Cycling and cardiovascular disease risk factors including body composition, blood lipids and cardiorespiratory fitness analysed as continuous variables: Part 2—systematic review with meta-analysis

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ABSTRACT

Objectives We aimed to examine the relationship between cycling (particularly commuter cycling) and risk factors associated with cardiovascular diseases (CVDs) including body composition, blood lipids and cardiorespiratory fitness. This study differed from our recent (Part 1) systematic review in that risk factors for CVD were analysed as continuous variables rather than being present or absent.

Design Systematic review and meta-analysis.

Eligibility criteria 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 risk factors were reported.

Methods We analysed body composition, physical activity (PA), cardiorespiratory fitness (CRF), blood lipids and blood pressure (BP). Skinfold, waist circumference and body mass index were analysed and prioritised in that order when more than one measure were available. PA included measures of counts per minutes, moderate-to-vigorous PA or minutes per week. CRF included results of maximal tests with or without expired air or submaximal test. For blood lipids and BP, separate analyses were run for low-density and high-density lipoprotein, triglycerides, total cholesterol, systolic BP and diastolic BP. Studies were excluded when reporting dichotomous outcomes or when cycling and walking were combined. Heterogeneity was investigated using I^2.

Results Fifteen studies were included; the majority reported commuter cycling. In total, we included 5775 cyclists and 39 273 non-cyclists. Cyclists had more favourable risk factor levels in body composition −0.08 (95% CI −0.13 to −0.04), PA 0.13 (95% CI 0.06 to 0.20), CRF 0.28 (95% CI 0.22 to 0.35) and blood lipids compared with non-cyclists. There was no sex difference in risk reduction.

Conclusion/implication Cycling mitigated the risk factor profile for CVD. A strength of this systematic review is that all the risk factors were analysed as continuous variables. These data provide evidence for practitioners, stakeholders, policy-makers and city planners to accommodate and promote cycling.

Systematic review registration PROSPERO CRD42016052421.

INTRODUCTION

Active travel is associated with reduced all-cause mortality,[1 2] and it could improve the health on a population level.[3] Active travel is inversely associated with obesity at both country[4] and individual levels.[5] Active travel has promising associations with lower levels of cardiovascular disease (CVD) risk factors,[6 7] and it is a feasible form of physical activity for those who do not enjoy sports.[8]

In the systematic review and meta-analysis of Hamer and Chida,[9] active travellers had 11% lower risk of CVD, with a potential for greater effects in women. Further, there appears to be even larger benefits of commuter cycling compared with walking.[10] Commuter cycling is often performed at a higher physical intensity compared with walking for transportation, which may explain the stronger health-enhancing effect.[10]

In our related systematic review and meta-analysis[11] (Part 1 of 2 where this is Part 2), cyclists had a 22% lower risk of CVD incidence, CVD mortality and CVD risk factors presented as dichotomous outcome.[11] To our knowledge, there exists no meta-analysis of studies examining risk factors associated with CVD assessed as continuous variables and cycling. Nevertheless, there is one meta-analysis examining the effect of active travel and CVD as a dichotomous outcome,[7] one scoping review on body weight,[12] and one literature review on cycling and health.[3]

Due to the growing number of published studies concerning active travel and the possible heterogeneity between walking and cycling, this systematic literature review and meta-analysis aimed to summarise the associations of cycling on CVD risk factors of continues outcome variables compared with non-cyclists. We hypothesised a similar dose-dependent association of cycling and risk factor associated with CVD for both men and women.

METHODS

Search strategy and selection criteria

We conducted a systematic review and meta-analysis. The protocol for this systematic literature review and meta-analysis was registered at PROSPERO on 6 December 2016, with registration number CRD42016052421, and complied with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 guidelines.[13]

