Cycling is associated with a lower incidence of cardiovascular diseases and death: Part 1 – systematic review of cohort studies with meta-analysis

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ABSTRACT

Objectives Physical inactivity is a risk factor for cardiovascular disease (CVD). Cycling as a physical activity holds great potential to prevent CVD. We aimed to determine whether cycling reduces the risk of CVD and CVD risk factors and to investigate potential dose-response relationships.

Design Systematic review and meta-analysis of quantitative studies.

Eligibility criteria for selecting studies We searched four databases (Web of Science, MEDLINE, SPORTDiscus and Scopus). All quantitative studies, published until August 2017, were included when a general population was investigated, cycling was assessed either in total or as a transportation mode, and CVD incidence, mortality or risk factors were reported. Studies were excluded when they reported continuous outcomes or when cycling and walking were combined in them. We pooled adjusted relative risks (RR) and OR. Heterogeneity was investigated using I.

Results The search yielded 5174 studies; 21 studies which included 1,069,034 individuals. We found a significantly lower association in combined CVD incidence, mortality and physiological risk factors with total effect estimate 0.78 (95% CI (CI): 0.74–0.82; P<0.001; I^2=58%). Separate analyses for CVD incidence, mortality and risk factors showed estimates of RR 0.84 (CI, 0.80 to 0.88; P<0.001; I^2=29%), RR 0.83 (CI, 0.76 to 0.90; P<0.001; I^2=0%), and OR 0.75 (CI, 0.69 to 0.82; P<0.001; I^2=66%), respectively. We found no dose-response relationship or sex-specific difference.

Conclusions Any form of cycling seems to be associated with lower CVD risk, and thus, we recommend cycling as a health-enhancing physical activity.

Systematic review registration Prospero CRD42016052421.

What is already known?

- The rise of non-communicable diseases is a growing challenge worldwide.
- Physical inactivity is associated with CVD as well as its risk factors.
- Thus, it is necessary to increase physical activity levels by means of multi-sectorial and multidisciplinary public health actions.
- Active transport may be a promising approach to increase levels of physical activity and reduce CVD risk.

What are the new findings?

- Cycling was associated with 22% lower risk of combined CVD risk than using passiv transport.
- There was no sex-difference or dose-response relationship of cycling and risk of CV
- Politicians, stakeholders and city planners may promote cycling as public health action.

INTRODUCTION

The rise in non-communicable diseases (NCDs) is a growing challenge worldwide.[1 2] In 2016, cardiovascular disease (CVD) was one of the five leading causes of years of life lost.[3] Physical inactivity is associated with CVD and CVD risk factors,[4 5] and the WHO has declared physical inactivity the fourth leading risk factor for global mortality.[6] Approximately a quarter of the world's adults are physically inactive.[7] Globally, the level of physical activity has decreased over previous decades[8] and is still decreasing.[7] Multi-sectorial and multidisciplinary public health actions are needed to tackle the problem of physical inactivity.[9]

Changes in the built environment are likely to increase the activity level among children and adults.[10] Walking and cycling separately, adjusted for other physical activity, may reduce the all-cause mortality at a population level.[11] Active transportation may also reduce the incidence of NCDs, including CVD.[8] Therefore, active transportation may be a promising approach to increase physical activity levels and reduce CVD risk. In addition, cycling as transportation may appeal to many people who are not interested in participating in sport as a means of being physically active.

One limitation of research studies investigating active transportation is that they often combine walking and cycling.[12] This is a problem since cycling often is performed at a higher exercise intensity than walking,[13] and higher exercise intensity is associated with a further reduction in risk of coronary heart disease.[14] Therefore, cycling may be more effective than walking in preventing CVD.[12] To our knowledge, there has not been a meta-analysis examining prevention of CVD and cycling. Nevertheless, there are two meta-analyses examining CVD and active transport[15 16] and one literature review of cycling.[12] Therefore, this systematic review with meta-analysis of cycling and CVD adds increased power to investigate the association, as data are pooled, and accounts better for

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the observed heterogeneity than when walking and cycling are combined.

We aimed to assess the strength of association between cycling and (1) CVD and (2) CVD risk factors. We hypothesised there would be similar associations for men and women, and a dose-response relationship between cycling and health.

METHODS

We conducted a systematic review with meta-analysis. The protocol was registered with the PROSPERO database on 6 December 2016 (PROSPERO ID: CRD42016052421) (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42016052421) and complied with Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 guidelines.[17]

Literature search

We searched for published quantitative studies (prospective, retrospective, cohort, longitudinal design and cross-sectional studies or randomised controlled trials) that examined the association of cycling with CVD or CVD risk factors to 8 August 2017. The first author (SN), in cooperation with a librarian, performed the search. Published and peer-reviewed articles in English were identified from four electronic databases: Web of Science, MEDLINE, SPORTDiscus and Scopus. The search strategy consisted of the terms 'cycling' OR 'bicycling' OR 'biking' OR 'commuter cycling' AND 'CVD' OR 'CVD risk factors' OR 'CVD risk factor' OR 'cardiovascular disease risk factors' OR 'cardiovascular disease' OR 'cardiovascular diseases' OR 'cardiovascular disease*." In total, 5174 records were identified: Web of Science (3525), MEDLINE (via EBSCO) (522), SPORTDiscus (41)and Scopus (1086). After elimination of duplicates, 4785 records remained (figure 1).[17] See online supplementary table 1, for example, of full search strategy run in MEDLINE via EBSCO. We searched the reference lists of included studies and contacted experts in the field to identify any studies that may have been missed in our electronic database search.

Inclusion criteria and selection process

Studies were excluded if they measured domains other than cycling, such as stationary cycling, or if cycling was a part of a rehabilitation programme/intervention or investigated an unhealthy population. We had no criteria for sample size.

