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A nationwide cohort study of slipped capital femoral epiphysis

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/archdischild-2016-312328>).

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Received 8 November 2016

Revised 22 March 2017

Accepted 17 May 2017

ABSTRACT

Objectives To describe the epidemiology of slipped capital femoral epiphysis (SCFE), to examine associations with childhood obesity and socioeconomic deprivation, and to explore factors associated with diagnostic delays.

Design Historic cohort study using linked primary and secondary care data from the Clinical Practice Research Datalink and Hospital Episode Statistics.

Setting All contacts with healthcare services, including emergency presentations, outpatient appointments, inpatient admissions and primary care visits, within the UK National Health Service.

Patients All individuals <16 years old with a diagnosis of SCFE and whose electronic medical record was held by one of 650 primary care practices in the UK between 1990 and 2013.

Main outcome measures Annual incidence, missed opportunities for diagnosis and diagnostic delay.

Results Over the 23-year period the incidence remained constant at 4.8 (95% CI 4.4 to 5.2) cases per 100,000 0–16-year-olds. There was a strong association with socioeconomic deprivation. Predisease obesity was also strongly associated with SCFE; mean predisease z-score of body mass index was 1.43 (95% CI 1.20 to 1.68) compared with the UK reference mean. Diagnostic delays were common, with most children (75.4%) having multiple primary care contacts with relevant symptomatology, and those who presented with knee pain having significantly longer diagnostic delay (median 161 (IQR 27–278) days) than those with hip pain (20 (5–126)) or gait abnormalities (21 (7–72)).

Conclusions SCFE has a strong association with both area-level socioeconomic deprivation and predisease obesity. The majority of patients with SCFE are initially misdiagnosed and those presenting with knee pain are particularly at risk.

INTRODUCTION

Slipped capital femoral epiphysis (SCFE) is the most common hip disease of adolescence.¹ Severe cases can lead to complete collapse of the femoral head, and SCFE is the most common reason for hip replacement surgery in both adolescence and early adulthood.² Early recognition of SCFE is important as the deformity may worsen if the slip remains untreated.³ Previous studies have found that symptom duration is associated both with the degree of slip and clinical outcome, as determined by surrogate measures such as compensation payments.^{4–6}

Unfortunately, hip disorders may present atypically in children, which can lead to diagnostic delays.^{3 7 8} It is therefore important to understand

What is already known on this topic?

- Slipped capital femoral epiphysis (SCFE) is an important cause of disability in children and young adults.
- Delay between onset of SCFE symptoms and treatment may worsen the prognosis.
- There is an association between SCFE and obesity, but this might be explained by reduced activity levels following onset of symptoms.

What this study adds?

- Diagnosis of SCFE is often delayed and there is evidence of missed opportunities for diagnosis in primary care.
- Children with atypical symptoms (particularly knee pain) are at greatest risk of misdiagnosis, despite this being a recognised presentation of SCFE.
- SCFE is strongly associated with area-level socioeconomic deprivation and premenstrual obesity.

both the epidemiology of SCFE and the spectrum of symptoms with which new cases present to healthcare providers. In particular, there have been a number of recent calls to raise awareness among non-specialists to ensure prompt recognition and referral of patients.^{9 10}

The epidemiology of SCFE is poorly documented. The few studies of incidence vary considerably in methodological quality, and meaningful comparisons are difficult because of their heterogeneous denominator populations.^{1 11–13} SCFE incidence has been ecologically linked to childhood obesity,^{1 11–13} although there is little strong evidence to support this association. Most studies have been retrospective case series from specialist centres^{14–16} that may suffer from referral bias and poor generalisability to the wider population. These studies also typically recorded patient weights *after* diagnosis, and it is plausible that obesity could result from exercise modification following disease progression.

This study is the first to use linked hospital and community-based records to describe the epidemiology of SCFE in a population cohort. It sought to test for an association with premenstrual obesity, socioeconomic deprivation and comorbid diseases and to explore factors associated with diagnostic delays.



