SYSTEMATIC REVIEW OF LIFE COURSE SOCIAL DETERMINANTS OF HEALTH AND THEIR ASSOCIATION WITH ADULTHOOD METABOLIC SYNDROME

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Abstract

Introduction: Metabolic Syndrome (MetS), refers to the clusters of metabolic abnormalities which increase the individual's risk in developing cardiovascular diseases, and various types of cancers. Studies show that genetic, environmental, and social factors may also have a role in the pathogenesis of MetS, but the association between life course social determinants of health (SDH), and MetS, has yet to be established. The current systematic review aims to summarize the outcomes derived from previous studies which have links between life course SDH and MetS, and in that regard, this review also explores the common indicators of the SDH.

Methods: Three electronic databases were used: Medline, CINAHL, and Scopus. Articles published from 1st January 1990 until 10th January 2017 were utilised. These studies contained at least one single indicator of childhood structural determinants of health as the independent variable, and adulthood metabolic syndrome as the outcome variable. Only English articles were included.

Results: There were twelve articles were retrieved for analysis: three were from Asia, five were from Europe, and three were from the US. The commonest measurement of childhood SDH was noted to be parental socioeconomic status (SES), with some even reporting car, house, and sewing machine ownership as household SES. It is possible that women with SDH adversity throughout their life course may be associated with higher risks of MetS while the findings among men were inconclusive.

Conclusion: The association between MetS and SDH depends on gender, indicators of SDH, time of adversity, and geographic location. In order to achieve the UN's Sustainable Development Goal on tackling NCD, policies to prevent MetS must include action for taking the SDH at all stages of life.

Keywords: *Social determinants of health, Metabolic syndrome, Life course*

Introduction

Metabolic syndrome (MetS) is a challenge to public health throughout the world. This cluster of condition is known to increase the individual's risk in developing cardiovascular diseases and diabetes (1). MetS also increases the risk of many types of cancer, such as bladder, liver, and colorectal cancers among men, and endometrial, pancreatic and colorectal cancers among women (2). Genetic and environmental factors may also play a role in the pathogenesis of MetS (3). Other influencing factors that are receiving more attention in research include the Social Determinants of Health (SDH). It is described by the World Health Organisation (WHO) as "the condition, in which people are born, grow, work, live and age, and the wider set of forces and systems shaping the conditions of the daily life" (4). These social determinants include age, gender, ethnic group, lifestyle factors, psychosocial factors, and socioeconomic status (SES) (5).

The United Nation's (UN) Sustainable Development Goal on tackling non-communicable disease (NCD) is to reduce premature death from NCD by one third. As the global burden of MetS increases, approaches to tackle the issue of the SDH is through looking at the individual's life course. Therefore, understanding SDH and MetS across the life course are critical for preventing MetS globally. To date, there has been no systematic review on the life course SDH and MetS. The current review thus aims to examine the association between life-course SDH with MetS among the adult population.

Method
Study eligibility
All studies that used either a cross-sectional, case-control or cohort study design were eligible for inclusion in the systematic review.

Search strategy
The systematic review was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (See Supplementary Material) (6). Three electronic databases were sourced as the primary research sites, and these journals must be published from 1st January 1990 to 10th January 2017. The databases were Medline, CINAHL and Scopus. The search strategies for Medline and CINAHL are presented in the supplementary sheet.

Study selection
Data selection were based on the following criteria: a) Population-based studies on any adults (≥ 18 years) which assessed the association between life course or childhood SDH and adulthood MetS; b) Studies where at least one indicator of childhood SDH was adopted as the exposure; c) Studies in which the outcome was defined as MetS, based on any one of the respective definitions: International Diabetes Federation (IDF) criteria (7), National Cholesterol Education Program (NCEP) Adult Treatment Panel-III (ATP-III) criteria (8), modified IDF or modified NCEP ATP-III criteria with Asian cut-offs for BMI and waist circumference (9), and harmonized criteria (1); and d) Published in the English language.

Data extraction
Two selected reviewers independently extracted the articles from each of the databases by using the agreed search terms. Both reviewers independently reviewed the titles, abstracts, and full texts, based on the predetermined criteria. Any discrepancies noted in the articles chosen were resolved by mutual consensus.

