



Annabelle, under 11 years of age.

Aims of the British Paediatric Surveillance Unit

To:

- Facilitate research into uncommon childhood infections and disorders for the advancement of knowledge and to effect practical improvement in prevention, treatment and service planning.
- Allow paediatricians to participate in the surveillance of uncommon disorders and to lessen the burden on reporting doctors of such requests arising from numerous different sources.
- Increase awareness within the medical profession of the less common disorders studied and respond rapidly to public health emergencies.

Front Cover artwork:

Annabelle, winner of the BPSU art competition in the under 11 years of age category asking children and young people to design an image based on the theme of 'rare disease and me'.

Annabelle's picture shows her "'bones' having a fight with her rare disease - chronic recurrent multifocal osteomyelitis. The 'spikey' pain getting a 'super hero' I.V. (complete with a yellow cape!) to take the pain away."



<http://www.bpsu.org.uk>

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Foreword

My first year as the chair of the BPSU has been busy, exciting and very productive, and it's all thanks to the continued support of my paediatric colleagues from across the five nations. Before I outline some of the BPSU's achievements over the past 12 months I must firstly thank my predecessor, Richard Reading, who chaired the BPSU for over five years. My task has been to build on the strong foundations that Richard set in place, ensuring that the BPSU is uniquely positioned to face the emerging challenges and opportunities in a confident and enthusiastic manner.



Dr Shamez Ladhani
Chair, BPSU

Despite compliance remaining at over 90%, I must report that there has been a 2.5% fall in the response rate in 2018. This might be due to a variety of reasons - individuals 'opting-out' of returning their Ecards; new consultants, who are less aware of the BPSU's active surveillance methodology, failing to return their Ecards, even when they do not have any cases to report. We have also had reports from the research teams regarding low questionnaire completion rates. We are working hard with the research teams to support data collection and to ensure that the questionnaires are as short and succinct as possible. We encourage all paediatricians to complete the Ecard and return questionnaires. In recognition of this clinicians will receive a biannual revalidation certificate and, for those who report a case, they will also receive a certificate for completing the questionnaires, for inclusion in their revalidation portfolios.

It is easier than ever to report cases on the orange Ecard system however, we are continuing to look at ways in which to develop this system. I'm pleased to announce that over the coming 12 months, the BPSU will develop an online integrated case notification and data collection platform - for the first-time reporting clinicians will be able to report cases and return clinical information in one simple, unobtrusive process.


The findings of several studies have been published in peer-reviewed journals. I would like to specifically highlight the recent publication on congenital Zika syndrome. This study is an excellent example of the collaborative work that the BPSU undertakes with Public Health England to rapidly implement national surveillance for emerging infectious disease threats. The near-real time monitoring of cases through the BPSU played an important part in providing reassurance of the low risk to our population.

The BPSU has an important role to play in the education and training of healthcare professionals and the public. The Sir Peter Tizard Research Bursary remains an important plank of the BPSU's work offering early career paediatricians the opportunity to lead a national BPSU study. We were excited to award the 2018 bursary to Dr Chenqu Suo from Addenbrooke's Hospital for her study on chronic recurrent multifocal osteomyelitis. This year also saw the launch of RCPCH-BPSU rare disease webinar series where BPSU study teams present their study findings. The first webinar was on Kawasaki disease and was very well received (<https://bit.ly/2Wr0rVW>). With the RCPCH, we plan to hold four a year with webinars on nutritional rickets and lead poisoning planned for the first half of 2020.

The BPSU continues to play an important part in public health engagement and our lay committee members play a critical role in advising on patient and public involvement on all the BPSU studies. The BPSU also held its magnificent summer rare disease tea party (<https://www.rcpch.ac.uk/bpsu/teaparty>) - the event was opened by Baroness Blackwood, Minister for rare diseases, who called for a 'national conversation' on rare diseases and delegates also had the pleasure of hearing young people speak on their experience of rare disease.

Internationally there is continued collaboration between the national surveillance units which make up the International Network of Paediatric Surveillance Units (INoPSU). Richard Lynn, our scientific coordinator, is now co-chair of INoPSU and has encouraged the sharing of protocols studies such as congenital Zika syndrome, microcephaly, congenital ichthyosis and fetal alcohol syndrome to allow comparative analysis.

This work is only possible because of a successful team and I would like to thank the members of the BPSU scientific committee for contributing their personal time, Richard and Jacob who run the BPSU office and the research teams themselves. But most of all I would like to thank you the clinicians who by return the Ecard and complete the questionnaires, without your support the BPSU would not have the impact it has.

A handwritten signature in black ink, appearing to read 'Ladhani'.

Shamez Ladhani, Chair BPSU,
October 2019

1 How the Surveillance System Works

Background

Rare diseases and infections are a numerically important cause of illness and death and mortality in childhood. There are upwards of 8,000 rare diseases and though individually uncommon, together they affect thousands. Many are characterised by chronicity, high rates of disability or death. These conditions pose a large financial and emotional burden for affected children, their families and health systems.

To address this problem in the UK and Ireland, the BPSU was set up in July 1986, enabling paediatricians to participate in the surveillance and further study of rare disorders affecting children.

Several agencies founded and continue collaborating to support the work of the BPSU: the Royal College of Paediatrics and Child Health (RCPCH), Public Health England (PHE), University College London GOS Institute of Child Health (UCL GOS ICH), GOSH Children's Charity and the Faculty of Paediatrics of the Royal College of Physicians of Ireland. The BPSU's Scientific Committee meets five times a year to consider individual applications and the progress of studies.

Selection of studies for inclusion in the scheme

Details on the selection process and application process for the BPSU is available at <http://www.rcpch.ac.uk/bpsu/apply>.

Each application requires approval from the BPSU Scientific committee, a Research Ethics Committee (REC), the Confidentiality Advisory Group (CAG) of the Health Research Authority and the Scottish Public Benefits and Privacy Panel (PBPP).

The reporting system

Surveillance is 'active' in that the BPSU office actively sends out an electronic orange card (eCards) to consultant paediatricians in the UK and Ireland asking for cases to be reported on the BPSU orange 'eCard' (Figure 1). Each month, all clinicians participating in the surveillance scheme are sent an eCard listing the conditions currently under surveillance; follow-up reminders are sent to those who have not returned their eCard. A set of instructions for completing the card, including the case definition of the conditions under surveillance can be accessed via the eCard. When a new study begins, the mailing also includes a specially produced protocol card and other information about the study.

Participants are expected to return eCards even if they have no cases to report - there is a 'nothing to report' box for them to tick. This is an important feature of the surveillance scheme as it allows us to measure compliance, which is continually monitored, to the reporting system.

Figure 1: Orange eCard

Orange E-Reporting Card

BPSU DECEMBER 2018 Reporting Card

Please complete the E-card below to indicate whether or not you have seen cases for DECEMBER 2018. The reporting instructions for DECEMBER 2018 are available to download at [BPSU 2018](#).

Notice

With your contribution to the BPSU's reporting scheme the BPSU continues to have a major impact on child health. The BPSU's Privacy Notice is available to view at [https://www.rcpch.ac.uk/bpsu/privacy-notice](#). The BPSU's reporting scheme is voluntary. If you wish to opt-out of the reporting scheme or from receiving either a newsletter or evidence of contribution certificates, please contact the [BPSU office](#).

E-card

Have you seen any cases in the month DECEMBER 2018?

☐ Yes ☐ No

Cases to report

Please specify in the appropriate box the number of cases seen:

To access the study information page on our Web site, click on the condition name:

- 1. HIV Infection & Perinatal HIV Exposure
- 2. Progressive Intellectual & Neurological Deterioration
- 3. Congenital Rubella
- 4. Juvenile-onset Systemic Lupus Erythematosus
- 5. Listeria infection in infants < 90 days
- 6. Acute severe osteomyelitis (accidental / non-intentional)
- 7. Fetal alcohol syndrome
- 8. Congenital atresia
- 9. Infant's choice

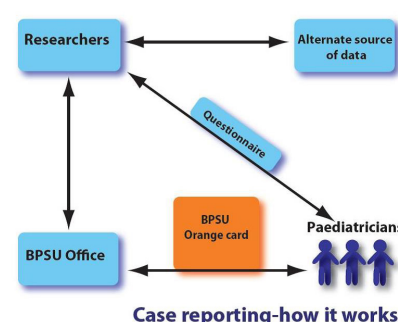
Thank you for reporting a case. Please make a note of the case details for future reference. Please keep a record of the report as an aide memoire. The Study Investigator will contact you shortly with a questionnaire.

