

# openheart Predictors of cardiovascular health in teenagers (aged 13–14 years): a cross-sectional study linked with routine data

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## ABSTRACT

**Objective** To examine the predictors of cardiovascular health in teenagers (aged 13–14 years).

**Methods** Measures of arterial stiffness (augmentation index (Alx)), blood pressure and cardiovascular fitness were taken from 234 teenage children (n=152 boys) and subsequently linked to routine data (birth and general practice records, education data and hospital admission data). Deprivation at school and at individual level was measured at birth, at 1 year old, at 13 years old and at secondary school using the Welsh Index of Multiple Deprivation. Multivariate regression analysis determined associations between routinely collected data and cardiovascular measures.

**Results** Teenagers had higher Alx (2.41 (95% CI 1.10 to 3.72)), ran fewer metres (–130.08 m (95% CI –234.35 to –25.78)) in the Cooper Run Test if they attended a more deprived school. However, higher individual level deprivation was associated with greater fitness (199.38 m (95% CI 83.90 to 314.84)). Higher systolic blood pressure was observed in first born children (10.23 mm Hg (95% CI 1.58 to 18.88)) and in those who were never breastfed (4.77 mm Hg (95% CI 1.10 to 8.42)).

**Conclusions** Improving heart health in deprived areas requires multilevel action across childhood namely, active play and programmes that promote physical activity and fitness and, the promotion of breastfeeding. Recognition of the important early indicators and determinants of cardiovascular health supports further development of the evidence base to encourage policy-makers to implement preventative measures in young people.

## INTRODUCTION

Cardiovascular disease (CVD) affects seven million people in the UK and is the leading cause of death in the Western world.<sup>1</sup> CVD risk factors should be low in young people, but the rise in childhood inactivity and poor fitness levels has led to an increase in prevalence and potential impact on lifetime CVD risk.<sup>2,3</sup> Identifying and addressing important CVD risk factors in early life could prevent symptoms in later life. Pathological changes in the arterial wall are well recognised to begin in childhood.<sup>4</sup>

## Key questions

### What is already known about this subject?

► Cardiovascular disease (CVD) is the leading cause of death in the Western world. More recently, greater emphasis has been placed on the role of increased arterial stiffness, high blood pressure and sedentary behaviour as predictors of CVD risk in populations. Identifying and addressing CVD risk factors in early life could prevent or delay disease in later life. We reviewed the literature and found that positive associations have been shown between a child's body mass index and CVD risk in adulthood, particularly among those from lower socioeconomic status. A meta-analysis of interventions targeting obesity and activity as methods of prevention in children concluded that high levels of leisure time activity benefit cardiovascular health. However, there was little evidence regarding the prognostic impact of a child's early environment and cardiovascular phenotype on cardiovascular outcomes. Breastfeeding has been identified in three studies as a protector against high blood pressure but this link has been described as modest.

### What does this study add?

► Our study identifies predictors of cardiovascular health in teenagers through data linkage with the Secure Anonymised Information Linkage databank. Routine health data was linked with baseline data collected during a physical activity intervention. There is relatively little previous research into early life and environmental impacts on young people's cardiovascular health. Our study suggests that supporting breastfeeding, improving physical activity opportunities for teenagers in deprived areas, enabling teenagers with chronic health conditions to be active and encouraging active transport at all ages may be beneficial to heart health and reducing CVD risk and warrants prospective evaluation.

### How might this impact on clinical practice?

► Our findings highlight issues where public health interventions (eg, breast feeding, parent groups, improving physical activity provision) may improve long-term cardiovascular health outcomes.

Positive associations have been shown between a child's body mass index and CVD risk in adulthood, particularly among those from lower socioeconomic status.<sup>5</sup> Deprivation has been associated with poorer cardiovascular fitness levels, higher obesity levels and consequently higher CVD risk.<sup>6</sup> Young people with lower socioeconomic status are less likely to engage in activity in the form of structured activities and competitive sports<sup>7</sup> and are subsequently at an increased risk of more sedentary lifestyles. These traits may also cluster with other health behaviours (eg, diet) which could also contribute to CVD risk when a child is older. Consequently, prevention strategies that decrease sedentary behaviour and improve nutrition have been designed to combat this issue.<sup>6,8–10</sup>

Early life behaviours may also contribute, for example, breastfeeding may protect against hypertension,<sup>11–13</sup> although this relationship has been described as modest. Less is known about the relationship between early life exposures and subsequent cardiovascular phenotype in young people and longer-term CVD risk. Therefore, increased study of these relationships in early life may provide important insights into how best to implement interventions in young people to prevent CVD.

