBP: diastolic blood pressure; HbA1c: glycated hemoglobin; HDL: high density lipoproteins; HS: healthy subjects; LDL: low density lipoproteins; NA: not available; PWv: pulse wave velocity; SAF: skin autofluorencence; SBP: systolic blood pressure; SD: standard deviation; UHS: unhealthy subjects.

Table S3. Quality assessment with the tool for observational cohort and cross-sectional studies of the National Heart, Lung and Blood Institute (outcome: PWv).

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Quality
Llaurado et al, 2014	Y	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Poor
Osawa et al, 2017	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Dadoniene et al, 2015	Y	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Poor
Ueno et al, 2008	Y	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Poor
Ninomiya et al, 2018	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Ueno et al, 2011	Y	N	Y	Y	N	N	N	Y	Y	NA	Y	NR	NA	Y	Fair
Hangai et al, 2016	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Osawa et al, 2018	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Hofmann et al, 2013	Y	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	N	Poor
McIntyre et al, 2011	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
McIntyre et al, 2013	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Igase et al, 2017	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Watfa et al, 2012	Y	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Poor

Table S4. Quality assessment with the tool for observational cohort and cross-sectional studies of the National Heart, Lung and Blood Institute (outcome: C-IMT).

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Quality
Araszkiewicz et al, 2015	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Hollander et al, 2007	Y	N	Y	Y	Y	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Blaauw et al, 2006	Y	N	Y	Y	Y	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Osawa et al, 2017	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
De Leeuw et al, 2007	Y	N	Y	Y	Y	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
De Groot et al, 2015	Y	N	Y	Y	Y	Y	N	NA	Y	Y	Y	NR	Y	Y	Good
De Leeuw et al, 2010	N	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	N	Poor
Den Dekker et al, 2013	Y	Y	Y	Y	Y	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Lutgers et al, 2010	Y	N	Y	Y	N	N	N	Y	Y	NA	Y	NR	NA	Y	Fair
Ninomiya et al, 2018	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Ueno et al, 2011	Y	N	Y	Y	N	N	N	Y	Y	NA	Y	NR	NA	Y	Fair
Hangai et al, 2016	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Osawa et al, 2018	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair
Yoshioka, 2018	Y	N	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Poor
Tanaka et al, 2009	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	N	NA	Y	Fair
Kimura et al, 2014	Y	Y	Y	Y	N	Y	Y	NA	Y	Y	Y	N	N	Y	Good
Temma et al, 2015	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y	Fair