Follow-up and confirmation of case reports

On receiving a case report the BPSU informs the relevant study team who send a short questionnaire to the reporting clinician to gather further information. Due to the need to discount duplicates a limited amount of patient identifiable data is collected. The study investigators report back to the BPSU, indicating when cases have been confirmed or are duplicate case reports (Figure 2). Duplication of reporting is most likely to occur when the condition requires referral to another clinician, but this is encouraged, as it is better to receive duplicate reports than to miss a case.

To improve case ascertainment for specific studies where a child may see specialist clinicians, consultants working in other specialties have been invited to participate in the scheme. Apart from helping to improve ascertainment such complementary data sources help to validate the surveillance system.

Figure 2: Surveillance mechanism



2 Scientific Coordinator's Yearly Review of Activities

Four studies commenced surveillance in 2018, acute severe poisoning, Dr Elizabeth Starkey, Derby Children's Hospital; fetal alcohol syndrome, Dr Kathryn Johnson, Leeds General Hospital; congenital ichthyosis, Dr Fozia Roked, Birmingham Children's Hospital and Sydenham's chorea, Dr Tamsin Newlove-Delgado, Exeter Medical School.



Richard Lynn,
Scientific Coordinator

Three studies had their period of surveillance extended: congenital rubella, progressive intellectual and neurological deterioration (PIND) and juvenile-onset systemic lupus erythematosus.

Surveillance on bronchopulmonary dysplasia, microcephaly and congenital Zika syndrome ended in 2018.

During 2018-19, there were 11 known publications relating to BPSU studies and 14 conference oral and poster presentations (see Appendices, p.26).

Participation in the scheme during the year 2018

Reporting rates for returning the electronic orange eCards remain high - the overall card return compliance rate for the year 2018, calculated as a proportion of orange cards returned, was 91.5% (46618/42633) a fall of 2.6% from 2017. Monthly response rates ranged from 95.9% in May to 88.9% in November with a median of 91.0%. Details of regional response rates are provided in Table 1 overleaf. Though above the BPSU target of 90% this still represents the largest one-year compliance rate fall. Many recently appointed consultants were added to the system and it may be there is a lack of awareness with regards negative reporting.

Table 2 summarises the outcome of the follow-up of cases and provides evidence for their level of accuracy of reporting by clinician. By the end of a study 80-95% of the questionnaires will have been returned. The time taken to follow-up varies between conditions and may be longer if microbiological/pathological details are required; or if a specialist committee has to convene to adjudicate on the case data.

Workload of those reporting in the scheme: 563 of 3860 (15%) receiving a card in 2018 reported a case in 2018. 397 (12%) reported a single case, 3% (126) reported between two and four cases and 40 (1%) reported five or more cases. The greatest number of cases reported was by HIV specialists, one of whom reported 26 cases.

Public and patient engagement

The BPSU is committed to wider public patient engagement (PPE) in the development and dissemination of our work and that of the studies. To support clinicians when preparing their protocols several resource packs have been introduced. These are available at <http://www.rcpch.ac.uk/bpsu/apply>.

The BPSU is contributing to work with patient advocacy groups such as Rare Disease UK and Findacure and specific groups such as Societi. BPSU has also contributed to the work of Medics 4 Rare Diseases helping to raise awareness of rare disease research amongst student medics and trainees.

Education

Several initiatives have been launched to help promote rare disease education. The BPSU produced a series of training aides in disease epidemiology, data analysis and public patient involvement. With the RCPCH it has launched a rare disease webinar series; the first on Kawasaki disease was one of the most viewed webinars the RCPCH have undertaken to date. It is planned to run at least four a year going forward.

International activities

The BPSU continues to take an important role in the activities of the International Network of Paediatric Surveillance Units (INoPSU). The BPSU developed a searchable database of over 200 rare paediatric conditions surveyed by units within INoPSU <http://www.inopsu.com>. Here you will also find information on affiliated national surveillance units, studies currently being undertaken; published papers; study protocols; and questionnaires.

Funding

BPSU is currently funded through grants from UCL GOS Institute of Child Health, RCPCH, and Public Health England with additional support from Great Ormond Street Hospital Children's Charity and with contributions from researchers.

Table 1: Regional Response rate 2018 and 2017

Region	% return	Rank 2018	Rank 2017
East Anglia	95.9%	2	3
Mersey	90.1%	17	13
NET	87.0%	20	18
North Scotland	95.9%	1	1
North Western	90.2%	15	14
Northern	94.5%	5	6
Northern Ireland	95.4%	4	16
NWT	89.0%	19	20
Oxford	93.0%	8	7
Republic of Ireland	90.3%	14	17
SET	89.0%	18	19
South Scotland	91.6%	11	4
South Western	93.7%	7	9
SWT	90.4%	13	12
Trent	90.2%	16	15
Wales	94.0%	6	5
Wessex	92.1%	10	10
West Midlands	92.6%	9	8
West Scotland	91.2%	12	11
Yorkshire	95.5%	3	2

Figure 3: Regional Response rate 2018



Table 2: Outcome of follow-up of the cases reported in 2018 for conditions under surveillance at July 2019

Condition under surveillance	Date when reporting began	Valid reports	%	Duplicates	Errors	(D&E) %	Not yet known	%	Total
HIV	Jun-86	9,649	77	925	786	14	1,228	10	12,588
CRU	Jun-91	93	45	42	67	53	4	2	206
PIND	May-97	2,316	53	566	1,135	39	389	9	4,406
RKT	Mar-15	125	39	11	117	40	66	21	319
BEH	May-15	58	40	21	59	55	8	5	146
VIB	Oct-15	207	59	7	85	26	49	14	348
FGM	Nov-15	79	68	6	21	23	10	9	116
ADHD	Nov-15	230	64	2	84	24	41	11	357
PRS	Jan-16	119	60	41	8	25	30	15	198
EPI	Nov-16	87	64	15	11	19	24	18	137
CDD	Nov-16	14	67	0	3	14	4	19	21
ZIKA	Apr-17	4	57	0	2	29	1	14	7
BPD	Jul-17	113	65	8	15	13	38	22	174
LUP	Sep-17	21	48	5	14	43	4	9	44
LIS	Oct-17	7	54	0	0	0	6	46	13
MIC	Oct-17	33	65	0	1	2	17	33	51
Total		13,155	69	1,649	2,408	21	1,919	10	19,131

HIV HIV infection and perinatal HIV exposure
CRU Congenital rubella
PIND Progressive intellectual and neurological deterioration
RKT Nutritional rickets
BEH Behçet's syndrome
VIB Visual impairment and blindness
FGM Female genital mutilation
ADHD Attention deficit and hyperactivity disorder

PRS Pierre Robin Sequence
EPI Deaths in children with epilepsy (excl. Scotland)
CDD Childhood disintegrative disorder
ZIKA Congenital Zika syndrome
BPD Bronchopulmonary dysplasia
LUP Juvenile-onset systemic lupus erythematosus
LIS Invasive listeria infection
MIC Severe microcephaly

3 Surveillance Studies Undertaken in 2018

Once again individual reports have concentrated on the summary of the condition and on the analysis. General methodology information is contained in the study protocols and can be found at <https://www.bpsu.org.uk>. Please take into consideration that the analysis presented here is provisional and has yet to be peer reviewed.

The investigators would like to acknowledge all those who are involved in their projects but are not mentioned. The BPSU would like to thank all those paediatricians who have returned cards, reported cases and completed the questionnaires.

