BMJ Global Health

Urban-rural differences in the association between blood lipids and characteristics of the built environment: a systematic review and meta-analysis

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To cite:

de Groot R, van den Hurk K, Schoonmade LJ, et al. Urban-rural differences in the association between blood lipids and characteristics of the built environment: a systematic review and meta-analysis. BMJ Global Health 2019;4. doi:10.1136/ bmjgh-2018-001017

Handling editor Seye Abimbola

Received 31 October 2018 Accepted 31 October 2018

ABSTRACT

Introduction The built environment defines opportunities for healthy eating and physical activity and may thus be related to blood lipids. The aim of this study is to systematically analyse the scientific evidence on associations between builtenvironment characteristics and blood lipid levels in adults. Methods PubMed, EMBASE and Web of Science were searched for peer-reviewed papers on population-based studies up to 9 October 2017. We included studies that reported on built-environment characteristics and blood lipid levels in adult populations (≥18 years). Two reviewers independently screened titles/abstracts and full-texts of papers and appraised the risk of bias of included studies using an adapted version of the Quality Assessment Tool for Quantitative Studies. We performed meta-analyses when five or more studies had sufficient homogeneity in determinant and outcome.

Results After screening 6902 titles/abstracts and 141 potentially relevant full-text articles, we included 50 studies. Forty-seven studies explored associations between urban versus rural areas with blood lipid levels. Meta-analyses on urban versus rural areas included 133 966 subjects from 36 studies in total. Total cholesterol levels were significantly and consistently higher in urban areas as compared with rural areas (mean difference 0.37 mmol/L, 95% Cl 0.27 to 0.48). Urban/rural differences in high density lipoprotein cholesterol were inconsistent across studies and the pooled estimate showed no difference (0.00 mmol/L 95% Cl -0.03 to 0.04). Low density lipoprotein (LDL) cholesterol and triglyceride levels were higher in urban than in rural areas (mean difference 0.28, 95% Cl 0.17 to 0.39 and 0.09, 95% Cl 0.03 to 0.14, respectively).

Conclusions Total and LDL cholesterol levels and triglycerides were consistently higher in residents of urban areas than those of rural areas. These results indicate that residents of urban areas generally have less favourable lipid profiles as compared with residents of rural areas. **Prospero registration number** CRD42016043226.

(C) Key questions

What is already known?

- Built-environment characteristics are known to influence lifestyle behaviours such as physical activity and dietary behaviour.
- These lifestyle behaviours are established determinants of blood lipid levels.

What are the new findings?

- ► This systematic review and meta-analysis shows that low density lipoprotein and total cholesterol and triglyceride levels are consistently less favourable in urban areas as compared to rural areas.
- ► No overall differences in high density lipoprotein cholesterol were found between urban and rural areas.

What do the new findings imply?

- ► The ongoing urbanisation worldwide may have health consequences related to blood lipid levels.
- ► Further research is needed to better understand in which way urbanisation may affect blood lipid levels.

INTRODUCTION

Elevated blood lipid levels are an established risk factor for cardiovascular diseases and contribute in a meaningful way to the global burden of disease. Globally, high total cholesterol (TC) levels are estimated to account for 4.5% of the total deaths. 1-3 Physical activity and low consumption of food high in saturated fat and dietary cholesterol, and high intake of food high in unsaturated fatty acids, especially omega-3 fatty acids, are associated with more favourable blood lipid profiles.⁴⁻⁶ In particular, the favourable effects of physical activity on high density lipoprotein (HDL) cholesterol and triglycerides is well documented. Dietary and physical activity behaviour is, in turn, influenced by built-environment characteristics



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that directly and indirectly facilitate or inhibit the maintenance of a healthy lifestyle. ⁸⁹ For example, the availability, accessibility and affordability of food and fast-food outlets have been found to be associated with dietary behaviour, ¹⁰ and the availability and proximity of opportunities to be physically active have been linked to leisure time physical activity. ¹¹¹² Hence, in their capacity to affect lifestyle behaviour, built-environment characteristics may be 'upstream' determinants of blood lipid levels. ^{13–20}

A common focus of the many studies that have investigated built-environment characteristics and blood lipid levels is the difference between residents of urban and rural areas. Urban-rural differences in blood lipid levels may be prevalent due to several aspects: urban areas may generally score higher on walkability as compared with rural areas, thereby facilitating light physical activity. 21 22 This could have beneficial effects in terms of reducing blood lipid levels for those living in more rural areas. Also, it may be that adults living in exposure to unhealthy food (outlets) may differ across urban and rural areas, which may influence blood lipid levels via dietary intake. Systematic reviews that examined urban-rural differences in relation to other health outcomes reported that rural residence is associated with higher bodyweight¹⁸ and urban residence with higher risk/prevalence of type 2 diabetes,²³ and, in India, with higher prevalence of hypertension.²⁴ A cross-country study with 17 countries reported the rate of major cardiovascular events (myocardial infarction, stroke and heart failure) was higher in rural compared with rural areas in low-income and middle-income countries (LMIC).²⁵ Interestingly, urban communities had higher risk factor scores. For policy makers, gaining insight into the health effects of urbanisation is highly relevant, as the United Nations projects that by 2050, 70% of the global population will reside in urban areas.²⁶ 27

In spite of it being a widely studied topic, a comprehensive overview of the relationship between built-environment characteristics and blood lipids is lacking. Therefore, we aimed to systematically review and meta-analyse the scientific evidence on associations between built-environment characteristics potentially related to physical activity, sedentary behaviour, dietary habits and blood lipid levels in adults.

METHODS

We conducted a systematic review and meta-analysis of studies seeking to assess the association between the built environment and total, HDL and low density lipoprotein (LDL) cholesterol; HDL/LDL cholesterol ratio and/or triglyceride levels. The structure of this review conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)-statement. The protocol of this systematic review was published and registered in PROSPERO in advance (www.crd.york.ac.uk/prospero, ID:CRD42016043226).

Literature search strategy

To identify all relevant publications, we performed systematic searches in the bibliographic databases

PubMed, EMBASE.com and the Web of Science Core Collection up to 9 October 2017 (LS, RdG). Search terms included indexed terms from MeSH in PubMed, EMtree in EMBASE as well as free texts in titles and abstracts. Search terms related to 'cholesterol' or 'triglycerides' were used in combination with search terms including 'built environment'. Full-text, peer-reviewed articles in English, French and Dutch were included. Duplicate articles were excluded. The full search strategy for all databases can be found in online supplementary appendix A. In addition, reference lists of the full-text articles included were searched for potentially eligible articles (ie, backward screening) and a citation search (ie, forward screening (RdG)).