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To cite: Perry DC, Metcalfe D, Costa ML, et al. *Arch Dis Child* Published Online First: [please include Day Month Year].
 doi:10.1136/archdischild-2016-312328

METHODS

Data sources

The Clinical Practice Research Datalink (CPRD) is the English National Health Service (NHS) observational data and interventional research service, jointly funded by the National Institute for Health Research and the Medicines and Healthcare Products Regulatory Agency (MHRA). CPRD GOLD is a large database containing the longitudinal medical records from approximately 650 primary care providers throughout the UK. It was launched in 1987 and now includes active records for 5.5 million individuals, that is, around 8% of the UK population. The data are well recorded¹⁷ and has been shown to provide results that are consistent with other data sources in the UK. A detailed description of CPRD is available elsewhere.^{17 18} Linked inpatient data using Hospital Episode Statistics (HES) are available from 1997 onwards following the introduction of a unique NHS number for each individual patient. HES data contain details of all contacts (admissions and attendances) with English NHS healthcare providers. All NHS healthcare providers in England, including acute hospital trusts, primary care trusts and mental health trusts, contribute data to HES. Linkage to HES was available for 357 of the 650 primary care providers contributing to the CPRD (HES does not cover Scotland, Wales or Northern Ireland, hence is not available at all of these sites, nor in a proportion of English primary care providers who do not contribute linked data).

Case identification and validation

Cases were extracted from both CPRD and HES if they had a diagnostic code indicative of SCFE between 1 January 1990 (CPRD) or 1 April 1997 (HES) and 31 March 2014 (see online supplementary appendix 1). When a case was identified, further support for the diagnosis was sought within both the same and the other data set. This was achieved by examining the diagnostic and procedural codes 2 years either side of the SCFE diagnosis date. The strength of the validation was classified using a validation algorithm (more details are available in online supplementary appendix 1).

Cases were included if they satisfied both the following criteria: (1) age above 6 years old, and 16 years or under on the day of the diagnostic record of SCFE and (2) at least 1 year of prior up-to-standard (UTS) data within their computerised record. UTS is a term used by CPRD to denote that a practice has continuous high-quality data sufficient for use in research.¹⁹ There were no exclusion criteria, although outliers with respect to age were examined to determine their validity.

Where linkage was available and there was good evidence to support the diagnosis, the index date of diagnosis was determined to be the earliest date within the two databases (if different). In all other instances the earliest diagnostic record was assumed to represent the index date.

Denominators were obtained from CPRD to calculate the annual incidence of disease for 0–16-year-olds stratified by age, sex, year, region and quintile of socioeconomic deprivation. Socioeconomic deprivation quintiles were available at a patient-level for patients within England.²⁰ External validity of the data set was assessed by comparing the age and sex distribution of cases identified to those published previously.¹

Socioeconomic deprivation quintiles were established by CPRD using small area-based measures of deprivation. Small area deprivation was determined using routinely collected national data that include seven components: (1) income, (2) employment, (3) health deprivation and disability, (4) education, skills and training, (5) barriers to housing and services, (6)

crime, and (7) the living environment.²⁰ Deprivation scores were assigned according to postcode by the National Statistics Office. The English Index of Multiple Deprivation divides England into 34 378 lower layer super output area with approximately 400 households or 1500 residents for each region.²⁰ Premorbid obesity was examined using the most recently recorded body mass index (BMI) prior to the index date of diagnosis within the primary care record.

Prediagnosis symptomatology was investigated among individuals for whom a diagnostic record was evident within both data sets (ie, validation code 1, 2 or 3). Predetermined symptom codes were categorised as ‘hip pain’, ‘knee pain’ and ‘altered gait’ and ‘miscellaneous leg pain’ (see online supplementary appendix 1). CPRD entries with a relevant symptom code were recorded if they occurred within 2 years of diagnosis. After the initial symptom code record, the number of subsequent primary care contacts with a relevant symptom code was determined.

Diagnoses commonly associated with SCFE within the literature (hypothyroidism, growth hormone deficiency, renal failure, renal osteodystrophy, Down’s syndrome and radiotherapy) were examined for their prevalence prior to the SCFE diagnostic code using CPRD diagnostic codes and associated prescription medication codes (see online supplementary appendix 1).

Ethics approval was given for the use of CPRD data for this study by the UK MHRA Independent Scientific Advisory Committee. The article conforms to the guidance of the REporting of studies Conducted using Observational Routinely-collected Data (RECORD) statement.²¹

Statistical analysis

Poisson CIs were calculated for rate estimations, and trends were examined using Poisson regression. The Wilcoxon-Mann-Whitney test was used to examine the age distribution of cases by gender. Kruskal-Wallis one-way analysis of variance was used to explore differences in days to diagnosis by presentation category. All statistical analyses were undertaken using Stata V.14.

