Kawasaki disease: a prospective population survey in the UK and Ireland from 2013 to 2015

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ABSTRACT

Objective Kawasaki disease (KD) is an increasingly common vasculitis with risk of coronary artery aneurysms (CAAs). The last UK survey was in 1990, whereas current epidemiology, treatment patterns and complication rates are unknown. The aim of this study was to address this knowledge gap.

Methods A British Paediatric Surveillance Unit survey in the UK and Ireland from 1 January 2013 to 28 February 2015 ascertained demographics, ethnicity, seasonal incidence, treatment and complication rates.

Results 553 cases were notified: 389 had complete KD, 46 had atypical KD and 116 had incomplete KD; 2 were diagnosed at postmortem with an incidence of 4.55/100 000 children under 5 years (2.5 months–15 years). Presentation was highest in January and in rural areas. Most were white (64%), and Chinese and Japanese Asians were over-represented as were black African or African mixed-race children. 94% received intravenous immunoglobulin (IVIG). The overall CAA rate was 19%, and all-cardiac complications affected 28%. Those with CAA received IVIG later than in those without (median 10 days vs 7 days). Those under 1 year had fewer symptoms, but the highest CAA rate (39%). Overall 8 of 512 cases (1.6%) had giant CAA, and 4 of 86 cases (5%) under 1 year of age developed giant CAA. Mortality from KD was 0.36%.

Conclusions The UK and Ireland incidence of KD has increased and is more frequently seen in winter and rural areas. Delayed IVIG treatment is associated with CAA, suggesting earlier and adjunctive primary treatment might reduce complications to prevent CAA, particularly in the very young.

BACKGROUND

Kawasaki disease (KD) is a self-limiting medium-vessel vasculitis of unknown aetiology that typically presents in children and adolescents with fever and mucocutaneous changes. If left untreated, 15%–25% of children will develop coronary artery aneurysms (CAAs); 2%–3% of untreated cases die as a result of coronary vasculitis causing myocardial ischaemia, sometimes many years later.1 The incidence of KD varies from 308 per 100 000 children under 5 years in Japan, to about 5–8 per 100 000 in England.2,3 The high rate in North-East Asians, which persists after migration to countries with low incidence,4 is strong evidence for a genetic factor, and there is clear evidence from genome-wide association studies of an important role of genetic variants in determining susceptibility. The aetiology of KD is unknown, but seasonal variation, occurrence of epidemics and association with wind patterns would be compatible with an infectious or toxic trigger.5,6

KD is the most common cause of acquired heart disease in children in the UK and USA.7,8 Prompt diagnosis is essential to minimise complications. Intravenous immunoglobulin (IVIG) has formed the mainstay of primary treatment following publication of a seminal clinical trial in the 1980s.9 However, IVIG resistance occurs in up to 20%–40% of unselected cases and is associated with increased coronary complication rates.1,10 Recent studies and meta-analyses of all published studies have suggested that addition of corticosteroids to IVIG reduces the risk of CAA, particularly in high-risk patients.1,11 However, there is currently no

What is already known on this topic?

- Kawasaki disease (KD) is the most common acquired heart disease in the Western world, with the highest incidence in North-East Asians and with unknown aetiology.
- Seasonal variation, with peaks in winter and spring, and reported epidemics suggest that there are environmental factors that trigger the condition.
- The original British Paediatric Surveillance Unit study in 1990 suggested that UK patients might have high coronary artery aneurysm (CAA) rates despite intravenous immunoglobulin (IVIG).

What this study adds?

- There is a rising incidence of KD, with increased incidence in Asians and Black Africans, and increased incidence in rural populations.
- Children under 1 year are at highest risk of CAA (39%), are more likely to present with atypical KD. Late diagnosis is associated with CAA.
- The overall frequency of CAA remains high at 19% despite more widespread use of IVIG, although mortality is now tenfold lower than documented in 1990.
reliable method to predict which patients are at risk of CAA and thus require additional treatment, as scoring systems that predict IVIG non-response in Japan have not been reliable in studies in the UK and North America.