Screening and eligibility criteria

Study designs that sought to assess associations between the built environment and TC, HDL and/or LDL cholesterol and/or triglycerides were considered eligible for systematic review. Two authors (RdG and JL) independently screened all potentially relevant titles and abstracts. Subsequently, full-texts were screened for eligibility using prespecified inclusion and exclusion criteria. Studies were included if they: (1) reported on adults (aged >18 years or mixed age groups, thus drawing separate conclusions/results for adults); (2) were population-based; (3) were peer-reviewed, published, fulltexts; (4) reported on the association between built and/ or physical-environment characteristics and total, HDL and LDL cholesterol; HDL/LDL cholesterol ratio and/ or triglyceride levels; (5) included objectively or subjectively measured built-environment characteristics; (6) and were written in Dutch, French or English. Studies were excluded if they reported on the same population as another study that was included (of these, only the most relevant article was included). There were no restrictions with regard to ethnicity or nationality of study populations. Studies were eligible for meta-analyses if descriptive statistics (mean, SD or SE and number of participants) were available as these are necessary to construct mean differences. Differences in judgement were resolved by reaching consensus (RdG and JL) and by consultation with a third author (KvdH) if disagreements were not resolved. Meta-analyses were performed in the event that more than five studies on the same environmental characteristic were identified with sufficient similarity in determinant and outcome.

Data extraction and study outcomes

A data extraction form was developed and pilot-tested on five randomly selected included studies and refined accordingly. Data were extracted by one author (RdG) and 5% were randomly checked (JL). The extraction form included author(s), country of study, year of publication, journal reference, participant characteristics (age, sex, number of participants and inclusion criteria pertaining to age), study design, data collection methods, environment characteristics and definition of the exposure. Only

two comparators were extracted: if multiple urbanisation levels—that is, urban, rural, semirural—were reported, these were pooled into two categories where possible, otherwise only urban and rural were extracted. For this study, data on urban and rural areas were extracted based on the categorisation as provided by the authors of the included studies. Hence, no uniform definition was used. As part of the quality assessment, an item regarding the reporting on the used definition was included (see Q16 of online supplementary appendix B). Furthermore, we extracted the unit of measurement of blood lipids, whether lipid measurements were taken while fasting or non-fasting, summary measures of the outcome(s) including type of analysis and, if applicable, regression coefficient, CIs, mean, SD and whether or not a statistical difference was found.

In the event that more clarification or additional information was required, the authors of the original studies were contacted up to five times. First, three attempts to contact the first author were made and, if unsuccessful, the second author and, subsequently, the last author were contacted. When contact details of any of these authors could not be found, attempts were made to contact any of the other authors until five attempts were made. We requested information from authors of 47 of the studies included and successfully contacted authors of 33 studies.

Quality assessment

To assess the quality of the studies included, we used an adapted version of the Quality Assessment Tool for Quantitative Studies (QATQS, online supplementary appendix B), used previously for similar purposes. 14 23 The adjusted QATQS was pilot tested for clarity on five studies included and consisted of the following six domains: study design, selection bias, withdrawals and dropouts, confounders, data collection and reporting. Although our research question differed from the majority of the research questions of the studies included, we assessed the quality of these studies in relation to our research question that is, the association between environment characteristics and the outcome. Analysis or reporting of the results may, therefore, have been appropriate for the research question of the original paper, but not sufficient in light of the aim of this systematic review. Each domain was rated as strong, moderate, weak or not applicable, which resulted in an overall quality score. Studies with at least three strong domains and no weak domains were classified as strong. Moderate was assigned to studies with two weak domains or fewer than three strong domains. Studies with more than two weak domains were rated as weak.

Data synthesis and analysis

A narrative of the findings from the studies included was written, structured around the type of outcome, the built-environment characteristics under study and the quality (strong/moderate vs weak). The meta-analyses were performed using R Studio V.0.99.896 and the Metafor package, using a random effects model. The

pooled estimates in the forest plots were presented as mean differences with 95% CIs between groups. The forest plots were grouped by study quality (moderate-strong and weak) and by sex. Heterogeneity in study outcomes was assessed using the I² statistic. We assessed potential publication bias by evaluating the symmetry of funnel plots for each blood lipid under study. Since the included studies were published over a considerable time span 1980–2017, additional sensitivity analyses were performed in which we meta-analysed studies stratified by three time periods: from 1980 to 1999, 2000–2009 and from 2010 to 2017.

RESULTS

Study selection

The search generated a total of 9602 articles, of which 3509 were duplicates, leaving 6134 unique articles, (see figure 1). We excluded 5993 articles after screening the titles and abstracts and reviewed the remaining 141 fulltexts. Of those 141 full-texts, (1) 54 did not report on a relevant outcome; (2) 10 were in a language other than English, French or Dutch; (3) 10 studies were excluded because of study design; (4) 7 studies were excluded because of the study population; (5) 7 studies were excluded because no relevant built-environment determinants were studied and (6) 5 studies reported on 2 of the same study populations, therefore 3 of these studies were excluded. As a result, a total of 50 studies met the eligibility criteria and were included. Evidence of heterogeneity across studies included in the meta-analysis was observed, I² ranged from 90.4% to 98.1%. The symmetry of the funnel plots (figure 2) suggests the absence of publication bias. The plots also show some dispersion on top, indicating heterogeneity in outcomes between studies, which is in line with the observed I² statistic values.