This paper aims to identify predictors of cardiovascular health in teenagers (aged 13–14 years) which is an under-researched area of teenage health. Cardiovascular phenotype data were collected as part of baseline data collection from the Active Children through Individual Vouchers—Evaluation (ACTIVE) project, a mixed method randomised control trial (RCT) based in south Wales, UK. The ACTIVE RCT aimed to improve the cardiovascular fitness, cardiovascular health and motivation of teenagers to be active<sup>10</sup> and, therefore, included measures of augmentation index (AIx), blood pressure and fitness. This paper is a cross-sectional analysis of baseline measures linked with routinely collected data from the National Community Child Health Database (NCCHD) and the Tagged Electronic Cohort Cymru (TECC). These databases include data from the child health system in Wales, including birth registration, maternal health and monitoring of child health examinations.

The relationships between arterial stiffness, blood pressure and fitness with important early life influences (eg, deprivation and maternal influences) at population level are less well known and exploring these will add to knowledge and inform novel approaches to clinical practice regarding CVD risk. Furthermore, findings can inform early public health intervention approaches in this area. This paper assessed if there are any early life indicators that make teenagers more vulnerable to cardiovascular risk.

## METHODS

### Participants and settings

The ACTIVE Project was a mixed method RCT based in seven secondary schools in South Wales<sup>10</sup> with the aim of improving the cardiovascular fitness and health and

**Table 1** Demographics of schools

	Wales Index of Multiple Deprivation of the school*
School 1	1660
School 2	326
School 3	84
School 4	56
School 5	1434
School 6	1610
School 7	426

\*The Welsh Index of Multiple Deprivation (WIMD) is the official measure of small area deprivation in Wales

motivation of teenagers. A detailed trial protocol (Trial Number: ISRCTN75594310) has been published.<sup>10</sup> A total of 13 schools were assessed for eligibility to take part in ACTIVE; four did not meet inclusion criteria of being located in one of Wales' most deprived areas. School and individual level deprivation was derived from the Welsh Index of Multiple Deprivation (WIMD) which is used to identify areas of deprivation based on income, employment, health, education, access to services, community safety, environment and housing.<sup>14</sup> For this study, the continuous WIMD scale was used for individual and school level deprivation with one equating to the most deprived areas and 1909 to the least deprived.

Two headteachers declined to participate, one of whom declined after randomisation occurred. This meant seven secondary schools took part in the RCT. The demographics of the schools can be seen in table 1. This paper examines the baseline data collected from ACTIVE and, therefore, includes one cohort prior to randomisation.

Following initial school recruitment and headteacher approval, participants (in school year 9, aged 13–14 years) were recruited for measures via school assemblies and information sheets. Consent was voluntary and involved both written parental consent and pupil assent forms. All pupils in school year 9 were eligible to participate to create a cohort representative of teenagers from deprived areas. No pupils were excluded from participation. A total of 234 (n=152 boys) out of 1023 pupils across the seven schools (23%) were recruited. Basic demographics of participants can be seen as table 2.

### Procedures

Cross-sectional measurements of baseline phenotype data were linked to routine data (general practice, hospital and education records) to develop a retrospective cohort. Routinely collected data from the NCCHD, which contains birth information of children, and the TECC, which provides GP visits and hospital admissions for key comorbidities, were linked via the Secure Anonymised Information Linkage (SAIL) databank. These databases include data from the child health system in Wales, including birth registration, maternal health and