The last comprehensive epidemiological study of KD in the UK was undertaken by the British Paediatric Surveillance Unit (BPSU) in 1990.12 This revealed an incidence of 3.4/100,000 children under 5 years from 1 January to 31 December 1990, and a higher than expected coronary complication rate of 29% in those children who had received IVIG, comparable with those patients who did not receive IVIG. More recent epidemiological studies noted a higher UK incidence of 8.39–9.1/100,000 children under the age of 5,13–15 but both were limited by indirect retrospective epidemiological methodologies and thus may not be accurate. Moreover, 24% of children with KD are older than 5 years,13–15 but accurate UK epidemiological data are lacking in this age group.

The incidence of KD has been reported to be increasing in many countries. Furthermore, the population demographics are changing, and there is therefore a need for updated information on KD in the UK.16–17 The purpose of this study was to establish the current incidence of KD in the UK, noting the seasonal variation; to assess complication rates and the factors influencing these; and to shape future management practice based on these data (box 1). Areas of particular interest included the potential influence of ethnicity, urbanisation and disease outcomes in the light of recently updated clinical guidance regarding the use of corticosteroids for KD.1

METHODOLOGY

The study used the BPSU methodology for the epidemiological research surveillance, similar to the 1990 BPSU KD survey.12 Each month all paediatricians and paediatric cardiologists (list available from the Royal College of Paediatrics and Child Health and the British Congenital Cardiac Association) were contacted by email to report if they had seen a case of KD (box 2). If notified, the BPSU would then make the research team aware and a questionnaire was posted. This surveillance methodology provided an active, real-time quantitative portrait of KD in the defined population. All of the UK and Ireland were included in the study. Also included were the Channel Islands and Isle of Man. Incidence was calculated by applying the most recent resident population data from the 2011–2015 Census of Population18 and their equivalents from Ireland.19

Inclusion criteria

In the first year, the protocol requested the reporting of only complete KD cases, but in the second year all cases of KD (ie, including atypical and incomplete KD as per the aforementioned definitions) were included. Where the interpretation of clinical features was uncertain, expert panel review (RMRT, RM-W, AVR, EJT, DS, PAB) of the case was undertaken to ascertain by consensus (defined as 100% agreement among experts) if the diagnostic criteria for KD had been fulfilled, and if so how to classify the subtype of KD (complete, atypical or incomplete) for inclusion in the study.

Exclusion criteria

The exclusion criteria were patients older than 16 years, outside the predefined study period and those with alternative final diagnoses. In addition, for the first year of the study, those with streptococcal infection were excluded, but not in the second year of study, since it is now recognised that streptococcal infection (and other infections) may be associated triggers for responses resulting in KD.20

Cardiac involvement

We defined CAA as a Z score of ≥2.5 internal diameter.21 The Z scores were checked or completed, using the Cardio Z software, based on the data supplied by Dallaire and Dahdah.22 Those with aneurysms were referred to as CAA+ and those without were CAA−. In addition, there were some children with bright coronary artery walls, dilated (but non-aneurysmal) coronary arteries, pericardial effusion or myocarditis. These were recorded as cardiac involvement, but not CAA. We recorded the early presence of CAA at diagnosis, and also in some cases later echocardiographic data were also presented. Giant aneurysms were defined as ≥8 mm or Z score ≥10.21

Duration of the study

In accordance with the most recent BPSU methodology, data collection was over a 25-month period, January 2013–February

Box 1 Summary of the British Paediatric Surveillance Unit Kawasaki disease (KD) research questions

| Incidence |
|-----------|
| ► What are the demographics (sex, age, ethnicity, area of residence) of those diagnosed with KD in the UK and Ireland less than 16 years old? |
| ► Has the incidence changed since the last survey in 1990? |
| ► Clinical presentation and cardiac complications |
| ► How does KD first present, and what is the interval between first presentation and diagnosis? |
| ► What is the frequency and nature of cardiac complications detected using echocardiography within 30 days of developing KD? |

Clinical management

► What acute treatment is being given to patients during their initial hospital presentation with KD?