Accidental poisoning

Key points

- In the first nine months of surveillance there have been 18 confirmed cases. There are 30 questionnaires still outstanding.
- As yet there have been no confirmed deaths secondary to accidental poisoning.
- 50% of confirmed cases are caused by medications and 33% by illicit substances.

Summary

Accidental or unintentional poisonings involve people poisoning themselves or others without wanting to cause harm. In children it is a common reason for attendance at healthcare providers. Young children, especially under the age of five, have an inquisitive nature, and frequently put things found in their environment into their mouths. Teenagers involved in risk-taking behaviour by taking illicit drugs or alcohol are also in danger of unintentionally poisoning themselves.

Serious consequences following accidental poisoning are rare. Child-resistant containers for medicines and other dangerous substances have contributed significantly to a reduction in serious harm. However, a number of children continue to suffer significant harm, with between five and 10 deaths each year and approximately 50 children admitted to intensive care within the UK.^{1,2} In particular, a single dose unit of certain adult medications can be fatal to a toddler. Most of these are in blister packs, which are not subject to current child resistant closure legislation. Accidental poisoning is essentially an avoidable problem and, as a result, remains an important public health issue.

This will be the first study in the UK and Republic of Ireland to determine the incidence and identify the circumstances surrounding serious accidental poisonings in children. The study will look at poisonings resulting in death, or signs and symptoms needing significant monitoring or support. By identifying specific trends for specific substances that frequently cause significant harm, it is hoped that our study results can inform policies for example, reducing harm by legislation around more robust child-resistant packaging.



Dr Elizabeth Starkey

Surveillance period

July 2018 - July 2019 (inclusive).

Methodology

Data capture uses standard BPSU methodology. Details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/poisoning>

Further information on number of deaths by accidental poisoning is being obtained from both child death overview panels in England and from the Office of National Statistics. Further information is also to be collected on admissions to PICU with accidental poisoning via the Picanet database during the study period. These sources are not to provide additional case reports but to check the accuracy of case reporting.

Analysis

A preliminary description of case reports during the first nine months of the study (July 2018 to March 2019 inclusive) is provided below. More detailed analysis will be completed at the end of data collection period.

Seventy-nine cases have been reported. 19 have been reported in error prior to questionnaires being completed. 18 have been confirmed (one duplicate) cases meeting the study definition and seven were excluded by the study team after the completed questionnaires did not meet the case definition. Four have been lost despite reminders to clinicians, and 30 questionnaires are currently awaited.

No deaths from accidental death have been reported. Among the confirmed cases, 12 (66%) are male and 15 (83%) are of white ethnicity.

Eighteen cases occurred, nine from medications, six from illicit drugs and three from household and industrial products. Of the nine medication poisonings, four were opioid related, four were from psychiatric medications and one from ophthalmology treatment. Of the illicit substances, five were from cannabis or synthetic equivalent and one related to amphetamine.

Fifteen cases had a low Glasgow coma scale (GCS) requiring frequent monitoring, 11 cases needed continuous oximetry plus oxygen and cardiac monitoring. Nine cases needed additional respiratory support.

Discussion

Although the number of confirmed case reports is lower than expected in the first nine months of the data collection period, it was difficult to predict the total number we would receive as there are no other reports in the literature on this problem. The incidence of acute severe poisoning cannot be estimated until data collection is complete.

A significant proportion of cases so far have been reported in error, a large proportion were when the surveillance first commenced. This has reduced since adjusting the definition on the orange eCard to include the wording accidental and non-intentional to prevent cases of self-harm being reported.

Public and patient engagement

Child Accident Prevention Trust
Web: <https://www.capt.org.uk>

References

1. Flanagan RJ, Rooney C, Griffiths C. Fatal Poisoning in childhood, England and Wales 1968-2000. *For Sci Int*: 2005;148; 121-129
2. Anderson M, Hawkins L, Eddleston M et al. Severe and fatal pharmaceutical poisoning in young children in the UK. *Arch Dis Child* 2016;101:653-656
3. Braitburg G, Oakley E. Small dose...big poison. *Aust FAM Physician* 2010;39:826-33

Acknowledgements

The study team are grateful to the Research and development department at Derby hospital, in particular Rachelle Sherman, for their guidance and support. We are also grateful to clinical and lay representatives for their comments on the study design, questionnaire and patient information.

Funding

This study is funded by Sir Peter Tizard Research Bursary.

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Bronchopulmonary dysplasia

Key points

- 329 notifications of cases have been received during the 13 month surveillance period.
- 63% (202/323) response rate for the notification questionnaire and 53% (86/162) for the follow-up questionnaire.
- 20% (40/202) cases were either ineligible or duplicate reports.

Summary

Many babies born more than eight weeks early will have some problems with their breathing and need oxygen for many weeks. This is known as chronic lung disease or Bronchopulmonary dysplasia (BPD) and happens because the lungs were immature at birth. Most babies recover well, but some may go home in oxygen. A small number have such severe lung problems that they need to stay in hospital on breathing machines for many weeks or months, and may even die. Because very small numbers of babies have such severe problems, little is known about this important group of preterm babies and how they are cared for or what might make their outcome better.

The study aims to estimate the minimum incidence of life threatening BPD in infants born at least eight weeks early; to describe maternal and infant characteristics of infants developing BPD. Also the study aims to describe the respiratory support options and medical treatments given and describe the outcomes over a year of life.

Surveillance period

July 2017 - July 2018 (inclusive).

Follow-up period: Follow-up questionnaire at one year of age of each eligible case.

Methodology

Data capture uses standard BPSU methodology. Details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/bpd>

Analysis

Over the 13 month surveillance period a total of 329 case notifications were received. Six cases were reported in error to the BPSU. So the actual cases notifications were 323. Information has so far been received on 202 (62.5%) reports. A large number (121) reporters did not return the notification questionnaire despite two or more contacts made in the form of email, telephone or re-sent questionnaire.

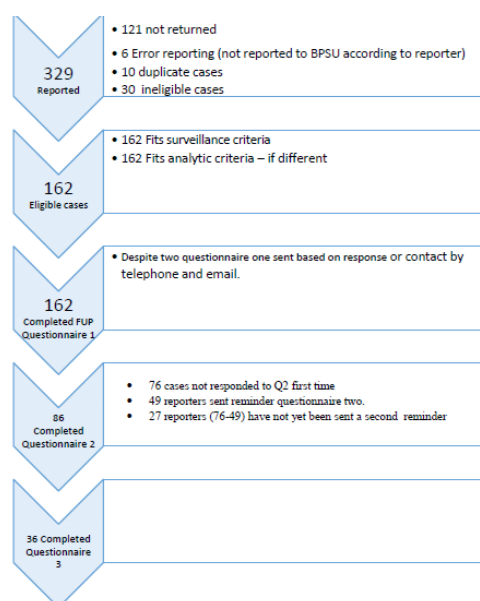
One hundred sixty-two (79%) cases have met the case definition, 10 cases were duplicates, 30 do not meet inclusion criteria. Of these 26 did not meet the gestation criteria, four cases were excluded for other reasons e.g. congenital anomaly, cardiac, pneumonitis and hydrops.



Drs S Harigopal, J Berrington & S Ramaiah

Of the 162 cases that met the case definition, Median gestational age was 26⁺⁰ (IQR: 24⁺³ – 28) and median birthweight was 720g (IQR: 611 – 900g). 90.4% received antenatal steroids. Only one baby did not receive surfactant. Median duration of invasive ventilation was 27.5 days. Median duration of non-invasive respiratory support was 64.5 days. 50% of the babies needed high frequency oscillatory ventilation and 27.9% received inhaled nitric oxide. 57% received postnatal steroids and 85% received diuretics.

Figure 4: Cases reported



Discussion

The study involves data collection through three questionnaires. The first at the time of reporting, the second – at the point of expected discharge from hospital or transfer to respiratory paediatrics and the third questionnaire at one year of age. The study is complete in terms of notification. It was estimated that there would be between 100-200 cases with life threatening BPD each year and to date 162 eligible cases have been reported.