When presenting the systematic review, the identified studies were grouped according to the study design. A table was created, based on the childhood and adulthood life course SDH exposures. This procedure followed the Commission on SDH framework (10). Each of the life courses was grouped into the structural or the intermediary determinants of SDH. Indicators of the structural determinants include socioeconomic status (educational level, occupational status, and income), race and gender. Indicators of the intermediary determinants encompass material circumstances, health behaviours, biological

and psychosocial factors. Figures 1 shows the flow chart of the systematic review.

The quality of the review was assessed by using a modified Newcastle-Ottawa scale (NOS) (11). Overall, three studies (12–14) were found to be moderate in quality while the remaining nine (15–23) were classified as high quality. None were of low quality.

Results
Study selection
The selected studies, upon following the set of criteria provided, yielded a total of 4,077 studies. However, only 12 studies qualified for this systematic review (12–24). (See figure 1)

Of these 12 studies, two were cross-sectional studies (13,19), and 10 were cohort studies (12,14–18,20–23). Three studies were from Asia (two from South Korea and one from China) (13,17,19), six were from Europe (one from Finland, two from Sweden, three from the UK) (14,15,18,21–23), and three were from North America (USA) (12,16,20). The smallest sample size in the study was 399 (18) while the largest sample size was 20,086 (17). Two studies (18,20) had female-only participants while the rest had both male and female participants. The final extracted studies are shown in Table 1.
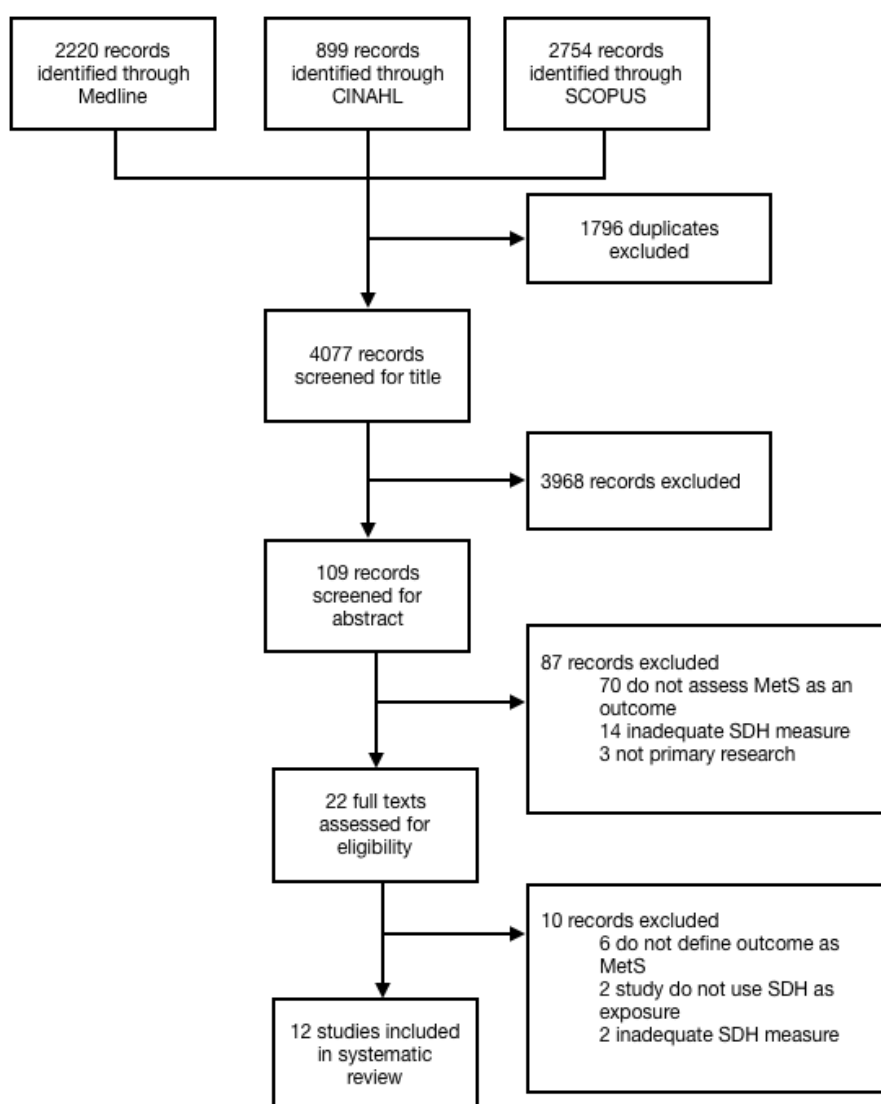

Figure 1: Flow chart of the systematic review

Table 1: Studies Assessing the Association Between Life-Course Sdh and Mets.