► Are treatments other than aspirin and intravenous immunoglobulin being used, and if so, have these impacted on outcome?

Other outcomes

► What is the frequency of non-cardiac complications within 30 days following KD?

► How are patients with KD being followed up within the UK and Ireland?

Box 2 Kawasaki disease (KD) case definition

Any infant or child up to the age of 16 years presenting for the first time in the UK or Ireland with fever of 5 or more days duration, plus 4 of the following (complete KD), or plus any 3 of the following (incomplete KD), or plus 2 or 3 of the following with coronary artery changes (atypical KD):

► Conjunctivitis: bilateral, bulbar, non-suppurative.

► Lymphadenopathy: cervical >1.5 cm.

► Rash: widespread, polymorphous, not vesicular.

► Lips and mucosa: red cracked lips, ‘strawberry tongue’, erythematous oral cavity.

► Changes in the extremities: erythema, oedema of palms and soles initially, later peeling of skin.
2015. All data were collected and retained in accordance with the Data Protection Act 1998.

**Data management, analysis and security**

As approved by the ethics committee, parental consent was not obtained as the identity of the cases was known only to the reporting clinician. Anonymous questionnaires were sent from our study centre after case notification. Use of the National Health Service number and date of birth allowed checks for duplication. Using the first four components of the postcode, the population density was estimated by area where each patient lived in the UK and by area in Ireland. As most of the data were categorical or not normally distributed, statistical methods based on the $\chi^2$ test were used. Statistical analysis was undertaken at Heriot-Watt University (MD, RS) using SPSS V.24. A P value of <0.05 was considered significant. The distribution of numerical values was summarised as medians and ranges; the Wilcoxon-Mann-Whitney test was used for group comparisons of those with or without CAA. A complex system-level security protocol was used and was risk-assessed on an annual basis.

**RESULTS**

Between 1 January 2013 and 28 February 2015, 601 reports of KD were received by the BPSU, with 38 duplicates, 9 other diagnoses and 1 with no clinical information. Of the remaining 553, there were 389 cases of complete KD; 46 atypical cases with fewer than 4 clinical features but with abnormal echocardiograms; and 116 cases of incomplete KD. Two cases were diagnosed retrospectively at postmortem without any clinical data to allow KD subtype categorisation (table 1).

Boys comprised a significantly greater proportion of the cases, and the proportion of Black and Asian patients was increased relative to the expected proportion of these groups in the population (table 1). There were significantly more children under 1 year old with atypical or incomplete KD (45/95; 47%), compared with children over 1 year old (102/428; 24%) ($\chi^2=21.31, p<0.0001$).

The annual incidence was estimated using the 257 cases that had been diagnosed between 1 February 2014 and 31 January 2015. Only those whose ages were reported are included. Only in the second year were all subtypes of KD reported. The age-specific annual incidences were 4.55/100 000 at age 0–4 years, 1.26/100 000 at 5–9 years, and 0.08/100 000 at 10–14 years.