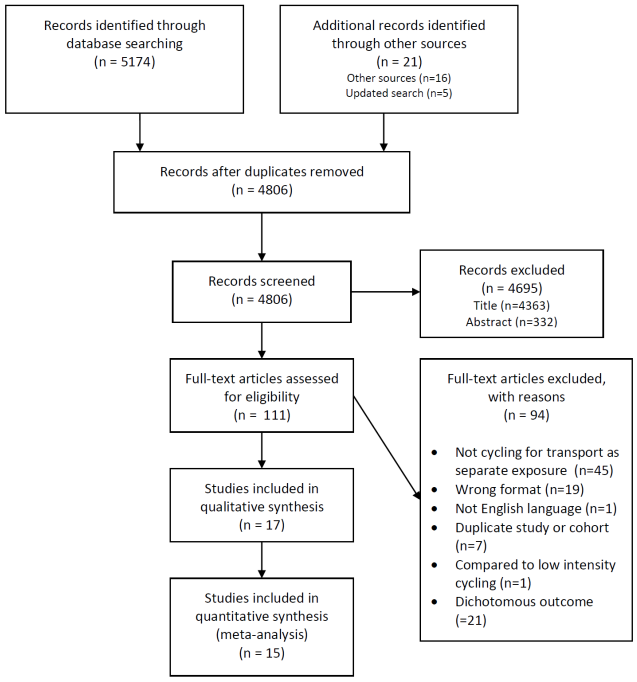

Figure 1 Flow chart of included studies as proposed by Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement 2009.

Literature search

A systematic search of published quantitative studies (prospective, retrospective, cohort, longitudinal design, cross-sectional studies and randomised controlled trials) that examined the association of cycling with CVD or CVD risk factors was performed on 1–2 December 2016. The first author (SN) performed the search in cooperation with a librarian. Published and peer-reviewed articles in English were identified from four electronic databases: Web of Science, MEDLINE, Sport Discus and Scopus. The search strategy consisted of two blocks 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, from Web of Science (3525), MEDLINE (via EBSCO) (522), SPORTDiscus (41) and Scopus (1086). After elimination of duplicates, 4785 records remained (figure 1). See online supplementary table 1 for example of full search strategy.

Inclusion criteria and selection process

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

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 incidence, CVD mortality or physiological CVD risk factors as an outcome; and (4) reported continuous outcome measures.

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. Studies that reported walking and cycling combined were excluded. We had no criteria for sample size.

Included studies

Following screening, 111 studies were selected for full-text eligibility assessment. Among the 111 full-text studies, 16 studies fulfilled the inclusion criteria, while 16 further studies were identified as eligible through the reference lists of included studies. In addition, an updated search was performed on 8 August 2017, when five more studies were included. In total, 36 studies fulfilled the primary inclusion criteria. As the present meta-analysis comprises continuous outcomes only, 21 studies with outcomes presented as dichotomous variables only were excluded. Thus, the present meta-analysis included 15 studies (see figure 1).

Study quality assessment

Included studies were assessed according to the Quality Assessment Tool of Quantitative Studies.[14] AR and SN independently assessed each study. In cases of disagreement of rating, agreement was solved by mutual consensus. For results from the study quality assessment, see online supplementary table 2.

Contact with authors

SN contacted the corresponding author when there was a lack of clarity or when additional information was needed. This resulted in reanalysis of all included outcome measures for de Geus *et al*.[15]

Analysis

Data extraction was conducted by SN based on the main exposure, which was defined in accordance with the protocol as any cycling. Main outcome was CVD risk factors. The risk factors were further categorised in seven categories after a systematic review of all risk factors reported in the included studies: body composition, physical activity, cardiorespiratory fitness (CRF), blood lipids, blood pressure, diet and other physical fitness measures than CRF. For diet[16] and physical fitness other than CRF,[17 18] both categories were excluded from meta-analysis due to too few (≤2) unique studies. In intervention studies lasting more than 6 months,[15 19] we included results from the first 6 months. All outcomes were additionally analysed stratified by design and combined to investigate possible sources of heterogeneity (online supplementary table 4).

Category 1: body composition

The risk factors covering body composition were ranked from high to low quality: (1) skinfold,[17 20 21] (2) waist circumference (WC)[22] and (3) body mass index (BMI).[23–26] To summarise the risk factors covering body composition, we included the most accurate measure in each study by the ranked quality above. In addition to body composition, each risk factor was also analysed in subgroups: skinfold, WC and BMI.

Category 2: physical activity

Physical activity was reported as either counts per minute,[20] daily moderate-to-vigorous physical activity (MVPA)[17 27] or minutes per week (min/week).[23] Physical activity was only analysed with one common analysis. However, meta-regression was used to measure the consistency of results (see table 2). Sedentary time[17] and light physical activity[17] were not meta-analysed due to interference with MVPA and the characteristics of cycling, respectively.