The age of the individual at the BMI record was only available to researchers in whole years and so a consistent midyear point (ie, 10.5 years) was used to determine SD scores. SD (z-) scores were calculated using the Medical Research Council lmsGrowth module²² for Excel (Microsoft, Redmond, Washington, USA), which calculates z-scores based on age and sex using UK 1990 reference data. BMI records from the first year of life were excluded.

RESULTS

Five hundred and ninety-six unique patients were identified with a diagnostic code of SCFE over the study period within the data sets (figure 1). The validation algorithm found that 88% of diagnoses could be validated, and 86% of cases for whom CPRD-HES link was available (n=394) could be externally

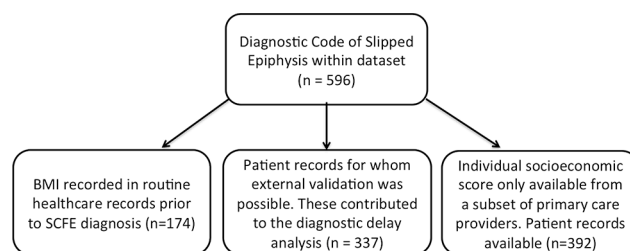


Figure 1 Flow diagram showing number of SCFE cases and missing data. BMI, body mass index; SCFE, slipped capital femoral epiphysis.

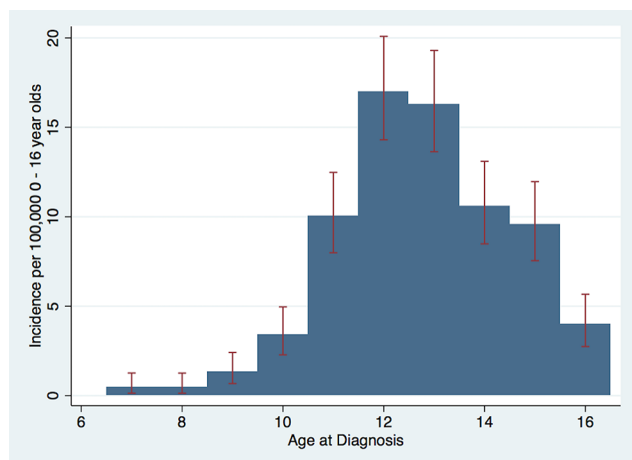


Figure 2 Histogram of age of onset of slipped capital femoral epiphysis. Each bar represents the incidence rate for age with 95% Poisson CIs.

validated. Given the high degree of validity of the diagnostic codes, all 596 remaining records were included within the subsequent analysis.

Incidence

The overall crude incidence rate was 4.8 (95% CI 4.4 to 5.2) cases per 100 000 0–16-year-olds. The disease incidence among boys was 1.7 times greater than among girls 5.7 (95% CI 5.1 to 6.3) vs 3.9 (95% CI 3.4 to 4.4) cases per 100 000 0–16-year-olds. The age distribution demonstrated that the peak age of diagnosis was 12–13 years old (figure 2, further breakdown is available as supplementary tables). Subgroup analysis suggested that the median age at diagnosis was 1 year earlier among girls, with the peak age of diagnosis being 12 years vs 13 years among boys ($p < 0.001$).

Over the 25-year study period there was no significant variation in the annual incidence of SCFE (figure 3), although there was a peak in diagnoses between 2000 and 2005. There were no significant seasonal differences in diagnosis or evidence of substantial regional variation.

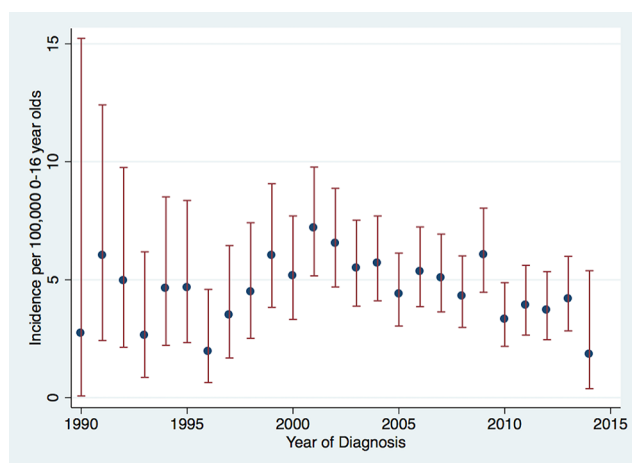


Figure 3 Scatter plot of disease incidence of slipped capital femoral epiphysis by year. Each point represents the annual incidence rate with 95% Poisson CIs.