**Table 1** Demographics of Kawasaki disease in the UK and Ireland

| Total number of cases | Complete | Atypical | Incomplete | Postmortem | Total |
|-----------------------|----------|----------|------------|------------|-------|
|                        | 389 %    | 46 %     | 116 %      | 2 %        | 553 100% |
| Sex                   |          |          |            |            |       |
| Male                  | 231 60   | 28 61    | 64 55      | 0          | 323 59 |
| Female                | 153 40   | 18 39    | 42 36      | 2          | 215 39 |
| Sex unreported        | 5 1      | 0 0      | 10 9       | 0          | 15 3   |
| Male to female ratio  | 1.50:1   | 1.56:1   | 1.52:1     | 0          | 1.51:1 |
| Age (years)           |          |          |            |            |       |
| <1                    | 50 13    | 20 43    | 25 22      | 2          | 100 18 |
| 1–4                   | 251 64   | 19 41    | 48 41      | 0          | 318 57 |
| 5–9                   | 69 18    | 5 11     | 28 24      | 0          | 102 18 |
| 10–16                 | 7 2      | 1 2      | 1 1        | 0          | 9 2    |
| Not reported          | 12 3     | 1 2      | 14 12      | 0          | 27 5   |
| Ethnicity             |          |          |            |            |       |
| White                 | 257 75   | 26 70    | 71 72      | 1          | 50 355 64 |
| White and black       | 12 6     | 4 5      | 4 2        | 0          | 20 7 |
| White and Asian       | 10 2     | 1 2      | 3 0        | 0          | 14 2 |
| Black                 | 39 3     | 4 6      | 3 0        | 0          | 46 4 |
| Asian subcontinent    | 25 7     | 5 8      | 12 9       | 0          | 42 10 |
| Other Asian           | 11 5     | 1 8      | 3 7        | 1          | 50 16 8 |
| Chinese/Japanese      | 14 3     | 4 2      | 2 9        | 0          | 20 5 |
| Others                | 21 5     | 1 2      | 18 16      | 0          | 40 7 |
| Country               |          |          |            |            |       |
| Scotland              | 19 5     | 3 7      | 7 6        | 0          | 28 5 |
| Ireland               | 23 6     | 0 0      | 9 8        | 0          | 31 6 |
| Wales                 | 24 6     | 7 15     | 6 5        | 0          | 35 6 |
| Northern Ireland      | 9 2      | 0 0      | 2 2        | 0          | 12 2 |
| Isle of Man/Channel Islands | 2 1 | 2 4 | 1 1 | 0 | 5 1 |
| England               | 312 80  | 34 74    | 94 79      | 2          | 100 442 80 |
| Date of illness       |          |          |            |            |       |
| 1 February 2013–31 January 2014 | 186 49 | 13 28 | 27 25 | 0 | 226 42 |
| 1 February 2014–31 January 2015 | 161 42 | 30 65 | 70 60 | 2 | 263 49 |
| Outside study period  | 36 9     | 3 7      | 9 8        | 0          | 48 9 |
Figure 1 Incidence of Kawasaki disease by month at diagnosis showing breakdown into complete, atypical and incomplete cases. PM was diagnosis at postmortem.

Date of diagnosis
Based on 479 cases reported between 1 February 2013 and 31 January 2015, more cases occurred in the winter (defined as December–February) and spring (March–May) than in the summer (June–August) and autumn (September–November) months (figure 1) ($\chi^2$ tests for monthly and seasonal variations were significant at $p=0.08$). These results controlled for length of month and confirmed the appreciable peaks in January in both ‘all’ and ‘complete’ cases.

Time to first point of clinical contact and diagnosis
Four hundred and forty-three (80%) children saw a general practitioner (GP) at a median (range) of 2 (0–27) days from the first onset of symptoms. The time from first GP consultation to hospital admission was 1 (0–32) days; the time from disease onset to formal diagnosis was 7 (0–36) days; and the time to diagnosis following admission to hospital was 1 (0–25) days, with 50 cases being diagnosed on day of admission.

We used the first four components of the postcode of patients in the UK to assign cases as resident in urban or rural areas and compared the proportion of cases occurring in rural or urban areas. Relative to the population density, we found significantly more cases occurring in rural areas (applying a non-linear cubic regression offered best fit with $r^2=0.867$, $F=30.290$, $p<0.005$) (figure 2).

Clinical features
Coronary artery status
The results of the initial echocardiograms were available for 523 of 553 children. There were 11 children in whom the weights and Z scores were missing, so these have been omitted from the analysis. Overall, 123 of 512 (24%) had abnormal coronary Z score (Z score >2) at echocardiography within 30 days of diagnosis. Of these, 95 of 512 had coronary Z score ≥2.5; thus, the overall CAA rate within 30 days of diagnosis was 19%.

