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Trends in socioeconomic inequalities in underweight and obesity in 5-year-old children, 2011–2018: a population-based, repeated cross-sectional study

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ABSTRACT

Objective To explore trends in prevalence and socioeconomic inequalities in underweight and obesity in 5-year-old schoolchildren in Scotland between 2011/2012 and 2017/2018.

Design A population-based, repeated cross-sectional study.

Setting Local authority primary schools in Scotland.

Participants 373 189 5-year-old schoolchildren in Scotland between 2011/2012 and 2017/2018.

Methodology Trends in prevalence and inequalities in underweight and obesity were examined across seven school years (2011/2012–2017/2018) for 373 189 5-year-old schoolchildren in Scotland. Body mass index SD scores were calculated, and epidemiological cut-offs relative to the UK 1990 references categorised underweight and obesity. Slope/relative indices of inequality (SII/RII) were calculated for underweight and obesity by school year using the area-based Scottish Index of Multiple Deprivation.

Results The prevalence of obesity rose slightly overall during the study period (9.8% in 2011/2012; 10.1% in 2017/2018). However, this masked a widening of inequalities, with children from the most deprived areas experiencing a greater risk of obesity in 2017/2018 than in 2011/2012 (risk ratio=1.14, 95% CI 1.04 to 1.25) compared with an unchanged risk in children from the least deprived areas (risk ratio=0.95, 95% CI 0.82 to 1.11). SII and RII indicate widening inequalities for obesity, with RII rising from 1.95 (95% CI 1.71 to 2.22) in 2011/2012 to 2.22 (95% CI 1.93 to 2.56) in 2017/2018. The prevalence of underweight was consistently low (1.2% in 2011/2012; 1.1% in 2017/2018), with no consistent evidence of social patterning over time.

Conclusions Inequalities in obesity in schoolchildren in Scotland are large and have widened from 2011, despite only a slight rise in overall prevalence. In contrast there has been little change in underweight prevalence or inequalities during the study period. Extra resources for policy implementation and measures which do not widen inequalities and focus on reaching the most deprived children are required to tackle the high prevalence and growing inequalities in childhood obesity in Scotland.

INTRODUCTION

In 2015, an estimated 5% (107.7 million) of children worldwide had obesity,1 and although the prevalence of childhood obesity in many high-income countries appears to be levelling off2 there is evidence in the UK to suggest that it is not consistent across all socioeconomic groups.3 4 Obesity is not the only form of malnutrition which is a cause for concern in childhood; there is increasing recognition of the need to consider the ‘double-burden’ of malnutrition, even in high-income countries.5 Double burden refers to the coexistence (potentially at individual, family, community and national level) of both underweight and obesity, even in high-income countries.5 Double burden matters because of the multiple adverse developmental and health consequences of both forms of malnutrition in early life.5

In the late 1990s in Scotland both underweight and obesity in early childhood were
much more prevalent than expected compared with the UK reference data from 1990, and both were socially patterned (much higher risk in more socioeconomically deprived families). Very little is known about more recent trends and inequalities in the double burden of underweight and obesity in children in the UK. Inequalities in childhood underweight and obesity may have worsened due to dramatic changes in the social and economic environment in the past decade. Life expectancy growth in the UK has stalled and health inequalities widened in the last decade of austerity (policies which produced massive public spending cuts with consequent loss of health and social services, reductions in welfare benefits and increased food insecurity). One English school study on over five million children conducted between 2007 and 2012 showed widening inequalities in the prevalence of obesity over time, low prevalence of underweight and no evidence of inequalities in underweight changing during the study period.

More recent trends in the double burden, and whether or not inequalities in the double burden are widening or narrowing, can be identified in Scotland because population-level body mass index (BMI) data are routinely collected, on an opt-out basis, on primary 1 (typically aged 5 years old at some point in the school year) schoolchildren as part of the Child Health Systems Programme School (CHSP-S). This is an important time to monitor population BMI as it corresponds to the physiological nadir of the growth curve in childhood and represents a transitional stage for children in terms of changing food and physical patterns. Reports on the prevalence of underweight, healthy weight, overweight and obesity are published annually by the Scottish Government; however, changes in patterns of inequalities have not been fully examined using measures of inequality. Other surveys conducted in Scotland lack population-level numbers, consistent methods and reporting on deprivation.