**Table 2** Population demographics

Variable	Male (n=129) (SD)	Obs	Female (n=105) (SD)	Obs
Arterial stiffness (%)	9.54 (5.58)	129	10.17 (4.67)	105
Blood pressure (mm Hg)	114.47 (13.86)	129	110.42 (11.62)	105
Cardiovascular fitness (metres ran)	2004.98 (412.92)	129	1604.98 (266.19)	105
School deprivation	674.60 (677.01)	129	642.76 (688.17)	105
Deprivation at birth	744.27 (559.9)	109	573.93 (468.94)	86
Deprivation at 1	665.25 (557.14)	108	595.45 (470.16)	84
Deprivation at 13	734.07 (534.4)	126	663.6 (482.38)	102
Birth weight (g)	3368.23 (576.38)	113	3257.35 (597.67)	90
Gestational age (weeks)	38.99 (1.82)	111	38.81 (2.48)	90
Birth number	1.02 (0.15)	128	1.01 (0.13)	102
Maternal age (years)	26.9 (5.78)	120	26.57 (5.88)	94
Breastfed (%)	48.44 (n=62)	128	40.20 (n=41)	102
C section (%)	19.38 (n=25)	129	23.81 (n=25)	105
Hospital admission (total number of admissions)	1.63 (2.01)	125	1.33 (2.85)	101
General Practice (GP) visits (total number of GP visits)	74.17 (43.24)	98	63.67 (34.00)	78
Sedentary time (Week) (min)	627.21 (82.53)	129	601.96 (79.08)	105
Sedentary time (Weekend) (min)	621.55 (115.31)	129	563.62 (120.11)	105
Moderate to Vigorous Physical Activity (MVPA) (Week) (min)	81.39 (22.10)	129	78.47 (24.25)	105
Moderate to Vigorous Physical Activity (MVPA) (Weekend) (min)	56.57 (20.67)	129	61.86 (26.06)	105

monitoring of child health examinations which include exposures that could predict cardiovascular risk.

Further information about the routine data included in the analysis can be seen as online supplementary file 1. All phenotype data included in this study were taken from the baseline data collection of the ACTIVE Project between September and December 2016. Data collection was organised in the schools with the aim of avoiding disruption to school timetables.

This paper uses measures of AIx, systolic blood pressure and cardiovascular fitness (Cooper Run Test (CRT)) as indicators of cardiovascular health. Higher AIx and blood pressure are both associated with increased CVD risk.<sup>15–17</sup> Poorer fitness has also been attributed to CVD risk.<sup>2,3</sup>

#### Aim

By using data linkage to routine data, this study assessed if there are predictors of poorer cardiovascular health and CVD risk in teenagers in relation to measures of AIx, systolic blood pressure and cardiovascular fitness.

#### Augmentation index (AIx)

AIx was assessed using the Vicorder (Skidmore Medical Limited, Bristol, UK). Measurements were taken with the participants seated following a 5 min rest during which a SC10 Hokanson cuff was positioned around their upper left arm. The cuff was inflated to measure

blood pressure; it was then reinflated to record the brachial artery pulse-pressure waveform. Central AIx was determined from the blood pressure and waveform using a transfer function integral to the software. This process was repeated and if both measures of AIx were within  $\pm 5\%$ , the two measures were accepted, if not, a third reading was taken and a mean of all three readings calculated.

#### Blood pressure

Blood pressure was measured with a standardised upper arm cuff methodology using an Omron M2 sphygmomanometer. After resting seated for 5 min, participants had three measurements taken from their left arm, with the average calculated. If there was a difference of  $\pm 5$  mm Hg between the readings, researchers took an additional measure. Participants did not fast prior to these measurements.

#### Cardiovascular fitness

Participants took part in the CRT to assess cardiovascular fitness.<sup>18</sup> This was a 12 min walk/run test conducted during physical education (PE) lessons where participants completed as many laps of a school sports hall as possible in the time. This was then converted to the total distance ran (in metres). The validity of the CRT has been tested in numerous studies in both girls and boys.<sup>19</sup>

### Data linkage

Data linkage was carried out through the SAIL databank<sup>20</sup> based at the Swansea University Medical School (UK). This occurred via linking AIX, systolic blood pressure and cardiovascular data with routinely collected health data, for example, deprivation at school and at home, birth weight and hospital admissions. A unique Anonymous Linking Field was assigned to person-based records before it was joined to clinical data via a system linking field.<sup>21</sup>

Routine data came from the NCCHD and the TECC. The full list of covariates and how they were cleaned can be seen as online supplementary file 1. Deprivation at school and individual level was the only variable to be measured at different time points (at birth, at 1 year old and at 13 years old). This was done to explore whether moving in and out of deprived areas during life affects heart health and whether deprivation impacts heart health at a specific age.

### Statistical analyses

Linear mixed effects multilevel regression was used to analyse the relationship between routine data on (1) AIX, (2) systolic blood pressure and (3) cardiovascular fitness. Covariates were excluded from the analysis if they had missing data on over 100 participants, and a full list can be seen as online supplementary file 1. Gender was included in the models to assess any differences by gender. The level of significance for the results of statistical analysis was set to  $p < 0.05$ . Structural equation modelling (SEM) in STATA was also used to show relationships between routinely collected data and the cardiovascular phenotypes collected in this study. Two independent statisticians conducted a parallel data analysis in STATA (V.15.1) to avoid researcher bias.

