Childhood/adolescent Sydenham’s chorea in the UK and Ireland: a BPSU/CAPSS surveillance study

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ABSTRACT
Objective To conduct the first prospective surveillance study of Sydenham’s chorea (SC) in the UK and Ireland, and to describe the current paediatric and child psychiatric service-related incidence, presentation and management of SC in children and young people aged 0–16 years.

Design Surveillance study of first presentations of SC reported by paediatricians via the British Paediatric Surveillance Unit (BPSU) and all presentations of SC reported by child and adolescent psychiatrists through the Child and Adolescent Psychiatry Surveillance System (CAPSS).

Results Over 24 months from November 2018, 72 reports were made via BPSU, of which 43 met the surveillance case definition of being eligible cases of suspected or confirmed SC. This translates to an estimated paediatric service-related incidence rate of new SC cases of 0.16 per 100 000 children aged 0–16 per year in the UK. No reports were made via CAPSS over the 18-month reporting period, although over 75% of BPSU cases presented with emotional and/or behavioural symptoms. Almost all cases were prescribed courses of antibiotics of varying duration, and around a quarter of cases (22%) received immunomodulatory treatment.

Conclusions SC remains a rare condition in the UK and Ireland but has not disappeared. Our findings emphasise the impact that the condition can have on children’s functioning and confirm that paediatricians and child psychiatrists should remain vigilant to its presenting features, which commonly include emotional and behavioural symptoms. There is a further need for development of consensus around identification, diagnosis and management across child health settings.

WHAT IS ALREADY KNOWN ON THIS TOPIC
Sydenham’s chorea (SC) is considered a rare disease, but there have been no previous prospective surveillance studies in the UK and Ireland.

WHAT THIS STUDY ADDS
This study provides the first estimate of the service-related incidence of SC in the UK.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
This study highlights the importance of remaining vigilant to the presenting features of SC.

INTRODUCTION
Sydenham’s chorea (SC) is a neuropsychiatric condition largely affecting children and adolescents, associated with prior Group A Streptococcal infection. SC is a major criterion for rheumatic fever diagnosis and occurs alone or alongside other features. SC is characterised by purposeless, involuntary, non-stereotypical movements of the trunk or extremities (chorea), often associated with muscle weakness and emotional lability. Symptoms range from mild to severe but can severely impact a child’s ability to perform activities of daily living. The chorea is often accompanied by emotional and behavioural symptoms, including anxiety, tics, obsessions and compulsions that may be severe and persistent. Symptoms usually resolve within 2 years, but for 20% may become chronic.

SC is currently considered a ‘rare disease’ but it is unclear how many children are affected by it, their clinical journey or their needs. Previously, only single-centre retrospective studies in paediatrics have taken place in Western Europe, but such methods have limitations in capturing cases and clinical detail. Reports also suggest that SC is often not recognised promptly. Rare conditions may have greater impact on families, who may become more isolated, lack information on prognosis and experience more diagnostic delays. This research was therefore developed in partnership with the Child and Adolescent Psychiatry Surveillance System (CAPSS), and the Child and Adolescent Mental Health (ChYMe) research collaboration, University of Exeter Medical School, Exeter EX1 2LU, UK; t.newlove-delgado@exeter.ac.uk

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with the family-led charity, the Sydenham’s Chorea Association (http://www.sydenhamschorea.org.uk/).

This paper describes the first prospective surveillance study of SC in the UK and Ireland, with paediatricians via the British Paediatric Surveillance Unit (BPSU) and with child and adolescent psychiatrists through the Child and Adolescent Psychiatry Surveillance System (CAPSS). The parallel surveillance method was chosen as children with SC may be seen by child psychiatrists due to the high prevalence of emotional and behavioural symptoms.

The study aimed to answer the following three main questions:

► What is the paediatric service-related incidence of first presentations of SC in children and young people aged 0–16 years in the UK and Ireland?

► What is the psychiatric service-related incidence of children and young people with SC and associated psychiatric symptoms in the UK and Ireland?

► What are the most common presenting features of SC, and what is the current clinical practice in terms of investigations, management and referral?

