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Review

Preschool children's physical activity and cardiovascular disease risk: A systematic review

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ABSTRACT

Objectives: Higher physical activity (PA) levels in adults are associated with lower cardiovascular disease risk, however it is unclear whether this association is evident in children younger than five years. Given that cardiovascular disease has early life origins, this study systematically reviews evidence of associations between PA and cardiovascular disease risk factors among children aged 3–5.5 years.
Design: Systematic review.
Method: A systematic search of multiple data bases was conducted to identify published papers reporting associations between any measure of PA and cardiovascular disease risk factors. Inclusion criteria: English language; peer-reviewed; original quantitative research; mean age or majority of sample to be between 3.0–5.5 years. Studies where the sample was characterised by a health condition (e.g. obese, hypertensive) were not eligible for inclusion.
Results: Twelve papers met the inclusion criteria. At least one study for each cardiovascular disease risk factor except inflammation was included. PA was not associated with insulin resistance, and inconsistently associated with the remaining cardiovascular disease risk factors. Studies were mostly cross-sectional and methodologically heterogeneous. Longitudinal and experimental study designs and objective measurement of PA may help provide a clearer indication of the interplay between PA and cardiovascular disease risk in the preschool population.

Practical implications

- In preschool aged children, evidence is inconsistent as to whether PA is associated with indicators of cardiovascular disease risk.
- Research identified was lacking longitudinal analysis, experimental study designs and objective measures of PA.
- No previous studies have investigated the association between PA and inflammatory markers in preschool aged children.
- Despite inconsistent evidence from this review, it is important to continue to promote PA among pre-schoolers consistent with current public health guidelines given the other benefits attributed to PA in this age group.

1. Background

Cardiovascular disease (CVD) continues to be the leading cause of death in Australia and worldwide.[1] Among adults, there is consistent evidence that physical activity (PA) is a key protective factor against CVD and benefits several parameters related to CVD progression, including reducing inflammation and blood pressure, improving blood lipid profile and insulin sensitivity, and thinner and more elastic arteries.[2] However, less is known about the association between PA and markers of CVD risk in children, especially children younger than five years.[3] Despite decades of latency before

Abbreviations: BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; CARS, children's activity rating scale; cpm, counts per minute; EE, energy expenditure; HDL, high density lipoprotein; ISI, insulin sensitivity index; LDL, low density lipoprotein; LPA, light intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PA, physical activity; PWV, pulse wave velocity; totalc, total cholesterol; VPA, vigorous intensity physical activity.

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CVD manifests, intimal alterations associated with acute cardiac events such as myocardial infarction and ischaemic stroke can be seen in newborn aortas.[3] Understanding early developmental origins of health and disease, such as early life CVD risk, is an essential first step to primary prevention.

Results from four systematic reviews[4–7] and one update[8] on children and adolescents aged 5–19 years suggests that PA may be inversely associated with multiple individual CVD risk factors including blood pressure, arterial thickness, blood lipids, markers of inflammation and a combined CVD risk score. In older children, there is some evidence that a combined CVD risk score comprising multiple CVD risk factors is more sensitive than any single CVD risk factor.[9]

To date, only one systematic review has investigated PA and CVD risk in children aged 0–5 years. Timmons et al.[10] reviewed a broad range of health benefits of PA in preschool aged children. The major outcomes of that review with regard to CVD risk were that PA was associated with a favourable blood lipid profile and CVD/cardiometabolic risk score in 3–5-year-old children. However, that review was limited by inclusion of only three eligible studies, and the overall quality of those studies was rated as 'low'. There has been increasing interest in the early childhood period since that 2012 review, and the subsequent increase in research in this population warrants a more focused evaluation of the evidence. PA in early life may help explain the attributable risk of CVD across the lifespan, however at present no reviews have focused specifically on the association between PA and CVD risk in early life. Therefore, the aim of this paper is to review evidence regarding the association between PA and CVD risk factors among preschool aged children (3.0–5.5 years).