We included studies that (1) employed a quantitative design and studied a general population; (2) assessed cycling exposure either as a mode of transportation, or as a recreational activity; (3) measured CVD, CVD mortality or physiological CVD risk factors as an outcome and (4) reported dichotomous outcome measures.

Two reviewers (SN and AR) independently assessed the studies for eligibility with subsequent consensus by discussion.

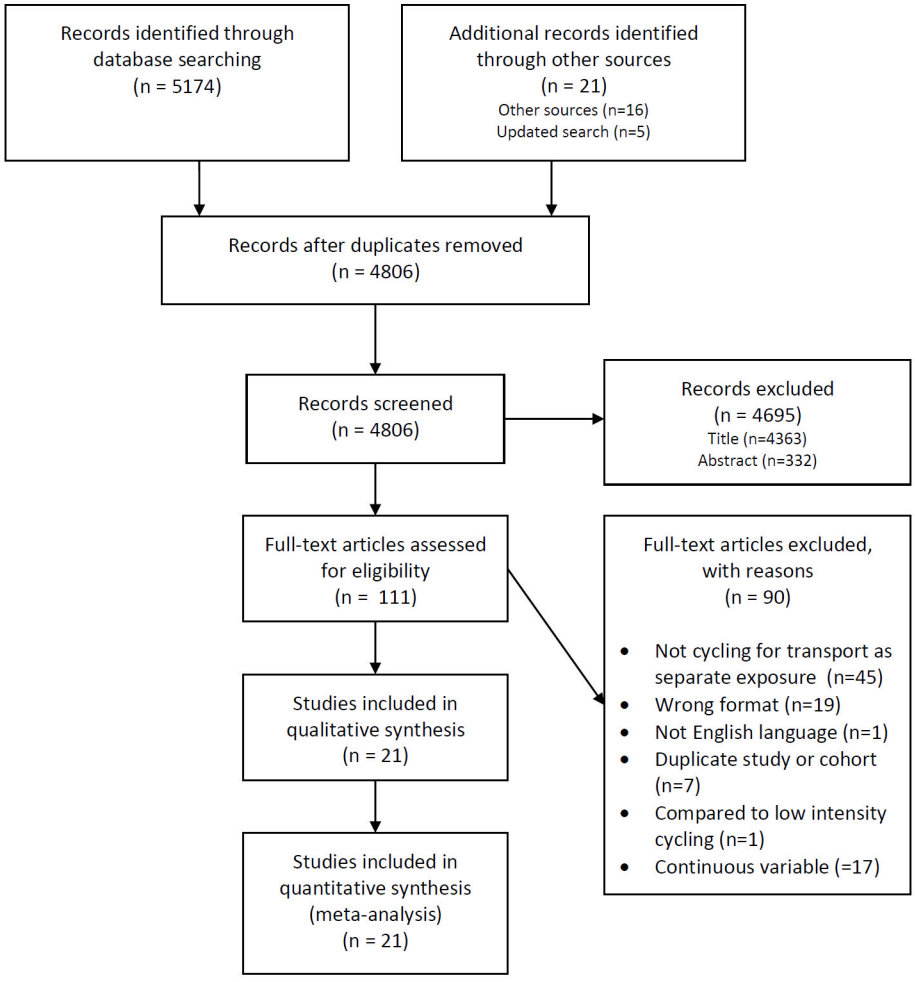

Figure 1 Flow chart of included studies as proposed by Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement 2009.[17]

Table 1 Quality assessments of included studies based on the Quality Assessment Tool of Quantitative Studies[18]

Study	Selection bias	Study design	Confounding factors	Blinding	Data collection	Withdraws and drop-outs	Global rating*
Hoevenaar-Blom *et al*[19]	Weak	Moderate	Strong	NA	Moderate	Strong	Moderate
Koolhaas *et al*[20]	Weak	Moderate	Strong	NA	Moderate	Moderate	Moderate
Armstrong *et al*[21]	Moderate	Moderate	Moderate	NA	Strong	Weak	Moderate
Blond *et al* [22]	Weak	Moderate	Strong	NA	Moderate	Moderate	Moderate
Andersen *et al* [23]	Weak	Moderate	Strong	NA	Moderate	Strong	Moderate
Celis-Morales *et al* [24]	Weak	Moderate	Strong	NA	Moderate	Strong	Moderate
Matthews *et al*[25]	Strong	Moderate	Strong	NA	Moderate	Strong	Strong
Besson *et al*[26]	Weak	Moderate	Moderate	NA	Moderate	Weak	Weak
Oja *et al*[27]	Moderate	Moderate	Strong	NA	Moderate	Strong	Strong
Sahlqvist *et al*[28]	Moderate	Moderate	Strong	NA	Moderate	Moderate	Strong
Grøntved *et al*[29]	Moderate	Moderate	Strong	NA	Moderate	Moderate	Strong
Laverty *et al*[30]	Weak	Weak	Strong	NA	Moderate	NA	Weak
Wen *et al*[31]	Moderate	Weak	Strong	NA	Moderate	NA	Moderate
Østergaard *et al* [32]	Moderate	Weak	Moderate	NA	Weak	NA	Weak
Bere *et al*[33]	Weak	Moderate	Moderate	NA	Moderate	Weak	Weak
Sahlqvist *et al* [34]	Weak	Weak	Strong	NA	Moderate	NA	Weak
Millett *et al*[35]	Moderate	Weak	Strong	NA	Moderate	NA	Moderate
Berger[36]	Weak	Weak	Moderate	NA	Weak	NA	Weak
Evenson *et al* [37]	Moderate	Weak	Strong	NA	Moderate	NA	Moderate
Hu *et al*[38]	Strong	Weak	Moderate	NA	Moderate	NA	Moderate
Ramirez-Velez *et al*[39]	Strong	Weak	Moderate	NA	Moderate	NA	Moderate

*Weak, moderate and strong indicated poor, moderate and high study quality, respectively.
NA, not applicable.