METHODS

BPSU surveillance

We conducted a prospective surveillance study of suspected or confirmed first presentations of SC in children and young people aged 0–16 years (case definition in table 1) with paediatricians in the UK and Ireland from November 2018 to November 2020 via the BPSU using their standard ‘Orange card’ anonymous notification methodology, summarised in figure 1. SC is frequently a clinical diagnosis, based on the distinctive presentation. Laboratory confirmation of streptococcal infection and echocardiographic findings provide supportive evidence of SC. However, the absence of these does not preclude clinical diagnosis, as SC onset may be delayed following infection with no persisting serological evidence. Consequently, our case definition of confirmed cases included all clinically confirmed cases.

Questionnaires were piloted by paediatricians before finalising and included items on characteristics of case and service; clinical presentation and antecedents; investigations and management, referrals, service-related outcomes, impairment and impact on activities of daily living using the Universidade Federal de Minas Gerais (UFMG) SC rating scale; impact on education (see online supplemental material).

CAPSS surveillance

CAPSS uses a very similar surveillance methodology to BPSU, with monthly e-cards sent to child and adolescent psychiatrists registered with the system. The case definition (table 2) and questionnaire (online supplemental materials) differed between the CAPSS and BPSU, capturing service-related incidence of any presentations of SC or associated psychiatric symptoms to child and adolescent psychiatrists, not only new onset SC, as psychiatric symptoms may appear much later. Surveillance through CAPSS took place from May 2019 to December 2020 (18 months).

Analysis

Our analysis of characteristics included all cases meeting the surveillance case definition were analysed, with sensitivity analysis in Stata V.17.0 performed using confirmed cases. Descriptive analysis was performed presenting data rounded percentages for the full sample following statistical disclosure principles. Where possible, incidence was calculated using official national mid-year population estimates for children aged up to 16 for the appropriate geographies.

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**Table 1** Case definitions for BPSU study

<table>
<thead>
<tr>
<th>Surveillance case definition</th>
<th>Please report:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children and young people aged 0–16 years presenting to the reporting clinician for the first time in the surveillance period with a first episode of suspected or confirmed Sydenham’s chorea (SC).</td>
<td>- Children and young people presenting to you for the first time in the surveillance period with a first episode of suspected or confirmed SC.</td>
</tr>
<tr>
<td></td>
<td>- According to the Jones criteria for acute rheumatic fever, SC is defined as ‘purposeless, involuntary, non-stereotypical movements of the trunk or extremities, often associated with muscle weakness and emotional lability’.</td>
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<td></td>
<td>- SC is typically of acute or subacute onset, meaning that the chorea reaches a peak within days or weeks rather than months. 2</td>
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<td></td>
<td>- The Jones criteria list the differential diagnoses which must be excluded in order to confirm a diagnosis of SC (detailed in full in the reporting card).</td>
</tr>
<tr>
<td></td>
<td>- Chorea is frequently a clinical diagnosis. It is important to note that laboratory confirmation of streptococcal infection provides supportive evidence of SC, but the absence of such laboratory evidence does not preclude clinical confirmation.</td>
</tr>
</tbody>
</table>

Please report cases presenting to you for the first time during the surveillance period, who are new cases of suspected or confirmed SC (with no prior diagnosis before the current episode). These cases may be either:

► Suspected: cases presenting with chorea with acute/subacute onset, but where no diagnosis has yet been made.

► Confirmed clinically: cases where a new diagnosis of SC has been made, with chorea presenting with acute or subacute onset, and lack of clinical or laboratory evidence of an alternative cause as defined above by the Jones criteria.

**Table 2** Case definitions for CAPSS study

<table>
<thead>
<tr>
<th>Case definitions for CAPSS</th>
<th>Suspected: Children and young people aged 0–16 years presenting to the reporting clinician for the first time in the surveillance period with a first episode of suspected SC.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children and young people</td>
<td>Confirmed: Children and young people aged 0–16 years presenting to the reporting clinician for the first time in the surveillance period with a first episode of confirmed SC.</td>
</tr>
</tbody>
</table>

**Figure 1** A summary of the BPSU ‘orange card’ surveillance study reporting and follow-up process. BPSU, British Paediatric Surveillance Unit.
RESULTS

Ascertainment
Over 24 months, 72 reports were made via BPSU, of which 43 met case definition (n=12 suspected, n=31 confirmed cases). The remainder were ineligible (n=8 not SC or not new, n=6 duplicates, n=15 unable to confirm). Returned questionnaire response rate was 79% (57/72).