Category 3: cardiorespiratory fitness

CRF was analysed independently of measurement methods. Nevertheless, we ranked the measurement methods from

high to low quality: (1) maximal test with analysis of expired air,[10 15 19 21 23 28] (2) maximal test without analysing expired air[22] and (3) submaximal approach.[17] Meta-regression was run to investigate relationship of measurement quality and effect (see table 2).

Category 4: blood lipids

Four risk factors from blood samples were included: high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG) and total cholesterol (TC). In online supplementary table 3, we standardised the outcomes to SI units for descriptive purposes, and we recalculated HDL, LDL, TG and TC from milligrams per decilitre to millimoles per litre using the factors recommended by the Society for Biomedical Diabetes Research[29]: 0.0259 for HDL and LDL, and 0.0113 for TG, respectively. Total cholesterol was only reported as millimoles per litre. Due to the obvious heterogeneity, that is, higher HDL level indicates a better result, while a higher LDL level would be a worse result, each component was analysed separately.

Category 5: blood pressure

Both diastolic blood pressure (DBP) and systolic blood pressure (SBP) were included. DBP and SBP were analysed separately to ensure that we did not analyse individuals twice (see online supplementary table 3 for details).

Statistics

In all analyses, we ensured that individuals were not analysed more than once. Analyses were performed in Stata V.12.1 (StataCorp LP, College Station, Texas, USA) using user-written commands described by Egger *et al*[30] with random estimate models. The estimates are presented as standardised mean difference (SMD) with 95% CIs. Dose–response relationships were analysed by meta-regression and are presented as β coefficients and p values. Heterogeneity is presented as I^2 and p value. The I^2 was calculated using Stata-derived test for heterogeneity (Cohen's Q) and df:

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

As proposed by Higgins *et al*,[31] 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.[31] Heterogeneity was tested in all analyses. The power of the test increases with higher number of studies, and should be interpreted with caution when low number of studies, due to the possibility of false homogeneity.[31]

Small-study effect

Small-study effect was investigated by regression of effect size (ES) and SE of ES as proposed by Egger *et al*.[32] Asymmetry, which indicates a small-study effect, was defined as p value <0.1 due to limits of the statistical power.[32] As for heterogeneity, tests for small-study effect are vulnerable for type I error when few studies are included.[31 32]

RESULTS

Study characteristics

Fifteen studies were included in the meta-analysis of the present study, where the majority of the studies reported commuter cycling.[15–27] In total, the meta-analysis included 5775 cyclists and 39 273 non-cyclists. Cyclists had more favourable risk factor levels in four of five risk factor categories (body composition, physical activity, CRF and blood lipids) compared with non-cyclists (table 1). Online supplementary table 3 summarises the included studies and distribution of risk factors. Randomised controlled trial (RCT) studies showed a significant improvement for body composition and CRF with SMD −0.99 and 1.06, respectively. However, both outcomes were heterogeneous (I^2=71%–94%); see online supplementary table 4 for details.

Analysis of risk factor categories

Body composition

Cyclists had a consistently lower skinfold, WC and BMI compared with non-cyclists. The combined score of body composition was lower for cyclists, with estimates heterogeneous (figure 2 and table 1). Cycling was associated with enhanced body composition, consisting of either skinfold, BMI or WC (see table 1