Risk of bias assessment

The included studies were assessed according to the Quality Assessment Tool of Quantitative Studies.[18] SN and AR independently assessed each study. Any case of disagreement was resolved by discussion. The tool consists of six components: representativeness of the target group, study design, confounding factors, blinding of both assessors and participants, reliability and validity of measures and number of withdrawals and drop-outs. Each component was rated 'weak', 'moderate' or 'strong' following a standardised rating system, where 'weak' and 'strong' indicates poor and high quality, respectively. Studies with no weak components were rated as 'strong', studies with one weak component were rated as 'moderate' and studies with more than one weak component were rated as 'weak'. For detailed information of distribution of study quality, se table 1 .[19–39]

Contact with authors

We (SN or LBA) contacted the corresponding author when there was a lack of clarity or when additional information was needed.[39]

Data extraction and main analysis

Data extraction was conducted by SN based on the main estimate exposure, which was defined in accordance with the protocol as any cycling. Main outcomes were defined a priori as CVD mortality, CVD incidence and CVD risk factors. CVD and coronary heart disease were treated as CVD for both CVD mortality and CVD incidence. In studies where relative risk (RR) was presented with more than one model of adjustment, the most conservative estimate was included. If both CVD mortality and CVD incidence were reported,[24] CVD incidence was included due to higher numbers of cases.

For single risk factors, each risk factor was included in the main estimate, but not when both 'overweight or obese' and 'obesity' were reported in a single study. In this case, only 'overweight or obese' was included due to higher numbers of cases. If studies only reported high and low dose or reported men and women separately or reported more than one level of dose, we meta-analysed each study and included the combined estimate (online supplementary table 2).

Among those 10 studies reporting either CVD mortality or CVD incidence only, the following was analysed: (1) CVD incidence and total cycling,[24] (2) CVD incidence and estimated total cycling,[20–22] (3) CVD mortality and estimated total cycling,[28] (4) CVD mortality and estimated commuter cycling,[25 26] (5) CVD mortality and total cycling[23 27] and (6) CVD incidence and estimated commuter cycling.[19] We included only the estimate of highest statistical power from each study. This was important to ensure that individuals were included in the meta-analysis only once.

Data extraction subgroup analysis

Due to a wide range in reporting of exposure and outcomes, we classified exposure as total cycling or commuter cycling. Outcomes were classified by subgroups for CVD mortality, CVD incidence, grouped CVD risk factors, and single CVD risk factors. CVD risk factors were only analysed when reported by ≥2 studies (online supplementary table 4). This resulted in subgroup analyses of (1) overweight or obese, (2) obesity, (3) hypertension, (4) HDL-cholesterol level and (5) triglyceride level. See table 2 for details of classifications of risk factors. We analysed hypertensive versus not hypertensive. All subgroups were analysed for men, women and men and women combined.

Dose-response

Each study was individually recoded into low-dose and high-dose cycling when possible. Low dose was defined as the lowest amount of cycling reported, and high dose was defined as

Table 2 Characteristics of included studies.

Study	Design/cohort /countries	Type of cycling	Population	Dates/years of follow up	Total N	Incidence /death	Outcome	Prevalence of cycling (%) Total/low/high	RR/OR (95% CI)	Dose	
										Low	High
Hoevenaar-Blom *et al*[19]	Prospective cohort/MORGAN/ The Netherlands	Commuter	Men, women; Aged 20–65 y at baseline	1993–2006/9.8	16442	923/NA	Incidence	75%/19%/5%	0.82 (0.73 to 0.92)	Regular cycling	>2.5 hour/wk
Koolhaas *et al*[20]	Prospective cohort/Rotterdam study/ The Netherlands	General	Men, women; aged>55 y at baseline	1997–2012/10.3	5901	642/NA	Incidence	58%/32%/26%	0.78 (0.67 to 0.91)	13 min/day	51 min/day
Armstrong *et al*[21]	Prospective cohort/ Million Women Study/ United Kingdom	Total	Women; Aged 55.9 (SD 4.8) y at baseline	1998/9	497857	6815/NA	Incidence	Not reported*	0.84 (0.80 to 0.88)	>0–2 hour/wk	>2 hour/wk
Blond *et al* [22]	Prospective cohort/ Diet, Cancer and Health/ Denmark	Overall, commuter	Men, women; Aged 50–65 y at baseline	1993–2013/20	53723	2892/NA	Incidence	Not reported	0.87 (0.82 to 0.93)	>0–2.5 hour/wk†	>2.5 hour/wk†
Andersen ZJ *et al*[23]	Prospective cohort/ Diet, Cancer, and Health/ Denmark	Commuter, leisure time	Men, women; Aged 50–65 y at baseline	1993–2010/13	52061	NA/1285	Mortality	68%/NA/NA	0.78 (0.69 to 0.88)	No dose reported. 3.2±3.4 hour/wk	
Celis-Morales *et al*[24]	Prospective cohort/ UK Biobank/ United Kingdom	Commuter	Men, women; 40–69 y at baseline	2007–2014/5	263540	1110/496	Incidence, mortality	3%/NA/NA	0.54 (0.33 to 0.88)	Short ‡	Long ‡
Matthews *et al*[25]	Prospective cohort/ Shanghai Women's Health Study/ China	Commuter	Women; Aged 40–70 y at baseline	1997–2004/5.7	67143	NA/251	Mortality	NA/19%/5%	0.72 (0.42 to 1.23)	0–1–3.4 METh/day	>3.5 METh/day
Besson *et al* [26]	Prospective cohort/ EPIC-Norfolk/ United Kingdom	Commuter	Men, women; Aged 45–79 y at baseline	1993–2006/7	14903	NA/370	Mortality	NA/NA/NA	0.77 (0.51 to 1.15)	<30 min/wk	>30 min/wk
Oja *et al* [27]	Prospective cohort/ HSE & SHeS/ England, Scotland	Any	Men, women; Aged 30–98 y at baseline	1991–2008/9.2	75014	NA/1909	Mortality	10%/5%/5%	0.93 (0.76 to 1.16)	min/wk low §	min/wk high §
Sahlqvist *et al*[28]	Prospective cohort/ EPIC-Norfolk/ United Kingdom	Commuter, Total	Men, women; Aged 40–79 y at baseline	1993–2011/15.3	22450 Commuter; 13346	NA/1639	Mortality	Total: 30%/NA/NA Commuter: NA/4%/2%	0.86 (0.74 to 1.00)	1–59 min/wk	>60 min/wk
Grøntved *et al*[29]	Prospective cohort/ Västerbottens Health Survey/Sweden	Commuter	Men, women; Aged 43.5 y at baseline	1990–2011/10	23732		Risk factors ¶**†† ‡‡	24%/NA/NA	1; 0.85 (0.73 to 0.99) 2; 0.87 (0.79 to 0.95) 3; 0.85 (0.76 to 0.94)		
Laverty *et al*[30]	Cross sectional/ Understanding society/ United Kingdom	Commuter	Men, women; Aged 16–65 y	NA	20458		Risk factors ¶**	3%/NA/NA	1; 0.63 (0.53 to 0.75) 2; 0.76 (0.56 to 1.01)		
Wen *et al*[31]	Cross-sectional/ New south Wales Adult Health Survey/ Australia	Commuter	Men, women; Aged≥16 y	NA	6832		Risk factors¶¶	3%–10%/NA/NA	1; 0.34 (0.13 to 0.89)		
Østergaard *et al*[32]	Cross sectional/ NA/ Denmark	Commuter	Men, women; Aged 12–16 y		3847		Risk factors¶¶	62%/NA/NA	1; 0.55 (0.42 to 0.72)		
Bere *et al* [33]	Longitudinal/ ENDORSE and Youth in Balance/ The Netherlands, Norway	Commuter	Men, women; Aged 13.2 y at baseline	2005–2008/2	890		Risk factors¶¶	48%/NA/NA	1; 0.44 (0.21 to 0.88)		