Study characteristics

The majority of the studies included (47) reported on differences in blood lipids between urban and rural environments. The characteristics of these studies are summarised in table 1. Most of these studies were conducted in Asia (30, of which 11 in India and 10 in China) and Africa (10). With the exception of two studies²⁸ ²⁹ that had a longitudinal observational design, all urban/rural studies had a cross-sectional design and were published between 1980 and 2017, the median year of publication being 2009 (IQR: 2001-2015. With the exception of one study published in French,³⁰ all studies were published in English. Seven studies provided a reference for their operationalisation of urban and rural areas, most often citing a national statistics bureau (see online supplementary appendix C). The majority of the studies (30) only stated which cities and villages were considered to be urban and rural, the remainder of the studies 10 reported no information on their definitions. Thirty-three studies reported blood lipid levels for men and women

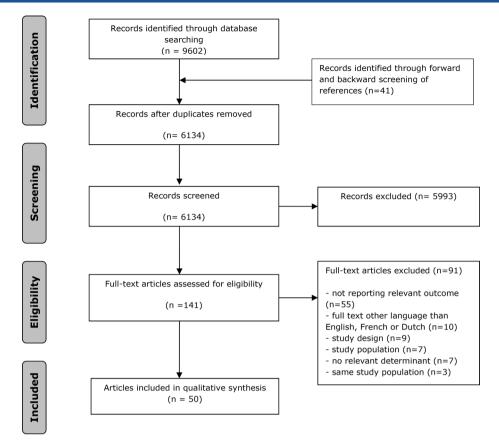


Figure 1 Flowchart.

separately, 12 studies for men and women combined, 3 exclusively for women and 2 for men. Of the 47 studies that investigated urban-rural environment differences, 2 investigated differences between people who lived in rural areas and those who migrated to an urban area. The remaining studies included in this review focused on accessibility of markets/parks (1) community-based interventions (1) and walkability (1).

Quality assessment

The overall rating of 12 studies (24%) was weak, 37 moderate (74%) and 1 strong (2%). ³³ A summary of the quality assessment scores of the studies included is shown in figure 3. The domain reporting was rated as weak in 22 studies (44%). The selection bias domain was assessed as strong in 7 studies (14%), as moderate in 26 studies (52%) and weak in 17 studies (34%). The ratings per domain per study are provided in online supplementary appendix D.

Environmental characteristics

Urban-rural

Total cholesterol

Forty studies provided information on TC levels, of which 30 were rated as being moderate in quality and 10 as weak. The majority of the studies of moderate quality reported TC levels in urban areas to be significantly higher compared with rural areas. Of the studies that reported results for men and women combined (10), 63% found significantly higher TC levels in urban areas.

Of the studies that were stratified by sex (25) in general, higher TC values were reported for women (65%) and men (81%) who lived in urban areas as compared with rural areas. More heterogeneous results were found for the studies classified as weak. The percentage of these studies that reported higher levels of TC in urban areas ranged from 33% to 50%. Of the 32 studies that were eligible for meta-analysis, 25 were rated as moderate and 7 as weak. The meta-analysis of the studies of moderate quality showed significantly higher TC levels in urban areas as compared with rural areas (mean difference 0.37, 95% CI 0.27 to 0.48). Although the CI of point estimates of the studies classified as weak was wider than the CI of the moderate studies, the point estimate was still significantly higher for those residing in urban areas (mean difference 0.37 mmol/L, 0.04–0.69; see figure 4).

HDL cholesterol

HDL cholesterol levels were reported in 36 studies. One such study was rated as strong, ³³ 27 as moderate and 8 as weak. No clear pattern could be found in the results of the studies of moderate quality. The studies rated as of moderate and strong quality showed higher levels of HDL cholesterol in urban areas for women (47%), whereas for men, more studies reported higher HDL cholesterol levels in rural areas (41%). Most studies rated as weak (five out of eight) found no statistically significant difference. The meta-analysis included 28 studies in total of which 1 was rated as strong, 22 as moderate

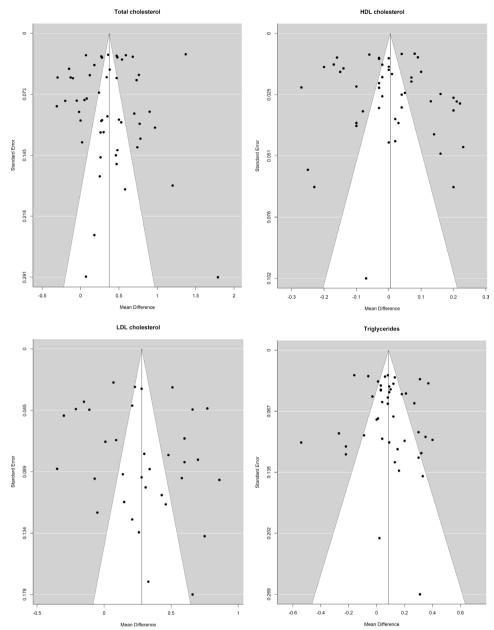


Figure 2 Funnel plots. HDL, high density lipoprotein; LDL, low density lipoprotein.

and 5 as weak. No differences in HDL cholesterol levels according to urban-rural were observed (0.00 mmol/L, -0.03 to 0.04) (figure 5).

LDL cholesterol

Information on LDL cholesterol levels was provided in 28 studies. Of these, 21 studies were rated as moderate and the remaining 7 as weak. In about 60% of the studies of moderate quality, significantly higher LDL cholesterol was reported in urban areas. The number of studies that were classified as weak was low (7) and comparisons made in those studies generally showed no statistically significant difference between urban and rural areas. Twenty studies were eligible for meta-analysis, of which 16 were rated as moderate and 4 as weak. The mean difference in the studies of moderate quality was 0.29 mmol/L (0.17 to 0.41), see figure 6, with higher levels in urban areas.

Figure 4 shows that the patterns of the point estimates are similar across studies that reported on men and women separately or combined. The studies included that were rated as weak showed a mean difference between urban and rural areas of 0.25 mmol/L (0.01 to 0.48).

Triglycerides

Of the 33 studies that reported triglyceride levels, 26 were rated as moderate and 7 as weak. Mixed results were found for studies that were rated as moderate and reported separately for women. In 30% of the comparisons (6) higher levels of triglycerides were found in urban areas; however, 38% reported no differences. Comparisons made by studies that reported triglycerides of men found 48% higher levels in urban areas. More than half of the comparisons (6 or 55%) of the studies of weak quality reported higher levels in urban areas.