It is concerning that data on 121 (38.5%) reports have not yet been received, even after several communications. The number of cases confirmed 162, represents 80% of the cases for which follow up data has been received, which suggests there could be more cases in the cohort for which we have no data as yet. Even so the number of cases

confirmed is still higher than expected. This may be due to changes in practice since our estimates, especially around the use of high flow therapy and thereby more babies may be on longer duration of respiratory support than if a baby was on CPAP thereby increasing the numbers reported. Data collection and analysis is still in progress and more information will be made following review.

Public and patient engagement

The Tiny Lives Trust
Web: <https://www.tinylives.org.uk>

Acknowledgements

The BPD team would like to thank Mrs Sue Morrison for the administrative support she has lent to the study, Tiny Lives for funding and supporting the study and Bliss Charity for their endorsement. The

BPD would also like to acknowledge the RCPCH members and parents helping with the study.

Lastly, the study team would like to acknowledge Newcastle Upon Tyne Hospitals NHS Foundation Trust for sponsoring the study.

Funding

This study is funded by The Tiny Lives Trust.

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Congenital rubella

Key points

- Since 2005, 13 congenital rubella births have been reported in the UK with one reported between April 2018 and March 2019.
- Congenital rubella syndrome can occur when a woman contracts rubella during the first trimester of pregnancy. It can cause deafness, blindness and heart defects in the fetus, amongst other symptoms.
- Antenatal screening for rubella susceptibility was discontinued in England in April 2016.

Summary

Surveillance of congenital rubella (CR) has been in place since 1971, when the National Congenital Rubella Surveillance Programme (NCRSP) was set up to monitor the impact of rubella vaccine; there has been active surveillance throughout the UK and Ireland through the BPSU since 1990.¹ The last confirmed CR birth reported was in 2018 (n=1).

Following policy reviews in 2003 and 2012,¹ antenatal screening for rubella susceptibility was discontinued in England in April 2016 (and subsequently also in Scotland and Wales) but continues in Northern Ireland and in the Republic of Ireland. The PHE's National Screening Programme supports on-going national surveillance of CR through the BPSU, in order to help maintain professional awareness of this rare but potentially devastating infection, and to provide a mechanism for the timely reporting of the circumstances of any cases which do occur. Congenitally infected infants can shed rubella virus for an extended period of time, and every infected infant must be diagnosed and managed appropriately to avoid the risk of contributing to further community transmission.

A review by the World Health Organization (WHO) in 2008 estimated that more than 110,000 infants were born with congenital rubella syndrome (CRS) each year in developing countries, and rates are highest in the WHO African and South-East Asian regions where vaccine coverage is lowest. In April 2015 the WHO Region of the Americas became the first in the world to be declared free of endemic transmission of rubella, and the WHO aims to eliminate measles, rubella and congenital rubella (elimination defined as <1 case of CRS per 100,000 births) from five of the seven WHO regions by 2020. Although in the UK reported cases of CRS have been below this level for many years, rubella outbreaks and associated CR births have been reported in several European countries in the last decade.

Between July 2018 and July 2019, 740 cases of rubella were reported in the WHO European Region, 50% of which occurred in Poland. Cases were also reported from Germany, Turkey and Italy. In addition, since 2016, there have been increases in measles cases globally with 84,462



Dr Helen Bedford

cases reported in the WHO European Region in 2018 and almost 1,000 confirmed cases reported in England and Wales. Many of these cases have occurred in older teenagers/young adults who are unvaccinated. With rubella still circulating in Europe, there is the potential for importation of infection posing a risk to individuals susceptible to rubella and so continued vigilance is necessary.

Surveillance period

January 1990 and is reviewed yearly.

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/congenitalrubella>

Analysis

Between April 2018 and March 2019 there were three reports to the BPSU. One case of CRS in an infant born in the UK was reported, the mother acquired the infection abroad. One report was made in error and the other was of a teenager who was born abroad. The surveillance case definition was revised in 2005 to include newly diagnosed children who were born abroad, in order not to miss any cases, and to contribute to European surveillance data.

Table 3: Confirmed and compatible congenital rubella births in the UK and Ireland 1990 to March 2019

Year of birth	Primary Source of notification		
	BPSU	Other	Total
1990-94 * ^	22	10	32
1995-99	12	4	16
2000-04 *	10	1	11
2005-09 *	4	2	6
2010-19 *	6	1	7
Total	54	18	72
* includes a stillborn infant			
^ includes a set of triplets, one of whom was stillborn			

Congenital rubella births in the UK or Ireland 1990-2019: Sixty-eight children and four stillborn infants with confirmed or compatible CR have been born and reported since active surveillance was established in 1990; 54 of these (76%) were first reported through the BPSU (Table 3).

Since 2005 there have been 13 confirmed reports, including one stillborn infant. None of the mothers were UK-born, and none had a previous pregnancy in the UK. Three women arrived in the UK in childhood, and at least one reported having had the MMR vaccination as a teenager. Half of the women acquired their infection abroad in early pregnancy, but six came into contact with rubella in the UK.

Discussion

Very few cases of CR have been reported in the last decade and most reports concern infants with neonatal symptoms who also have serious rubella-associated defects identified at birth or soon afterwards. About half of the recent maternal infections were acquired in the UK. Pregnant women may enter the UK having acquired infection in early pregnancy elsewhere, and susceptible women resident in the UK who travel abroad during early pregnancy may also come into contact with rubella. Health professionals, particularly paediatricians and those working in primary care and antenatal care, or with refugees or other recent migrants, must continue to be aware of the potential serious implications of rash illness in early pregnancy, the guidelines for the management of rash illness in pregnancy,² and also of the early signs of congenital rubella.

Funding

UCL Great Ormond Street Institute of Child Health and the NHS Infectious Diseases in Pregnancy Screening (IDPS).

Public and patient engagement

Sense.

Web: <http://www.sense.org.uk>

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HIV infection & vertical HIV exposure

Key points

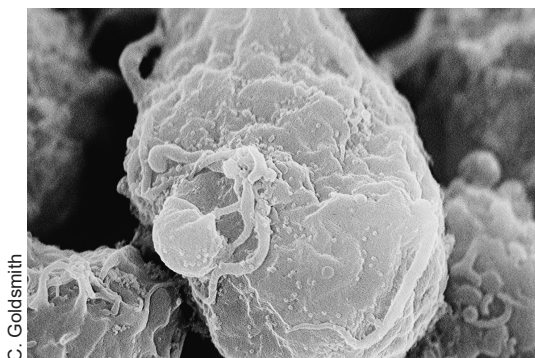
- The number of children born each year in the UK and Ireland to women with diagnosed HIV infection has stabilised in recent years and is currently around 1,000; the vertical transmission rate among diagnosed women remains stable at less than 0.3%.
- New diagnoses of children born in the UK and Ireland have fallen from 40-50 per year in the early 2000's to under 10 per year since 2012.
- The NSHPC continues to conduct enhanced surveillance of all HIV vertical transmissions reported to have taken place in the UK (from 2006); 145 children were reported from 2006 up to the end of 2018, with around two-thirds born to women undiagnosed at the time of delivery.

Summary

The National Surveillance of HIV in Pregnancy and Childhood (NSHPC) has been running for over 30 years. The NSHPC conducts active surveillance of pregnancies in women living with HIV, their babies and other children diagnosed with HIV in the UK and Ireland, as part of Public Health England's Infectious Diseases in Pregnancy Screening Programme. The NSHPC monitors changing patterns of HIV infection and diagnosis in pregnant women and children and tracks changes in obstetric and therapeutic management and vertical transmission (VT) rates. Full details are available on the NSHPC's website: <https://www.ucl.ac.uk/nshpc/>

In the UK and Ireland, there are around 1000 livebirths to HIV-diagnosed women per year. VT rates among diagnosed women have declined from 2.1% in 2000-2001 to below 0.3% since 2012¹. Fewer than 10 infants now acquire infection each year in the UK and Ireland, and most of these have mothers who were not aware of their HIV at the time of delivery. The circumstances of recent UK-born infected children continue to be explored in the NSHPC enhanced surveillance of vertical transmissions.