Continued

Table 2 Continued

Study	Design/cohort /countries	Type of cycling	Population	Dates/years of follow up	Total N	Incidence /death	Outcome	Prevalence of cycling (%) Total/low/high	RR/OR (95% CI)	Dose	
										Low	High
Sahlqvist *et al*[34]	Cross-sectional/ Bicycle Victoria/ Australia	Commuter	Men, women; Aged≥18 y	NA	1813		Risk factors¶	100%/NA/NA	1; 0.67 (0.50 to 0.90)		
Millett *et al* [35]	Cross-sectional/ Indian Migration Study/ India	Commuter	Men, women; Aged≥18 y	NA	3902		Risk factors¶**	45%–68%/NA/NA	1; 0.66 (0.55 to 0.77) 2; 0.51 (0.36 to 0.71)		
Berger *et al*[36]	Cross-sectional/ TCCS/ United States	Commuter	Men, women; Aged 20–64 y	NA	1450		Risk factors¶**††‡‡	100%/NA/NA	1; 0.69 (0.58 to 0.82) 2; 0.67 (0.50 to 0.90) 3; 0.72 (0.59 to 0.88) 4; 0.85 (0.67 to 1.07)		
Evenson *et al*[37]	Cross-sectional/YRBS/ United States	Commuter	Men, women; Youth in 6th–12th grades	NA	4448		Risk factors¶	13%/NA/NA	1; 0.71 (0.52 to 0.98)		
Hu *et al*[38]	Cross-sectional/ NA/China	Commuter	Men, women; Aged 20–49 y	NA	3708		Risk factors††‡ ‡	11%–19%/NA/NA	3; 0.71 (0.52 to 0.98) 4; 0.90 (0.66 to 1.23)		
Ramirez-Velez *et al*[39]	Cross-sectional/ FUPRECOL/Colombia	Commuter	Men, women; Aged 9–17.9 y	NA	1568		Risk factors†††‡	23%/NA/NA	3; 1.06 (0.81 to 1.37) 4; 1.03 (0.83 to 1.23)		

Risk factors:
*States that cycling is infrequent in this cohort.
†Commuter cycling: Low dose=0–1.5 hour/week; High dose >1.5 hour/week
‡Split into groups according to distance.
§Groups defined by using the sex-specific medians.
¶) Body mass index (BMI), overweight ≥25, and obesity ≥30 according to the WHO.[43]
** Hypertension (self-reported or doctor-diagnosed[30 36] or systolic blood pressure or diastolic blood pressure >140 and>90 mm Hg, and/or use of antihypertensive medications.[29]
††) Hypertriglyceridemia (>1.7 mmol/L,[29] self-reported or doctor diagnosed,[36] adverse log transformed scale,[38] or 'high triglycerides' not defined.[39]
‡‡) Low high-density lipoprotein level (self-reported or doctor-diagnosed,[36] adverse scale[38] or low high-density lipoprotein level (Friedwald formula).[39]
METh, metabolic equivalent hours.; NA, not applicable; RR, relative risk; wk, week.

the highest dose reported (table 2, characteristics of included studies). For the study by Blond *et al*,[22] low dose was generated after meta-analysis of low (>0–1 h/week) and moderately low (1–2.5 h/week) cycling. The dose-response relationship was analysed for total cycling and commuter cycling. When both CVD incidence and CVD mortality were reported,[24] CVD incidence was included in the dose-response analysis.