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Table 1 Character	Characteristics of included 'urban-rural' built environment characteristic studies	in, pepn	rban-ru	ral' built	environ	nent cha	racteristic	studies					
			Number	Number of participants	oants					Mean±SD mmol/L per blood lipid	lood lipid		
		Study	Urban			Rural			Blood	Urban		Rural	
Study	Country	design	% 0+	0+	€0	\$\dagger\$	0+	%	lipid	\$\$	60	55	60
Abdul-Rahim, Husseini ⁴⁶	Palestine	SS	492	200					TC	5.23±1.33		5.15±1.11	
									HDL	0.90±0.22		1.17±0.45	
									LDL	3.75±1.10		3.27±1.32	
									TG	1.86±2.66		1.53±1.57	
Aguilar-Salinas, Lerman-	Mexico	SS			167	81	56	40	70	5.75±1.12	5.6±0.95	5.5±1.1	5.02±0.97
Garber*'									HDL	1.26±0.33	1.08±0.26	1.26±0.28	1.31±0.36
									LDL	3.93±1.08	3.86±0.93	3.6±1.1	3.2±0.92
									TG.	1.68±0.42	1.96±1.38	1.56±0.49	1.65±1.4
Al-Nuaim ⁴⁸	Saudi Arabia	SS			864	875	584	601	72	4.35±1.5	4.2±1.4	4.4±1.5	4.4±1.6
									HDL	1.2±0.5	1.3±0.6	1.3±0.8	1.4±0.8
									LDL	3.3±1.3	3.1±1.5	3.0±1.5	2.5±1.0
Cai, Zhang ⁴⁹	China	CS							TC	5.14±1.04	86:00∓00:98	4.96±0.99	5.09±1.09
									HDL	1.60±0.48	1.37±0.40	1.57±0.41	1.37±0.48
									LDL	3.32±1.00	3.23±0.95	3.14±0.96	3.37±1.11
									TG	1.35±1.09	1.69±1.51	1.32±1.29	1.89±2.37
Campos, Bailey ⁵⁰	Costa Rica	SS			98	66	88	103	10	4.89±0.85	5 4.73±0.80	4.63±1.09	4.47±0.88
									HDL	1.19±0.26	3 1.01±0.23	1.16±0.23	1.09±0.23
									LDL	3.05±0.75	5 2.87±0.78	2.84±0.88	2.72±0.80
									TG	1.41±0.70	1.82±0.89	1.32±0.64	1.50±0.71
Das, Pal ⁵¹	India	CS			102	122	88	135	10	4.97±0.60	5.12±0.76	5.28±0.60	5.14±0.74
									HDL	1.15±0.12	1.18±0.12	1.17±0.13	1.17±0.15
									LDL	3.07±0.59	3.19±0.75	3.42±0.61	3.26±0.76
									TG	1.63±0.26	1.64±0.32	1.51±0.25	1.55±0.32
Delisle, Ntandou- Bouzitou ³³	Benin	SS			100	100	82	82	HDL	1.37±0.40	1.22±0.20	1.62±0.37	1.29±0.92
Du, Su ⁵²	China	SS	2879	918					70	4.34 (3.04 to 5.15)		4.20 (2.76 to 5.05)	
									HDL	1.15 (0.95 to 1.36)		1.03 (0.83 to 1.26)	
									LDL	2.77 (2.33 to 3.32)		2.78 (2.26 to 3.32)	
									TG	1.85 (1.13 to 3.94)		2.05 (1.27 to 4.13)	
Gharbi, Belhani ³⁰	Tunisia	SS			201	168	155	146	10	4.75±1.50	4.51±1.27	4.27±1.13	4.05±1.30
									HDL	1.07±0.39		1.05±0.44	0.80±0.15
									TG	1.41±1.12	1.50±1.42	1.06±0.67	1.34±0.91

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			Numbe	Number of participants	ipants					Mean±SD r	Mean±SD mmol/L per blood lipid	pid lipid			
		Study	Urban			Rural			Blood	Urban			Rural		
Study	Country	design	% 0+	0+	€0	₽\$+	0+	€0	lipid	₩ 4	0+	€0	% O+	0+	€0
Glew, Conn ⁵³	Nigeria	SO			77	55	79	42	10		4.40±0.77	4.09±0.75		3.62±0.80	3.62±0.77
									HDL		1.29±0.29	1.16±0.27		1.06±0.30	0.96 ± 0.34
									LDL		2.40±0.70	2.17±0.65		1.94±0.71	1.91±0.65
									TG.		1.52 ± 0.74	1.67±1.00		1.22±0.74	1.65±1.02
Gregory, Dai ⁵⁴	Guatemala	SO			155	119	372	241	70		4.26±0.85	4.35±0.91		4.21±0.79	4.00±0.83
									HDL		1.04±0.26	0.86±0.23		1.00±0.28	0.88±0.24
									LDL		2.42±0.71	2.58±0.82		2.33±0.65	2.24±0.69
									TG		1.82±1.01	2.06±1.15		1.91±0.91	1.93±1.00
Gu, Reynolds ⁵⁵	China	CS			4163	3730	3851	3796	70		5.08±1.23	5.00±1.22		4.81±1.24	4.72±1.29
									HDL		1.36±0.62	1.21±0.61		1.36±0.62	1.35±0.65
									LDL		3.05±1.23	3.03±1.22		2.82±1.24	2.75±1.29
									TG		1.50±1.23	1.75±1.83		1.42±1.24	1.38±1.29
Gupta, Prakash ⁵⁶	India	SS				199		202	72			4.55±1.11			4.27±0.96
									HDL			1.11±0.31			1.14±0.31
									LDL			2.78±1.01			2.50±0.85
									TG			1.42±0.62			1.38±0.52
He, Gu ⁵⁷ *	China	CS			4163	3730	3851	3796	10		5.08	4.99		4.8	4.71
									HDL		1.35	1.21		1.36	1.34
									LDL		3.06	3.02		2.81	2.75
									TG		1.50	1.75		1.42	1.38
Htet, Bjertness ⁵⁸	Myanmar	SS			379	376	362	369	10		5.4±0.95	5.5±0.97		5.4±1.75	5.0±1.73
									HDL		1.1±0.19	1.2±0.19		1.3±0.19	1.3±0.38
									TG		1.6±0.76	1.9±1.36		1.4±1.75	1.5±1.34
Huang, Wu ⁵⁹	China	CS			2361	2552	2341	1631	TC		4.85±1.00	4.73±0.90		4.17±0.92	4.25±0.91
									HDL		1.46±0.36	1.33±0.32		1.37±0.32	1.33±0.33
Joshi, Anjana ⁶⁰	India	CS	290	1452					10	4.32±1.11			3.98±0.98		
									HDL	1.01±0.31			1.01±0.31		
									LDL	2.51±0.85			2.3±0.83		
Kodaman, Aldrich ⁶¹	Ghana	CS			1293	972	583	469	10		4.70±1.09	4.41±1.1		3.94±0.95	3.68 ± 0.94
									HDL		1.27±0.38	1.12 ± 0.34		1.20±0.41	1.15 ± 0.38
									LDL		2.95±0.97	2.75±0.88		2.29±0.84	1.98±0.71
									5 <u>1</u>		0.94±0.64	0.87±0.53		0.93±0.59	0.93±0.60