Article	Quality	Year of Publication	Study Design	Sample Size	Population	Continent	Gender
Mosquera et al. (2017) (23)	High	2017	Cohort study	10612	Sweden	Europe	Both (male 49.65%, female 50.35%)
Puolakka et al. (2016) (22)	High	2016	Cohort study	2250	Finland	Europe	Both (1033 males, 1217 females)
Delpierre et al. (2016) (21)	High	2016	Cohort study	3798	United Kingdom	Europe	Both (1876 males, 1922 females)
Montez et al. (2016) (20)	High	2016	Cohort study	1109	United State	North America	Female only (white 56.1%, black 43.9%)
Choi et al. (2014) (13)	Moderate	2014	Cross-sectional study	10106	Korean	Asia	Both (4,357 males, 5,749 females)
Yang et al. (2014) (19)	High	2014	Cross-sectional study	14888	Korean	Asia	Both (6324 men, 8564 women)
Gustafsson et al. (2012) (18)	High	2012	Cohort study	399	Sweden	Europe	Female only
Elwell-Sutton et al. (2011) (17)	High	2011	Cohort study	20086	Guangzhou, China	Asia	Both (5381 males, 14705 females)
Chichlowska et al. (2010) (16)	High	2010	Cohort study	10997	United State	North America	Both (3812 white men, 884 black men, 4724 white women, 1577 black women)
Lucove et al. (2007) (12)	Moderate	2007	Cohort study	1195	African Americans	North America	Both (No gender breakdown)
Kivimäki et al. (2006) (14)	Moderate	2006	Cohort study	1922	Finland	Europe	Both (856 men, 1066 women)
Langenberg et al. (2006) (15)	High	2006	Cohort study	2629	England, Wales, and Scotland	Europe	Both (1311 men and 1318 women)

Social determinants of health indicators
Five cohort studies (14,15,18,21,22) assessed the childhood and adulthood SDH whereas the rest of the five studies (13,16,19,20,23) measured childhood exposure only. All these studies typically investigated the structural determinants of SDH during childhood based on the indicators of household income, parental income, education, and occupation

Association between life course social determinants of health and MetS
a) Childhood SDH and MetS
Out of the 12 studies identified, only 10 had assessed childhood SDH independently in their analysis (12–15,17,19–23). Chichlowska et al.(16) found that there was an association between life-course SDH and MetS among females, but not among the males. Gustafsson et al.(18) conducted a females-only study, and they noted an association between life-course SDH and MetS.

Two studies found significant association between low childhood SES, and adulthood MetS (18,22). Puolakka et al. (22) found that those with a higher childhood SES have a lower risk ratio (RR) for MetS (RR: 0.93, 95% CI: 0.90–0.97). Gustafsson et al. (18) reported that those with socioeconomic disadvantages at the age 16 have an OR of 1.96 (95% CI: 1.18–3.26) in having MetS. However, the Z-score for adversities experienced at the age of 16 was not significant (OR of 1.22 (95% CI: 0.96–1.56)) (18).

Delpierre et al. (21) reported a significant association based on a crude OR analysis, where men with a higher adverse childhood experiences (ACE) have an cOR of 1.38 (95% CI: 1.05–183), and women with a higher ACE, have a cOR of 1.19 (95% CI 0.96–1.48) (21). Nonetheless, the results of this crude OR analysis were found to be not significant after adjustment of confounders were made in the subsequent regression model.