Multiple imputation of missing data was conducted using chained equations (MICE) command in STATA as data was assumed to be missing at random due to absence during some aspects of baseline testing. Data for the primary outcome of cardiovascular fitness was imputed for 27 participants using gender and deprivation. This generated one complete dataset which was used for analysis.

## RESULTS

Table 2 shows the demographics of participants. Boys had higher measures across most variables including deprivation levels, hospital and GP visits and sedentary time. However, these differences were marginal except for differences in cardiovascular fitness which shows boys as a population were fitter than girls at this age. Results from the multilevel analysis are presented as tables 3–5, respectively. Figure 1 shows relationships via SEM.

### Augmentation index

Analysis showed higher AIX measures was associated with a lower school WIMD score (indicating higher levels

**Table 3** AIX (linear mixed effects multilevel regression)

Variable	Coefficient	P value	95% CI
School deprivation	−0.003	0.010	−0.005 to −0.0007
Deprivation at birth	0.0008	0.506	−0.001 to .003
Deprivation at 1	0.001	0.488	−0.002 to .005
Deprivation at 13	−0.0002	0.886	−0.003 to .002
Gender	1.26	0.383	−1.57 to 4.10
Birth weight	−0.002	0.088	−0.005 to .0003
Gestational age	0.314	0.403	−0.423 to 1.05
Birth number	−8.10	0.019	−14.85 to −1.34
Maternal age	−0.072	0.536	−0.300 to .156
Breastfed	1.22	0.513	−0.181 to .050
C-section	0.472	0.780	−2.83 to 3.78
Hospital admissions	−0.363	0.007	−0.627 to −0.099
GP visits	0.030	0.006	0.008 to 0.052
Sedentary time week	−0.011	0.054	−0.046 to .024
Sedentary time weekend	0.011	0.196	−0.005 to .028
MVPA time week	−0.054	0.065	−0.113 to .003
MVPA time weekend	−0.003	0.907	−0.066 to .059
Blood pressure	−0.065	0.268	−0.181 to .050
Fitness	−0.001	0.581	−0.005 to .002

Those highlighted in bold indicate significance ( $p$  value  $< 0.05$ )

**Table 4** Blood pressure (linear mixed effects multilevel regression)

Variable	Coefficient	P value	95% CI
School deprivation	−0.001	0.530	−0.008 to 0.004
Deprivation at birth	0.003	0.000	0.001 to 0.007
Deprivation at 1	−0.007	0.276	−0.019 to 0.005
Deprivation at 13	0.004	0.348	−0.005 to 0.014
Gender	5.32	0.111	−1.22 to 11.87
Birth weight	−0.0008	0.802	−0.007 to 0.005
Gestational age	0.333	0.795	−2.18 to 2.84
Birth number	−29.96	0.000	−46.04 to −13.88
Maternal age	0.205	0.630	−0.631 to 1.042
Breastfed	−6.09	0.042	−11.96 to −0.22
C-section	5.15	0.012	1.13 to 9.16
Hospital admissions	0.096	0.769	−0.544 to 0.736
GP visits	−0.011	0.677	−0.064 to 0.041
Sedentary time week	0.069	0.010	0.28 to 0.11
Sedentary time weekend	−0.032	0.037	−0.06 to −0.001
MVPA time week	−0.07	0.972	−0.22 to −0.085
MVPA time weekend	−0.01	0.839	−0.189 to −0.154
AIX	−0.44	0.310	−1.29 to 0.40
Fitness	−0.007	0.079	−0.015 to 0.0008

Those highlighted in bold indicate significance ( $p$  value  $< 0.05$ )

AIX, augmentation index.