Table 1 Continued	pe														
			Number	Number of participants	pants					Mean±SD mmol/L per blood lipid	ool/L per blood	lipid h			
		Study	Urban			Rural			Blood	Urban			Rural		
Study	Country	design	₩ +	0+	Q.	₽ 3	0+	8	lipid	₩ 4	0+	Z.	55	8	
Lim, Jang ²⁸	South Korea	LT			2497	2523	2784	2240	TC		5.19±0.97	5.33±0.92	5.12±0.93		4.86±0.93
									HDL		1.34±0.31	1.21±0.27	1.30±0.31		1.27±0.33
									LDL		3.21±0.89	3.37±0.93	3.14±0.88		2.86±0.99
									TG		1.47±0.93	1.92±1.27	1.89±1.40		1.63±1.07
Mbalilaki, Hellènius ⁶²	Tanzania	CS			225	259	256	245	TC		4.5±1.0	4.5±1.1	3.8±1.1		3.6±1.0
									HDL		1.2±0.3	1.1±0.3	1.0±0.4		0.9±0.3
									LDL		2.7±0.9	2.7±1.0	2.1±0.9		2.0±0.8
									TG		1.4±1.0	1.8±1.2	1.4±0.6		1.5±0.8
Miranda, Gilman ³² †	Peru	SS	199	201					72	5.04±1.03			4.03±0.86		
									HDL	1.15±0.28			1.14±0.34		
									LDL	3.10±0.88			2.21±0.70		
									TG	1.52±1.23			1.28±0.80		
Mohan, Gupta ⁶³	India	CS			2229		2616		TC		4.90±1.00		4.31±0.79	62	
Mollentze, Moore ⁶⁴	Orange Free	SS			468	290	574	279	72		5.09±1.15	4.99±1.19	4.85±1.12		4.72±1.30
	State								HDL		1.36±0.45	1.38±0.51	1.20±0.34		1.24±0.49
									LDL		3.16±1.06	2.94±1.16	3.15±1.11		2.80±1.01
									TG		1.21±0.93	1.52±1.29	1.24±0.66		1.48±1.03
Ntandou, Delisle ⁶⁵	Benin	CS			100	100	85	85	TG		0.75±0.3	0.89±0.4	0.72±0.3		0.81±0.4
Obirikorang, Osakunor ⁶⁶	Ghana	SS	312	360					72	5.00 (4.65 to 5.50)	.50)		4.80 (4.55 to 5.20)		
									HDL	1.00 (0.80 to 1.20)	.20)		1.00 (0.80–1.20)		
									LDL	3.40 (3.05 to 3.80)	(08)		3.10 (2.70 to 3.60)		
									TG	1.20 (0.80 to 1.40)	.40)		1.35 (1.10 to 1.70)		
Oommen, Abraham ⁶⁷	India	CS			1341	1058	2132	1667	TC		4.7±1.08	4.91±1.05	4.52±1.10		4.53±1.18
									HDL		0.87 ± 0.28	0.79 ± 0.34	1.03±0.30		0.96±0.31
									TG		1.40±0.89	1.73±1.20	1.27±0.81		1.55±1.28
Pandey et al 2013	India	SS			2008		2616		10		4.67±0.81		4.31±0.93	93	
Patel, Woodward ⁶⁸	Thailand	CS			2002	1130	1210	963	10		5.71±3.58	5.54±3.70	5.18±2.43		4.80±2.48
									HDL		1.34±0.89	1.19±0.67	1.13±0.67		1.06±0.62
									LDL		3.71±3.13	3.61±3.70	3.28±2.78		2.86±2.48
									TG		1.51±3.13	1.88±2.17	1.73±2.78		2.15±2.02
Pongchaiyakul,	Thailand	CS			290	305	187	134	10		5.28±1.04	5.35±1.10	4.98±1.38		4.38±1.08
nongsplablias									HDL		1.53±0.34	1.36±0.29	1.31±0.29		1.32±0.30
									LDL		3.16±0.94	3.1±1.00	2.85±1.15		2.24±0.88
									TG		1.26±0.88	1.94±1.24	1.80±1.20		1.79±0.96
														(

Table 1 Continued	р														
			Number	Number of participants	oants					Mean±SD mi	Mean±SD mmol/L per blood lipid	lipid			
		, vbiidy	Urban			Rural			Blood	Urban			Rural		
Study	Country	design	₽\$+	0+	%	£94	0+	6	lipid	₽	0+	€	\$d	0+	€0
Prabhakaran, Roy ⁷⁰ ‡	India	ᆸ	9504						10		4.98±0.97	4.96±1.14		4.35±1.01	4.93±1.09
Reddy, Ramachandraiah ⁷¹ India	1 India	SS				190		190	70			4.62±1.17			3.85±0.92
									HDL			1.15±0.31			1.13±0.38
									LDL			2.67±1.04			2.09±0.77
									T G			1.70±0.64			1.43±0.49
Richter, Baumgartner ⁷²	South-Africa	SS			591	393	633	333	TC		5.02 (4.18 to 0.09)	4.68 (3.84– 5.71)		4.85 (4.11 to 5.95)	4.50 (3.81 to 5.53)
									HDL		1.36 (1.03 to 1.78)	1.50 (1.12 to 2.04)		1.39 (1.09 to 1.84)	1.45 (1.02 to 1.94)
									TDF		3.35 (2.55 to 4.12)	2.86 (2.17 to 3.73)		3.15 (2.50 to 4.09)	2.85 (2.9 to 3.62)
									TG		1.18 (0.87 to 1.78)	1.00 (0.78 to 1.46)		1.09 (0.81 to 1.49)	0.97 (0.76 to 1.35)
Russell-Jones, Hoskins ⁷³	Fijian Mela- nesian	SS			7	35	109	87	5		5.2±1.3	5.6±1.6		4.0±1.0	3.81±1.0
Sarrafzadegan, Talaei ⁷⁴	Iran	SS	4572	1751					72		5.64±1.35	5.33±1.34		5.74±1.38	5.46±1.29
									HDL		1.24±0.27	1.16±0.26		1.27±0.27	1.19±0.25
									LDL		3.41±1.10	3.13±1.11		3.52±1.14	3.34±1.07
									TG		2.15±1.14	2.25±1.23		2.05±1.09	2.04±1.16
Seck, Dia ⁷⁵	Senegal	SS	557	469					70	6.75±0.52			5.38±0.26		
Silambuselvi and Murugu India	ı India	CS							10		5.44			5.11	
Valavan									HDL		1.16			1.39	
									LDL		3.56			3.42	
									TG		1.84			1.80	
Singh, Rastogi ⁷⁷	India	CS			139	172	115	140	HDL		1.27±0.24	1.25±0.20		1.22±0.15	1.18±0.12
Snehalatha and	India	SS	1521	2145					10	4.47±0.94			3.93±0.93		
Kamacnandran									HDL	1.17±0.26			1.09±0.24		
									TG	1.39±0.85			1.33±0.89		
Song, Li ²⁹ ‡	China	CS	19 841	20 029					10		4.05±6.24	4.66±4.23		3.79±5.21	4.54±5.66
Tatsukawa, Sawayama ⁷⁹	Japan	CS			703	375	1688	929	10		5.37±0.92	5.03±0.77		5.52±1.00	5.33±0.90
									HDL		1.52 ± 0.35	1.43±0.34		1.67±0.37	1.46±0.37
									LDL		3.22 ± 0.84	2.92±0.72		3.37±0.89	3.22±0.81
									TG		1.38±0.75	1.49±0.82		1.07±0.61	1.41±0.79
Tazi, Abir-Khalil ⁸⁰	Morocco	CS	755	1047					TC	4.89±1.16			4.42±1.06		