Four studies (14,19–21) found no significant association between childhood SDH and MetS. Two studies which followed men and women in Asia, recorded mixed findings. Their findings suggest that inverse association was only significant among women (13,17). Elwell-Sutton et al. (17) assessed childhood SDH by using a three-point childhood SES questionnaire. They found that among women, there was an inverse association between lower childhood SEP and adulthood MetS (OR: 1.16, 95% CI: 1.07–1.26). In contrast, men who had a lower childhood SES were less likely to have MetS (OR 1.91, 95% CI: 1.56–2.35). Elwell-Sutton et al. (17) also argued that even though low SES was usually associated with MetS among Western men and women, it was noted that the association between ischemic heart disease (IHD) and SES changed over time, and it is epidemiologically stage-specific.

Choi et al. (13) noted that among Korean women, there was a significant association between maternal education and occupational status with MetS, but this was not detected among the men. Studying the individual components of childhood SES (maternal education and occupation), Choi et al. (13) stated that female participants with a medium and high maternal education had a significant association with MetS (medium: OR 0.56, 95% CI: 0.43–0.71, high: OR 0.46 CI: 0.21–0.99). It appears that mother's occupation (manual work) among the female participants had higher OR of having MetS when compared to those who did not work or unemployed (OR: 1.34, 95% CI: 1.05–1.47).

In comparison, Chichlowska et al. (16) found mixed results when their samples were stratified by gender. They observed that the OR of having MetS for white women with low SES was 1.23 (95% CI: 1.17–1.42) while for black women it was 1.21 (95% CI: 1.21: 1.00–1.47). However, the results were not significant for both white and black men.

Chichlowska et al. (16) then hypothesized that the higher prevalence of central obesity in women may be the most likely reason highlighting the significant association between SES and MetS among women. Further, when compared to men, women were more likely to experience psychosocial disadvantages, such as higher likelihood of being unemployed, and becoming a single parent, both of which can lead to chronic stress.(25)

b) Childhood and Adulthood SDH and MetS

Nine studies (12,15–22) had analysed the association of both childhood and adulthood SDH with adulthood MetS. Elwell et al. (17) found that the higher the total number of SES disadvantages throughout the life course, the higher the OR (1.55, 95% CI 1.30–1.84). After stratifying the gender, they found that females with the highest score in respect of SES disadvantages, had higher OR of having MetS (OR 1.91, 95% CI: 1.56–2.35). In comparison, a different observation was noted among the males, who had the highest cumulative SES disadvantages score. It was observed that males had a lower OR of 0.64 (95% CI: 0.43–0.94) of having MetS.

Similar to the result of the females as reported by Elwell et al. (17), the female-only study conducted by Gustafsson et al. (18) showed that a higher life course adversity score resulted in an OR of 1.46 (95% CI: 1.14-1.87) of having MetS. Moreover, Chichlowska et al. (16) also found that having a low cumulative SES (combination of parent's education, occupation, occupational role, and parental ownership of house) score led to a higher and significant OR of MetS among the black (1.55, 95% CI: 1.30–1.84) and white (1.30, 95% CI; 1.17–1.43) women, but not among the men.

Another study that produced mixed findings with regards to gender is traced to Yang et al.(19) They found a significant association between MetS and lower adulthood SES (quartiles 3 and 4) with father's occupation standing as manual-skilled. However, this was only the case for the females [Q3 SES: OR 2.18 (95% CI: 1.47–3.25) and Q4 SES: OR 3.10 (95% CI 2.01–4.78)]. As before, there was no significant findings among the men. Table 2 provides a summary of the life course model, type of analysis, prevalence of MetS and results of the associations derived from the reviewed studies.

Table 2: Life Course Model, Type of Analysis, Prevalence of Mets and Results of Association Presented in the Reviewed Studies.

Article	Life course model	Statistical analysis for association between childhood SDH and MetS	Prevalence of MetS in the study (stratified by gender where available)	Result and direction of the association
Mosquera et al. (2017)	Social mobility (intergenerational) model	Concentration index with Wagstaff-type decomposition analysis	33.4% in males, 25.1% in females	Results are stratified by gender. However, in both genders' childhood conditions predict MetS in adulthood. Nevertheless, adult health inequalities have greater influences than childhood ones.
Choi et al. (2014)	Social mobility (intergenerational) model	Univariate and multivariate logistic regressions model	21.0% in males, 19.3% in females	In females, the higher the SES, the lower the odds of having MetS. In males, there is no significant association.
Puolakka et al. (2016)	Social mobility (intergenerational) model	Poisson logistic regression	21.4% (overall)	Higher childhood SES is associated with lower risk of MetS >30 years later in adulthood.