No reports were made via CAPSS over the 18-month reporting period.

Incidence
Based on a mid-year UK population estimate (including all four nations) of 13 468 262 children aged 0–16 years, the cases (suspected and confirmed) reported to our study would result in a paediatric service-related incidence rate of new SC cases of 0.16 per 100 000 children per year (95% CI 0.11 to 0.25). Using only confirmed cases to generate an estimate, the incidence rate would decrease to 0.12 per 100 000 children per year (95% CI 0.07 to 0.19). Applying an alternative assumption, that 84.3% of the population would meet the case definition (using the mean titre was 600 IU/mL. The majority of patients had an anti-streptolysin titre (ASOT) was performed. ASOT measures levels of anti-streptolysin antibodies, indicating previous streptococcal infection. Nineteen per cent of reported cases had an elevated ASOT (200 IU/mL or above) and the mean titre was 600 IU/mL. The majority of patients had an ECG (95%), MRI head (86%), echocardiogram (84%) and a throat swab for microscopy, culture and sensitivity (77%). Other tests reported as performed are presented in online supplementary table 1.

Characteristics
Mean age of presenting cases was 9.4 years (range 4–16), with 68% being female. Of these cases, 87% were of white ethnic background, slightly exceeding the UK Census estimates (81.7%). About 74% of cases reported were from England; few cases were from Wales (n<5), Scotland (n<5) or Northern Ireland (n<10). Of these, 55.6% of cases were reported by consultant general paediatricians and 30.2% by consultant paediatric neurologists.

Presenting features
Categories of clinical features at presentation are reported in figure 2. All cases had chorea, as dictated by our case definition, which was moderately severe at presentation in 72% of cases (n=31), with the remaining either severe (14%), or minimal or mild (7%). The most common presenting symptoms (besides chorea) were gait disturbance and loss of fine motor skills, both of which were reported in 91% of cases (n=39).

Overall, at least one neuropsychiatric, emotional or behavioural feature was reported in 86% (n=37) of cases. Emotional lability was seen in 77% of all cases, some form of anxiety was present in 51%, tics in 37% and inattention/attention deficit in 35%. Other criteria for rheumatic fever (besides SC itself) such as erythema marginatum, subcutaneous nodules, carditis and polyarthitis appeared rare as presenting features in this sample (see figure 2). A sensitivity analysis of presenting features in confirmed cases only found no statistically significant differences in presentation (p<0.05 threshold).

Clinicians were asked to rate the child’s functioning at presentation. The mean score on the UFMG rating scale functional impairment domains was 2.0 (0 is ‘no impairment’ and 4 is ‘severe impairment’); 51% of children had severe impairment due to chorea on at least one of the six domains (hygiene, handwriting, dressing, speech, walking and handling utensils).

Investigations and results
In all reported cases, anti-streptolysin titre (ASOT) was performed. ASOT measures levels of anti-streptolysin antibodies, indicating previous streptococcal infection. Nineteen per cent of reported cases had an elevated ASOT (200 IU/mL or above) and the mean titre was 600 IU/mL. The majority of patients had an ECG (95%), MRI head (86%), echocardiogram (84%) and a throat swab for microscopy, culture and sensitivity (77%). Other tests reported as performed are presented in online supplementary table 1.

Antecedents
About 54% (n=24) of cases reported sore throat in the 6 months prior to the onset of chorea and 21% were diagnosed with acute antecedents.