Table 1 Main findings: meta-analysis for each outcome measure

Outcome	Number of reported results	Meta-analysis of each outcome			Back transfer from SMD	Test of heterogeneity		Dose–response		
		SMD	95% CI	p value		I^2*	p value	β	95% CI	p value
Combined score of body composition†	13	−0.08	−0.13 to −0.04	**<0.001**	NA	69%	**<0.001**	0.185	−0.46 to 0.83	0.540
Skinfold (mm)	5	−0.09	−0.17 to −0.01	**0.029**	−5.22 mm	88%	**<0.001**	0.453	−3.67 to 4.57	0.749
WC (cm)	6	−0.58	−0.64 to −0.51	**<0.001**	−9.6 cm	99%	**<0.001**	−1.588	−1.81 to −1.38	**<0.001**
BMI (kg/m^2)	12	−0.10	−0.14 to −0.05	**<0.001**	−0.45 BMI	41%	0.069	0.022	−0.11 to 0.16	0.714
Physical activity‡	7	0.13	0.06 to 0.20	**<0.001**	2.99 MVPA	80%	**<0.001**	−0.153	−0.93 to 0.63	0.635
CRF	15	0.28	0.22 to 0.35	**<0.001**	195.63 mL O_2/min	84%	**<0.001**	−0.339	−1.93 to 1.25	0.656
Total cholesterol (mmol/L)	8	−0.06	−0.12 to −0.00	**0.037**	−2.28 mmol/L	43%	0.091	0.014	−0.36 to 0.39	0.928
HDL cholesterol (mmol/L)	7	0.18	0.12 to 0.24	**<0.001**	2.95 mmol/L	24%	0.250	−0.024	−0.23 to 0.16	0.764
LDL cholesterol (mmol/L)	5	−0.15	−0.22 to −0.07	**<0.001**	−5.35 mmol/L	39%	0.161	−0.033	−0.44 to 0.37	0.809
Triglycerides (mmol/L)	8	−0.17	−0.23 to −0.11	**<0.001**	−8.62 mmol/L	20%	0.272	−0.135	−0.47 to 0.19	0.355
DBP (mm Hg)	7	0.03	−0.05 to 0.11	0.405	NA	74%	**<0.001**	0.105	−0.75 to 0.96	0.764
SBP (mm Hg)	7	−0.06	−0.14 to 0.02	0.122	NA	34%	0.172	0.030	−0.79 to 0.86	0.927

Bold font indicates significant results. Dose–response calculated from three levels of exposure (1–3).
*25%, 50% and 75% correspond to low, moderate and high I^2 values, respectively.[31]
†Sample of best measure reported. The risk factors were ranked from high to low quality: (1) skinfold,[18 20 21] (2) waist circumference[22] and (3) BMI.[23–26]
‡CPM, MVPA or min/week.
BMI, body mass index; CPM, counts per minute; CRF, cardiorespiratory fitness; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MVPA, moderate-to-vigorous physical activity; NA, not applicable; SBP, systolic blood pressure; SMD, standardised mean difference; WC, waist circumference.

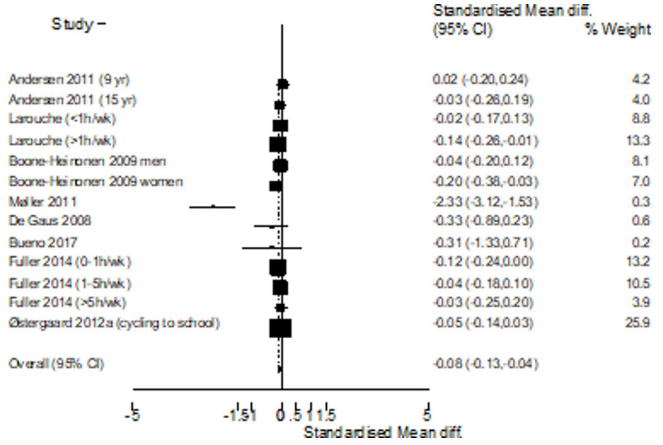

Figure 2 Forest plot of body composition, cyclists vs non-cyclists. Being a cyclist was significantly associated with more favourable body composition compared with non-cyclists, standardised mean difference −0.08 (95% CI −0.13 to −0.04), I^2=69%.

for details). The associations were similar when skinfold, WC and BMI were analysed separately. See online supplementary figures 1–3 for forest plots. Regression analysis of design and SMD showed a relationship where high-quality design (based on quality assessment) was associated with greater effect size in sum of skinfolds (see table 2 for details). Total estimate of combined score of body composition and separate analysis of BMI, skinfold and WC showed all moderate to high heterogeneity. Visually, in the analysis of combined score of body composition, Møller *et al*[21] differed from the rest of the studies. Since Møller *et al* is a RCT, we ran sensitivity analysis excluding RCTs.[10 21 23] The result became homogeneous (I^2=0%, p=0.799) and remained significant, SMD −0.7 (95% CI −0.12 to −0.03, p<0.001). For skinfold, results were also highly heterogeneous. Again, Møller *et al*[21] differed from the other results. When the analysis was run without RCT studies, including Møller *et al*,[21] cyclists no longer had lower sum of skinfold (SMD −0.07 (−0.15 to 0.01), p=0.109). Results, however, became homogeneous, I^2=0%, p=0.514. For WC, Larouche *et al*[17] >1 hour/week was considerably staggered to the left, indicating a higher effect than the rest of the studies. When Larouche *et al*[17] >1 hour/week was excluded from analysis, the result stayed significant (SMD −0.13 (−0.20 to −0.05), p=0.002) and became homogeneous, I^2=0%, p=0.616.