With efforts to mitigate the impact of rising food insecurity and child poverty in Scotland through free school meals, breakfast clubs and food banks, there is a clear need to monitor recent trends and inequalities in underweight and obesity as the mitigation of underweight could inadvertently lead to increasing the risk of obesity. This understanding should help inform policy and track progress towards the Scottish Government’s target to halve the prevalence of childhood obesity by 2030 and to reduce health inequality more generally. In summary, we need to understand recent trends in the double burden of early childhood malnutrition in order to test whether recent economic and policy changes have reduced or increased social inequality in Scotland. Improved understanding of trends in Scotland may also be helpful for other high-income countries— in general public health nutrition research and policy in high-income countries has neglected childhood underweight.

Aim
The aim was to explore the trends in prevalence and socioeconomic inequalities in underweight and obesity in 5-year-old schoolchildren in Scotland from 2011/2012 to 2017/2018.

METHODS

Data sources
Data for this population-based, child-level analysis were collected annually between 2011/2012 and 2017/2018 as part of the CHSP-S, a population-level data set routinely collected by Public Health Scotland (PHS) (formerly Information Services Division (ISD)) of the National Health Service (NHS) Scotland. The CHSP-S offers a review to all children in primary 1 (typically aged 4–5 years old at the start of the school year) of local authority schools and some private schools. Measurements are conducted on a parental/carer opt-out basis at any point within the school year by healthcare professionals, generally school nursing teams, who are trained to Royal College of Paediatrics and Child Health guidelines. Children’s heights are measured in centimetres to one decimal place and weights in kilograms to two decimal places.

CHSP-S collected data on the child’s date of birth and examination date—for which an age at examination could be calculated—sex and area-based socioeconomic deprivation. Area-based deprivation, measured by the Scottish Index of Multiple Deprivation (SIMD) at a national level, is based on the child’s home postcode. SIMD is an area-level measure of relative deprivation based on 38 indicators of deprivation categorised into seven domains (income, employment, health, housing, geographical access, crime, and education, skills and training). The list of areas was ordered by deprivation and split into tenths, where areas in SIMD 1 represent the 10% most deprived areas and areas in SIMD 10 represent the 10% least deprived. The SIMD was used in accordance with PHS (published as ISD) guidelines and CHSP-S publications, using SIMD 2012 for examinations between 2011/2012 and 2013/2014 and SIMD 2016 for examinations between 2014/2015 and 2017/2018.

In 2011/2012, CHSP-S captured 95.0% (n=52 972) of the National Records of Scotland’s (NRS) 5-year-old population estimate of 55 769 children. In 2017/2018, CHSP-S captured 88.4% (n=53 016) of the NRS estimate of 60 001. PHS suggests the reasons for decline in coverage include shortage of staff to conduct reviews and technical issues with recording review findings in the system. The decline was distributed equally across the socioeconomic scale and for each sex and thus should have no effect on the results.

Patient and public involvement
The project for which this study is involved in was scrutinised and approved by the NHS Scotland information governance board, the Public Benefit and Privacy Panel. This study involved secondary analyses of routine administrative
and health data sets, and all data were fully anonymised and made available to us for analyses within the National Safe Haven. Therefore, the patients or the parent/guardian of the patient could not be involved in the study.

Definitions
SD scores (SDS) for BMI (BMI=\(\frac{\text{weight (kg)}}{\text{height (m)^2}}\)) were calculated based on Cole et al’s UK 1990 references.20 Using epidemiological age-specific and sex-specific cut-offs, children in <2nd centile (SDS circa <−2) were classed as underweight and children in ≥95th centile (SDS circa ≥1.645) had obesity. Children who were overweight (≥85th centile and <95th centile; SDS circa ≥1.036 and <1.645) were kept separately from children of healthy weight (≥2nd centile and <85th centile; SDS circa ≥−2 and <1.036), although as our focus was on the double burden of underweight and obesity the results for overweight were not included in the main analysis.

Inclusion criteria
The study included individual records from pupils from all NHS Health Boards in Scotland who were between 4.0 and 7.0 years old inclusive (referred to as 5 years old herein) in Scottish Local Authority (and some private) schools for the school years 2011/2012-2017/2018 that had a record for the CHSP-S review. Initially there were 374 067 children. After excluding children due to age limits, extreme values for BMI SDS and height/weight SDS,18 and missing data for deprivation, the final sample consisted of 373 189 children (online supplemental figure S1).