Figure 5: Scanning EM of HIV, grown in cultured lymphocytes. Virions are seen as small spheres on the surface of the cell



C. Goldsmith



NSHPC team (names L-R): Dr Claire Thorne, Helen Peters, Kate Francis

Methodology

All maternity and paediatric reports are made through the NSHPC's secure online reporting portal. The majority of paediatric cases are reported directly to the NSHPC. Other sources include data linkage with PHE lab data. Details of the NSHPC data collection process are available at: <https://www.ucl.ac.uk/nshpc>. For details of the BPSU surveillance protocol see <https://www.rcpch.ac.uk/bpsu/HIV>.

Surveillance period

June 1986 - June 2019 (inclusive). *Follow-up period:* Infection status of HIV-exposed infants is established by their confirmatory antibody test at ≥ 18 months. Long-term follow-up information on children with confirmed HIV infection is collected through the Collaborative HIV Paediatric Study (CHIPS), a collaboration between the NSHPC, the MRC Clinical Trials Unit at UCL, and clinicians (<http://www.chipscohort.ac.uk>).

As of June 2019 surveillance of HIV infection and vertical HIV exposure has been discontinued on the BPSU orange eCard. Surveillance will continue to be conducted by the NSHPC. Please report any HIV exposed or infected children directly to the NSHPC team via your secure online account or contact nshpc@ucl.ac.uk to register.

Analysis

By the end of 2018 there were 12,510 BPSU reports to the NSHPC. Of these 9,517 were confirmed cases of HIV infection or exposed infants at risk of vertical transmission; 1,106 BPSU reports could not be confirmed as cases by the NSHPC (Table 4, overleaf). The remaining 1,887 reports were duplicates or errors. A further 14,000 confirmed cases of HIV diagnosed children and exposed infants have been reported through other sources (mostly direct reporting to the NSHPC). The remainder of this report includes verified data from all reporting sources (i.e. including those external to BPSU).

A cumulative total of 23,517 HIV-infected or exposed children had been reported to the NSHPC by the end of 2018. The majority of these paediatric reports (22993/23517, 98%) were children born to HIV-positive women.

Table 4: Breakdown of BPSU Reports to the NSHPC (notified by 31 December 2018)

Place of birth / report	Confirmed or compatible cases	Duplicate	Errors	Not yet confirmed
England	6949	949	587	995
Wales	127	26	26	20
Scotland	509	78	90	24
N Ireland	110	8	22	4
Republic of Ireland	1822	60	41	63
Total	9517	1121	766	1106

There are currently around 1,000 livebirths to HIV-diagnosed women in the UK and Ireland. The NSHPC recently reported an overall transmission rate of under 0.3% for births to diagnosed women 2015-2016 (4/1438, 0.28%, 95% CI: 0.08%, 0.71%),¹ remaining stable since 2012 (Figure 6). The main reasons for the low transmission rate are the high proportion of women already diagnosed and on combined antiretroviral therapy (cART) at conception or starting this in early pregnancy. In 2015-2016, 88% of children were born to mothers who were diagnosed prior to pregnancy, 70% of women conceived on cART, and over 90% of deliveries were to women with undetectable viral load.¹

HIV-diagnosed children: Since 1986 when surveillance started, 2,412 children diagnosed with HIV have been reported. Among these, around 90% were vertically infected; 45% were born in the UK or Ireland. A fifth of children (442/2412) were under 16 at the end of 2018 and 75% (333/442) have been seen for care since 2017; 12% are known to have died.²

NSHPC enhanced surveillance of vertical transmissions: All UK-born children identified as being vertically infected are included in the ongoing enhanced surveillance carried out by the NSHPC. The purpose of the enhanced surveillance is to evaluate antenatal screening pathways and the management of women whose infants acquire HIV vertically to contribute to:

- monitoring and improvement of antenatal HIV screening protocols
- understanding timing and circumstances of maternal and infant acquisition of infection.

There have been 145 vertical transmissions among children born in the UK since 2006, with over two thirds born to undiagnosed women.^{3,4} Contributing factors included declined antenatal HIV testing, seroconversion, late booking and adherence issues. An Expert Review Panel meets on an annual basis to discuss anonymised cases and findings to date have been fed into PHE's Infectious Diseases in Pregnancy Screening Programme's national standards and guidelines.

NSHPC enhanced surveillance of supported breastfeeding: All cases of planned and/or supported breastfeeding by HIV-diagnosed mothers are included in the NSHPC enhanced data collection. This enhanced surveillance is ongoing and includes all children born from 2012. To date there have been over 100 reports of clinically supported breastfeeding in the UK.⁵ Findings will be used to inform national guidelines and policy.

Discussion

The epidemiology of HIV in pregnancy in the UK has changed significantly since surveillance started. Now, over 85% of pregnancies are to women diagnosed prior to pregnancy, with an increasing proportion on cART at conception, and over 90% delivering with undetectable viral load.

Changes in management and epidemiology of HIV in pregnancy and childhood, such as the increasing proportion of women on ART at conception, brings new challenges; these include questions around the safety of in utero exposure to antiretroviral drugs throughout gestation and on the impact of a potential increase in clinically-supported breastfeeding by a sub-group of women living with HIV. Updates to antenatal screening standards and pathways are taking place, and surveillance by the NSHPC will be necessary to monitor the outcomes of antenatal HIV screening for the Infectious Diseases in Pregnancy Screening Programme and the impact of these changes.

The vertical transmission rate in the UK and Ireland has remained stable in recent years, at under 0.3% since 2012. Risk of vertical transmission is even lower among women who have an undetectable viral load at the end of pregnancy, most of whom have a suppressed viral load throughout pregnancy.

Despite high uptake of antenatal testing and interventions to prevent vertical transmission, some infants are still acquiring HIV infection during pregnancy or through breastfeeding. The enhanced surveillance of vertical transmissions found that over two-thirds were born to the minority of women with HIV infection who remain

Figure 6: Vertical transmission rates of HIV among diagnosed women, 2000-16



undiagnosed at delivery. The main reasons identified for transmission amongst undiagnosed women were seroconversion and declining antenatal HIV testing. In diagnosed women, these were late antenatal booking and difficulties with adherence. The enhanced surveillance enables us to better understand the circumstances around transmissions that occur despite such low background vertical transmission rates and highlights where the challenges remain.

Acknowledgements

During 2018 the NSHPC team at UCL GOS Institute of Child Health included Helen Peters (Surveillance Manager), Kate Francis (Surveillance Coordinator), Rebecca Sconza and Laurette Bukasa (Surveillance Assistants) and Anna Horn (Surveillance Administrator).

Funding

The NSHPC is funded by Public Health England's Centre for Infectious Disease Surveillance and Control, and NHS IDPS programme (part of PHE).

Public and patient engagement

Children's HIV Association (CHIVA).
Web: <http://www.chiva.org.uk/>

Positively UK.
Web: <http://www.positivelyuk.org>

Salamander Trust.
Web: <http://salamandertrust.net>

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Dr Pat Tookey; Professor Mario Cortina-Borja



The winners of the BPSU's inaugural BPSU rare disease art competition were announced at the BPSU's rare disease tea party held on 10th July 2019. Entrants were asked to design an image based on the theme of 'rare disease and me'.

Daisy was announced as the winner of the 11-17 age category and her work (image above), will feature on the front cover of the next Child and Adolescent Psychiatry Surveillance System annual report. In describing her work she said that the artwork reflects how she thinks of her condition, 22q11.2 Deletion Syndrome, the mental health issues it causes and how she can get lost in her music to cope with the condition.

Annabelle's picture, the winner of under 11 age category, is presented on the front cover of this annual report.

Invasive listeria infection

Key points

- Fifty-Seven patients have been notified through BPSU and Public Health England (PHE) of which 14 were confirmed cases.
- Of the 14 cases for which full data are available all were infected in their first day of life.
- Two babies died.