**Table 5** Cardiovascular fitness (linear mixed effects multilevel regression)

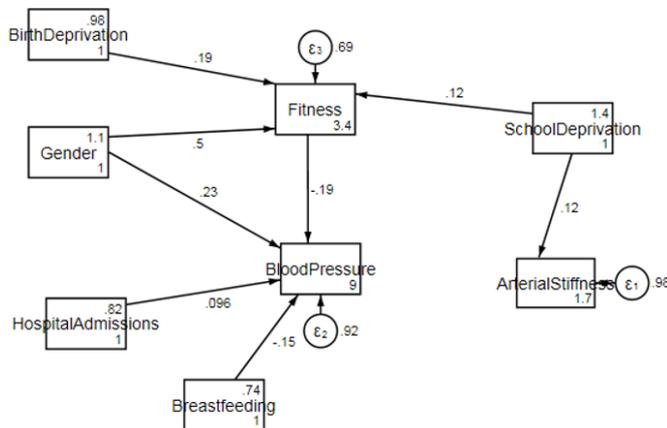
Variable	Coefficient	P value	95% CI
School deprivation	0.020	0.673	-0.070 to 0.116
Deprivation at birth	0.163	<b>0.007</b>	<b>0.045 to 0.281</b>
Deprivation at 1	-0.002	0.983	-0.233 to 0.228
Deprivation at 13	-0.112	0.371	-0.358 to 0.133
Gender	<b>389.50</b>	<b>0.000</b>	<b>233.693 to 545.307</b>
Birth weight	-0.001	0.987	-0.202 to 0.198
Gestational age	-9.30	0.729	-61.98 to 43.37
Birth number	<b>-1216.631</b>	<b>0.000</b>	<b>-1500.44 to -932.81</b>
Maternal age	<b>16.33</b>	<b>0.044</b>	<b>0.454 to 32.21</b>
Breastfed	195.72	0.063	-10.69 to 402.13
C-section	93.22	0.372	-111.61 to 298.06
Hospital admissions	-3.74	0.800	-32.77 to 25.27
GP visits	1.23	0.341	-1.30 to 3.76
Sedentary time week	-1.24	0.374	-4.42 to 1.92
Sedentary time weekend	1.48	0.099	-0.375 to 3.35
MVPA time week	-2.85	0.052	-5.73 to .026
MVPA time weekend	-2.08	0.448	-8.38 to 4.20
AIx	-5.42	0.606	-26.05 to 15.20
Blood pressure	-5.16	0.013	-9.23 to -1.08

Those highlighted in bold indicate significance (p value < 0.05)

of deprivation) (-0.003 (95% CI -0.005 to -0.0007), [table 3](#)). Lower hospital admissions (-0.363 (95% CI -0.627 to -0.099)) but higher number of GP visits (0.030 (95% CI 0.008 to 0.052)) also had significant relationships with higher AIx. School deprivation was also significant in the SEM ([figure 1](#)).

### Blood pressure

Lower systolic blood pressure was observed in teenagers who were first born (-29.96 mm Hg (95% CI -46.04 to -13.88), [table 4](#)) and those who were breast fed as infants (-6.09 mm Hg (95% CI -11.96 to -0.22)). Being born as a result of caesarean meant blood pressure was higher as a teenager (5.15 mm Hg (95% CI 1.13 to 9.16)). As well



**Figure 1** Path analysis.

as this, being more sedentary in the week was associated with higher blood pressure (0.068 mm Hg (95% CI 0.28 to 0.11)). SEM included gender as a predictor of having higher blood pressure too ([figure 1](#)).

### Fitness

Teenagers who were more deprived at birth ran further in the fitness testing (0.163 (95% CI 0.045 to 0.281), [table 5](#)). Boys were more likely to run further than girls (389.50 m (95% CI 233.69 to 545.30), [table 4](#)). Interestingly, teenagers were less fit if they were not first born (-1216.63 (95% CI -1500.44 to -932.81)) but were more fit if their mothers were older (16.33 (95% CI 0.45 to 32.2)). SEM showed that school deprivation also had a relationship with fitness that was not present in the multi-level regression.

### DISCUSSION

Although a relatively small study, our work demonstrates the feasibility and great value of linking paediatric clinical study data to routinely held healthcare records. This study has revealed interesting relationships between school deprivation and the cardiovascular phenotype in teenagers. First, AIx was greater in pupils attending deprived schools (schools in socioeconomically deprived areas) suggested they already had stiffer arteries by their early teens. Other confounders could explain the adverse cardiovascular phenotype in children attending deprived schools such as poor nutrition, tobacco exposure and increased psychosocial stress but this would require further evaluation.

Teenagers whose mothers reported breastfeeding were associated with lower systolic blood pressure consistent with previous literature.<sup>11</sup> These findings add to the evidence base supporting a beneficial impact of breastfeeding on blood pressure as a teenager. Longer duration breastfeeding has also been shown to have a beneficial effect on cardiorespiratory fitness.<sup>12</sup> Future research should explore this relationship further as supporting and promoting breastfeeding could provide beneficial long-term implications for teenager's health.