In 25 children, there was a pericardial effusion recorded, and in 7 there was either valve regurgitation or depressed ventricular function. Taking these into account, the all-cardiac complication rate (coronary Z>2, or any other cardiac complication) was 28% within 30 days of diagnosis (table 2). It is of note that a much higher proportion of children under the age of 1 year had CAA+ (39%) compared with those over the age of 1 (13%, $p<0.01$). Overall, 8 of 512 cases (1.6%) developed giant CAA, and 4 of 86 cases (5%) under 1 year of age had giant CAA.

Variables associated with CAAs
We reviewed the association of CAA status with features highlighted in previous publications (table 3) to determine whether there were any associations with CAA. In addition, we explored if there were any differences in coronary outcomes
between 2013 and 2014 which may have been influenced by the publication of a new UK clinical guideline paper at the end of 2013.1 In 28 cases, we did not know the coronary artery status, and in both of the postmortem cases there were CAAs. The presence of fever plus four diagnostic features of KD at the time of diagnosis (complete KD) was associated with a lower rate of coronary artery involvement. Younger age at presentation, longer time to receive treatment, and presentation between December and May were all associated with increased risk of CAA. Additional factors associated with the presence of CAA were lower albumin and higher corticosteroid use in those with CAA (table 3).

### Treatment with IVIG and aspirin

Excluding the two cases diagnosed after death and excluding the 20 cases with incomplete data, 502 of 531 received IVIG (95%), with the recommended dose of 2 g/kg (97%). Twenty-nine of 2013 cases with incomplete data, 502 of 531 received IVIG (95%), and in both of the postmortem cases there were CAAs. Overall, 8 of 49 had persistent giant CAA, including the 4 cases of giant CAA under the age of 1 year. Three had arthralgia, one had anaemia, one had hypertension and one had leucopaenia. In addition to the two cases who were diagnosed after death, a third child with pre-existing neurological disease died from CAA. In one case the parents refused therapy (table 3). Anti-inflammatory dose aspirin (30–50 mg/kg/day, divided into four daily doses) was given to 472 of 537, while 41 did not receive any aspirin; data regarding aspirin were missing for the other cases. Following this, an antiplatelet dose of aspirin (3–5 mg/kg once a day) was given to 460 (83%) children. As shown in table 4, the proportion of patients with CAA was lowest in those treated with IVIG within 7 days of onset and increased progressively in the group treated between 7 and 10 days and above 10 days.

### Adjunctive therapy

Overall, corticosteroids were used in 49 of 512 (10%) cases where CAA status was documented, either as primary adjunctive (4.6%) or as late rescue therapy (4.8%) (table 3). Infliximab was given to 10 of 551 cases (1.8%). Many children were commenced on antimicrobials (n=73) before the diagnosis of KD was made. No other treatments were reported.

### Other outcomes

Of the 523 cases with echocardiography performed within 30 days of diagnosis, data on follow-up echocardiography beyond 30 days were available in 49 of 523, of whom 40 had persistent CAA. Overall, 8 of 49 had persistent giant CAA, including the 4 cases of giant CAA under the age of 1 year. Three had arthralgia, one had anaemia, one had hypertension and one had leucopaenia. In addition to the two cases who were diagnosed after death, a third child with pre-existing neurological disease died from intractable seizures, providing an all-cause mortality rate of 3 of 553 (0.54%), and mortality directly attributable to KD of 2 of 553 (0.36%).

## DISCUSSION

This prospective UK population-based study shows that the incidence of KD as reported by paediatricians in the UK and Ireland has risen since the last survey in 1990 (from 3.4 to 4.55/100 000 children under 5 years, with a male to female ratio of 1.51:1). It is noteworthy that estimates of KD incidence based on hospital admission or GP database statistics previously reported more than double the number of cases in our survey.26 This BPSU survey used rigorous diagnostic criteria to ensure accurate case inclusion. In contrast hospital admission data are not based on strict epidemiological KD case definitions, usually relying on diagnoses assigned by junior doctors or coding clerks, and are thus likely to significantly over-record KD cases. Conversely, the voluntary reporting system used by the BPSU could under-record cases, as busy paediatricians may not respond or recall all the cases or may believe their colleagues are doing the reporting. Therefore, our BPSU data are likely to provide a minimum estimate of annual incidence. Many features observed in this UK and Ireland study are also seen in studies from other countries, including the majority of cases being less than 5 years old, seasonal occurrence with more cases in winter and spring, and increased proportion of Chinese or Japanese Asians and black Africans relative to their proportion in the general population. We found an increased