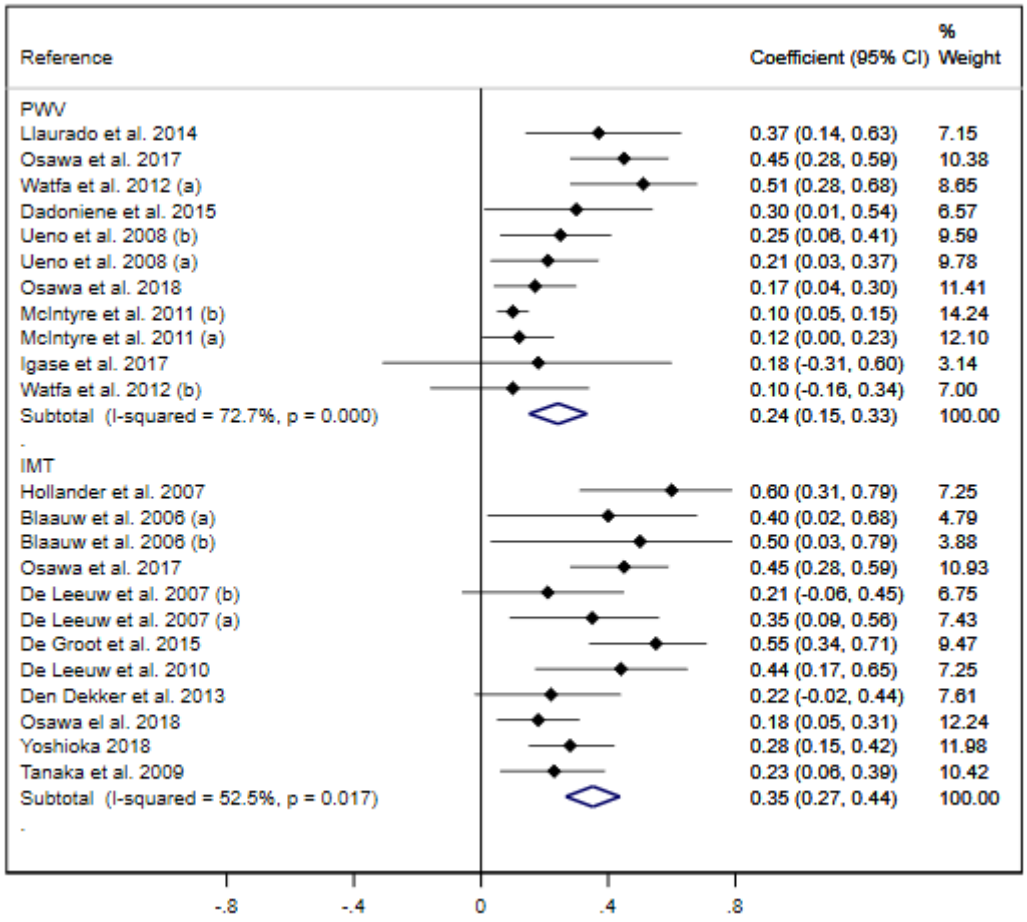
Table S5. Random effects meta-regression analysis of to determine if variables included in studies are significant moderators of relationship between PWv or C-IMT and SAF.

Variables	PWV			C-IMT		
	n	Coef. (95% IC)	p	n	Coef. (95% IC)	p
Age	16	**-0.008 (-0.013, -0.003)**	**0.007**	19	**-0.007 (-0.011, -0.003)**	**0.004**
BMI	12	0.008 (-0.42, 0.059)	0.725	18	-0.008 (-0.042, 0.026)	0.633
Ct	10	-0.014 (-0.12, 0.092)	0.768	13	-0.129 (-0.368, 0.109)	0.259
HDL	13	0.03 (-0.249, 0.309)	0.817	18	0.251 (-0.005, 0.507)	0.054
LDL	12	-0.031 (-0.162, 0.099)	0.604	18	-0.0003 (-0.136, 0.136)	0.997
TRIG	9	-0.012 (-0.187, 0.166)	0.890	14	-0.034 (-0.168, 0.099)	0.590
SBP	13	-0.005 (-0.015, 0.004)	0.253	15	**-0.008 (-0.014, -0.003)**	**0.008**
DBP	13	0.005 (-0.028, 0.038)	0.732	14	-0.009 (-0.022, 0.004)	0.166
HbA1c	7	**-0.108 (-0.209, -0.007)**	**0.040**	10	-0.058 (-0.116, 0.002)	0.055

C-IMT	-	-	-	16	-0.119 (-0.286, 0.047)	0.146
PWV	14	-0.003 (-0.026, 0.021)	0.815	-	-	-
SAF	15	-0.117 (-0.273, 0.038)	0.127	17	-0.012 (-0.183, 0.158)	0.880

Data are shown as coefficients ± 95% IC; BMI: body max index; C-IMT: carotid intima-media thickness; Ct: total cholesterol; DBP: diastolic blood pressure; HbA1c: glycated hemoglobin; HDL: high density lipoproteins; LDL: low density lipoproteins; PWV: pulse wave velocity; SAF: skin autofluorencence; SBP: systolic blood pressure.

Figure S1. Forest plot including the correlation between pulse wave velocity or carotid intima media thickness and skin autofluorescence in studies that included control group.



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2,3

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	3
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	3
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	3,4
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10,11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12,13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14