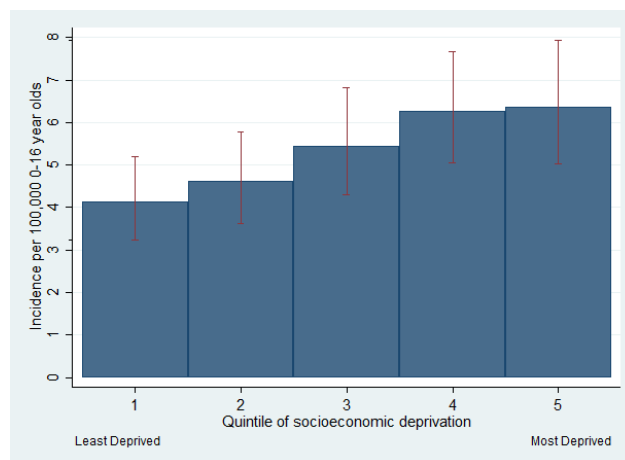


Figure 4 Scatter plot of disease incidence of slipped capital femoral epiphysis by quintile of patient-level socioeconomic deprivation. Individual quintiles of deprivation were available for 392 patients from practices within England.

Socioeconomic deprivation

Three hundred and ninety-two cases within England had an available patient-derived area-level socioeconomic deprivation score. There was a strong association between area-level deprivation and incidence of SCFE (figure 4). The incidence of SCFE increased from 4.1 (95% CI 3.2 to 5.2) cases per 100 000 in the least deprived quintile (quintile 1), to 6.4 (95% CI 5.0 to 7.9) cases per 100 000 children in the most deprived quintile (quintile 5). Poisson regression revealed a significant increase in the rate of SCFE with each quintile of worsening deprivation incidence rate ratio (IRR) 1.12 (95% CI 1.05 to 1.21, $p < 0.001$) (figure 4).

Symptomatology and diagnostic delays

Two hundred and fifty-four of 337 children (75.4%) had a relevant diagnostic code that preceded their SCFE diagnosis by less than 2 years. The median number of additional primary care contacts with a relevant symptom code, following the first symptom presentation to the time of the diagnostic record, was 1 (IQR 1–2). The median number of days from first presentation with a relevant symptom code, to diagnostic record was 26 (IQR 5–156). Symptom category was significantly associated both with time to diagnosis and the number of presentations before a diagnosis was recorded (table 1). Presentations with an initial record of knee pain demonstrated the greatest delay (median days to diagnosis 161 (IQR 27–278) vs 20 (5–126) with record of hip pain,

Table 1 Relationship between first symptom code recorded (within 2 years prior to slipped capital femoral epiphysis diagnosis) and the time/number of attendances until diagnosis

Initial symptom code	Median time to index date of diagnostic record (IQR)	Median number of additional visits with a relevant symptom code from first record of symptoms to diagnosis (IQR)
Hip pain (n=164)	20 days (5–126)	1 (1–2)
Knee pain (n=78)	161 (27–278)	2 (1–3)
Gait (n=23)	21 (7–72)	2 (1–3)
Misc leg pain (n=62)	74 (15–192)	2 (1–3)
Total (n=254)	26 (5–156)	1 (1–2)
Kruskal-Wallis	$p < 0.001$	$p < 0.001$