2. Methods

In the current review, the exposure variables were measures of PA and the outcome variables included seven key indicators of CVD risk: inflammation; lipid profile; insulin resistance; blood pressure; arterial thickness; arterial stiffness; and a CVD combined score from two or more CVD risk outcomes. The review is registered with PROPSERO (registration number: CRD42016041767), and followed the PRISMA checklist (see additional online file). Ethical approval was not required for this systematic review.

Systematic searches were conducted in May 2016, and updated October 2018 using EBSCO (Academic Search Complete, CINAHL Complete, Global Health, Medline Complete, SPORTDiscus with Full Text), Scopus, Informit and Embase databases. Search strings including are presented in supplement 1. Search terms and Boolean operators such as "and", "or" and "not" were adapted for use with other bibliographic databases in combination with database-specific filters. A separate search was conducted for each CVD outcome.

English language, peer-reviewed, original quantitative research was eligible for inclusion. Studies were included if the mean age of participants or majority of sample was 3.0–5.5 years. All forms of PA measurement (e.g., questionnaire, activity diary, pedometer, and accelerometer) and study designs (e.g. observational and experimental) were eligible for inclusion. Baseline data of longitudinal and experimental studies were eligible for inclusion if mean age or majority of sample was older than 5.5 years at follow up. Studies with a sample selected based on a health condition (e.g. obese, hypertensive) were not eligible for inclusion, nor were studies that examined the association between fitness, but not PA, and CVD risk.

The flow of papers through the review process is described in Fig. 1. Overall, there were >20,000 citations identified in searches after duplicates were removed. Two authors (LB and EF) independently screened the first 100 titles and compared results (99% agreement). One author (LB) screened the remaining titles and reviewed the abstract of each paper to determine eligibility. Full text articles were then retrieved and reviewed by two authors (LB and EF) to determine final inclusion in the review. Any differences between the two reviewers were resolved in discussion with at least one other author. Reference lists of included articles were also screened for eligible papers.

Key study characteristics were extracted by one reviewer (LB), including year of publication, country, study design, sample size, sex, age, measure of PA, measure of CVD and results. From each study, only data that met eligibility criteria were included in this review (i.e. additional measures or data from older children were excluded).

Two authors (LB and EF) independently assessed the quality of the included studies using an adapted tool for observational, cohort and cross-sectional studies (supplement 1). The 15-point tool is based on the criteria developed by Tooth et al.[11] which has been previously adapted by Singh et al.[12] and Fletcher et al.[13] It rates studies based on methodological aspects including study design, sample, measurement and statistical methods. Each criterion was worth one point (a single item of 1 point or two items worth 0.5 points each). Each item was scored 0.5 or 1 for 'yes' or 0 for no/unclear, with a possible total score ranging from 0 to 15 points. The score was divided by 15 and multiplied by 100 to generate a percentage score. Adaptations of the quality assessment tool for this study were made to distinguish between objective and subjective measures of PA. Use of accelerometers to measure PA automatically scored full points without needing to reference validity or reliability, given these qualities are well established for accelerometry in preschool aged children.[14–16] Subjective measures could only score half points for referencing either validity or reliability (0.25/0.05 points for one, or 0.5/1 if both). Quality assessment was conducted for the data eligible for inclusion, if only baseline data from a longitudinal study was included in this review it was classified as cross-sectional.

3. Results

A total of 12 unique articles from 11 different studies met the inclusion criteria (Fig. 1). Four articles reported two or more CVD risk outcomes with the remainder reporting a single outcome. Six articles reported on lipid profile, four on insulin resistance, six on blood pressure, one on arterial thickness, one on arterial stiffness, and two articles included a CVD combined score. None of the studies eligible for inclusion reported on inflammation. A list of all articles included in the final analysis and the corresponding CVD risk measures and quality assessment scores are shown in Table 1. The mean quality assessment score was 60%, and the range was 20–73%. The most common reasons for scores less than 100% in the quality assessment were not reporting the response rate, a response rate of <60%, and a lack of justification for the number of subjects needed to detect anticipated effects.