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**Table 2** Echocardiographic data showing cardiac complications

| Time of echo | Assessed (n) | Coronary Z<2 | Coronary 2sZ<2.5 | Coronary 2.5sZ<5 | Coronary 5sZ<10 | Coronary Z≥10 | Pericardial effusion | Valve regurgitation |
|-------------|-------------|-------------|-----------------|-----------------|----------------|--------------|-------------------|-------------------|
| At diagnosis | 523         | 389         | 28              | 59              | 28             | 8            | 25                | 7                 |
| >30 days    | 49          | 9           | 20              | 12              | 8              | 0            | 0                 | 0                 |

There were 11 children in whom the weights and Z scores were missing and so have not been included in the table.

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**Table 3** Association of coronary artery status with individual variables

| Criterion | CAA+ (n=95) | CAA− (n=417) | P values |
|-----------|-------------|--------------|----------|
| Male      | 62 (69%)    | 247 (59%)    | 0.27, NS |
| Median lowest albumin, g/L | 26 | 31 | 0.049 |
| Range     | (13–41) n=83 | (21–49) n=72 |          |
| Median lowest sodium, mmol/L | 134 | 134 | 0.92, NS |
| Range     | (125–142) n=48 | (123–141) n=415 | |
| Median lowest platelet count, x10^9/L | 212 | 245 | 0.15, NS |
| Range     | (30–442) n=95 | (54–450) n=415 | |
| Median age at presentation | 21.6 | 36.0 | 0.005 |
| Range     | (2.4–190.0) n=93 | (1.2–190.0) n=409 | |
| Median time to treatment (days) | 10.0 | 7.0 | 0.005 |
| Range     | (2–37) | (1–36) | |
| Mucosal involvement at diagnosis | 77/95 (81%) | 360/416 (87%) | 0.19, NS |
| December–May presentation | 64/95 (67%) | 245/416 (59%) | 0.12, NS |
| Presentation before 1 February 2014 | 53/95 (56%) | 210/416 (50%) | 0.35, NS |
| Primary steroid use | 11/95 (12%) | 13 (3%) | |
| Late corticosteroid use | 13 (14%) | 12 (3%) | |
| No corticosteroid use | 67/92 (73%) | 359/384 (93%) | 0.03 |

P value is the difference in median; NS: The numbers of patients receiving corticosteroids were too small for meaningful statistical testing. There were 11 children in whom the weights and Z scores were missing and so have not been included in the table.

CAA+, those with coronary artery aneurysms; CAA−, those without aneurysms.
Our study confirms that children under 1 year are more likely to have atypical KD and higher rates of coronary sequelae (39%), as reported in other series.\(^1\) Diagnosis of KD is difficult in the absence of all the typical features. As a high proportion of infants under 1 year of age do not fulfil the KD diagnostic criteria, there is a need for increased awareness of the possibility of KD in any infant with evidence of persistent inflammation (raised C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) or white cell count) and no response to antibiotics. In these infants, echocardiography is an urgent investigation required as part of the diagnostic work-up of suspected incomplete KD. A high index of suspicion is thus required, and early treatment with IVIG and additional anti-inflammatory agents, and referral to specialist units for suspected atypical KD cases in view of the high risk of CAA are advised. Our findings also support the previous suggestion that children under 1 year should be regarded as high risk for coronary sequelae,\(^4\) and therefore be targeted for more aggressive primary treatment. It is also of note that there was a higher rate of CAA in children in the second half of the study, after 1 January 2014. The most likely reason for this is that we included atypical KD in the second half of the study, which has CAA by definition.