Physical activity

Cyclists were observed to have a significant higher level of other forms of physical activity compared with non-cyclists, with a moderate to high level of heterogeneity. See table 1 for details. We observed a positive correlation of design and observed effect of cycling, so better designed studies had a higher effect size. See table 2 for details.

Cardiorespiratory fitness

In total, 10 studies reported any CRF as a risk factor associated with CVD. Overall, cyclists had a higher CRF compared with non-cyclists (figure 3). However, the results were heterogeneous (table 1). Møller *et al*[21] showed a stronger result than the rest of the analysed studies. When performing meta-analysis excluding RCTs including Møller *et al*,[21] the result remained significant (SMD 0.23 (95% CI 0.16 to 0.29), p<0.001) and became heterogeneous (I^2=52%, p<0.001). Increased quality of design

Table 2 Regression of SMD against study design, study quality, quality of measurement, age at baseline and gender, respectively

	Design		Study quality		Measurement quality		Age at baseline		Gender	
Category	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value
Combined score of body composition*	−0.24 (−0.61 to 0.14)	0.199	0.01 (−0.54 to 0.56)	0.973	NA	NA	−0.01 (−0.04 to 0.02)	0.434	−0.07 (−0.73 to 0.58)	0.808
BMI	0.00 (−0.09 to 0.09)	1.00	0.06 (−0.48 to 0.16)	0.260	NA	NA	0.00 (−0.01 to 0.01)	0.766	0.01 (−0.13 to 0.14)	0.922
Skinfold	**−1.14 (−1.26 to −1.02)**	**<0.001**	−0.70 (−3.88 to 2.48)	0.532	NA	NA	−0.02 (−0.12 to 0.07)	0.525	†	NA
Waist circumference	†	NA	0.77 (−0.62 to 2.16)	0.200	NA	NA	−0.01 (−0.06 to 0.04)	0.584	−0.22 (−1.26; 0.82)	0.594
Physical activity	**0.71 (0.55 to 0.87)**	**<0.001**	0.10 (−1.18 to 1.39)	0.844	0.59 (−0.01 to 1.20)	0.053	0.01 (−0.02 to 0.05)	0.359	†	NA
Cardiorespiratory fitness	**0.45 (0.12 to 0.79)**	**0.012**	0.30 (−0.32 to 0.91)	0.320	**0.55 (0.10 to 1.00)**	**0.021**	0.01 (−0.12 to 0.04)	0.287	0.10 (−0.35 to 0.56)	0.631
Total cholesterol	0.02 (−0.25 to 0.30)	0.851	0.08 (−0.29 to 0.45)	0.601	NA	NA	0.00 (−0.01 to 0.02)	0.645	0.10 (−0.14 to 0.34)	0.362
HDL cholesterol	0.03 (−0.11 to 0.17)	0.653	**−0.16 (−0.29 to −0.03)**	**0.026**	NA	NA	0.00 (−0.00 to −0.01)	0.067	0.52 (−0.07 to 0.18)	0.331
LDL cholesterol	−0.08 (−0.28 to 0.13)	0.329	†	NA	NA	NA	−0.01 (−0.02 to 0.00)	0.150	−0.01 (−0.26 to 0.24)	0.919
Triglycerides	0.18 (−0.02 to 0.37)	0.065	−0.00 (−0.36 to 0.35)	0.983	NA	NA	0.00 (−0.01 to 0.01)	0.767	0.02 (−0.23 to 0.26)	0.868
DBP	−0.15 (−0.44 to 0.14)	0.242	0.09 (−0.52 to 0.69)	0.721	NA	NA	−0.01 (−0.03 to 0.01)	0.167	0.16 (−0.69 to 1.00)	0.657
SBP	−0.13 (−0.41 to 0.15)	0.290	0.02 (−0.56 to 0.61)	0.932	NA	NA	−0.01 (−0.02; 0.01)	0.367	0.03 (−0.08 to 0.87)	0.907

*Sample of best measure reported. The risk factors were ranked from high to low quality: (1) skinfold,[17 20 21] (2) waist circumference.
†Omitted due to collinearity.
‡All analysis was of combined gender.
BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NA, not applicable; SBP, systolic blood pressure; SMD, standardised mean difference.

