Surveillance of rare diseases: a public health evaluation of the British Paediatric Surveillance Unit

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ABSTRACT

Background The British Paediatric Surveillance Unit (BPSU), a joint undertaking between the Royal College of Paediatrics and Child Health, Institute of Child Health and Health Protection Agency, undertakes nationwide surveillance of rare paediatric disorders. In 2007–09, formal evaluation to examine its effectiveness commenced.

Methods Centres of Disease Control guidelines for appraising public health surveillance systems were applied. Data sources included BPSU databases, published and unpublished reports. Questionnaires were sent to 600 participating paediatricians and 27 researchers. Half of the questionnaires were administered online to assess the feasibility of electronic reporting.

Results Three thousand UK paediatricians report monthly to the BPSU (94% return) and eighty BPSU studies have been published. These studies have influenced immunization and screening policy, altered clinical practice and informed health service configuration. Surveillance operations are simple, stable, representative and responsive to changing demands. Returns from the paediatricians’ survey were 75%; investigators 89%. Paediatricians valued the BPSU and did not find participation burdensome. Most supported online questionnaires (56%) but not monthly electronic reporting (35%).

Conclusions Evaluation demonstrated the effectiveness of the BPSU as a valuable resource for clinicians and policy-makers. Opportunities identified for future development include secure online reporting, improved responsiveness to urgent health threats and promoting public involvement.

Keywords child health, public health evaluation, rare disease, surveillance

Introduction

An individual rare disease affects fewer than five per 10 000 individuals1 yet collectively these conditions affect more than 3 million people in England.2 Many rare disorders begin in childhood, thus accurate and rigorous systems for defining the health burden attributable to rare diseases and measuring their impact on carers and healthcare systems are valuable tools. The British Paediatric Surveillance Unit (BPSU) was established in 1986 as a partnership between the Royal College of Paediatrics and Child Health (RCPCH), Health Protection Agency (HPA) and the UCL Institute of Child Health (ICH) and has undertaken active surveillance of rare childhood disorders and infections for 25 years.1 It was a pioneering arrangement providing a method for...
collection of information about the distribution of disorders at a national level from consultant paediatricians. Although originally funded through charities and study fees, the BPSU currently receives funding from the Department of Health.

The BPSU system is available to any researcher to investigate UK-wide case ascertainment of rare childhood disorders. Conditions are accepted for study based on rarity, public health relevance and the scientific merits of research objectives. The surveillance methodology (Fig. 1) is designed to minimize the burden on reporting clinicians and facilitate participation. In 2009, 3209 consultant paediatricians (around 94% of all UK and Irish paediatricians) participated in the monthly active reporting scheme known as the ‘Orange Card’. This card lists up to 14 conditions under surveillance. Clinicians indicate the number of relevant cases that they have seen within the past month, or state they have nothing to report, before returning the card to the BPSU. Researchers are notified of cases and undertake clinical data collection directly through short postal questionnaires to clinicians.

Conditions are usually surveyed for up to 2 years. Each study is peer reviewed by the BPSU committee and additionally requires approval by a Research Ethics Committee and the National Information Governance Board (Section 251). On occasions surveillance for specific conditions continues longer because of a public health need, for example paediatric HIV. The BPSU can initiate surveillance at short notice to facilitate effective healthcare responses, such as for H1N1-related paediatric Guillain–Barré syndrome in 2010.

The BPSU Executive Committee oversees the activities of the BPSU and includes representatives from the RCPCH, HPA, ICH, Health Protection Scotland and Royal College of Physicians (Ireland). Consultant paediatricians serve as committee members. Since 2006, two lay members have been co-opted to represent public and patient views, and facilitate public involvement in BPSU activities. Individual investigators have also increasingly sought to engage patient groups.