Ninety-four per cent of children received IVIG in line with current guidance, along with high-dose aspirin in almost all, although as previously highlighted those children with CAA+ were treated later (median 10 days) than those without CAA (7 days), highlighting the importance of instituting treatment as early as possible (ie, not just within 10 days) to improve outcomes.\(^5\)

Corticosteroids were only used in 10% of cases (table 3): 4.6% of cases as primary therapy and 4.8% as rescue therapy. This overall relatively low use of corticosteroids, combined with delay in initiating treatment, could explain the high CAA rates we observed, since a recent meta-analysis of 2746 patients has now demonstrated that early addition of corticosteroids is associated with reduced risk of CAA compared with IVIG therapy alone, particularly for high-risk cases (OR 0.424; 95%CI 0.270 to 0.665).\(^6\) Arguably, however, all UK patients with KD could be deemed ‘high-risk’, since 19% developed CAA within 30 days despite IVIG treatment, with even higher risk for children under the age of 1 year, of whom 39% developed CAA, and of which 5% had giant CAA with poor prognostic outcomes. We would have liked to have had follow-up on the CAA after 30 days, but we were obliged by our protocol approval by the BPSU and National Information Governance to keep this within the acute phase. We hope to be able to return to these patients and obtain ethical approval and consent for a follow-up study in the future.

**Limitations**

The BPSU methodology relies on busy doctors to complete data entry, and thus a surveillance-based study of this nature is limited since it is entirely dependent on the entry of data and case ascertainment for completeness. Therefore, although ours was a prospective study, it is expected that there will be a small proportion of cases that are not reported, as evidenced in a recent German study suggesting that up to 44% of cases can...
be missed. This will only serve to increase the incidence of KD above that in the present reported study. Also, by the nature of the BPSU study methodology, follow-up data examining late cardiac sequelae are limited.

CONCLUSIONS
KD has a rising incidence in the UK and Ireland, and cardiac sequelae are higher than reported for other countries despite most patients receiving IVIG therapy. Treatment delay is likely to have been contributory to high CAA rates. A future national UK comparative clinical trial of corticosteroids as primary adjunctive therapy for unselected patients with KD is now planned. In the meantime, GPs and paediatricians should be aware that treatment to completely ablate systemic inflammation as early as possible is required to prevent lifelong cardiac sequelae, and that the historic KD therapeutic adage of ‘treatment within 10 days’ is no longer fit for purpose.

Contributors RMRT, AH, RM-W, PAB and RML designed the project. Cases were assessed by the expert panel review (RMRT, RM-W, AVR, EJT, DS, PAB), and PC collected and recorded the data. SD provided patient participation support and informed families involved in the study of the ongoing progress. CAM, AH and ODF provided local support and assisted with recruitment. RM-W, RS and MD undertook informed families involved in the study of the ongoing progress. CAM, AH and ODF undertook statistical analysis.