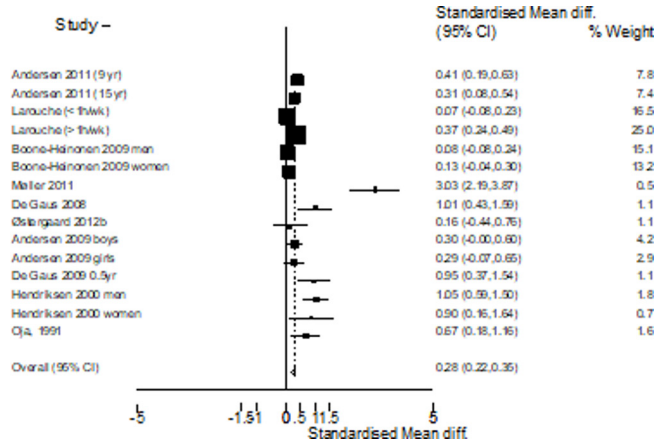

Figure 3 Forest plot of cardiorespiratory fitness, cyclists vs non-cyclists. Being a cyclist was significantly associated with improved cardiorespiratory fitness compared with non-cyclist, standardised mean difference 0.28 (95% CI 0.22 to 0.35), I^2=84%.

was significantly correlated with increased effect of cycling on CRF. Improved measurement quality (direct vs indirect VO_{2max} test) was significantly correlated with effect size. However, the total study quality (based on 'global rating' in online supplementary table 2) was not correlated with the effect size (table 2).

Blood lipids

For blood lipids, we analysed each outcome separately. TC, HDL, LDL and TG were all significantly enhanced in cyclists. TC, LDL and TG were all significantly lower and had low to moderate heterogeneity (see table 1 for details). For cyclists, HDL was found to be SMD 0.18 higher compared with non-cyclists (table 1). See online supplementary figures 4–7 for forest plots. However, the effects were small, SMD −0.06 to −0.17 for TC, LDL and TG, and 0.18 for HDL, and were all slightly heterogeneous (I^2=20%–43%).

Blood pressure

Neither DBP nor SBP were related to cycling (p=0.122 and 0.404, respectively). Low-to-moderate heterogeneity was found for SBP, whereas a high degree of heterogeneity was found for DBP. The number of studies that reported BP were approximately the same as for the other risk factor categories.

Dose–response

All exposure measures had at least two levels of cycling, but only BMI and physical activity had three levels.

WC showed a graded association with level of cycling (β −1.59, p<0.001). Andersen *et al*,[20] Boone-Heinonen *et al*[22] and Larouche *et al*[17] reported WC where only Larouche *et al*[17] reported three levels of cycling. Thus, the relationship should be interpreted with caution.

Small-study effect

A small-study effect was found among half of the outcome measurements: combined score of body composition (β=−2.50, p=0.030), BMI (β=−0.58, p=0.026), skinfold (β=−7.07, p=0.003), physical activity (β=5.98, p=0.006), CRF (β=4.72, p=0.001), total cholesterol (β=−0.92, p=0.024) and triglycerides (β=0.77, p=0.066). A small-study effect was less common among outcomes such as blood lipids and BP.

DISCUSSION

Overall, being a cyclist was associated with a reduced CVD risk compared with non-cyclists, with reductions in four out of five CVD risk factor categories. Notably, the results should be interpreted with caution as only WC and CRF had a small-to-moderate effect in accordance to Cohen's rule of thumb,[33] and the associations were mainly heterogeneous. The health effects of being a cyclist compared with non-cyclist were stronger when RCTs are only considered. Being a cyclist is associated with both improved both body composition (SMD −0.99, 95% CI −1.49 to −0.54) and improved CRF (SMD 1.06, 95% CI 0.85 to 1.28).