The BPSU model has been replicated by other UK specialties and countries. Two national surveillance units, in Australia (APSU) and Canada (CPSP), have established a methodology for formally reviewing performance against internationally recognized Centres for Disease Control (CDC) criteria for evaluating public health surveillance programmes. These units, and the British Ophthalmological Surveillance Unit (BOSU) surveyed the views of participating clinicians. Whilst case ascertainment of the BPSU have previously been appraised, formal evaluation of the Unit has not.

**Methods**

CDC Guidelines are widely accepted for evaluation of public health surveillance systems and facilitate comparisons between surveillance units. Qualitative and quantitative evaluation of the BPSU’s usefulness, data quality, flexibility, simplicity, stability, timeliness, representativeness and acceptability was conducted through a structured appraisal of process and outputs directed by these guidelines. Data were extracted from electronic and paper records, including peer-reviewed publications, annual reports, monthly card monitoring databases and committee minutes.

Views of participating clinicians were assessed using a structured questionnaire sent to a sample of 600 (20%) paediatricians, selected by random number generator from those reporting to the BPSU for at least 9 months prior to September 2007. The first 300 clinicians were sent an email link to access the survey online (‘SurveyMonkey’; Portland, Oregon, USA); the remainder were sent postal questionnaires with reply-paid envelopes. Questions concerned the usefulness, simplicity, timeliness and acceptability of the system, as well as user views of electronic reporting. An email reminder was sent to non-responders after 2 and 6 weeks and offered the choice to respond in either format.

An online questionnaire was sent to all investigators (n = 27), who had used the BPSU to undertake surveillance for at least 12 months between October 2003 and

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**Fig. 1** Diagram of the BPSU reporting system.
September 2007. This sought opinions on the usefulness and effectiveness of the BPSU.

No measures were made of the sensitivity of case detection, including assessment of the number of ‘missed’ or unreported cases, in BPSU studies as this has been addressed in a previous paper.12

Results
Survey responses
Of 600 paediatricians approached, 451 (75%) responded to the survey; 192 (43%) responded by post and 259 (57%) online. Only three respondents receiving the online survey requested it in paper format, whilst 59 who originally received the postal questionnaire responded online after a reminder. Characteristics of survey respondents were similar to the entire BPSU reporting base (Table 1). Of 27 lead investigators surveyed, 24 (89%) responded.

Performance of the system
The performance of the BPSU was appraised for usefulness and against relevant system attributes.

Table 1 Characteristics of survey respondents

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>BPSU reporting base (n = 2923)a</th>
<th>Survey sample (n = 600)</th>
<th>Survey respondents (n = 428)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>n; %</td>
<td>n; %</td>
<td>n; %</td>
</tr>
<tr>
<td>Male</td>
<td>1651; 56</td>
<td>261; 57</td>
<td>246; 57</td>
</tr>
<tr>
<td>Female</td>
<td>1272; 44</td>
<td>339; 43</td>
<td>182; 43</td>
</tr>
<tr>
<td>Type of practice</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community based</td>
<td>517; 82</td>
<td>477; 80</td>
<td>340; 79</td>
</tr>
<tr>
<td>Hospital based (or academic)</td>
<td>2406; 18</td>
<td>123; 20</td>
<td>88; 21</td>
</tr>
<tr>
<td>Period reporting to BPSU</td>
<td>n = 2640c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 months to &lt;5 years</td>
<td>835; 32</td>
<td>178; 30</td>
<td>129; 30</td>
</tr>
<tr>
<td>5 years to &lt;10 years</td>
<td>685; 26</td>
<td>177; 30</td>
<td>131; 31</td>
</tr>
<tr>
<td>10 years or more</td>
<td>1120; 42</td>
<td>245; 40</td>
<td>168; 39</td>
</tr>
</tbody>
</table>

aBPSU records for all respondents (n = 2923 responding consultants) on 1 December 2007.
bTwenty-three paper questionnaires were excluded as they were returned anonymously and characteristics of respondents are unknown.
cThis excludes 283 consultants who had been reporting for less than 9 months.