Summary

Listeriosis is a rare bacterial infection that can cause severe disease in young babies, pregnant women, people with weakened immune systems and the elderly. Pregnant women can become infected by eating contaminated food, such as fresh cheese and unpasteurised milk, and may then pass on the infection to their unborn babies. This can cause miscarriage, premature birth, death or severe disease in babies, often leaving the baby with long-term disabilities. Listeria may be becoming more common, particularly in ethnic minority groups.

This study aims to establish how common this infection in babies and at what age babies are getting the infection. It will also establish how the babies are treated and what is the mortality and the long term consequences of the disease.

The importance of the study is to inform the national policy on antibiotics: current national guidelines (e.g. the NICE guidelines), advising doctors on antibiotic treatment for babies younger than 3 months, recommend an antibiotic combination that will treat listeria infection. Unfortunately, this does not happen everywhere and some babies with possible listeria infection do not get the right antibiotics. Conversely, we know from a recent national study of meningitis that only babies younger than 1 month of age had listeria meningitis. This raises the possibility that thousands of babies between two and three months of age may be receiving antibiotics that are not needed. This study will provide data to establish whether a more targeted policy is required.

Surveillance period

September 2017 - September 2019 (inclusive).

Follow-up period: Follow-up questionnaire at 12 months after initial diagnosis, ending in September 2020.



Dr Stefania Vergnano

Methodology

Data capture uses standard BPSU methodology. In addition, microbiologists in each country will continue reporting cases through established routine public health laboratory reporting systems. The reference public health laboratories are regularly contacted, and the cases reported will be compared with the cases detected through the BPSU orange eCard system to ensure all cases are detected.

In England, the Office for National Statistics (ONS) and the Hospital Episode Statistics (HES) will also be contacted to ensure all admissions and deaths due to listeria in infants less than 90 days are captured.

Details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/listeria>.

Analysis

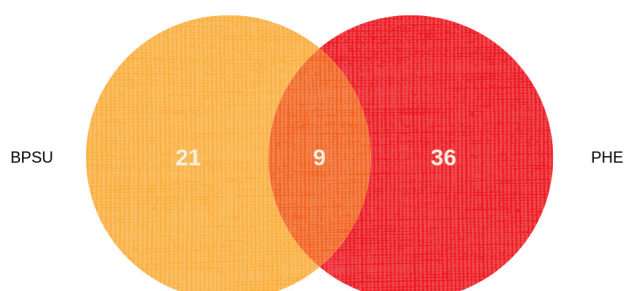
From September 2017 to February 2019 there have been 21 BPSU and 36 PHE notifications and two cases identified through neonIN, a voluntary UK neonatal surveillance network.

After deduplication and verification of the BPSU cases, seven were excluded as duplicate notifications, two did not meet the definition and for two full information is pending.

Data for the two neonIN cases are available, one was a duplicate of the BPSU reports. Data from PHE included 11 miscarriages/stillbirths and eight duplicates with the neonIN and/or BPSU data. Of the remaining 15 cases six cases were verified and complete information were collected, one was excluded as not affected.

Complete information is still pending for seven further cases: two from the BPSU notifications and five from PHE, it is possible that there is overlap between these cases.

Figure 7: Cases reported by BPSU and PHE



The study will continue until September 2019. All cases will be followed-up 12 months after notification. To this date 14 cases have been verified and full information are available. The incidence of listeria in young infants was 0.018 per 1000 live births (LB). Nine infants were late preterm (≥ 30 weeks). The median Birth weight was 2420g (range 605- 3240g), gestational age was 35 (range 24-39) and eight were girls. All cases presented within the first 24 hours from birth. Two babies died giving a case fatality rate of 14%. Of the affected babies three were white, two were African, four Asian, two mixed race: white and black African, and three unknown.

Data were available from the one year follow-up for two babies, both were well and had no hearing, visual or neuro developmental impairment.

Discussion

The survey is showing a much lower number of cases of listeria than expected with an incidence of 0.018 per 1000 LB. In the Republic of Ireland incidence is higher at 0.06 per 1000 LB. Case fatality rate is high with two deaths (14%). All cases presented within the first 24 hours of birth making a very compelling case for changing the national empiric antibiotic therapy for infants under 90 days to include amoxicillin only for the first post-natal week. Of the babies with known ethnic background 73% (8/11) were from either Asian or African or mixed background. Data about medium term follow-up are still awaited.

Following from this study it is realistic to expect that the current NICE guidelines would need amending. It is also hoped that an international comparison with other surveillance units will be undertaken. – the Canadian Paediatric Surveillance Program and a Swiss Paediatric Surveillance Unit are collecting very similar data and the aim is to write a joint publication to compare incidence, age of infection and outcome of Listeria infection in young infants

Funding

This study has been funded by St George's University of London.

Public and patient engagement

Bliss.

Web: <https://www.bliss.org.uk>

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St. George's University of London:
Professor Paul Heath
Temple Street Children's Hospital, Dublin:
Dr Robert Cunney
University Hospital Galway:
Professor Martin Cormican

Juvenile-onset Systemic Lupus Erythematosus

Key points

- Surveillance of juvenile-onset systemic lupus erythematosus through the BPSU with additional reporting by adult clinicians including dermatologists, nephrologists and rheumatologists commenced September 2017 for a period of 25 months.
- Over the first 18 months 60 cases have been reported in total (after excluding duplicates, cases not meeting case definition and those falling outside study dates). There are a further 33 cases with pending clinical data.

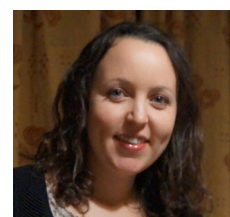
Summary

Juvenile-onset systemic lupus erythematosus (JSLE) or 'childhood lupus' is a rare disease where the immune system attacks many parts of the body. JSLE can be very variable in how it presents, with some children having a mild disease and others having a very severe disease (e.g. developing kidney failure or brain abnormalities). It is not known exactly why JSLE develops. It is likely to be a complicated combination of genetic and environmental factors. It is also not known how many children and young people in the UK and Ireland develop JSLE. This study will help us understand how many children are affected by JSLE and which medical teams look after them. Children with JSLE present with different features and it can be difficult to classify children with JSLE. Classification criteria are important to help doctors diagnose JSLE and to help research better treatments for JSLE. The study aims to determine clinical features of JSLE on presentation, and how new classification criteria used for adults perform in children being treated as JSLE.

Surveillance period

September 2017 - September 2019 (inclusive).

Follow-up period: Follow-up questionnaire at 12 months after initial diagnosis, ending in September 2020.



Dr Hanna Lythgoe

Methodology

Data capture uses standard BPSU methodology.

In addition, adult clinicians including dermatologists, nephrologists and rheumatologists who may see young people with a new diagnosis of JSLE also report all new cases they might have seen on a monthly basis in parallel to the BPSU reporting system.

Details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/lupus>

Analysis

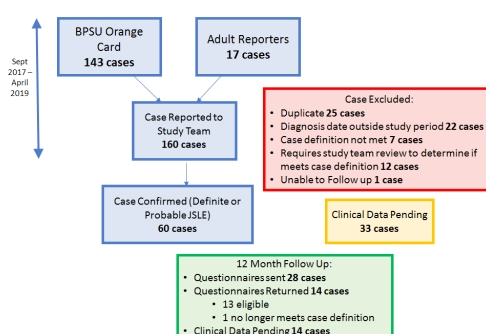
Figure 8 shows cases reported over the first 18 months of the study from the BPSU and adult reporters.

The original number of patients expected was 150 – 160 patients per year. At present there are 60 confirmed cases, 12 possible cases and 33 with outstanding questionnaires. This number is below the expected number of cases. The expected number was based on incidence rates in other countries as well as a UK incidence study which looked at GP records.

This analysis is performed on data from the first 13 months of reporting (September 2017 – October 2018). 102 cases were reported between September 2017 and October 2018. At the point of this analysis 37 cases were included and 65 excluded (duplicate cases, diagnosis date outside study period, case definition not met, clinical data still pending).