To our knowledge, no other studies have meta-analysed cycling and its associations on CVD risk factors such as blood lipids, body composition and fitness measured with continuous outcome variables. However, active travel has been shown to reduce all-cause mortality,[7] CVD[7 11] and CVD risk factors.[11] Although cycling has been shown to be associated with reduced rate of CVD,[11] there is uncertainty as to the effect of cycling on CVD risk factors.[11] Cycling was associated with 18%–33% lower risk of overweight, obesity, hypertension and triglycerides, but results were heterogeneous.[11] In the present study, we found a similar result for continuous variables, but BMI and blood lipids were homogeneous. For other risk factors, the degree of heterogeneity differed between 34% and 99%. Our results underpin the uncertainty of the association between cycling and CVD risk factors by continuous outcome measures.

Among the five CVD risk factor categories, the strongest association of cycling compared with non-cycling was observed for CRF (SMD −0.28, 95% CI 0.22 to 0.35). The result was heterogeneous, I^2=84%. The large degree of heterogeneity was investigated, but the reason for heterogeneity was not clear. We investigated the associations of study design and effect on CRF and found that improved study design was positively associated with the effect. This association was not observed for the global rating for study quality. This indicates an inter-relationship between study design and observed association. The challenge of meta-analysing outcomes from different designs is well known.[30] One major difference between RCT and cross-sectional designs is the possibilities of selection bias and the degree of random sampling. In addition, there is a possibility for recall bias for the cross-sectional studies due to usage of questionnaires, and selection bias for RCT.[30] When we analysed the studies of cross-sectional design separately, the result remained significant, but the degree of heterogeneity was reduced from 84% to 52%. The remaining degree of heterogeneity may be the observed positive association between effect of cycling and measurement quality and the fact that exposure is often controlled better in RCTs.

For single risk factors, the strongest association was observed in the sensitivity analysis of body composition. In our combined score of body composition, the association of cycling was significant with a moderate level of heterogeneity (SMD −0.08, 95% CI −0.13 to 0.04, I^2=69%). When we performed sensitivity analysis of each of the included risk factors, a moderate effect was observed for WC (SMD −0.58, 95% CI −0.64 to −0.51) for any cycling. The result was highly heterogeneous, I^2=99%. The chance of erroneous calculated heterogeneity increases if few studies are analysed.[31] Only six studies were analysed in the WC analysis, and thus the test of heterogeneity might be erroneous. Even though the uncertainty of consistency in analysis of WC, we found no difference between either gender or age (see table 2 for details). When we back transfer the SMD to an adult male population,[22] any cycling can be interpreted as a reduced WC of 9.5 cm.

In our present meta-analysis, cycling was associated with lower BMI compared with non-cyclists. Flint and Cummins[5] found promising results of active travel and its effect on reduction of BMI in mid-life. Our finding is in accordance with previous findings where it has been observed that the reduction may be smaller than previously expected.[12]

Dose–response relationship

We hypothesised that there was a dose–response relationship. Of the 11 outcome measures, only WC showed a dose–response relationship. This is in contrast with previous findings where both active travel[7] and cycling[3] were reported to have a dose–response relationship for health outcomes. When analysing the effect of cycling, there are several challenges. First, when risk factors are analysed by prospective cohorts, there is a great possibility of misclassification[34] and an uncertainty in results and an increased possibility of drawing an erroneous conclusion. Second, the definition of cycling and amount needed to be classified as a cyclist varied among the included studies. The majority of the included studies categorised cycling from self-reported questionnaire, where cycling is defined as the usual mode of travel,[20] mode of travel during the past 3 months,[17 26] 7-day recall about transport modes,[27] dominant mode of transport during summer months,[18] daily commute by cycling over 60 min[35] and amount of weekly recreational cycling.[16] The RCTs also had different definitions of cycling. The definitions varied between definitions of minimum daily time,[21] distances cycled,[15 23] destinations[10 28] and frequency and distance.[19] The definitions of cycling may surely influence the effect of cycling, as more and more frequent cycling is likely to increase effect. The RCT studies were the source of heterogeneity in the combined score of body composition, skinfold and CRF. When we analysed without RCT studies, the result remained significant and became homogeneous. Further, Larouche *et al*[17] seemed to be the source of heterogeneity for WC for the results of cycling more than 1 hour per week. When WC was analysed except Larouche >1 hour, the result remained significant and became homogeneous. This points in the direction that the source of heterogeneity may be the unequal definitions of cycling and that there may be a dose–response relationship even though it was only observed for WC in this meta-analysis.