We reanalysed the dose-response relationship in post-hoc analysis by redefining the criteria for low and high dose. First, we redefined the cut-off for high dose as >1 h/week, then as >2 h/week and finally we analysed at three dosage levels.[21]

Statistics

In all analyses, we ensured that individuals were not analysed more than once for the same outcome, that is, 'overweight or obese' and 'obesity.' Due to this, studies were only included once for CVD incidence and CVD mortality but may have been included in different subgroup analyses or for equivalent CVD risk factors. For analyses of CVD incidence or CVD mortality, we calculated pooled RR or pooled HR. For analyses of each CVD risk factor, we calculated adjusted OR.

All analyses were performed in Stata v.12.1 (StataCorp LP, USA), using user-written commands described by Egger *et al*.[40] The estimates are presented as multivariate adjusted RR (CVD incidence and CVD mortality) or OR (CVD risk factors) with 95% CIs.

We used random effect models.[40] Dose-response relationships and differences between sexes were analysed using meta-regression and presented as β-coefficients and P values. Heterogeneity was assessed using the I^2 statistic, Q (Cochran's heterogeneity test) and P value. The I^2 statistic was calculated using Stata based on Q and df.

$I^2 = 100\% \times (Q - df)/Q$

As proposed by Higgins *et al*,[41] I^2 describes the percentage of total variance across studies, with values between 0% and 100%, where 0% indicates no heterogeneity. Negative values were set equal to zero.[41] Heterogeneity was tested in all analyses, but should be interpreted with caution when few studies were analysed due to the possibility of false homogeneity.[41]

Following the rule of thumb described by Sterne *et al*,[42] the test for funnel plot asymmetry was only used when there were more than nine studies in the meta-analysis (figure 2). Sensitivity analyses, tests for heterogeneity and regression analyses are presented in online supplementary table 5a-12b.

Small-study effect

The small-study effect was investigated for the total estimate CVD using the 'metabias' and 'metainf' commands as described by Egger *et al*.[40] We also performed subgroup analyses for study quality and for CVD incidence compared with CVD mortality.

Role of the funding source

There was no funding source for this systematic review.

RESULTS

In total, 38 studies fulfilled the primary inclusion criteria. As the present meta-analysis comprises dichotomous outcomes only, 17

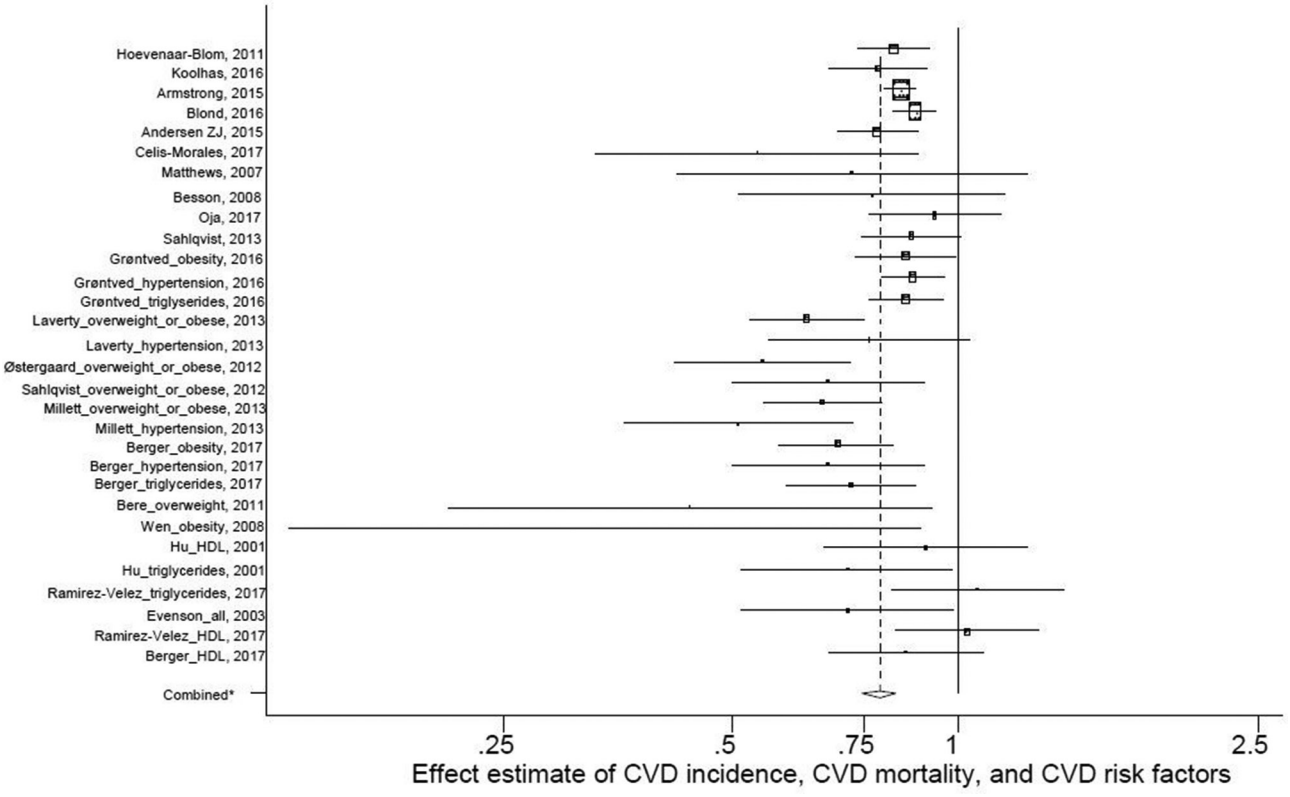

Figure 2 Forest plot of the main analysis of cycling on CVD incidence (risk ratio), CVD mortality (risk ratio), and CVD risk factors (OR). *The combined random effect estimate was 0.783 (CI: 0.744 to 0.824) for CVD incidence, CVD mortality and CVD risk factors combined, indicated by the diamond in the bottom of the diagram. The combined estimate was statistically significant, but were moderately heterogeneous (I^2=58%). From the top, the first ten studies are either CVD incidence or CVD mortality estimates, and the latter studies are CVD risk factors. See table 2 details of included studies.