Delpierre et al. (2016)	Social mobility (intergenerational) model and critical period model	Logistic regression	37.5% in males, 19.8% in females	The link between exposure to adversity during childhood and the risk of MetS is less clear because this association is not significant after considering early socioeconomic and birth conditions that are independently associated with the risk of MetS. A lower socioeconomic position (SEP) during childhood, emergency caesarean delivery, low birthweight, mother younger than 23 years old at birth, smoking during pregnancy, and not being a homeowner during early adulthood are independently associated with MetS.
Chichlowska et al. (2010)	Accumulation model	Poisson regression implemented using generalized estimated equation	28.5% in white women, 39.4% in black women, 23.6% in white men, 28.6% in black men.	Cumulative SES over the life course, as well as its components, are inversely related to MetS in middle-aged women but not in men.
Kivimäki et al. (2006)	Social mobility (intergenerational) model	Multiple logistic regression	9.6% in men, 6.7% in women	No robust association is seen between early SES and adult MetS.
Montez et al. (2016)	Accumulation model and social mobility (intergenerational) model	Prevalence analysis for baseline (multiple logistic regression) and incidence analysis after baseline (Cox proportional hazards model)	24.6% in women (female-only study)	Childhood and adult SES predict the odds of MetS among women as they approach menopause transition; however, adult SES (measured by education) is more important thereafter.
Gustafsson et al. (2012)	Accumulation model	Multiple logistic regression	19.8%	Socioeconomic disadvantage manifests as MetS in mid-adulthood and is partially conveyed through the cumulative effects of social and material hardships encountered across the life course.
Lucove et al. (2007)	Social mobility (intergenerational) model	Poisson regression	25%	A higher level of education and a lesser degree of skilled occupation protect against MetS.
Elwell-Sutton et al. (2011)	Accumulation model and social mobility model	Multi-variable logistic regression	18.1% overall (11.4% in males, 20.6% in females)	Socioeconomic disadvantage across the life course is associated with MetS in women only.
Langenberg et al. (2006)	Accumulation model and social mobility (intergenerational) model	Logistic regression	33.4% in men, 23.6% in women	Among men, only personal educational level is associated with MetS. Among women, childhood social class, educational level and adult social class are associated with MetS.
Yang et al. (2014)	Accumulation model and social mobility (intergenerational) model	Multi-variable logistic regression	26.6% in men, 21.3% in women	Sex-specific socioeconomic disparities in childhood and adulthood have a differential impact on the prevalence of MetS and its individual components in Korea.

Discussion

This systematic review focused on 12 studies which assessed the association between life course SDH, and MetS. Due to the wide range of SDH indicators, the SES, a structural determinant, was thus used in the review because it is the commonest indicator used by most to assess both the childhood and adulthood life course for SDH. Following previous studies, the parents' SES, such as their occupation, and education level were then applied. It seems that parents' SES also included collected items such as cars, houses, and sewing machines. These items were used as the proxy for childhood SDH. Clearly, the number of indicators used to assess the exposure of life course SDH varied from single to multiple indicators of SDH.

Due to the small number of studies that were extracted for our review, and also due to the high heterogeneity of the SDH indicators, the current systematic review was inevitably, limited in terms of its ability to draw a firm conclusion. Nevertheless, from this review, it could be deduced that life-course social disadvantages may result in higher risk of developing of adulthood MetS. This deduction is dependent on the type of SDH indicators used, such as gender, race, and geographical location.

Moreover, the SDH indicators seemed to overlap, hence they were difficult to categorize. The problem was further compounded by the lack of a gold standard set of indicators. Thus it exacerbated the challenges researchers faced.(26) Measurements were often not applicable, or they may not have been tested for their validity for use in socioeconomically, and culturally diverse groups. Hence, why most SDH studies were based on a single measurement of exposure, such as the SES. However, other indicators of the SDH, such as material circumstances, assets owned, and social class, should not be treated lightly either, especially when health inequalities were assessed over the life course. Moreover, using weak measuring variables that had been assessed multiple times may also lead to poor

fitting models, such that it may not reflect the whole exposure to the SDH (27). In comparison, applying too many indicators, primarily in the absence of an unstandardized measurement, would lead to the issue of a lack of comparability among studies.