Statistical analysis
The analyses were conducted within the NHS National Safe Haven19 and reported following best practice guidance.21 22 Data cleaning and statistical analyses were completed using RStudio V.1.2.133523 and various packages within the program.24–29

Trends in prevalence and inequalities in underweight and obesity were calculated across seven school years: from 2011/2012 to 2017/2018. Line graphs were used to show the change in prevalence of underweight and obesity over the years according to sex and area-based deprivation (SIMD). Linear regression was used to examine if the prevalence of each disease had changed over the years.

Differences between sex and area-based deprivation (SIMD) overall and over time were estimated using a modified Poisson regression model, which uses a binary outcome of underweight versus healthy weight and obesity versus healthy, with interaction terms for school years (as a continuous variable) with both sex and SIMD, separately in the same model. Risk ratios (RR) were calculated by taking the exponential of the model estimate and 95% CIs calculated using robust SEs.

To investigate whether the risk of underweight and obesity had increased in 2017/2018 vs 2011/2012, the modified Poisson regression models described above were used, although the sex variable was removed. Linear combination analysis was used to compare the prevalence of underweight and obesity in 2017/2018 vs 2011/2012 partitioned within each tenth of area-based deprivation (SIMD). RRs were calculated by taking the exponential of the sum of the estimate for 2017/2018 and the respective SIMD tenth and year interaction term, and robust SEs were used to calculate 95% CIs.

Recognising that inequalities cannot be captured in a single number, absolute and relative inequalities were calculated by the slope index of inequality (SII) and the relative index of inequality (RII), with 95% CIs, respectively, for the prevalence of underweight and obesity. The SII and RII were modelled using additive and multiplicative Poisson regression, respectively, using the rate of underweight and obesity versus healthy weight as the dependent variable and the midpoint of the cumulative population for each tenth of the socioeconomic scale, ranked from the least deprived to the most deprived, as the independent variable for each school year over the study period,30 using robust SEs. The SII should be interpreted as the absolute inequality in underweight and obesity, respectively, between the top and bottom of the socioeconomic scale in terms of rate difference.31 The RII should be interpreted as the ratio of the underweight and obesity rates of those from the most deprived areas compared with those from the least deprived areas.31 To test the hypothesis of increasing or decreasing trend in SII and RII, a linear regression modelled using the SII and RII estimates was regressed against the school year (treated as a continuous variable).

Population attributable risk (PAR) is a measure of the potential impact of control measures in a population, which can be relevant to public health decisions.32 The PAR for social deprivation was calculated by subtracting the prevalence of underweight and obesity in those in the least deprived tenth (SIMD 10) from the overall prevalence. Dividing by the overall prevalence of the condition gave population attributable risk percentage (PAR%), which was used to estimate the percentage of disease that could be avoided if the risk factor (deprivation in this instance) was removed.33 This was calculated for 2011/2012 and 2017/2018 for underweight and obesity separately.

RESULTS

Data completeness
The seven cohorts represented 93.6% (n=52 173/55 769), 94.6% (n=53 944/57 021), 91.7% (n=54 556/59 490), 91.1% (n=54 498/59 796), 91.0% (n=53 222/58 497), 84.6% (n=52 164/61 695) and 87.7% (n=52 632/60 001) of the NRS population estimate for the seven school years, respectively (online supplemental table S1).

The cohorts had an overall sex split of 50.9% (n=190 100/373 189) male and 49.1% (n=183 089/373 189) female. The SIMD distribution was skewed to the right, with the highest proportion of observations in SIMD 1 (most deprived tenth; 12.2%) and the lowest in SIMD 10 (least deprived; 8.7%) (online supplemental table S2), which is consistent with the NRS birth records.34

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Figure 1 Prevalence of underweight (A) and obesity (B) in 5-year-old schoolchildren in Scotland overall and by sex from school years 2011/2012 to 2017/2018 (online supplemental table S3).