All studies were cross-sectional except for one which was a longitudinal study. Two articles analysed data from the IDEFICS study, Jiménez-Pavón et al.[17] conducted analyses with accelerometer assessed PA and Bel-Serrat et al.[18] used proxy-reported PA in analyses. As the sample sizes, exposure outcomes and analyses were distinctly different they were considered unique articles in this systematic review. Seven of the eleven studies were conducted in European countries, two in United States of America, one in Canada and one in India. The number of participants ranged from 22 to 4619 with all studies including both boys and girls. Subjective measures of PA were used in six articles and objective measures were used in five articles. One study[19] utilised both subjective and objective measures of PA. There was no clear pattern of association with CVD

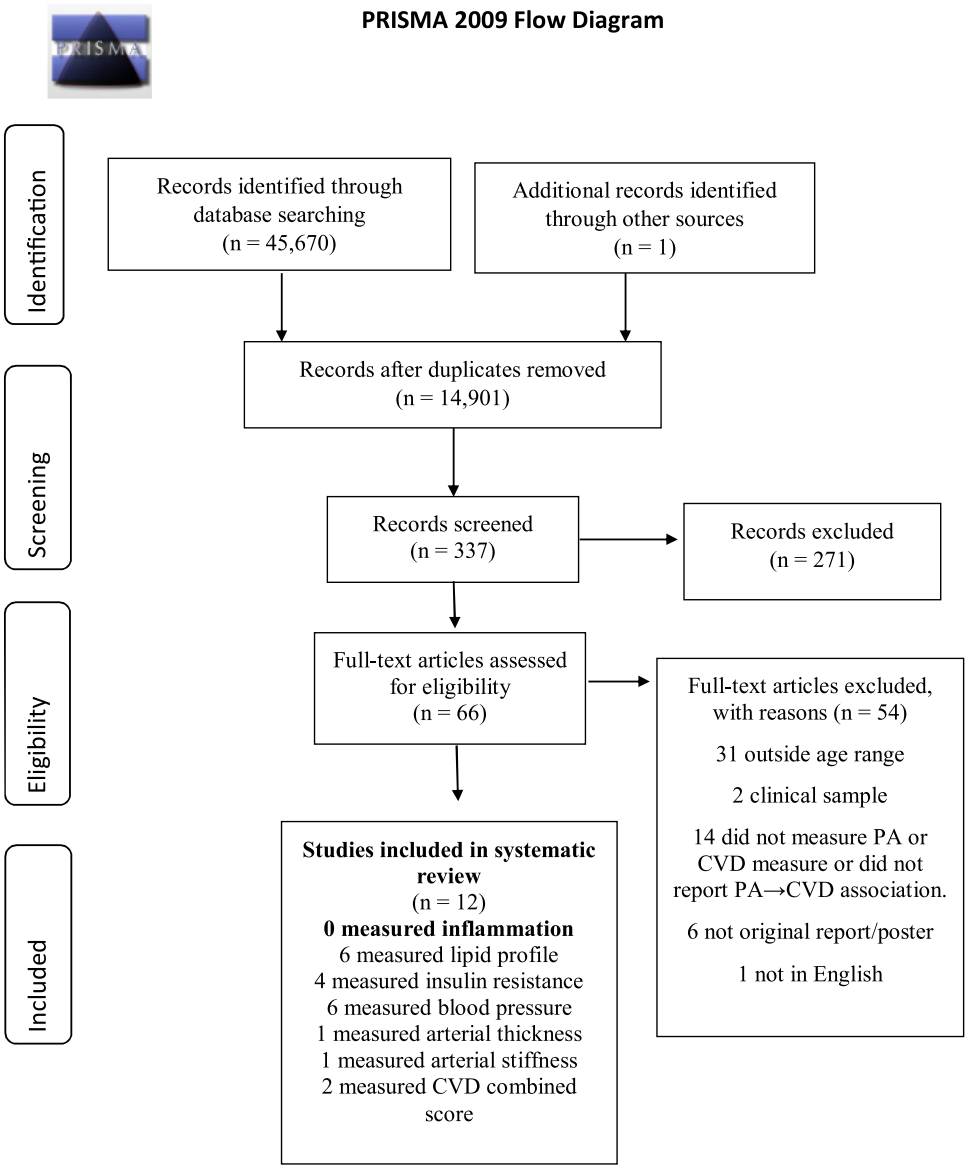

Fig. 1. Flow Chart of Citations (PRISMA).

Table 1
CVD measures included in each paper and quality assessment.

	Inflammation	Lipid Profile	Insulin Resistance	Blood Pressure	Arterial Thickness	Arterial Stiffness	CVD combined score	Subjective/ objective measure of PA	Quality Assessment*
Bel-Serrat et al. 2013[18]		√	√	√			√	Subjective	70%
Bunt et al. 2003[19]			√					Both	63%
DuRant et al. 1993[20]		√						Objective	63%
Huang et al. 2016[21]		√	√					Objective	73%
Idris et al. 2015[27]				√	√	√		Subjective	63%
Jiménez-Pavón et al. 2013[17]							√	Objective	76%
Murphy et al. 2004[26]			√					Objective	63%
Parizkova et al. 1986[25]		√						Subjective	**20%,**
Sääkslahti et al. 1999[23]		√		√				Subjective	**42%**
Sääkslahti et al. 2004[24]		√		√				Subjective	57%
Vale et al. 2015[29]				√				Objective	60%