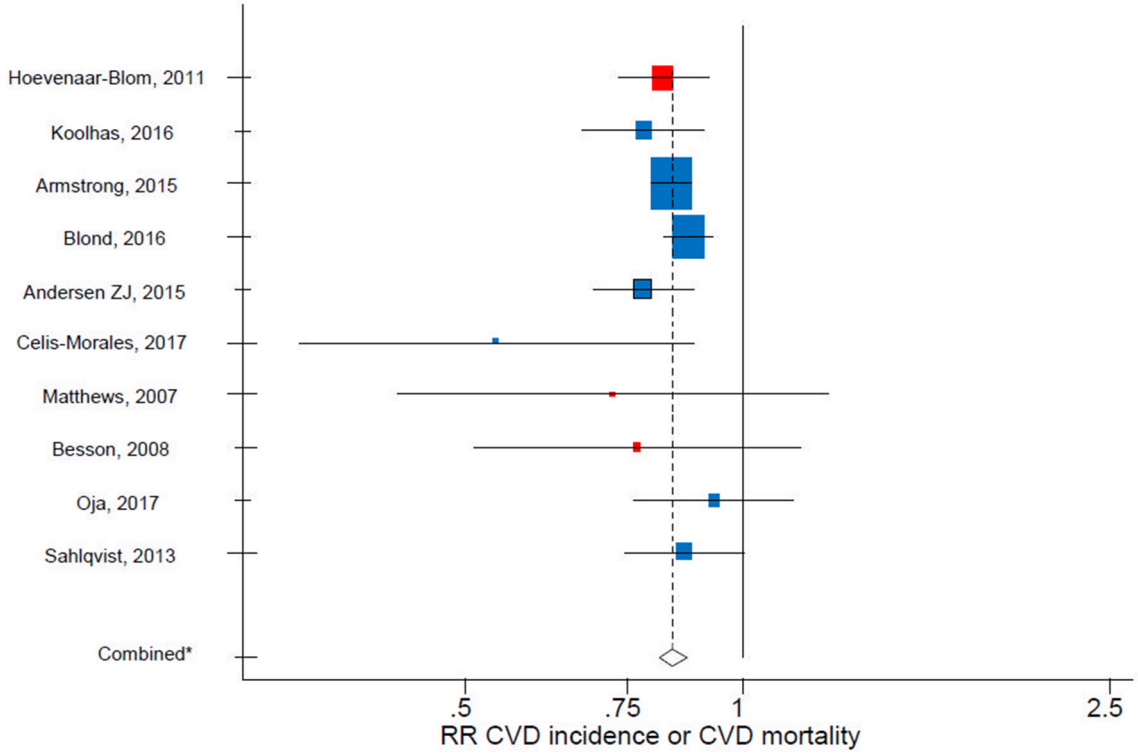

Figure 3 Forest plot of sensitivity analysis of main analysis on CVD incidence and CVD mortality. Total cycling is indicated by blue colour, and commuter cycling is indicated by red colour. *The combined random RR was 0.840 (CI: 0.812 to 0.868, I^2=0%) for CVD Incidence and CVD mortality, indicated by the diamond in the bottom of the diagram. For CVD incidence the combined RR was 0.837 (0.797–0.880, I^2=30%), and for mortality the combined RR was 0.827 (0.761–0.899, I^2=0%). The inconsistent result of homogeneity is most likely due to few studies in the separate analysis.

studies with outcomes presented only as continuous variables were excluded. Thus, the present meta-analysis included 21 studies (figure 1). Data were reanalysed of high-density lipoprotein (HDL)-cholesterol and triglyceride levels from the study of Ramírez-Vélez *et al*[39] due to lack of clarity.

In total, 1,069,034 individuals from eight different cohorts and four different countries were included in the analysis of CVD incidence and CVD mortality. The estimates were based on 12,382 incidents and 5950 deaths during a follow-up time of 9.8±4.9 years. Further, 72,648 individuals from 10 countries were analysed for one or more CVD risk factors. figure 1 presents detailed information regarding the review process and exclusions. table 2 summarises the characteristics of the 21 included studies.[19–39]

Main analysis of outcome

For the overall analysis of CVD incidence, CVD mortality and CVD risk factors, there was a significant total effect estimate of 0.78 (95% CI: 0.74 to 0.82, P<0.001; I^2=58%, Q P<0.001) (figure 2). The RR for CVD incidence was 0.84 (0.80–0.88, P<0.001; I^2=30%, Q P=0.22). The RR for CVD mortality was 0.83 (0.76–0.90; P<0.001; I^2 <0%, Q P=0.58). The OR for CVD risk factors was 0.75 (0.68–0.82; P<0.001; I^2=64%, Q P<0.001).

Sensitivity analysis of total cycling and commuter cycling in the main analysis

For total cycling, there was a RR of 0.80 (0.71–0.90, P<0.001; I^2=45%, Q P=0.16) for CVD incidence and a RR of 0.84 (0.71–0.99, P=0.037; I^2=53%, Q P=0.14) for CVD mortality (figure 3). For commuter cycling, there was a RR of 0.86 (0.85–0.91, P<0.001; I^2 <0%, Q P=0.33) for CVD incidence, a RR of 0.84 (0.74–0.97, P=0.014; I^2 <0%, Q P=0.73) for CVD mortality and an OR of 0.75 (0.69–0.82, P<0.001; I^2=66%, Q P<0.001) for CVD risk factors (figure 3).