Table 2. Case definition and reporting instructions for CAPSS study

<table>
<thead>
<tr>
<th>Surveillance case definition</th>
<th>Reporting instructions to child and adolescent psychiatrists</th>
</tr>
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<tbody>
<tr>
<td>Children and young people aged 0–16 years that have or have had a suspected or confirmed diagnosis of Sydenham’s chorea (eg, by paediatrician) and present to the reporting clinician for the first time within the current episode of care with psychiatric symptoms.</td>
<td>Please report:</td>
</tr>
<tr>
<td>► Children and young people aged 16 years or under who have or have had a suspected or confirmed diagnosis of Sydenham’s chorea (eg, by paediatrician) and present to you for the first time within the current episode of care (regardless of whether this is their first contact with CAMHS or not) with one or more psychiatric symptoms.</td>
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<tr>
<td>► Chorea is defined as a state of excessive, spontaneous movements, irregularly timed, non-repetitive, randomly distributed and abrupt in character. These movements may vary in severity from restlessness with mild intermittent exaggeration of gesture and expression, fidgeting movements of the hands, unstable dance-like gait to a continuous flow of disabling movements.</td>
<td></td>
</tr>
<tr>
<td>► Sydenham’s chorea is frequently a clinical diagnosis. Laboratory confirmation of streptococcal infection (eg, by throat swab) provides supportive evidence of Sydenham’s chorea but the absence of investigation does not preclude clinical confirmation. Cases may fall into any of these categories:</td>
<td></td>
</tr>
<tr>
<td>– Suspected Sydenham’s chorea: cases presenting with chorea but where no clear diagnosis has yet been made.</td>
<td></td>
</tr>
<tr>
<td>– Confirmed Sydenham’s chorea: where a diagnosis of Sydenham’s chorea has been made (eg, by paediatrician) and alternative causes have been excluded.</td>
<td></td>
</tr>
</tbody>
</table>

CAPSS, Child and Adolescent Psychiatry Surveillance System.

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rheumatic fever (ARF) according to paediatrician report. There was only one case with a family history of SC and no reports of family histories of rheumatic fever or other movement disorders.

Management
About 77% of patients (n=33) were admitted to hospital during the clinical episode, with a median stay of 5 days. All but one were prescribed antibiotics, but dose and duration were not specified by most respondents. The most commonly prescribed course was 10 days of penicillin V followed by long-term prophylaxis (23%, n=10), but antibiotic regimes varied. Other treatments used included symptomatic treatment of chorea with anticonvulsants and neuroleptics (53%, n=23), most commonly sodium valproate, haloperidol or carbamazepine. About 28% of patients received immunomodulation, with 16% prescribed steroids, and 12% receiving intravenous immunoglobulins. A total of 51% of children were referred to occupational therapy or physiotherapy, and 14% to clinical psychology or neuropsychology. Fewer than five patients were referred to CAMHS.

DISCUSSION
Our estimates of incidence of 0.16 per 100 000 per year (or 0.21 per 100 000 corrected for reports which could not be followed up) are the first prospective estimates of incidence of SC for children in the UK, and align with Crealey et al’s earlier retrospective case note study from the Republic of Ireland, which estimated an incidence rate of 0.23 per 100 000.10 We report similar age and gender profiles of children to other epidemiological studies from other settings.13 24 The very low incidence of family history of SC identified in this study is comparable with recent Italian and Turkish findings.9 23

In the vast majority of cases, chorea was associated with moderate or severe functional impairment. ‘Mild’ cases may not be identified or recognised by families or professionals, reducing specialist referrals. The most common presenting features reported (besides chorea) were gait disturbance, loss of fine motor skills and dysarthria. Our reported rates of carditis (12%) were much lower than the rates of ‘around 60%’ found in an older Australian study and 81% presented by Orsini et al in 2022.9 26 Despite the association of SC and rheumatic heart disease, 16% were reported as having no echocardiogram.

Neuropsychiatric, emotional and behavioural symptoms were common in line with the systematic review by Punukollu et al.4 However, most children were not referred to CAMHS and no SC cases were reported via CAPSS over an 18-month period. This may be because co-occurring emotional and behavioural problems are not recognised or prioritised during the acute presentation of chorea, due to low confidence among paediatricians in assessing and making appropriate referrals, or because symptoms may be managed within paediatric services rather than referred onto CAMHS.

Alternatively, the absence of case reports from CAMHS consultants may be due to children being seen in CAMHS but not seen by the consultant child and adolescent psychiatrists, who are reporting into CAPSS, or to clinicians in CAMHS not making the link between a child’s emotional or behavioural symptoms and a history of SC.