Usefulness
Since 1986, 80 studies using BPSU methodology have been completed, of which 51 have published findings in peer-reviewed journals. BPSU studies have generated 169 papers, 222 conference presentations and 8 book chapters, while committee members have authored 7 papers on methodology13,14–18 and contributed to three international collaborative papers.5,19,20

Surveillance through the BPSU has influenced vaccine policy, enabling evaluation of polio eradication19 and providing essential data to the World Health Organization (WHO) for appraising the effectiveness of rubella immunization.21 Research into HIV4, congenital syphilis,22 Group B streptococcus,23 neonatal herpes simplex24 and medium-chain acyl CoA dehydrogenase deficiency25 have supported national screening policy, whilst studies of vitamin K deficiency bleeding26,27, Reye’s syndrome28 and biliary atresia29 have been prominent in informing clinical practice and service configuration.

Active participation in surveillance increases awareness amongst paediatricians of rare disorders and epidemiological methods.18 In survey responses, 379 (84%) paediatricians rated the study of rare conditions as important/very important and 43% identified studies that have changed their clinical practice, citing vitamin K deficiency bleeding (15%), Kawasaki disease (8%), diabetic ketoacidosis (7%), Group B streptococcal infection (7%) and progressive intellectual and neurological deterioration (6%).

Over 90% of investigators surveyed felt their research objectives could only have been achieved through national surveillance and regarded BPSU studies as key evidence sources for clinical practice and health policy. At least 73% of studies had stimulated further research. Investigators identified improved understanding of surveillance and the establishment of new specialty-specific surveillance schemes as additional benefits.

Data quality
Data quality reflects the validity and completeness of surveillance data. The BPSU recruits all consultant paediatricians who are members of the RCPCH, the professional body responsible for the training and examination of paediatricians in the UK. In 1996, validation of the reporting base identified a need to monitor new appointments and recruit community paediatricians,13 which was subsequently implemented.

The monthly Orange Card return rate is high, at 94% monthly (2008/09), with duplicate reports comprising around 10% (2008/09) of all notifications. Clinical details to confirm the diagnosis are available in 92–95% of cases.
(2008/09). Of paediatricians responding to the survey, 212 (47%) had not reported a case in the past 2 years; most had not seen a child with a listed condition (n = 172), however 28 (13%) had not reported a case because they knew a colleague had done so.

**Flexibility**

The BPSU system has proven flexible in response to changing demands, such as emerging public health concerns or governance requirements. Survey respondents expressed willingness to rapid reporting in health emergencies; 80% indicating that email would be their preferred method.

The BPSU system has adapted to involve multiple sources to improve case ascertainment, including joint studies with other surveillance units, adding non-paediatric specialities to the mailing list and establishing new reporting systems. Sustained surveillance of conditions of major public health importance is accommodated.

Crucially studies of paediatric HIV, new variant Creutzfeld-Jakob disease, water births, and haemolytic uraemic syndrome were initiated in direct response to public health concerns. The recent H1N1 pandemic provided an opportunity to pilot a faster process for initiating surveillance, for paediatric Guillain–Barré Syndrome, whilst maintaining the rigour of scientific peer review. Nevertheless barriers were encountered that could not be addressed by the BPSU, specifically the timeliness of information governance approvals.

Review of BPSU guidance documents indicated these had been adapted as research ethics and governance requirements altered, but procedures for regular updating were lacking.

**Simplicity**

The postal card has proven a straightforward reporting system and paediatricians can record notified cases on a detachable counterfoil. Of 239 survey respondents who had recently reported a case, 18 (8%) had recorded incomplete details, 20 (8%) misplaced the counterfoil and 11 (5%) could not locate patient notes. Most (92%) found the clinical questionnaire easy to complete using patient casenotes (n = 153 [70%] respondents), laboratory reports (n = 47), maternal casenotes (n = 17) or information from other hospitals (n = 5).