Wilson et al. 1992[28]				√				Subjective	63%
Total	**0**	6	4	6	1	1	2		

* Papers were rated on an adapted 15 point scale and considered 'high quality' if they scored >50% **bold** papers that scored <50%.

Table 2
Summary of results by CVD risk outcome.

CVD risk outcome	Overall	Results by measure of PA		Sex		Association altered by:		
	Overall results	Subjectively measured PA	Objectively measured PA	Boys	Girls	Adiposity	Intensity of PA	Domain of PA/PA survey item
Lipid profile:								
HDL	+[23],25 0[20,21]	+[23,25]	0[20,21]	+[24]	0[24]			√[23,24]
LDL	0[20,21,25]	0[25]	0[20,21]					
Triglycerides	0[25] −[20]	0[25]	−[20]	0[18,24]	0[18,24]		√[20]	
Total cholesterol	−[23] 0[20,21]	−[23]	0[20,21]	0[24]	0[24]			√[23,24]
Total cholesterol/ HDL ratio	0[21]	N/A	0[21]	+[24] 0[18]	0[18,24]			√[24]
Insulin resistance	0[18,19,21]	0[18,19,*]	0[19,21]	0[26]	0[26]	√[19]		
Blood Pressure								
systolic	0[23,29,28] +[24] U[27]	0[23,28] +[24] U[27]	0[29]	+[18]	0[18]	√[23,29]	√[29]	√[23,24]
diastolic	+[23,24] 0[27,28]	+[23,24] 0[27,28]				√[23,24]	√[24]	√[23,24]
Arterial thickness	−[27]	−[27]	N/A			√[27]		√[27]
Arterial stiffness	0[27]	0[27]	N/A					
Combined CVD score	−[17]		−[17]	−[17] 0[18]	0[17,18]		√[17]	

+ positive association, − negative association, 0 no association, U u shape association, PA physical activity.
[*] Objective and subjective measures included in study by Bunt et al. Results from the most adjusted analyses included in table. If multiple measures of physical activity were reported the strongest association is presented in the table.

risk based on type of PA assessment (Table 2). A comprehensive summary of all studies included is available in Supplement 3.