The current review had shown that adverse structural determinants of SDH through the life course could lead to MetS. The review also showed the adulthood's structural determinants of SDH might influence more than the childhood's SDH on having MetS. This outcome concurred with the Cumulative Inequality Theory, where health outcomes from early life exposures are not permanent. Instead, they unfold along the individual's life course (28).

Poverty condition is significantly correlated with low health literacy (29) and low health literacy is associated with limited access to preventive healthcare (30). These adverse conditions may lead to poor health behaviours, such as unhealthy life styles, poor dietary intakes, and poorer health outcomes (31).

The review found that when analyses were done by considering gender, the reviewed studies also showed a significant association between life-course SDH and MetS among females. One of the reviewed studies had even proposed that the socio-biological hypothesis could be used to explain the differences in the results when taken by gender. This hypothesis suggests that improved environmental conditions allowed the upregulation of sex steroids which have detrimental effects on the IHD risk in men, but not in women (32).

The study by Chichlowska et al. (16) forwarded two potential mechanisms for the gender differences: obesity and stress. Firstly, due to the higher prevalence of obesity among females as compared to males, it was argued that obesity could be one of the factors for MetS; it may influence the economic trajectories, especially among women (33). Nevertheless, it should be noted that Chichlowska et al (16) had failed to find any

significant association between obesity, and SES in their study. Secondly, it has been hypothesized that there is a relationship between low SES, and stress-related neuroendocrine dysfunction, which affects women more than men (34).

A different systematic review by Newton et al. (35) found an inverse association between life course SES and obesity among women. The MetS risk factors of weight gain due to pregnancy, gestational diabetes, and pre-eclampsia emerged as the three significant factors which were specific to women (36). Women and girls are society's most vulnerable people. Limited access to disease prevention services due to financial and social burden would increase the risk among women disproportionately, as compared to men (37). Thus, there is a need to investigate how gender health disparity was affected, not only by SES but also by the health system, governance, policies, culture and societal values.

To prevent MetS through the life course SDH approach, the Commission on SDH has provided a framework for the policy makers to reduce health inequalities. It should also be noted that the vast majority of studies were done in developed countries, with very few being focused on middle-income countries, and none at all for Africa. The cost of the high funding involved may be one of the factors causing this lack of research. Moreover, such research requires a long follow-up time with the necessity of laboratory investigations to diagnose MetS, both of which are expensive. Despite this, the World Health Organization (WHO) had reported that more than three quarters of deaths occur globally due to NCDs, among the low- and middle-income countries. The paucity of data on MetS in the low- and middle- income countries, coupled with the rising prevalence of MetS, means that tackling MetS based on the SDH framework and achieving the SDG for

NCDs could be very challenging.

Strengths and limitations

The main strength of this systematic review is that, it could possibly be the only one of such reviews of studies looking at the association between MetS and life course SDH. Thus far, our comparison had not uncovered any similar reviews. Although the search terms we used had resulted in the extraction of a large number of studies, there was no major medical database (Embase) that was accessible at the time of this review. Although the findings of the studies may not be exhaustive, the three databases have processed a large number of studies.

With regards to the robustness of the results presented in the reviewed studies, majority of the studies were based on retrospective data about early-life SES. This data may therefore, have been subjected to recall bias which could have led to an underestimation of the true effects. Also, the use of subjective questions which relied heavily on interpretation or judgement is also a questionable approach. However, most of the items of the childhood indicators were framed as objective questions (such as parental occupation), and these were regarded as reasonably reliable and valid (38,39).

Conclusion

The indicators of the life course SDH had shown some possible associations with adulthood MetS. Due to the small number of studies, and the high heterogeneity of the SDH indicators, this systematic review was inevitably, constrained by its ability to draw a firm conclusion. Nevertheless, this review sheds light on the fact that there is an urgent need for a more in-depth analysis of life course SDH inequality to be conducted, and also for a validated standard instrument to be used to measure life course SDH, especially in low- and middle-income developing countries.

Declaration of interest

The authors declare no conflicts of interest.

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