Trends in the prevalence of underweight and obesity by sex

Figure 1 shows the prevalence of underweight and obesity for boys, girls and overall over time (2011–2018). Overall, the prevalence of underweight ranged from 1.2% in 2011/2012 (n=635/52 173) to 1.1% in 2017/2018 (n=560/52 632; β=0.0, 95% CI −0.1 to 0.0, p=0.27) (figure 1A, online supplemental table S3). The prevalence of underweight within the female population was 0.9% (n=228/25 507) in 2011/2012 and 0.7% (n=185/25 735) in 2017/2018 (β=0.0, 95% CI −0.1 to 0.0, p=0.07), while the prevalence of underweight in the male population was 1.5% (n=407/26 666) and 1.4% (375/26 897) for 2011/2012 and 2017/2018, respectively (β=0.0, 95% CI −0.1 to 0.0, p=0.27). Boys had a higher risk of being underweight than girls (RR=1.68, 95% CI 1.46 to 1.93, p<0.001), with this risk being consistent over the years (p for sex/year interaction=0.26).

The overall prevalence of obesity was 9.8% (n=5111/52 173) in 2011/2012 and 10.1% (n=5336/52 632) in 2017/2018 (β=0.1, 95% CI 0.0 to 0.2, p=0.15) (figure 1B, online supplemental table S3). The prevalence of obesity within girls was 9.5% both in 2011/2012 (n=2424/25 507) and 2017/2018 (n=2456/25 735; β=0.1, 95% CI −0.1 to 0.3, p=0.27). The male prevalence of obesity was 10.1% (n=2687/26 666) in 2011/2012 and 10.7% (n=2880/26 897) in 2017/2018 (β=0.1, 95% CI 0.0 to 0.5, p=0.11). Boys had a higher risk of having obesity compared with girls (RR=1.06, 95% CI 1.02 to 1.11, p=0.004), although the risk was consistent over the years (p for sex/year interaction=0.46).

Trends in socioeconomic inequalities in underweight and obesity

Within children from the 10% most deprived areas (SIMD 1), the prevalence of underweight was 1.2% (n=75/6355) in 2011/2012 and 1.1% (n=70/6246) in 2017/2018 (β=0.0, 95% CI 0.0 to 0.1, p=0.86) (figure 2A, online supplemental table S4). The prevalence of underweight in the 10% least deprived areas (SIMD 10) was 1.1% (n=51/4439) in 2011/2012, reducing to 0.8% (n=40/4837) in 2017/2018 (β=−0.1, 95% CI −0.2 to 0.0, p=0.08).

The prevalence of obesity in children from the 10% most deprived areas increased from 11.9% (n=755/6355) to 13.5% (845/6246) between 2011/2012 and 2017/2018 (β=0.3, 95% CI 0.0 to 0.6, p=0.030) (figure 2B). The prevalence in the 10% least deprived areas remained steady over the years, where 6.6% (n=295/4439) of children had obesity in 2011/2012 and 6.4% (n=308/4837) in 2017/2018 (β=−0.1, 95% CI −0.3 to 0.2, p=0.60) (figure 2B).

Changes in risk of underweight and obesity in 2011/2012–2017/2018 according to area-based deprivation

There was no change in risk of underweight in 2017/2018 for children from the 10% most deprived areas in Scotland (RR=0.97, 95% CI 0.70 to 1.34, p=0.86) when compared with children from the same areas in 2011/2012.
Figure 2  Prevalence of underweight (A) and obesity (B) in 5-year-old schoolchildren in Scotland by area-based deprivation (Scottish Index of Multiple Deprivation) from 2011/2012 to 2017/2018 (online supplemental table S4).

Figure 3  Risk ratio and 95% CI for the prevalence of underweight (A) and obesity (B) in 2017/2018 vs 2011/2012 for each decile of the Scottish Index of Multiple Deprivation. LD, least deprived; MD, most deprived; SIMD, Scottish Index of Multiple Deprivation.
(figure 3A). Similarly, the risk of underweight did not change for children in the 10% least deprived areas between 2011/2012 and 2017/2018 (RR=0.72, 95% CI 0.47 to 1.08, p=0.11). The only change in risk of underweight between 2011/2012 and 2017/2018 was evident in children from SIMD 2, where children in 2017/2018 had a lower risk of underweight than their counterparts in 2011/2012 (RR=0.67, 95% CI 0.48 to 0.94, p=0.019).

Although the prevalence of obesity remained constant overall in Scotland, children from the 10% most deprived areas had an increased risk of obesity in 2017/2018 than in 2011/2012 (RR=1.14, 95% CI 1.014 to 1.25, p=0.005) (figure 3B), while the risk remained unchanged in children from the 10% least deprived areas (RR=0.95, 95% CI 0.82 to 1.11).