PA and lipid profile: two[20,21] of the six studies that reported lipid profile measured PA objectively by direct observation,[20,22] and accelerometers.[21] The remaining studies relied on parent-reported survey,[18] validated parent-reported activity diary[23,24] and teacher-reported survey[25]. Measures of lipid profile included high-density lipoprotein (HDL) cholesterol[20,21,23,24], low-density lipoprotein (LDL) cholesterol[20,21,25], triglycerides[18,20,24,25], ratio of total cholesterol:HDL[18,20,21,24] and total cholesterol.[21,23–25]

In five studies that reported HDL cholesterol, two studies[24,25] reported a positive association with PA, one study[23] reported an inverse association with PA and two studies[20,21] reported no association. In the study by Parízková et al.[25] children whose kindergarten teacher reported that they engaged in high level of PA had higher mean HDL cholesterol than children whose teacher reported that they exhibited a low level of activity.[25] Two studies by Sääkslahti et al.[23,24] measured HDL cholesterol and used the same PA diary to derive four exposure variables: 'outdoor play', 'indoor play', 'low-active playing' and 'high active playing'. One of these studies[24] found that parent-reported playing outdoors correlated positively with HDL cholesterol ($r = 0.29$, $p = 0.016$) in boys only, with no other measures of PA showing an association. Conversely, and contrary to expected, the other study[23] found an inverse correlation ($r = -0.21$, $p = 0.016$) between 'very active outdoor play' and HDL cholesterol, even after adjusting for BMI and sex.[23] All of these studies measured PA subjectively, and two studies[23,25] scored <45% on the quality assessment. The only study that measured PA objectively (via direct observation) reported no association with HDL cholesterol.[20]

Three studies[20,21,25] examined the association between PA and LDL cholesterol; two measured PA subjectively, one objectively[21] and all reported no evidence of association. Four studies[18,20,24,25] measured triglycerides. The only study that used an objective measure of PA found a negative correlation between PA and triglycerides.[20] The three studies[18,24,25] used a subjective measure of PA and found no evidence that PA was associated with triglycerides. Of four studies that considered the ratio of total cholesterol/HDL cholesterol[18,20,21,24] three included subjective measures of PA,[18,20,24] one measured PA objectively[21] and all reported no associations. However, in stratified analyses, Sääkslahti et al.[24] reported that parent-reported playing outdoors was positively correlated ($r = 0.35$, $p = 0.003$) with the ratio of total cholesterol/HDL cholesterol in boys.

Five studies[20,21,23–25] included a measure of total cholesterol, four of which reported no association with parent-reported PA.[20,21,24,25] Sääkslahti et al.[23] found that parent-reported 'high active playing' was inversely correlated ($r = -0.21$, $p = 0.034$) with total cholesterol, but the strength of the association was attenuated ($p = 0.066$) after adjusting for sex and BMI.[23] Parent-reported 'outdoor play' was also negatively associated ($p = 0.017$, coefficient was not reported) with total cholesterol in the regression analysis after adjustment for BMI and sex.[23]

PA and insulin resistance: the four studies[18,19,21,26] that measured PA and insulin resistance reported no overall association between PA and insulin resistance in preschool aged children. However, some inconsistent results were reported when results were stratified by sex and by PA on weekends/weekdays. Bel-Serrat et al.[18] reported a positive association between parent-reported PA and insulin resistance (HOMA-IR) in boys but not girls, while Bunt et al.[19] reported no association between number of parent-reported physical activities per week and insulin resistance, after adjusting for weight or body fat. Two studies[21,26] measured PA objectively and found no association with homeostatic model assessment of insulin resistance (HOMA-IR). Huang et al.[21] reported that percentage of time spent in LPA was positively associated ($r = 0.417$, $p < 0.05$) with adiponectin (adipokine involved in glucose regulation) on weekdays but not weekends. Other PA variables: total time in LPA, total time MVPA and proportion of time in MVPA were not associated with adiponectin.[21]

PA and blood pressure: six studies considered blood pressure. All conducted analyses with systolic blood pressure, and four studies[23,24,27,28] also analysed diastolic blood pressure. Five[18,23,24,27,28] used a subjective measure (proxy-reported surveys) of PA; the other[29] used accelerometers.