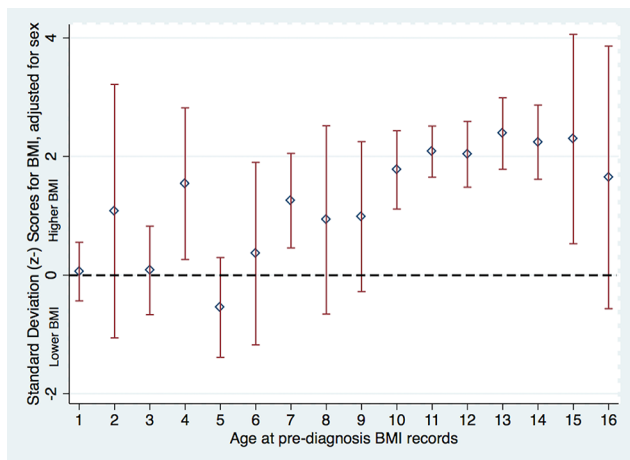


Figure 5 BMI prior to diagnosis, using the most recent BMI recorded in primary care before slipped capital femoral epiphysis diagnosis. Red diamonds represent the standard deviation (z-) score and error bars represent 95% CIs. z-Scores derived using British 1990 data set. BMI, body mass index.

Kruskal-Wallis $p < 0.001$). In some instances more than 10 separate primary care contacts with relevant symptoms codes, typically knee pain, were recorded before a SCFE diagnostic code appeared in either CPRD or HES.

Childhood BMI

One hundred and seventy-four children had a BMI recorded within their electronic medical records prior to the diagnosis of SCFE. A diagnostic record of SCFE was strongly associated with a higher mean z-score, with the mean recorded BMI being 1.43 (95% CI 1.20 to 1.68) SD above the UK reference mean (figure 5).

Comorbid disease associations

Of the 596 children within the cohort, 16 (2.7%) children had either a diagnostic code of hypothyroidism or a prescription record for thyroid hormone replacement therapy. Other comorbidities investigated (Down's syndrome, renal failure, renal osteodystrophy, growth hormone deficiency and radiotherapy) had very low overall prevalence, with only 8 (1.3%) children having either a diagnostic or drug code of any of these diseases. We are unable to report these numbers in further detail in accordance within our licence agreement regulating the reporting of small numbers.

DISCUSSION

This is the first study to examine the epidemiology of SCFE using linked primary and secondary care records. The overall incidence throughout the study period was 4.8 (95% CI 4.4 to 5.2) cases per 100 000 0–16-year-olds, that is, approximately 624 (95% CI 572 to 676) new cases of SCFE per year in the UK, based on 2015 population estimates of 13 million children in this age range, or a lifetime SCFE risk of approximately 1:1300 to individuals. We found a strong association with premorbid obesity and socioeconomic deprivation, as well as frequent delays in correctly diagnosing new SCFE cases.

External validation

The sex ratio demonstrated a strong male predominance, with the mode age of disease presentation between 12 and 13 years

old, and an earlier peak among girls. These findings are consistent with other studies.^{1 12 14 23} The incidence rates were comparable with those published for Scotland (approximately 5 per 100 000 6–18-year-olds).¹ These similarities suggest that the diagnostic codes used in this study are a true reflection of SCFE incidence in the UK.

Longitudinal and geographical trends

There was no significant fluctuation in incidence rates by time or geographical area. The highest incidence of SCFE occurred in 2001. Murray and Wilson¹ and Maffulli and Douglas²³ both independently analysed data from Scotland between 1980 and 2000, and identified a gradual increasing frequency of SCFE. Our data suggest that, after a peak incidence in 2001, there was a gradual decline in the incidence of SCFE. Interestingly, data from the Health and Social Care Information Centre suggest a peak in prevalence of UK childhood obesity at a similar time (2004), with a gradual reduction afterwards.²⁴ These observations may provide further ecological evidence to support an association with obesity. Our study was unable to reproduce the seasonal association reported by one previous study, which suggested that children were at higher risk of SCFE during the summer months.¹⁴

Obesity

Previous case series have reported an association between obesity and SCFE. However, these often recorded BMI following diagnosis, which is problematic because obesity could also be a consequence of exercise limitation caused by SCFE. However, our study found that individuals with SCFE have a much higher BMI (recorded before SCFE diagnosis) than a comparable British reference population.²² The mean BMI was approximately 2 SD above 'normal' for all children with SCFE whose height and weight were recorded between 10 and 16 years old. This supports the finding of one previous small study ($n=26$) that found early BMI abnormalities in children prior to the diagnosis of SCFE,¹⁶ and several larger series from specialist centres that report strong associations with obesity among children affected by SCFE.^{12 14 15} However, only 174 children had a BMI recorded within their medical records prior to diagnosis, which may introduce a selection bias. Such individuals may have had their BMI recorded owing to a particular concern (eg, obesity), which may therefore misrepresent the cohort. The consistent evidence from various study designs is however suggestive that there is a strong association between obesity and SCFE. The true nature of the obesity association requires a prospective cohort study of childhood BMI linked to subsequent morbidity outcomes, although a sufficiently large cohort of children is difficult to identify.