Table 1 Continued	pe														
			Number	Number of participants	ipants					Mean±SD mi	Mean±SD mmol/L per blood lipid	d lipid			
		Study	Urban			Rural			Blood	Urban			Rural		
Study	Country	design	°\$+	0+	%	£94	0+	8	lipid	£9+	0+	6	\$ d+	0+	€0
Vrdoljak, Marković ⁸¹	Croatia	SS	1824	642					10	5.90			5.72		
									HDL	1.57			1.60		
									LDL	3.53			3.52		
									TG	1.80			1.94		
Wang, Wei ³¹	China	SS			547	763	862	929	72		4.32±0.90	4.64±0.98		4.10±0.89	4.03±0.94
											1.20±0.30	1.05±0.28		1.18±0.31	1.09±0.32
											2.52±0.75	2.58±0.95		2.43±0.70	2.38±0.78
											1.31±1.00	2.28±2.35		1.07±0.73	1.24±1.27
Weng, Liu ⁸² §	China	CS			80	81	191	177	72		4.45±0.72	4.22±0.72		3.39±1.11	3.39±1.73
									HDL		1.42±0.54	1.09±0.18		1.20±0.41	1.22 ± 0.40
									LDL		2.73±0.89	2.73±0.72		1.99±0.83	1.98±1.60
									TG		1.04±0.80	1.52±0.99		0.78±0.41	0.65 ± 0.67
Woo, Chook ⁸³	China	SS	116	116					2	5.16±0.96			5.14±1.02		
									HDL	1.49±0.36			1.33±0.40		
									LDL	3.16±0.87			3.21±0.94		
									TG.	1.08±0.67			1.30±1.04		
Wyatt, Griew ⁸⁴	Papua New Guinea	CS			23	98	49	22	5		3.96±0.88	3.64±0.86		3.78±1.09	3.57±1.29
									TG		0.61 ± 0.25	0.63±0.19		0.60±0.38	0.60±0.18
Xu, Ming ⁸⁵	China	SS	1467	890					HDL	1.30±0.30			1.32±0.31		
									TG.	1.58±1.18			1.49±1.03		

*Only SEM reported but no information on number of participants per group.

*Migration study, Chiy data on ruban and rural levels are provided in this table. Aguilar-Salinas, Lerman-Garber.**

*Holigration study, Chiy data on urban and rural levels are provided in the urban male cell. Urban levels of first wave are provided in the urban female cell. Accordingly, the rural levels of the first and second wave are provided in the cells for rural males and females, respectively.

\$Migration study, Rural represents data of "Yf farmers". Urban nepresents "Yf migrants.

\$Migration study, Rural represents data of "Yf farmers". Urban nepresents "Yf migrants.

\$\tilde{\text{c}}\$ females; \$\tilde{\text{c}}\$, males and females combined; CS, cross-sectional; HDL, high density lipoprotein; NR, not reported; TC, total cholesterol; TG, triglycerides.

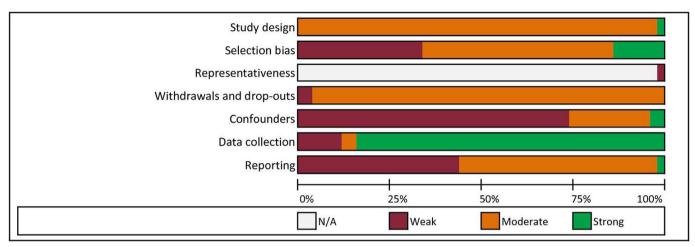


Figure 3 Quality assessment overview.

Three out of four studies that made separate comparisons for men did not show statistically significant differences between urban and rural areas. The meta-analysis included 25 studies, of which 21 were rated as moderate and 4 as weak. The forest plot of the moderately rated studies shows significantly higher triglyceride levels in urban areas as compared with rural areas (mean difference 0.08 mmol/L, 0.02 to 0.14, figure 7). The studies that were rated as weak showed higher triglyceride levels in urban areas (mean difference 0.13 mmol/L, 0.04 to 0.21).

Sensitivity analyses with time periods

Studies performed in different time periods were quite consistent, apart from some small non-significant differences (online supplementary appendixes E1–4).