Two studies[24,27] reported an association between PA and systolic blood pressure. Idris et al.[27] found that children with lower parent-reported levels of PA (time-weighted metabolic equivalents [METs] score < 4095) and children with higher parent-reported levels of PA (time weighted METs score > 6055) had higher systolic blood pressure than children who participated in a moderate amount of PA (time weighted METs score 4095–6055). Sääkslahti et al.[24] reported that outdoor play, but not indoor play or low active or high active play, was correlated with systolic blood pressure among boys ($r = 0.23$, $p = 0.041$) in BMI-adjusted partial correlation analyses.[24] The remaining three studies found no associations between PA and systolic blood pressure.[18,28,29] While the only study[29] to measure PA objectively reported no overall association with blood pressure, it found that overweight children who undertook less than 60 min/day of moderate-vigorous intensity PA had three times greater odds (OR 3.8, CI 1.6–8.6) of having high systolic blood pressure compared to normal weight, more active children.

Two of four studies found no association between PA and diastolic blood pressure reported. Outdoor play ($r = 0.31$; $p = 0.033$)[23] and high-active play ($r = 0.25$; $p = 0.026$)[24] were associated with higher diastolic blood pressure in boys but not girls, which is opposite to the expected direction of association.

PA and arterial stiffness: one study examined associations with arterial thickness and arterial stiffness.[27] Ultrasonography of the carotid artery was used to measure intima-media thickness (cIMT), arterial distensibility and elastic modulus. PA was assessed using a time weighted metabolic equivalents (MET) score, derived from a parent survey. The parent survey obtained information about the time their child spends in non-sport activities, active travel, and leisure activity (cycling, outdoor play, indoor play and free-time sports). Time weighted MET from sports activities, but not total time weighted MET, were associated with a thinner cIMT. There was no association with arterial distensibility or elastic modulus.[27]

PA and combined CVD risk score: the IDEFICS study was the only study to measure CVD combined score.[17,18] The combined CVD score was computed according to Andersen et al.[30] derived from age and sex specific z-scores of: systolic blood pressure, triglycerides, total cholesterol/HDL ratio and HOMA, and the sum of two skinfolds. Bel-Serrat et al.[18] reported results from PA measured subjectively (parent proxy-report), whereas Jiménez-Pavón et al.[17] measured PA objectively (accelerometer). Neither article reported whether the CVD combined score used was validated. No associations were reported between parent-reported nor accelerometer measured total PA and combined CVD risk score. Analysis with accelerometer assessed PA found that vigorous-intensity PA, but not light- or moderate-intensity PA, was inversely associated with the CVD combined score.[17]

4. Discussion

This systematic review assessed the current evidence regarding the association between PA and CVD risk factors among preschool-aged children. It included twelve unique articles, nine more than the only previous similar review.[10] Despite the larger number of studies eligible for inclusion in the current review, the total number investigating any one CVD indicator is small and there remains insufficient evidence to draw a definitive conclusion on whether PA is associated with any measure of CVD risk, including lipid profile, blood pressure, arterial thickness, arterial stiffness or combined CVD score. Overall, PA was either not associated with CVD risk outcomes or beneficially associated with CVD outcomes. When an association was observed, the correlation between physical activity and CVD outcome(s) was usually weak. While there is developing evidence that PA is associated with aspects of CVD risk in older children aged 5–17 years[5–8], there is insufficient evidence to draw conclusions in preschool aged children. This difference may be because the adverse cardiovascular risk profile in preschool aged children is less progressed and therefore more subtle and difficult to detect. Despite inconsistent evidence from this review it is important to continue to promote PA among pre-schoolers, consistent with current public health guidelines, given the other benefits attributed to PA in this age group.[31]

There was some evidence that associations between PA and CVD risk in preschool aged children may be modified by intensity of PA, adiposity, and/or sex of the child. Generally, higher intensities of PA were more consistently associated with improved cardio-metabolic health indicators (CVD combined score[23] and blood pressure[24]) than lower intensities of PA. This is consistent with evidence from a recent systematic review on children aged 5–17 years.[6] Subjective measures of PA commonly used in studies in the current review captured minimal data on the intensity of PA which may have limited the sensitivity of such studies to detect associations.