Deprivation

This study is the first to examine the association between SCFE and socioeconomic deprivation. It demonstrated that quintiles of small area-level socioeconomic deprivation are associated with increased disease incidence. One limitation of this approach is that area-based deprivation may lead to ecological error by assuming homogeneity among individuals enumerated within each region. Assigning an area score to an individual may therefore misclassify individuals who are atypical for their region. Although the mechanism underlying the association between area-level deprivation and SCFE incidence is unclear, one possibility is childhood obesity, which is known to be independently associated with socioeconomic deprivation.²⁵ This association may therefore represent further ecological evidence of an association between SCFE and obesity.

Diagnostic delay

The majority of patients (75.4%) had multiple contacts with primary care displaying relevant symptoms before a diagnosis was established. Importantly, patients who initially presented with knee pain were less likely to be diagnosed promptly than those with hip pain or gait abnormalities. This is important because one-third of patients initially presented with knee symptoms. The finding that patients with SCFE with knee pain are less likely to be diagnosed promptly supports the conclusions of smaller studies from specialist centres.^{3,26} There is evidence to suggest that increased time to diagnosis worsens both the degree of hip deformity and prognosis.^{6,14} Diagnostic delays are therefore a major source of litigation in both hospitals and primary care.⁷ The Medical Defence Union, which is just one of the providers of medical indemnity to doctors in the UK, manages 5–10 claims related to diagnostic delays in SCFE each year, which can each settle for up to £500 000 (US\$612 000) (Medical Defence Union, personal communication, 2016). It is therefore particularly important that non-specialist doctors recognise the potential significance of knee pain in children, as they are most likely to encounter patients with undifferentiated SCFE at their initial presentation. Examination and documentation of hip movements are therefore fundamental when examining a child with knee pain, particularly if pretest probability (eg, based on age and body habitus) is high for SCFE. We acknowledge the limitation that there is uncertainty that the child did not have an alternative cause of pain at initial consultation; however, even closely reviewing individual medical records, it would not be possible to differentiate these from SCFE. The finding that diagnostic delays were associated with knee pain supports the existing literature of hospital case series.

Comorbid diseases

The overall prevalence of associated diseases was very low, and these diseases appear to contribute little to the development of SCFE at a population level. Nevertheless, we recognise that the risk to an individual of SCFE may be higher once diagnosed with an associated disease, particularly hypothyroidism. Although this association could not be quantified in the absence of a control group, the absolute contribution of comorbid diseases to SCFE in the UK appears to be small.

CONCLUSION

This is the first study to link primary and secondary care data in order to describe the epidemiology of SCFE. In addition to characterising patients who are at greatest risk, it has confirmed the ecological association between obesity and SCFE. It also highlighted the difficulties inherent in correctly diagnosing SCFE in primary care, particularly when children present 'atypically' with knee pain. The data suggest that these patients are less likely to be diagnosed promptly, which might contribute to worse clinical outcomes and claims for clinical negligence. This highlights the need for judicious clinical examination and due consideration of hip signs when children present with knee pain.

Correction notice This paper has been amended since it was published Online First. Owing to a scripting error, some of the publisher names in the references were replaced with 'BMJ Publishing Group'. This only affected the full text version, not the PDF. We have since corrected these errors and the correct publishers have been inserted into the references.

Contributors DCP conceived the study, undertook the data analysis and drafted the manuscript. DM contributed to the study design, data analysis and drafting of the manuscript. MLC and TVS contributed to the study design, helped interpret the data and made important critical revisions to the manuscript.

Funding This work was supported by the Academy of Medical Sciences Starter Grants for Clinical Lecturers (cofunded awards from the Academy, Wellcome Trust, Medical Research Council, British Heart Foundation, Arthritis Research UK, the Royal College of Physicians and Diabetes UK). DCP is funded by a National Institute for Health Research as an NIHR Clinician Scientist.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Pursuant to the terms of our data sharing agreement with the data owners, no additional data are available from the corresponding author. Further data may be available on application directly to NHS Digital.

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Arch Dis Child published online June 29, 2017

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