**SII and RII for underweight and obesity**

In 2011/2012 there was evidence to suggest that there were absolute and relative inequalities in the prevalence of underweight between the most and the least deprived areas (SII=0.4, 95% CI 0.1 to 0.8; RII=1.42, 95% CI 1.06 to 1.90), followed by fluctuations in both SII and RII over the study period, with no systematic trend observed (figure 4A, online supplemental table S5).

For obesity, the SII was estimated at 6.5 (95% CI 5.6 to 7.5) in 2011/2012, rising to 8.1 (95% CI 7.2 to 9.0) in 2017/2018, with evidence to suggest the absolute inequalities followed an upward trend (slope=0.30, 95% CI 0.05 to 0.55, p=0.028) over the study period (figure 4B, online supplemental table S5). The RII, too, followed an upward trend (slope=0.05, 95% CI 0.01 to 0.08, p=0.013) between 2011/2012 and 2017/2018, rising from 1.95 (95% CI 1.71 to 2.22) to 2.22 (95% CI 1.93 to 2.56) (figure 4B, online supplemental table S5).

**PAR% for underweight and obesity**

The PAR% for obesity in 2017/2018 suggests that 37.2% (n=1984/5365, 95% CI 29.0% to 45.3%) of cases of obesity in 5-year-old schoolchildren could have been avoided if inequalities were eradicated, rising from 32.2% (n=1645/5111, 95% CI 23.7% to 40.6%) in 2011/2012. The equivalent calculations for underweight in 2017/2018 suggested 22.2% (n=124/560, 95% CI −59.0% to 100.0%) of cases of underweight in 5-year-old schoolchildren could be avoided, rising from 5.6% (n=35/635, 95% CI −65.8% to 77.1%) in 2011/2012; however, these estimates for underweight should be interpreted with caution due to the small numbers and large CIs.

**DISCUSSION**

**Main findings and study implications**

This population-based, child-level analysis of over 350,000 5-year-old children in Scotland between 2011/2012 and 2017/2018 is the first study, to our knowledge, to examine trends in socioeconomic inequalities in both underweight and obesity during a decade of austerity economic policies in the UK. Overall, the prevalence of...
obesity has risen very slightly; however, this has masked widening inequalities due to higher and increasing levels of obesity in children from more deprived areas, and lower plateauing levels of obesity in children from less deprived areas.

Despite increasing concern over the public health impact of the increasing levels of child poverty, food insecurity and the use of food banks in the UK over the past decade of austerity, there is very little evidence on prevalence, trends and inequalities in childhood underweight. In contrast to obesity findings in the present study, the prevalence of underweight across the seven school years was consistently low relative to the UK 1990 references, with no evidence of an increase or decrease and no clear social gradient observed over the years. These results for the underweight population are best taken with caution due to the low prevalence, and thus small sample size, of underweight in the study. Any misclassification of children with BMI SDS close to the cut-off for underweight could drastically change the results presented in this study.

Comparisons with other studies

As noted above, awareness of the double burden has increased only recently, and there has been a perception that early childhood underweight is a public health problem for low-income to middle-income countries rather than high-income countries. As a result, there are relatively few similar studies from high-income countries which can be compared against the findings of the present study. This dearth of evidence also means that the causes of social inequalities and widening inequalities are poorly understood. Further research will be required to understand why social inequalities in early childhood underweight decreased in Scotland from the late 1990s to 2011/2012 (present study), and then remained relatively stable from 2011/2012, and why social inequalities in early childhood obesity increased over the decade of austerity in the UK as suggested by the present study. This could be part of a wider picture observed across England in recent years, with a report from the Health Foundation reporting on falling life expectancy in people from the most disadvantaged (and marginalised) groups. Although it is difficult to attribute causality, this report strongly suggests that a decade of austerity has adversely impacted the social determinants of health in the short, medium and long term, with the impact of child poverty most likely showing their effects in the long term.

In a previous Scottish study of social inequalities of underweight and obesity in early childhood which used routinely collected data from 1998/1999, there was marked social patterning of both underweight and obesity in those years. We are not aware of any Scottish trend data in social patterning of childhood underweight and obesity since that time.

Despite some methodological and consent differences, White et al in an earlier analysis of routine data from children aged 5 and 11 years old in England showed similar widening inequalities in obesity, but these remained stable for underweight, and suggested more sophisticated implementation of policy to protect the health of children from the poorest areas.