Adiposity has previously been associated with CVD risk factors, including blood pressure,[32,33] and both sex and adiposity have previously been associated with insulin resistance[26,34] among older children. In the current review, there was some evidence that both adiposity and sex may moderate the association between PA and both blood pressure and insulin resistance. In one study, the benefits of PA on systolic blood pressure were limited to overweight, underactive children.[29] PA and adiposity independently predict CVD mortality in adults,[35] however the interplay between PA, age, sex, genetics, environmental factors and adiposity to contribute to CVD risk is not well understood. In addition to the degree of adiposity, the velocity of weight change over time in the early life period may be important. Infants' BMI increases rapidly from birth to six months then plateaus and declines until it increases again or 'rebounds' at around 5–6 years of age. An earlier rise in BMI has been associated with higher CVD risk.[34,36] Given that most of the studies in this systematic review were cross-sectional, the timing of adiposity rebound was not examined.

This review was limited by the small number of studies that met the eligibility criteria, most of which were cross-sectional and scored relatively low on the quality assessment tool. A causal relationship between PA and CVD risk could not be examined as there were no experimental studies included. None of the included studies measured inflammation, despite inflammation being integral to the development of atherosclerosis.[37] A systematic review of school aged children[4] found some evidence that PA may be beneficial to vascular structures (intima-media thickness) and inflammatory status (c-reactive protein). However, most studies included in that review focused on children with obesity so may not be generalisable to the broader population. High sensitivity c-reactive protein has been shown to predict cardiovascular events in adults, however limitations of common inflammation bio-markers including c-reactive protein are limited specificity to CVD and low negative predictive value.[38] As more sensitive inflammatory markers for CVD are tested there is a novel opportunity to examine the association between PA and inflammation in pre-school aged children.

Study heterogeneity may have contributed to discrepancies between results. For example, parent proxy-reported total PA may be inherently different from teacher proxy-reported total PA. Teachers may not have a good sense of children's PA outside of preschool time and parents may not accurately estimate their child's PA when they are not with them. Teacher reported physical activity has been found to correlate better to objectively measured physical activity, however, the magnitude of correlation remains modest. Proxy-reported surveys also provide different types of results to objective measures of children's PA such as accelerometers, as they are dependent on recall and often cannot provide precise information about intensity.[39–42]

Future research with preschool aged children should use objective measures of PA and consider intensity, as well as adiposity and sex in analyses. Longitudinal and experimental study designs are required to determine whether a causal relationship between physical activity and CVD risk exists. In addition, future research should consider less commonly examined CVD risk factors; inflammatory markers, arterial stiffness and arterial thickness.

5. Conclusions

There are currently few studies and only limited and inconsistent evidence of an association between early life PA and various markers of CVD risk. Given associations observed in older children and adults, and the limited associations observed in this age group, there is reason to suspect PA in early life has potential for later

impacts on CVD risk. Regardless, evidence of other health and well-being benefits of PA reinforce the need to promote PA from early life.

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Authors' contributors statement

Ms Bell assisted the conceptualisation and design of the review, conducted the searches and screened all citations titles, abstracts and full texts and drafted the initial manuscript.

Dr Fletcher screened 100 titles, reviewed full texts, conducted the quality assessments and revised the manuscript.

Alfred Deakin Professor Timperio, Associate Professor Hesketh and Professor Vuillermin assisted with the conceptualisation and design of the review, resolving screening conflicts and interpretation of the findings.

All authors revised and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jsams.2018.11.021.

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