This study has shown that being first-born is better for systolic blood pressure and cardiovascular fitness. There is some evidence that early born children have greater access to resources and attention.<sup>22</sup> This may account for better fitness measures if first-born children are having greater access to physical activity opportunities, equipment and facilities. This is worthy of further investigation and, coupled with the finding that older mothers have fitter children, provides evidence that support for larger families, with younger mothers is needed to facilitate equality of activity and socialisation opportunities and resources. Being active in this way at an early age could track into later life and could reduce the risk of poor heart health.<sup>6</sup> Early physical activity promotion in children may provide an accessible and low-cost method of preventing poor heart health in later life.

Boys were significantly fitter than girls were (based on metres ran in the CRT). This is unsurprising as most literature suggests boys are more active and thus fitter.<sup>9 23–25</sup> Boys generally have a higher amount of lean body mass at this age, which could contribute to better cardiovascular fitness levels.<sup>26</sup> Programmes that target girls activity and fitness have been implemented,<sup>27–29</sup> but this study provides evidence there are still differences between boys and girls and more needs to be done. There were no other significant differences between genders for the measures.

Teenagers in more deprived schools appeared fitter. Schools in deprived areas typically offer less PE time<sup>30</sup> and provide fewer opportunities for sports and physical activities in and after school.<sup>30 31</sup> However, this finding suggests that despite being less likely to engage in physical activity, in the form of structured (competitive) sports clubs, it may be that participants from more deprived areas engage more low cost, unstructured activities or active travel due to the cost of running a car or using public transport.<sup>6</sup> This could account for higher fitness levels as, despite being an exposure, MVPA was not significant in influencing fitness.

Research has shown that there are cardiovascular benefits associated with all levels of activity.<sup>32</sup> Active travel in particular has been associated with healthier body compositions and cardiovascular fitness in this age group.<sup>33</sup> As shown by previous research, the importance of promoting different types of activity in young people cannot be overstated,<sup>2 32 34</sup> particularly in the deprived school settings as highlighted by this study. In this instance, school level deprivation was more strongly associated with an adverse cardiovascular phenotype in teenagers than home deprivation, which is worthy of further study.

### Limitations

This study was only able to measure cardiovascular measures in teenagers who consented to participate in this study, thus these individuals may have been more motivated and interested in being active. It is possible that the teenagers who did not consent were less interested or motivated to be active. Therefore, this study may be illustrative of the factors associated with the cardiovascular phenotype in predominantly more active teenagers with better cardiovascular fitness and heart health.

This is a relatively small study reporting the findings of 234 teenagers in south Wales; the results may not be generalisable to the wider UK or international populations and will require validation in larger, prospective studies. ACTIVE did not collect data on existing medical conditions, medications, recent infections or anthropometry, which can influence cardiovascular health. This can be seen as a limitation. Future studies could use this level of participant information for more detailed analysis of predictors of cardiovascular health.

The path analysis shows that even though relationships were present, these relationships only explained a small proportion of variation in A1x and blood pressure

in particular and warrant further evaluation in larger prospective studies ideally with careful documentation of important covariates including anthropometric and serological measurements to add greater depth to analysis.

### CONCLUSION

This study provides evidence of early life indicators, which may make teenagers more vulnerable to poorer cardiovascular health in adolescence and potentially greater lifetime risk of CVD. Interventions could target schools in deprived areas to improve heart health. For example, improving access to and uptake of a variety of activities that promote different types of physical activity, rather than simply aiming to reduce sedentary behaviour such as active travel or low cost, easy to access physical activities outside the school environment. Promotion of breastfeeding and play/socialisation support for younger, larger families may also have a beneficial effect.

Recognition of the important early indicators and determinants of cardiovascular health would warrant further development of the evidence base to encourage policy-makers to implement preventative measures in young people.

**Contributors** MJ wrote the first draft of the paper and all authors provided critical input and revisions for all further drafts, SB wrote analysis and results section and provided critical input and revisions for all further drafts. MJ, CT, SS, JD and SB undertook data collection and data analysis. DC, CT, SB, GS, JH, SA, SM, EE designed the study, aided in interpretation of findings and supervision of study quality. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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**Disclaimer** The lead author (MJ) affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The College of Human and Health Science Ethics Committee granted ACTIVE ethical approval (reference: 090516). The study was linked to anonymised routine data and therefore the need for further ethical approval and participant consent was waived by the approving IRB (Institutional Review Board), UK National Health Service Research Ethics Committee. The SAIL independent Information Governance Review Panel (IGRP), which contains members from the UK National Health Service Research Ethics Committee, experts in information governance and members of the public, approved the study.

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**Data availability statement** Data are available on reasonable request.

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