Migration studies

Two studies focused on migration to urban areas.^{31 32} In their investigation, Miranda *et at*³² categorised three groups; urban residents, rural residents and those who migrated to urban areas at least 5 years ago. They found that total and LDL cholesterol, and triglyceride levels were similar in urban and migrant residents, but both were significantly higher than rural areas. The HDL cholesterol levels were approximately 1.44 mmol/L across all resident groups. In the other migration studies, similar patterns were reported, with the exception of HDL cholesterol levels in men, which were significantly lower in urban residents.³²

Miscellaneous

We identified three studies investigating accessibility to parks, the impact of community-based interventions and walkability and blood lipid levels. The study investigating accessibility of parks and markets reported a positive association between distance to markets and HDL cholesterol. The community-based obesity and chronic disease prevention intervention study initiated various interventions on the physical, economic, social and political environments depending on the needs of the

community. Slight improvement in blood lipid levels was reported after a 3-year follow-up.³⁵ Increased walkability scores were unexpectedly found to be associated with increased triglyceride levels in the Multi-Ethnic Study of Atherosclerosis.³⁶

DISCUSSION

The studies on built-environment characteristics and blood lipid levels that are available to date focus predominantly on urban-rural differences. The current review reveals that LDL and TC and triglyceride levels are consistently less favourable in urban areas as compared with rural areas. No overall differences in HDL-cholesterol were found between urban and rural areas.

In the studies meta-analysed here, the pooled mean urban-rural differences in LDL, TC and triglyceride levels were 0.28 (0.17 to 0.39), 0.37 (0.27 to 0.47) and 0.09 (0.03 to 0.14) mmol/L. Guidelines from the National Cholesterol Education Program (NCEP) classify LDL cholesterol levels of <2.59 mmol/L as optimal, the range of LDL cholesterol levels of the included studies in the meta-analysis ranged from 1.06 to 3.93 mmol/L.37 TC levels below 5.18 mmol/L are considered desirable and triglyceride levels below 1.69 mmol/L are classified as normal by the NCEP guidelines. The range of TC and triglyceride levels of studies included in the meta-analysis ranged from 3.57 to 6.75 mmol/L and from 0.60 to 2.15 mmol/L respectively. On an individual level, the pooled mean differences may be considered small, but at a population level and from a public health policy perspective, this can be regarded as relevant.³⁸ Although quantification in terms of the population attributable risk is difficult to estimate for our study population, a previous meta-analysis investigating the effect of statin use to reduce blood lipid levels identified a decrease of 1.00 mmol/L in LDL cholesterol to reduce the risk of ischaemic heart disease events by 11%.39 In addition, Rodger et al state that

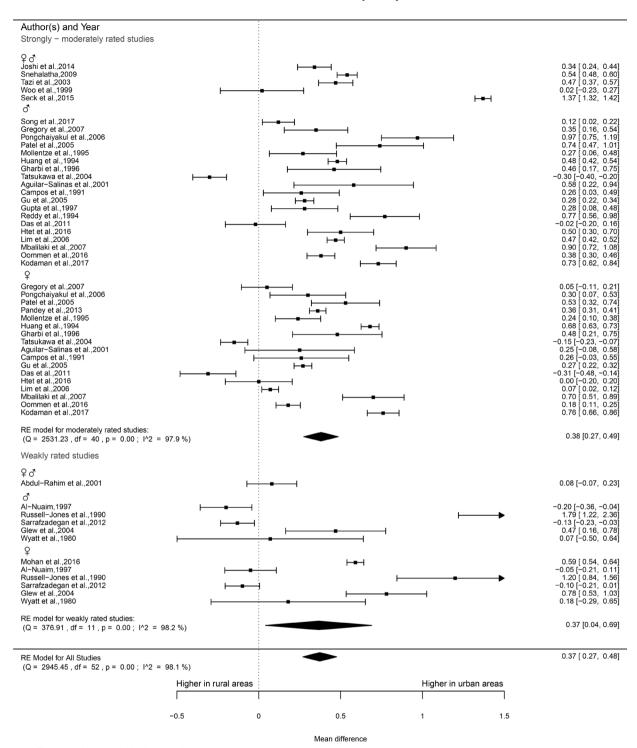


Figure 4 Forest plot total cholesterol.

although associations of TC levels and risk of cardiovascular diseases attenuate with age, they remain strong and positive in the oldest age groups; 1 mmol/L lower cholesterol is associated with 15%–20% lower stroke risk and 20%–25% lower ischaemic heart disease. Anyway, differences in urban and rural areas are likely to become even more relevant as it is projected that

70% of the world's population will reside in urban areas by $2050.^{2627}$

Potential explanations for the urban-rural differences in blood lipids include differences in socioeconomic status, diet as well as occupational activities. ¹⁰ ²⁶ ⁴¹ ⁴² To date, most of the studies on this topic have been carried out in LMIC, in which there is a stark contrast between

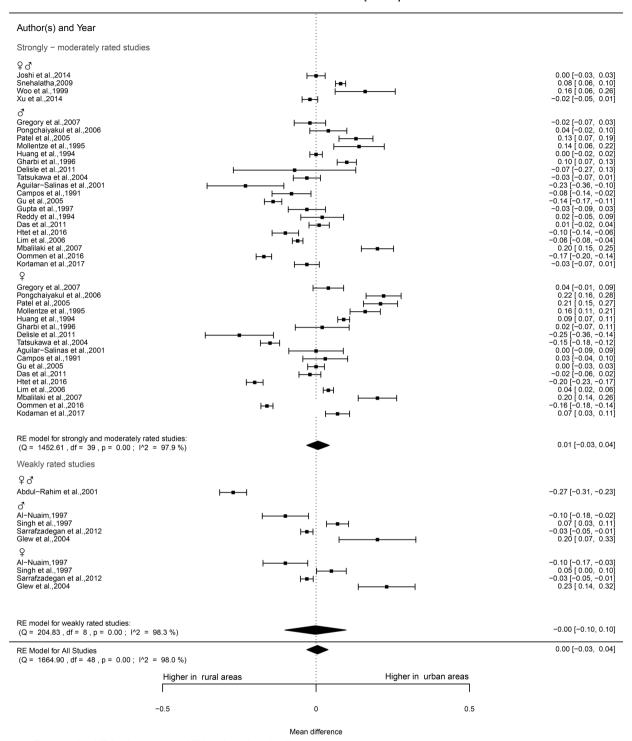


Figure 5 Forest plot HDL cholesterol. HDL, high density lipoprotein.