All 37 patients met Systemic Lupus International Collaborating Clinics classification criteria (SLICC-2012) and 35 patients met American College of Rheumatology classification criteria

Figure 8: Cases reported to the BPSU JSLE study over the first 18 months



(ACR-1997). Of the two patients meeting SLICC-2012 but not ACR-1997, one had lupus nephritis on renal biopsy and a positive ANA, and the other met the SLICC-2012 hypocomplementaemia immunological criterion.

Of the 35 patients meeting ACR-1997, median age at diagnosis was 12.8 years (interquartile range (IQR) 11.8–14.7 years) with female:male gender of 4.8:1 respectively. 24/35 (69%) were non-Caucasian. Median time from symptom onset to diagnosis was 2 months (IQR 1 – 6 months). The longest delay was 106 months (patient initially diagnosed with Henoch Schnölein Purpura). Of 35 patients, 9 (26%) experienced a delay in diagnosis measured by at least one of: established organ damage due to JSLE at diagnosis (five patients), review by ≥ 1 paediatric sub-specialist prior JSLE diagnosis (three patients) or patient not referred despite seeking medical review (six patients).

The diagnosis was made by or in conjunction with paediatric rheumatology in 21/35 (60%) patients. Of 35 patients, 4/35 (11%) patients were diagnosed solely by paediatric nephrology, 2/35 (6%) by adult rheumatology, 7/35 (20%) by general paediatrics and 1/35 (3%) by the paediatric infectious diseases team. Of 12/35 (34%) patients where diagnosis did not involve a rheumatologist 10 were referred to either adult or paediatric rheumatology and two patients were managed solely by paediatric nephrology.

Regarding treatment, 31/35 (89%) patients were treated with oral and/or intravenous steroids and 33/35 (94%) with hydroxychloroquine. Other treatments used were: mycophenolate mofetil (17/35, 49%); rituximab (8/35, 23%); azathioprine (6/35, 17%); methotrexate (5/35, 14%); cyclophosphamide (3/35, 9%); ofatumumab (1/35, 3%); IV immunoglobulin (1/35, 3%); plasmapheresis (1/35, 3%). No patients had died within one month of diagnosis.

Discussion

These are only initial findings based on early data. However, they suggest very variable delay in diagnosis and further analysis will focus on diagnostic pathways and factors impacting this. It is also notable that almost a quarter of patients were commenced on rituximab very early in the disease course with the majority of these patients (6/8 (75%)) having lupus nephritis. Analysis of the full data will define current patterns of prescribing in JSLE in the UK and Ireland. The number of cases reported is lower than expected but the incidence of JSLE in the UK and Ireland is unknown. Analysis of the final two year data will facilitate estimation of the current incidence rate.

Funding

This study has been funded through the Sir Peter Tizard Bursary and LUPUS UK.

Public and patient engagement

LUPUS UK.

Web: <https://www.lupusuk.org.uk>

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Dr Orla Killeen
Royal Hallamshire Hospital:
Dr Ruth Murphy

Progressive intellectual and neurological deterioration in children (including Creutzfeldt - Jakob disease)

Key points

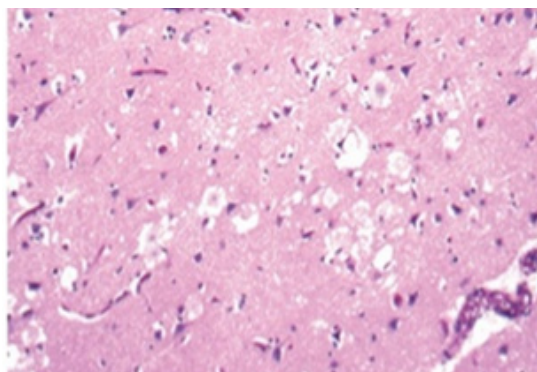
- Continuing surveillance of UK children with progressive intellectual and neurological deterioration (PIND) is important to ensure that new cases of variant Creutzfeldt-Jakob disease (vCJD) are not being missed.
- 188 children with suspected progressive intellectual and neurological deterioration were reported to the PIND study this year.
- Six cases of vCJD have been identified by the study. 1960 of the notified children have been confirmed as having a diagnosis other than vCJD, with more than 190 different rare neurodegenerative disorders in the diagnosed group. A paper on autopsy rates in children reported to the study was published in *Archives of Disease in Childhood* in October 2018.¹

Summary

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997² with the main aim of determining whether or not any children have developed variant Creutzfeldt Jakob disease (vCJD) (Figure 9). vCJD is a rare disorder that was first described in print in 1996. It is caused by a small protein particle called a prion which leads to deterioration in brain function over the course of months and eventually to death. Measures have been taken to remove the risk of transmission of vCJD via meat or meat products from cattle infected with BSE ("mad cow disease"). However there is still a risk that vCJD could infect humans via other routes (e.g. from blood transfusions or surgical or dental instruments or directly from mothers to babies around pregnancy).

The clinical presentation of vCJD is not typical of classical CJD and could be different in children, so the aim is to detect suspected cases by looking at a broader group of conditions. Paediatricians were asked to report all children that they see with worsening intellectual and neurological problems.

Figure 9: A florid plaque in the cerebral cortex in vCJD comprising a dense core with a paler outer layer of amyloid fibrils surrounded by spongiform change (haematoxylin and eosin stain)



The PIND Expert Group

The PIND Study Expert Group then reviews the anonymised clinical details for each child and decides whether or not that child has vCJD or has another diagnosis. By October 2018 there had been 178 deaths in the UK due to vCJD in patients of all ages (including six children). The risk of vCJD continues and the PIND Study remains the only practical means of carrying out surveillance for the disease in children.

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/pind>

Surveillance period

May 1997 – April 2022 (inclusive)

Analysis

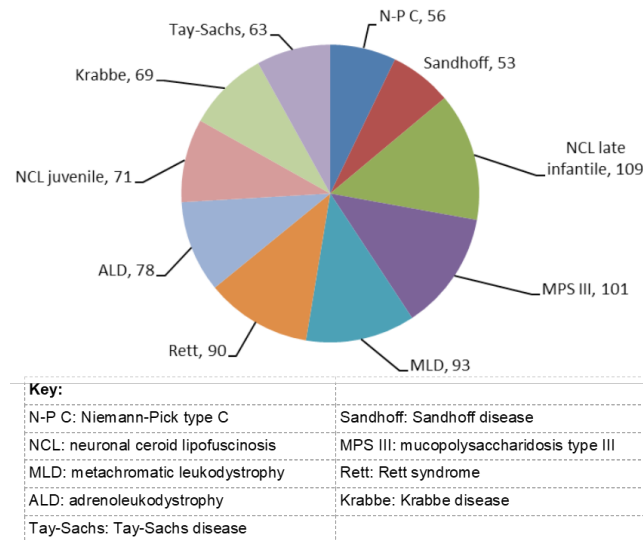
Between April 2018 and March 2019 188 children with suspected progressive intellectual and neurological deterioration were reported to the PIND study. This brings the total notified since the beginning of the study to 4517. 125 were still 'under investigation' by their paediatricians, 2037 did not meet the PIND definition or were duplicate or error notifications and 145 cases were outstanding.

The remaining cases were classified as follows:

Definite and probable cases of vCJD: Six cases of vCJD (four definite and two probable) have been notified - the youngest was a girl aged 12 years at onset. There were three other girls (two aged 14 years and one aged 13 years at age of onset) and two boys aged 15 years at onset. The last child who developed symptoms did so in 2000. All have now died and neuropathology has confirmed vCJD in four cases; a post-mortem was not carried out on the remaining two cases.²

Children with PIND who have definite diagnoses other than vCJD: More than 190 distinct disorders were diagnosed in these 1960 children. The most common diagnoses in the diagnosed group were late infantile neuronal ceroid lipofuscinosis (NCL), mucopolysaccharidosis type III and metachromatic leukodystrophy (MLD). Figure 10 shows the ten commonest groups in the diagnosed cases.