Subgroup analysis of total cycling

CVD incidence and CVD mortality

When performing subgroup analysis of total cycling, we found a RR of 0.806 (0.741–0.877, P<0.001; I^2=41%, Q P=0.132) for combined CVD incidence and CVD mortality. Subgroup analysis showed similar results when CVD incidence was analysed separately, with a RR of 0.800 (0.712–0.899, P<0.001; I^2=45%, Q P=0.162). Matthews *et al*[24] analysed women only, and no studies analysed men separately. No studies reported results for combined or single risk factors of total cycling, and thus, all analyses of risk factors were derived from commuter cycling; see online supplementary table 10a-12b for sex differences.

CVD risk factors only

No study reported total cycling and CVD risk factors.

Subgroup analysis of commuter cycling

CVD incidence, CVD mortality and CVD risk factors

A total of 46 different estimates were reported for commuter cycling. When CVD incidence, CVD mortality and CVD risk factors were combined, there was a RR of 0.77 (0.73–0.82, P<0.001; I^2=53%, Q P<0.001). Subgroup analysis including only CVD incidence gave a RR of 0.859 (0.814–0.907, P<0.001; I^2 <0%, Q P=0.465); see online supplementary table 12a-b.

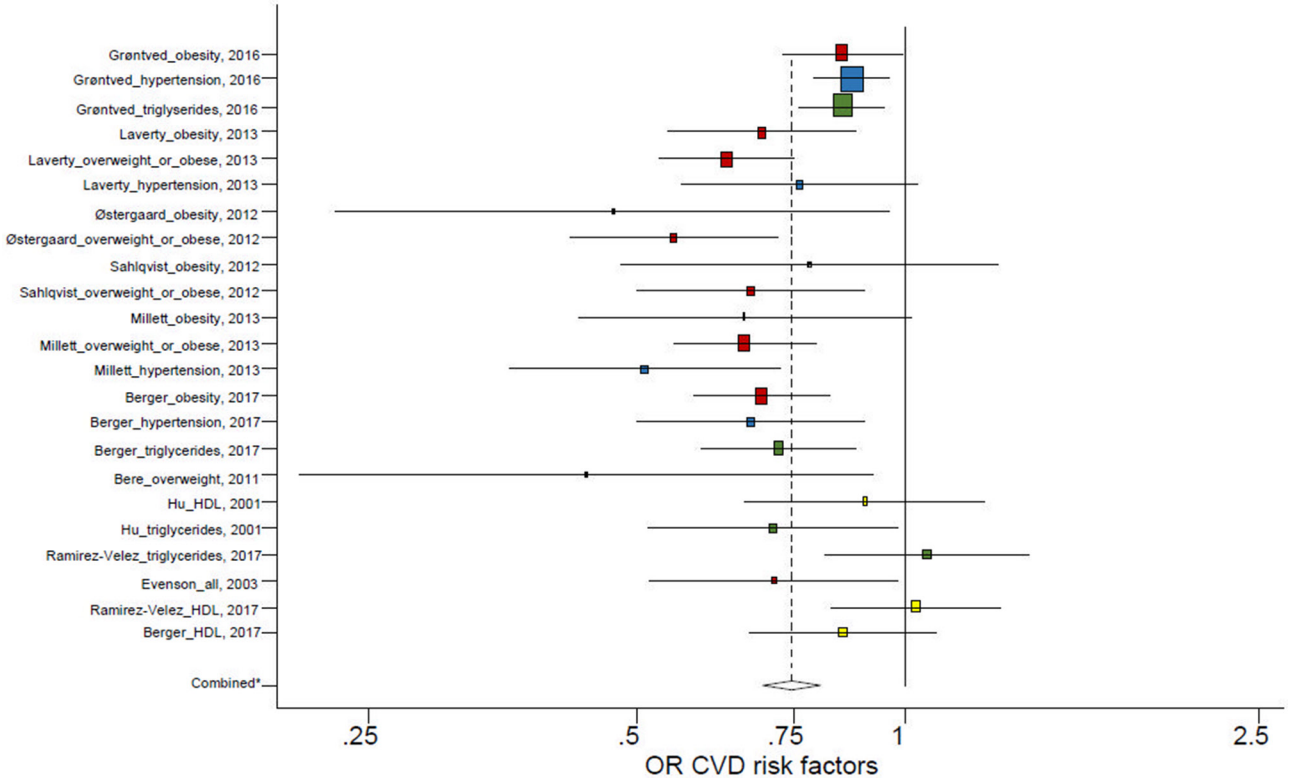

Figure 4 Forest plot of sensitivity analysis of CVD risk factors for commuter cycling. *Combined OR was 0.749 (0.689–0.815, I^2=54%) indicated by the diamond in the bottom. Red boxes indicates overweight or obese, blue box indicates hypertension, green box indicates triglycerides and yellow box indicates HDL. All risk factors independently beside HDL were significant. For detailed information of each outcome see table 6a-b in online supplementary tables.

CVD risk factors only

CVD risk factors were reported for commuter cycling. Overweight and obesity were the most commonly reported risk factors (figure 4), and were classified according to WHO.[43] In total, 'overweight or obese' or 'obesity' were reported 14 times. When analysing 'overweight or obese' and 'obesity,' there was an OR of 0.633 (0.574–0.669, P<0.001; I^2 <0%, Q P=0.814) and OR 0.722 (0.631–0.826, P<0.001; I^2=29%, Q P=0.204), respectively. There was an OR of 0.714 (0.566–0.900, P=0.004; I^2=72%, Q P=0.014) for hypertension, 0.827 (0.712–0.961, P=0.013; I^2=52%, Q P=0.098) for triglyceride level and 0.983 (0.822–1.176, P=0.855; I^2 <0%, Q P=0.502) for HDL-cholesterol level. Triglyceride level remained significant only when analysing men and women combined. HDL-cholesterol was the only risk factor not significant for men, women, or combined.