the socioeconomic position of various inhabitants. In LMIC, living in certain urban areas—often referred to as slums—poses grave health risks due to the poor living conditions in such neighbourhoods and may negatively impact individuals' lifestyles. ⁴³ In addition, urban areas, in general, are characterised by a relatively high availability of (fast-)food outlets and are conducive to the adoption of more western diets, rich in salt, sugar and saturated fat, potentially contributing to

the unfavourable blood lipids observed. ^{10 42 44} Another possible explanation is that in urban areas, occupations often involve office work that generally requires less physical activity as compared with labour in rural, agricultural settings. ⁴⁵ Some of the studies included selected very remote places as research contexts, where traditional dietary habits and frequent occupation-related physical activity (due to agriculture) are more prevalent. This may have introduced some selection bias that

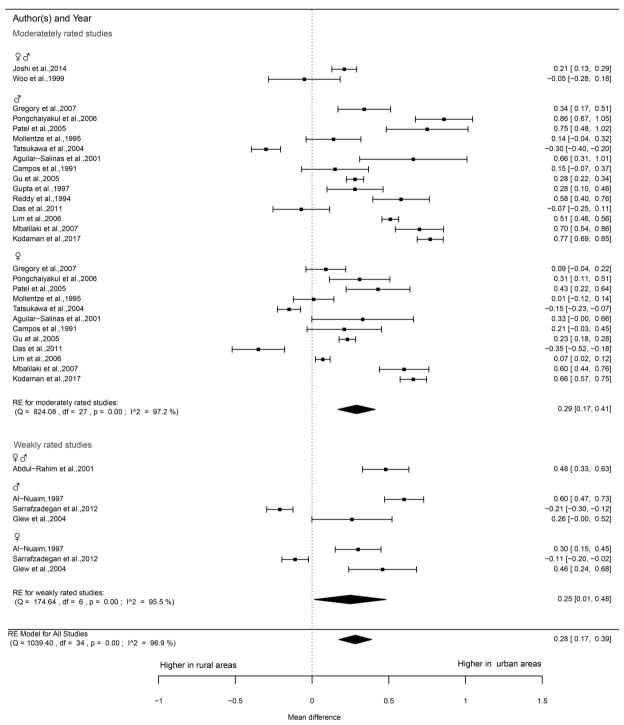


Figure 6 Forest plot LDL cholesterol. LDL, low density lipoprotein.

increased the contrast between urban and rural areas. Also, less heterogeneity might exist between urban and rural areas in non-LMIC at the level of occupation-related physical activity, food availability and dietary habits and social-economic status in comparison with LMIC. However, only few studies from high-income countries were included in this review.

This systematic literature review and meta-analysis provides strong evidence of an association between

the built environment and lipid levels on the basis of a meta-analysis of 36 studies and 133 966 subjects. The findings contribute to our understanding of the relationship between urban versus rural areas, as a characteristic of the built environment and blood lipid levels. Our study also has certain limitations: the majority of the studies included were cross-sectional, preventing us from drawing causal inferences. The available studies to date, in general, do not allow for

Mean difference triglycerides [95% CI]

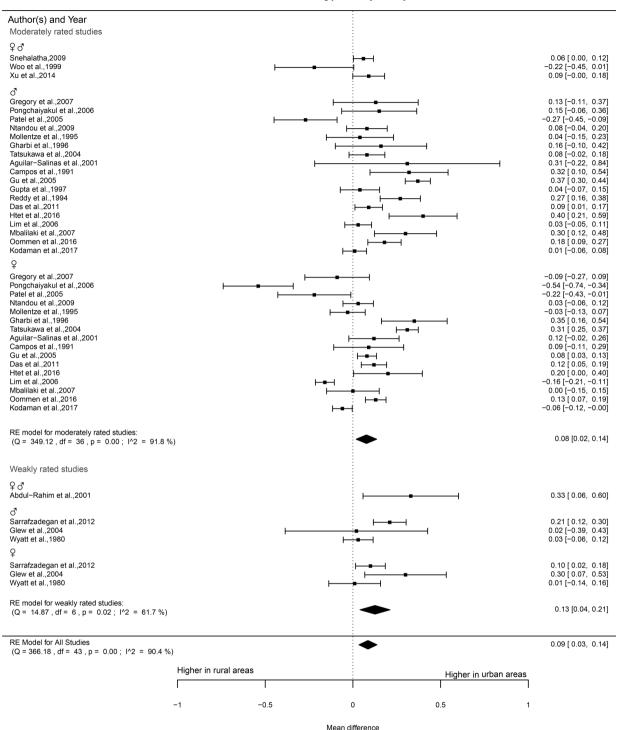


Figure 7 Forest plot triglycerides.

adjustment for potential confounding variables such as age, sex and socioeconomic position. Reliance on the quality as well as the reporting, of the original studies is, however, an inherent aspect of any systematic review. The large heterogeneity of settings and variation in quality of included studies made pooling of the results and synthesis challenging. However, reporting separately for studies rated as of weak and moderate/high quality provides at least some quantitative assessment

of the overall association. Moreover, the findings were quite consistent, even across different time periods. The distribution curve for population blood lipid levels likely changed in the timespan that the included studies were published in 1980–2017. However, as we investigate associations of urban versus rural areas with these blood lipid levels, changes in population levels over time may not have a large impact. Another potential limitation is that there is no generally accepted definition of

urban and rural. The majority of the included studies merely provided names of places and abstained from providing any definition of concepts or explaining why certain places were considered to be either rural or urban. Even when studies referred to census data, these data were not comparable between studies. It is, therefore, unclear as to whether relative rurality in a certain country is linearly associated with blood lipid levels or if there is a more absolute threshold level.

This comprehensive review shows a consistent association between LDL and TC and triglyceride levels and urban areas. The current focus of research on built-environment characteristics and blood lipids is largely on urban and rural differences, especially in LMIC. The lack of evidence on the association between urbanisation and blood lipid levels in more high-income countries needs to be addressed. Further study of the way in which urbanisation affects blood lipid levels is warranted in order to better inform and guide policy makers and urban planners to help diminish unfavourable blood lipid levels and, in doing so, combat associated non-communicable disease.

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Contributors RdG, KvdH, WLAMdK, JB and JL conceived and designed the study. RdG, LJS and JL developed the search strategy. RdG and JL screened and performed the assessment of bias. RdG extracted the data. RdG, KvdH, WLAMdK, JB and JL interpreted the data. All authors gave final approval of the version to be published and have contributed to the manuscript. RdG is the guarantor.

Funding This study was financially supported by a Product and Process Development Grant (PPOC-14-028) from Sanquin Blood Supply Foundation and by the VU University Medical Center.

Competing interests None declared.

Patient consent for publication Not required.

Data sharing statement The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

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