A slowing of previous increases in childhood obesity prevalence in the past decade has been observed in other high-income countries, probably due to increased awareness of the problem and/or public policy efforts. However, our study shows that childhood obesity over the past decade in Scotland has not only increased in prevalence but has experienced marked widening inequalities. Reducing health inequalities is a high priority of public health policy in the UK, so the trends observed in obesity inequality in the present study are unwelcome. In addition, the PAR% estimates for obesity from this study give cause for concern because they suggest that the inequalities observed have affected large numbers of individuals, and in future years they will contribute substantially to inequalities in non-communicable diseases given the well-established comorbidities of childhood obesity.

Marmot et al highlighted the importance of experiences in early years to later health outcomes with inequalities at this age having potential lasting impact throughout the child’s life. This is reinforced again by Marmot et al, noting that at this age interventions to reduce inequalities which focus on proportionate universalism are most effective and are shown to be the most cost-effective. As noted above, the double burden of early childhood underweight and obesity is a relatively new concern for high-income countries and the issue of social inequalities in the double burden is even newer, so there is a dearth of evidence of interventions intended to reduce inequalities in the double burden. However, in general terms the evidence suggests that public health interventions which operate ‘upstream’ are both more likely to be effective and less likely to increase social inequalities than interventions which operate ‘downstream’, focusing on individuals.

Strengths and limitations

The study’s main strength is the high capture rate of the population in primary 1 in Scottish schools from large routinely collected administrative data sets, and this is the first time a study of this size has reported on inequalities in underweight and obesity in a contemporary population sample during a period of austerity policies. Our study used population-wide administrative data sets established for other purposes and therefore the variables available were limited. The data set had regular quality and completeness checks. The linkage process was robust and did not exclude many records from the expected total in the published reports. Due to our study having a high linkage rate, it is a representative cohort of the population.

Limitations in this study mainly come from the BMI measurement. Obesity is an excess of body fatness rather than an excess of body weight. Since body fatness is difficult to measure directly in large population-based
surveys, a high BMI-for-age is used widely as a proxy for high body fatness. Using BMI-for-age as a proxy underestimates ‘true’ obesity substantially compared with excessive fatness. It is therefore likely that the true obesity prevalence in Scotland is greater than the estimates presented which were based on BMI-for-age and that we have provided conservative estimates of obesity prevalence among 5-year-olds in Scotland.

The proportion of children reviewed from the population estimate reduced in each year of the study, although this change was proportionate across socioeconomic groups (online supplemental table S2). Children from more deprived areas are more likely to be absent from school than their less deprived peers, so may be missed by the reviews; however, those children attending private schools (1%–2% of population) may also be under-represented. It is unlikely either group will sufficiently change the direction of the results. The proportion of children in each area-based deprivation tenth is consistent with NRS population estimates.

Individual-level socioeconomic measures were not available as part of the routine administrative data and therefore area-based deprivation level was used. This has limitations when targeting individuals based on inferences made about the group (ie, ecological fallacy) and does not allow for heterogeneity in individual-level risk factors and disease levels within areas of residence.

CONCLUSIONS

This large population-based, child-level analysis suggests that the prevalence of childhood obesity has slightly risen, while absolute and relative socioeconomic inequalities in Scotland are large and worsening over time. In contrast, the prevalence of underweight was low, not obviously socially patterned, with no obvious change over the study period despite increasing levels of child poverty. Extra resources for policy implementation and measures which do not widen inequalities and focus on reaching the most deprived children are required to tackle the high prevalence and growing inequalities in obesity among children in Scotland.

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Contributors RS designed the study, developed the statistical design, wrote the statistical analysis plan, performed the statistical analysis, collated all reviewer comments and updated accordingly, and wrote the manuscript. JRR designed the study, provided critical review of the findings and wrote the manuscript. AH designed the study, provided critical review of the findings and wrote the manuscript. LAK developed the statistical design, provided critical review of the statistical analysis and wrote the manuscript. DC wrote the grant for the overall project, designed the study, provided critical review of the findings and wrote the manuscript. DY developed the statistical design, provided critical review of the statistical analysis and wrote the manuscript. AS wrote the grant for the overall project, designed the study, developed the statistical design, provided critical review of the findings and wrote the manuscript. All authors provided comments and updated accordingly, and wrote the final manuscript.

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