Gender difference

As we hypothesised, we did not observe gender differences for any of the CVD risk factors in our meta-analysis. There were several challenges when analysing gender differences as only five studies reported separate results for men and women. We therefore recommend researchers to report gender separated data when appropriate.

Strengths and limitations

Our results confirm a previous finding.[2 36] In the present meta-analysis, all risk factors were analysed separately. This provided new and in-depth insight of the effect of cycling for the separate risk factor.

There is a well-known challenge of meta-analysing different designs and types of studies.[30] The possibility of a misleading overall estimate of an association is a problem in general with meta-analysis and bigger when different designs are combined (Egger *et al*[30]). Even though it is appropriate to review a body of data systematically, it may be inappropriate to meta-analyse all designs together. To meet these challenges, Egger *et al*[30] recommend to carefully investigate sources of heterogeneity, such as design and type of study.

The study quality of the included studies was investigated by the Quality Assessment tool of Quantitative Studies.[14] This tool consists of seven categories (selection bias, study design, confounding factors, blinding, data collection, withdraws and drop-outs, and global rating). We used both the overall rating (global rating) and the design score when we by meta-regression investigated the association between study quality and effect size between studies investigating the same outcome variable. The result of this analysis are presented in table 2.

Meta-regression analyses were performed on both design and quality based on our included tool of quality assessment.[14] In general, we did not observe any consistent pattern for systematic dependence of quality. However, we observed that design may be a source of heterogeneity. Therefore, we investigated the heterogeneity for design further (see online supplementary table 4 for details). Systematically, we observed a stronger *effect* of any cycling when RCTs were analysed separately, compared with the *association* observed when all designs were analysed together.

Our aim is to summarise the literature as broadly as possible, and therefore all quantitative studies were included. This approach has some known challenges, but through a careful investigation of heterogeneity, this approach may outweigh the disadvantages of analysis designs combined.[30]

Further, in the present meta-analysis, the population consisted of 15% cyclists. The relatively low number of cyclists may cause selection bias and residual confounding for observational studies. In our analysis, we have consequently included only the most adjusted effect estimate, where almost all included studies were adjusted for other forms of physical activity.

This meta-analysis only comprises published results and thus might be affected by publication bias since unpublished studies often differ from studies that have been published.[37] This might be why we observed a small-study effect for 7 of the 11 included outcomes, which indicated that smaller studies tend to show a greater effect.[30]

Meta-analyses of observational studies are often more distorted by confounding and selection bias than meta-analyses of randomised controlled trials,[30] but they can to a larger degree generalise the results. The inclusion criteria for the present systematic review and meta-analysis were quantitative studies. This means that the observed association might be a result of an underlying confounder due to a large range of designs.[30] Differences in design and adjusted variables may further lead to residual confounding. List of design and adjusted variables per study may be found in supplementary table 5. We are aware of this possible pitfall and therefore analysed all outcomes by regression for both study design, overall study quality and measurement quality. We found

What is already known

- Active travel, including cycling, is associated with increased physical activity and reduced cardiovascular risk factors.

What are the new findings

- Being a cyclist was associated with more beneficial risk factor levels, except for blood pressure, compared with non-cyclists.
- Cycling activity was associated with lower waist circumference (dose dependent).
- The benefits of cycling were equally prominent in women and men.

a significant association for WC, physical activity and CRF (see table 2 for details). Interestingly, better study design improved the association of cycling on physical activity and CRF, but reduced the association of skinfold. For study quality, only HDL had a significant association with effect size and study quality.

Interpretation of results

The present study, which summarises all scientific evidence, shows that known risk factors for CVD are lower in those individuals who undertake cycling. The studies with the highest quality finds the greatest associations. Surprisingly, we did not observe a dose–response relationship or gender differences, even though it is most likely that it is more beneficial to bicycle more. For policy-makers, urban planners and stakeholders, this study provides an argument for the green shift and makes a case for cycling-friendly cities. It may well be that a cycling city is a healthy city.

Conclusion

Cycling was associated with lower levels in CVD risk factors. There was no sex difference or dose-response relationship between amount of cycling and effect size.

Contributors All authors contributed to the design of the study and reviewed the report. SN and LBA generated the hypotheses. SN and AR did the literature search. SN, AR and LBA analysed the data. SN wrote the first draft of the manuscript. LBA, AKS and AR revised the manuscript critically for important intellectual content. All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. LBA is the study guarantor.

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