**Timeliness and stability**

BPSU operations were well documented and resilient to staff changes. The Orange Card has been sent out without fail every month since inception; over 80% of cards are returned within 60 days and final return rates have remained stable at 90–95% throughout the last 20 years. Electronic reminders are sent after 2 months and only 4% of these are rejected (‘bounced’) by email accounts.

Of surveyed clinicians who had reported cases, 153 (64%) had received clinical questionnaires within 2 weeks, however 3% waited over 4 weeks. Some investigators described difficulties in obtaining completed questionnaires despite reminders and three investigators reported delays in receiving notifications from the BPSU. As no individual study data are held centrally by the BPSU, it was not possible to validate these reported difficulties.

Study applications took a mean of 16 months from submission to approval, but this period could be as long as 34 months. Delays were often related to study development throughout the peer-review process, which ensures that research effectively addresses clinical and public health objectives. It was evident that increased support for questionnaire development would be welcomed. Most investigators (83%) found peer-review helpful, particularly the opportunity to discuss their proposal with the BPSU committee.

**Representativeness**

The BPSU reporting base includes general, specialist and community paediatricians and has good regional coverage, with at least 89% of clinicians responding from each region (Fig. 2). Of 27 studies undertaken in 2003–08, 21 were based in England, four in Scotland and two in Wales.

Studies were mainly based in teaching hospitals (50%) and academic institutions (38%).

Participation in the BPSU by paediatricians from a wide range of specialities is essential to ensuring that children diagnosed after specialist referral are reported to the BPSU. Often children with rare conditions are cared for by general/community paediatricians and BPSU studies rely on both specialist and generalist paediatricians for case ascertainment as demonstrated in an audit of 11 studies performed in 2003–05. General/community paediatricians notified at least 50% of cases in over two-thirds of studies (Fig. 3); surveillance through either general/community paediatricians or through specialist groups would not contribute all cases.

Acceptability
The willingness of paediatricians and researchers to participate in the BPSU was investigated through the questionnaires; 385 (85%) paediatricians stated that they had returned every card they received and the remainder had returned over 50%. Interestingly, 275 (61%) paediatricians indicated a preference for 5–8 conditions being listed, fewer than the number on the card at the time of the survey. Barriers to reporting included the lack of a reply-paid envelope, hospital post systems, working across several locations, inadequate administrative support and heavy clinical workload.

In 2009, 1685 cases were reported by 721 paediatricians. While most paediatricians ($n = 449; 62\%) reported only one case, 119 (15\%) reported three or more, representing a significant workload. Moreover, survey respondents commented on the work involved in completing questionnaires, stating that some were time consuming to complete. Despite this, 83% surveyed paediatricians were not discouraged from reporting future cases.

In response to specific enquiry about the acceptability of online reporting, 293 (65\%) paediatricians preferred the postal Orange Card to an electronic system. However, over half ($n = 123 [56\%]$ of those who had reported a case would consider online clinical questionnaires. Most investigators ($n = 20 [83\%]$) would be interested in using online questionnaires to reduce postage costs and decrease response times, but they raised concerns about data security.

Discussion
Main findings of this study
Evaluation of the BPSU confirmed the effectiveness of this national surveillance system. For 25 years, the BPSU has been a valuable resource for clinicians and policy-makers providing high-quality surveillance data concerning a wide range of rare paediatric disorders. Participation rates are consistently high and paediatricians value the research outcomes, considering these to have been instrumental in informing clinical practice. Key priorities for the future development of the BPSU were highlighted.
What is already known on this topic
Appraisal of surveillance units in Australia and Canada also demonstrated high levels of participation by paediatricians and significant contributions to clinical practice.\textsuperscript{8–11,39} These evaluations emphasized the need to minimize the burden of reporting by ensuring that the clinical questionnaires developed by investigators are easy to complete.\textsuperscript{10} Additional aims were to improve dissemination of study findings and to develop methods for auditing the wider impact of surveillance.\textsuperscript{9–11}

Comparison of postal and electronic methods reporting methods were not included in these previous evaluations, however a recent study which compared electronic and postal methods for reporting adverse drug reactions in Scotland found no significant differences.\textsuperscript{40}

What this study adds
Evaluation of the BPSU has provided important audit data for international comparison and contributed additional information about the potential for electronic reporting within a successful and established surveillance system.