There was no dose-response relationship for total cycling, commuter cycling or combined total and commuter cycling (online supplementary table 7a-9b). All post-hoc analyses remained nonsignificant (coefficient = −0.010–0.002, P=0.648–0.909).

Small study effects

There was a significant small study effect, indicating possible publication bias (online supplementary figure 1-2).

DISCUSSION

Cycling was associated with a 16% lower risk of CVD incidence, 17% lower risk of CVD mortality and a 25% lower risk of CVD risk factors. When CVD incidence and mortality were combined, cycling was associated with a 22% lower risk. However, the main analysis was heterogeneous (I^2=58%), possibly because we included cross-sectional and prospective studies of populations of children and adults. To assess CVD incidence and CVD mortality, we analysed prospective cohort studies of adult populations.

Our results support those of a previous study of approximately 173,000 adults – that active transportation, especially cycling, reduces CVD risk.[15] We analysed an almost 10-fold larger population and included only cycling as an activity. Our results were slightly more consistent, and we found a stronger association for cycling compared with studies combining walking and cycling. Our results should be of interest for policy-makers and politicians, since they provide evidence of the protective effect of cycling on CVD.

CVD risk factors

In our systematic review, the most commonly reported and most frequently reduced risk factor was overweight or obesity. In a scoping review, Brown *et al*[16] found a small but significant reduction in body mass index with active transportation, but concluded that the effect might be smaller than indicated in the literature. However, in contrast, we found a 36% lower risk in cyclists for both overweight and obesity (OR 0.64, CI: 0.58 to 0.70, I^2=0%) combined, and a 27% lower risk for obesity (OR 0.73, CI: 0.57 to 0.94, I^2=66%). The relatively low heterogeneity could be erroneous, due to a smaller number of studies.[41] Therefore, it is possible that our results overestimate the risk reduction associated with cycling. However, our main analysis is supported by our subgroup analysis of commuter cycling and CVD risk factors (online supplementary table 12a-b), adding strength to our conclusions.

Hypertension was the second most reduced risk factor (OR 0.71, CI: 0.57 to 0.90). Two studies[30 36] defined hypertension based on a self-reported diagnosis by a physician, while Grøntved *et al*[29] used systolic and diastolic blood pressure of >140 and >90 mm Hg, respectively, or usage of antihypertensive medications. Further, risk of high triglyceride level was reduced by 18% for commuter cycling compared with that of passive commuters. Finally, HDL-cholesterol level was the only non-significant, homogeneous risk factor. Cycling therefore seems to be associated with an enhanced CVD profile and thus cycling may be able to prevent CVD incidence or CVD mortality.

Sex differences

In contrast to a previous meta-analysis,[15] we found no evidence that women experienced a greater effect from cycling compared with that of men. In our systematic review, CVD incidence and CVD mortality results were mainly presented in both sexes combined, whereas CVD risk factor results more often included a sex-specific analysis. There was a tendency for women to have greater risk reduction for both high triglyceride and HDL-cholesterol levels compared with men (online supplementary table 10a-12b).

Dose-response relationship

In contrast to previous suggestions,[11 12] we found no difference between low-dose and high-dose cycling. Increased cycling dose was associated with lower CVD risk, especially for commuter cycling and CVD mortality. This is in accordance with the finding of Kelly *et al*,[11] where the steepest risk reduction for all-cause mortality was for 0–101 min per week of cycling, but with further reduction in risk among those cycling >101 min per week.

When analysing the dose-response relationship, there were several challenges. First, we divided each study individually into either high or low doses based on the amount of cycling reported in each study. This resulted in heterogeneity of the definition of low and high dose: high dose in some studies[26 28] was similar to low dose in other studies (See table 2 for details). Second, there were few individuals in high-dose groups compared with those in low-dose groups; this was due to the low prevalence of cycling in general and a lower prevalence of high-dose cycling. Therefore, the results regarding the dose-response relationship should be interpreted with caution. We encourage researchers to be more consistent when creating categories for cycling doses and to report data, including that of low prevalence, in each category.

Strength and limitations

One of the greatest challenges of analysing cycling behaviour is that cycling is not a singular behaviour – often individuals engage in multiple physical activities. This means that people engaged in other forms of activities may be more likely to choose active transport as well. Even though 15 of 21 included studies adjusted for other physical activities, there may be residual confounding from leisure-time physical activity. In addition, in included studies with a low prevalence of cycling, cyclists may be a select group of individuals with superior health (and lower CVD risk profile). However, the majority of included studies adjusted for smoking status, alcohol consumption and level of education (see online supplementary Table 13 for details of adjustments).

Cycling and walking have different benefits such as an increased amount of vigorous activity[12]; therefore, cycling might be more protective than walking. Forty five studies were excluded due to merged groups of walking and cycling. This might be because few of the included studies were designed to evaluate the effect of cycling but rather aimed to register activity levels in large populations. If studies were not primarily designed to investigate the independent association of cycling and CVD, this may explain the publication bias we found in our funnel plot.

All studies used self-reported measurements of cycling and aimed to register physical activity levels. Self-report measurements may have recall bias, and social desirability bias by over-reporting of activity and underestimation of body weight. There was evidence for a small-study effect, and studies of negative results were less likely to be published.[40] This may have influenced our results by increasing the possibility that we overestimated the true association between cycling and CVD. On the other hand, the main analysis was primarily based on high-quality studies that consistently reported positive associations between cycling and reduction in CVD incidence and mortality. However, the results were less certain for the association between cycling and CVD risk factors since the studies included in those analyses were of moderate and low quality.

CONCLUSION

Cyclists had lower risk of CVD incidence, CVD mortality and some CVD risk factors. Similar lower risk of CVD were observed for men and women. Health professionals, city planners and stakeholders can recommend cycling to prevent CVD and should aim to increase the amount of any cycling.

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