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REFERENCES
1. Eleftheriou D, Levin M, Shingadia D, et al. Management of Kawasaki disease. Arch Dis Child 2014;99:74–83.
2. Nakamura Y, Yashiro M, Uehara R, et al. Epidemiologic features of Kawasaki disease in Japan: results of the 2009-2010 nationwide survey. J Epidemiol 2012;22:216–21.
3. Harnden A, Mayon-White R, Perera R, et al. Kawasaki disease in England: ethnicity, deprivation, and respiratory pathogens. Pediatr Infect Dis J 2009;28:21–4.
4. Holman RC, Curns AT, Belay ED, et al. Kawasaki syndrome in Hawaii. Pediatr Infect Dis J 2005;24:429–33.
5. Burns JC, Herzog L, Fabri O, et al. Seasonality of Kawasaki disease: a global perspective. PloS One 2013;8:e74529.
6. Rodó X, Curcoll M, Robinson M, et al. Tropospheric winds from northeastern China carry the etiologic agent of Kawasaki disease from its source to Japan. Proc Natl Acad Sci U S A 2014;111:7952–7.
7. Ghelani S, Sable C, Wiedermann BL, et al. Increased incidence of incomplete Kawasaki disease at a pediatric hospital after publication of the 2004 American Heart Association guidelines. Pediatr Cardiol 2012;33:1097–103.
8. Hall GC, Tulloh LE, Tulloh RM. Kawasaki disease incidence in children and adolescents: an observational study in primary care. Br J Gen Pract 2016;66:e271–e276.
9. Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med 1986;315:341–7.
10. Chen KY, Curtis N, Dahdah N, et al. Kawasaki disease and cardiovascular risk: a comprehensive review of subclinical vascular changes in the longer term. Acta Paediatr 2016;105:752–61.
11. Wardle AJ, Connolly GM, Seager MJ, et al. Corticosteroids for the treatment of Kawasaki disease in children. Cochrane Database Syst Rev 2017;1:C001188.
12. Dhillon R, Newton L, Rudd PT, et al. Management of Kawasaki disease in the British Isles. Arch Dis Child 1993;69:631–8.
13. Holman RC, Belay ED, Curns AT, et al. Kawasaki syndrome hospitalizations among children in the United States, 1988-1997. Pediatrics 2003;111:448.
14. Chang RK. The incidence of Kawasaki disease in the United States did not increase between 1988 and 1997. Pediatrics 2003;111(5 Pt 1):1124–5.
15. Stockheim JA, Inocentini N, Shulman ST. Kawasaki disease in older children and adolescents. J Pediatr 2000;137:250–2.
16. Brogan PA, Bose A, Burghner D, et al. Kawasaki disease: an evidence based approach to diagnosis, treatment, and proposals for future research. Arch Dis Child 2002;86:286–90.
17. Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004;110:2747–71.
18. ONS. 2011-2015 census. Ethnic group, local authorities in the United Kingdom”. Office of National Statistics 2017.
19. Central Statistics Office. Census 2011 small area population statistics (SAPS). 2015 https://www.cso.ie/en/census2011smallarea/populationstatistics/saps/.
20. Berselmi SM, McCrindle BW, Silverman ED, et al. Infections and Kawasaki disease: implications for coronary artery outcome. Pediatrics 2005;116:e60–e766.
21. McCrindle BW, Li JS, Minich LL, et al. Coronary artery involvement in children with Kawasaki disease: risk factors from analysis of serial normalized measurements. Circulation 2007;116:174–9.
22. Dallaire F, Dahdah N. New equations and a critical appraisal of coronary artery Z scores in healthy children. J Am Soc Echocardiogr 2011;24:60–74.
23. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, Treatment, and Long-term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. Circulation 2017;135:e927–e999.
24. Kobayashi T, Inoue Y, Morikawa A. [Risk stratification and prediction of resistance to intravenous immunoglobulin in Kawasaki disease]. Nihon Rinsho 2006;66:332–7.
25. Davies S, Sutton N, Blackstock S, et al. Predicting IVIG resistance in UK Kawasaki disease. Arch Dis Child 2015;100:366–8.
26. Harnden A, Alves B, Sheikh A. Rising incidence of Kawasaki disease in England: analysis of hospital admission data. BMJ 2002;324:1424–5.
27. Tizard EJ, Suzuki A, Levin M, et al. Clinical aspects of 100 patients with Kawasaki disease. Arch Dis Child 1991;66:185–8.
28. Mossberg M, Segelmark M, Kahn R, et al. Epidemiology of primary systemic vasculitis in children: a population-based study from southern Sweden. Scand J Rheumatol 2004;18:295–302.
29. Lyksina G, Bockeria O, Shirinsky O, et al. Cardiovascular outcomes following Kawasaki disease in Moscow, Russia: A single center experience. Glob Cardiol Sci Pract 2017;23:e201723.
30. Chen S, Dong Y, Kuchiy MG, et al. Coronary-Artery Complication in Kawasaki Disease and the Importance of Early Intervention: A Systematic Review and Meta-analysis. JAMA Pediatr 2016;170:1156–63.
31. Jakob A, Whelan J, Kordecki M, et al. Kawasaki Disease in Germany: A Prospective, Population-based Study Adjusted for Underreporting. Pediatr Infect Dis J 2016;35:129–34.