The suitability of CDC criteria as a framework for evaluating surveillance systems has been established through review of the published literature\textsuperscript{10} and previous national evaluations.\textsuperscript{8,10,11} Our evaluation additionally included the piloting of an online user survey, which allowed us to explore the feasibility and acceptability of electronic reporting amongst clinicians. The response rate to the BPSU survey was 75%, thus compared favourably with previous evaluations (48–68%).\textsuperscript{5,10,11,39}

Rare disease surveillance through the BPSU is valued by paediatricians and has significantly influenced clinical and public health responses to rare childhood conditions. Formal evaluation identified the key strengths of the BPSU as its simplicity, quality of the data collected, responsiveness to changing healthcare needs and the high level of acceptance by participating clinicians. Future development opportunities supported by participating clinicians and researchers included improving responsiveness to urgent health concerns and piloting online reporting.

The system has demonstrated considerable flexibility in the face of emerging public health concerns and paediatricians have expressed willingness to use rapid-reporting methods. The H1N1-related Guillain–Barré syndrome study\textsuperscript{46} demonstrated that information governance approvals are greater barriers to timely initiation of surveillance than the BPSU peer-review process. Nevertheless, the BPSU must ensure it has capacity to adapt to alternative reporting methods and address the challenge of urgent data collection.

Only Orange Card ‘reminders’ are sent electronically to paediatricians at present, although electronic methods have been introduced within other surveillance systems.\textsuperscript{39} The risk of jeopardizing the high response rate of the BPSU by moving to an electronic system remains a concern. Although paediatricians and researchers expressed support for online questionnaires, this did not extend to the routine Orange Card reporting system. Perhaps the novel concept of an online Orange Card requires testing, as changes to the Orange Card would affect all paediatricians and this survey excluded the newer consultants who may be more accepting of electronic methods. Crucially, any electronic data collection must accommodate the imperative to maintain patient confidentiality through secure data management.

Limitations of this study
BPSU monitoring systems maintain an accurate record of Orange Card notifications and of the proportion of notified cases that are confirmed by investigators as meeting their case definition, thus providing the basis for estimating disease incidence. However, the BPSU office does not have access to investigators’ monitoring systems so cannot, for example, audit or confirm questionnaire return rates within an individual study.

Capture–recapture analyses to assess completeness of ascertainment within BPSU studies have been reported previously.\textsuperscript{12} The vast majority of BPSU studies fail to meet the essential criteria for use of capture–recapture methodology due to the lack of independent sources for comparison. Surveillance of childhood cataract, undertaken in parallel through the BPSU and BOSU, estimated that up to 8% of cases may have been ‘missed’ in this study. To address lack of reporting, the BPSU recommends use of additional sources for case reporting and encourages positive dependency, such that any new case reported through an additional source (e.g. laboratory) should lead to a request being made to the responsible paediatrician for a completed questionnaire. Investigators are expected to record the proportion of cases reported through additional sources.

Summary
This evaluation confirmed the significant role played by the BPSU in providing national incidence and clinical data for rare childhood disorders. Individuals with rare disorders are often isolated and commissioning health services for them requires good data relating to the burden of disease. BPSU studies support reliable estimation of disease frequency and a better understanding of health needs to underpin clinical care pathways and service provision. Crucially, the BPSU is
dependent upon participating paediatricians for its success and the surveys demonstrated that it is vital to monitor their views relating to the burden of reporting and to achieve a balance with the requirements of investigators. The evaluation exercise highlighted key priorities for the future of the BPSU, in particular the further development of public engagement at all points of its mission.38

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We declare that this paper is not under consideration elsewhere.

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