Strengths and limitations
The main strength of this study is the use of established prospective active surveillance methodology through the BPSU and CAPSS, meaning that clinicians are requested to return a response monthly even if no cases have been seen. The BPSU had an 88% response rate for surveillance cards in 2020.27 In this study, another strength was also the high response rate: 80% of all questionnaires sent out were returned.

There are a number of weaknesses to consider in the methodology. During our study period, CAPSS had a lower response rate for surveillance cards (an average of 60% over the study period), meaning that cases may have been seen but not notified. Furthermore, while the BPSU and CAPSS achieve high coverage of consultants, there is a delay in updating contact lists which may mean not all new consultants or retiring consultants are included in or removed from databases. Furthermore, where cases are seen by other team members, they will not be reported unless specifically notified to the consultant. It is also possible that non-response to both the surveillance cards and the questionnaires may be associated with characteristics such as a particularly heavy workload. However, without data from non-responders or cases that might be seen elsewhere, we are unable to adjust our incidence estimates to reflect these effects.

Finally, after extensive consultation, and as SC is a clinical diagnosis, consultants were given the option to report cases as suspected or confirmed. We therefore report incidence using both our surveillance definition of confirmed or suspected SC; and our analytic definition of confirmed SC only, but present the remaining data on presentation and management using the surveillance definition.

Implications for research and practice
This study contains a number of implications for research and practice. First, it confirms the need for clinicians to remain vigilant to the presenting features of SC. Although a rare condition, it has not disappeared, and the impact on children’s functioning can be severe.

Under-reporting of SC may also be linked to a question that has arisen in discussions with paediatricians and child psychiatrists, as well as through involvement with patient groups. This is the distinction between SC and paediatric autoimmune neuropsychiatric syndrome (PANS)/paediatric autoimmune neuropsychiatric disorder associated with Streptococcus (PANDAS). The distinctive feature of SC is the presence of clinically significant chorea resulting in functional impairment at disease onset.4 28 However, there are overlaps in presenting features. While SC has been thought of as ‘a thing of the past’, PANS and PANDAS have an increasingly high profile. Ensuring that SC is recognised is important clinically as it requires long-term penicillin prophylaxis to prevent further attacks of ARF, sequelae of rheumatic heart disease and recurrent SC. Consensus development is needed in this area to combine expertise and evidence and provide greater clarity for clinicians and families.

Similarly, the findings do suggest variability in clinical management reported in our study, and in particular the use of antibiotics and immunomodulation, implying that harmonisation of management is merited. However, while there is evidence for the effectiveness of steroids, further well-conducted trials are needed to determine best practice.24 There are challenges in conducting trials in rare disease research, but there are opportunities to address these through greater international collaboration, use of electronic medical records and adaptation of standard trial designs.29

In spite of the high proportion of psychiatric comorbidities among the children and young people reported there was minimal onward referral to CAMHS services and no reporting of cases from child and adolescent psychiatrists via CAPSS, this finding warrants further exploration. Assessment and
management in SC should take account of the high level of emotional and behavioural symptoms among children with SC; for example, including appropriate validated assessment tools for these symptoms and management strategies within guidance and care pathways.30

Finally, the surveillance we report here focusses on first presentations of SC in children. There has been very limited study of the course of SC over longer periods of time, and into adulthood, although older data suggest that recurrence of chorea may occur in up to 20 to 40% of cases.2 31

CONCLUSIONS

Our estimates of incidence suggest that SC remains a rare condition in the UK and Ireland but has not disappeared. Indeed, our findings also emphasise the impact that the condition can have on children’s functioning and confirm that paediatricians and child psychiatrists should remain vigilant to its presenting features. The findings also highlight the need for further research and development of consensus around diagnosis and management.

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Contributors The study was designed with input from a Steering Committee who also advised on development of the questionnaires and study protocol. The steering committee included all authors (TN-D, MISM, ML, OM, NM, ELW, AS, BK and TF). TN-D and OM oversaw the surveillance studies at BPSU and CAPSS, respectively. TN-D and ELW collated and presented the data which was discussed with all authors. ELW and TN-D led on manuscript drafting and editing and all authors contributed to the revision of all versions and approval of the final manuscript. TN-D is guarantor for the study, accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests MISM is Honorary President of the Sydenham’s Chorea Association.

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