Figure 10: Ten commonest confirmed cases in the PIND study children (reviewed July 2018)



The PIND Study has previously shown that the greatest numbers of cases come from areas with relatively large populations of Pakistani origin;³ more recent data from the study¹ confirm that a large proportion of children in the study are Asian British.

Children with PIND and no underlying diagnosis (idiopathic group): The Expert Group meets regularly to discuss this group of children, currently 244. If a “new” variant of vCJD should arise or if the paediatric presentation differed from the adult presentation, this group could include such a phenotype. However, there is currently no evidence of a “new” unrecognised disorder in this group.

Discussion

The National Creutzfeldt-Jakob Disease Research and Surveillance Unit in Edinburgh reports that there have been 178 deaths from definite or probable vCJD in UK patients of all ages. Until 2016 all these cases were methionine homozygous at codon 129 of the prion protein gene (PRNP). It is significant that the first and only confirmed methionine/valine heterozygous vCJD adult case was identified three years ago (2016).⁴ During nearly 25 years of surveillance, six children presenting with vCJD under 16 years of age have been notified to the study, including four with definite vCJD and two with probable vCJD. There remains concern that more childhood cases may appear, perhaps related to underlying genotype, and children within the ‘idiopathic’ PIND group are under regular review. Children are still at risk of vCJD infection by blood,⁵ plasma products, surgical and dental instruments and theoretically via vertical transmission. Continued surveillance is essential as there are still many unanswered questions about this relatively new disorder – in particular, the number of children who may be incubating vCJD, the length of the incubation period and the exact nature of transmission. Meanwhile the study continues to yield unique information about

the epidemiology of childhood neurodegenerative disorders in the UK. The PIND team continues to present these data at scientific meetings and to publish papers in the relevant journals. Data from the study on cases of SSPE and on Aicardi-Goutières syndrome were presented at the BPNA annual meeting in Liverpool in January 2019 and a paper on autopsy rates in children reported to the study was published in *Archives of Disease in Childhood* in October 2018.¹

Acknowledgements

The PIND team are very grateful for the support of the PIND Expert Group: Dr Peter Baxter, Dr Carlos de Sousa, Professor Paul Gissen, Professor Manju Kurian, Professor John Livingston, Professor Robert McFarland, Dr Helen Mundy, Dr Suvankar Pal, Dr Michael Pike, Professor Richard Robinson, Dr Evangeline Wassmer, Professor Robert Will and Professor Sameer Zuberi. The PIND team are also very grateful for the support of Mr Richard Lynn and Mr Jacob Avis of the BPSU.

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Funding

Department of Health England and Social Care Policy Research Programme [PR-ST-1216-10001]

Public and patient engagement

Creutzfeldt-Jakob Disease Support Network.
Web: <http://www.cjdsupport.net>

Batten Disease Family Association.
Web: <http://www.bdfa-uk.org.uk>

Society for Mucopolysaccharide Diseases.
Web: <http://www.mpsociety.co.uk>

Alex TLC (Adrenoleukodystrophy).
Web: <http://www.alextlc.org>

The Cure&Action for Tay-Sachs (CATS) Foundation.
Web: <http://www.cats-foundation.org>

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Severe microcephaly

Key points

- Up to June 2019, there were 49 confirmed cases of severe microcephaly reported.
- More than half of the children reported had at least one neurological or neurodevelopmental problem and several children had multiple problems.
- Congenital infections were reported as the likely cause of severe microcephaly for eight children, however no children were confirmed to have congenital Zika infection.

Summary

A baby with microcephaly has a 'small head', which may be due to poor head growth before or after birth. This can be associated with abnormal brain structure or development, or with disability, but some babies will develop normally. Many different causes of microcephaly have been described, including genetic disorders, exposure during pregnancy to environmental toxins, certain drugs, infection or malnutrition.

There is uncertainty about the number of babies affected by microcephaly in the UK and Republic of Ireland and about the outcomes for these children. This study will find out how many babies in the UK and Republic of Ireland are born with severe microcephaly each year and how this affects their health and development, including hearing and vision. It will report the clinical features, describe variation in investigation and management and describe clinical outcomes at one and two years of age. The study will also provide a better picture of the care and support these babies and their families currently receive. This will allow us to make sure the right services are available to meet the future needs of children and families. Importantly it will also provide us with a way to monitor changes in the frequency of microcephaly, for example due to infections during pregnancy such as rubella, cytomegalovirus or Zika-virus.



Dr Rachel Knowles

Surveillance period

October 2017 - October 2018 (inclusive).

Follow-up period: Follow-up questionnaires at one year of age and two years of age. Follow-up will end in early 2020.

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/microcephaly>

Analysis

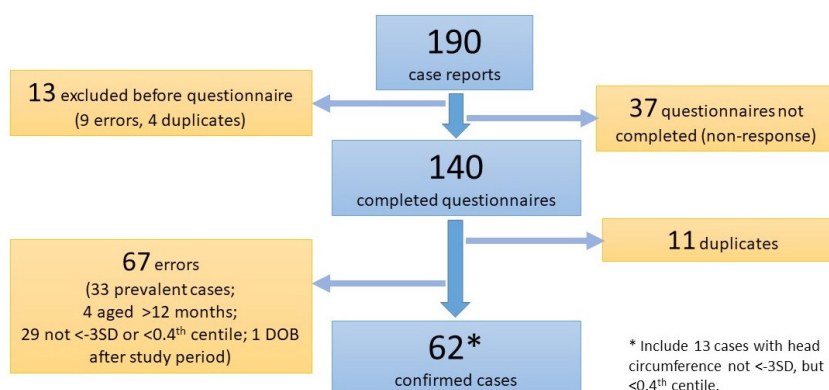
This interim analysis is based on data collected during the first 21 months (October 2017 – June 2019 inclusive) of the study. Some preliminary analyses based on these early data are reported below, however further questionnaires are still awaited and these figures may change.

The diagram flow of the cases reported to date can be seen in Figure 11.

Frequency of case reporting: Up to June 2019, 49 children with a confirmed head size $<-3SD$ below the mean for age and sex have been reported to the study; a further 13 children with a head size $<0.4th$ centile (equivalent to $<-2.67SD$) but not as severe as $<-3SD$ below the mean have additionally been reported. Incidence will be estimated once all cases have been fully reviewed and analysed.

Children's characteristics: The results below are based on 62 children with a head circumference below the 0.4th centile (including 49 children with a head circumference $<-3SD$ below the mean). The characteristics of these children are described in Table 5.

Figure 11: Flow diagram of microcephaly cases reported between October 2017 and October 2018 in the UK and the Republic of Ireland.



Clinical features at diagnosis: A range of abnormalities of neurodevelopment were reported, with some children having more than one problem. These included 18 children who had abnormal visual responses, 19 with eye abnormalities, 11 with hearing impairment, 14 who experienced seizures or fits, 29 who had other abnormal neurological signs and 23 with delayed motor milestones.

Table 5: Characteristics of microcephaly cases in UK and the Republic of Ireland reported to the BPSU between October 2017 and October 2018.

	%
Sex	
Girls	50.00
Boys	50.00
Ethnicity	
White	56.45
Asian	25.81
Other	12.90
Not known	4.84
Gestation at birth	
Term	55.74
Preterm	42.62
Not known	1.64
Total	100

* Term was defined as birth occurring on or after 36 weeks completed gestation.

Clinical investigation and management: Children had a variety of different tests and investigations, including tests for congenital infections and for metabolic disorders. Cranial MRI were performed on 41 children, ultrasound scans on 39 children and CT scans on ten. An EEG was completed in 19 children. Six children were reported to have genetic or syndromic conditions. Congenital infections, such as toxoplasmosis and CMV, were identified as a potential cause of the microcephaly in eight children, however no children were confirmed as having Congenital Zika Syndrome.

Clinical outcomes: At notification, most children were living at home and no child with confirmed microcephaly had died. The clinical outcomes at one and two years of age are currently being collected.

Discussion

The number of children with severe microcephaly reported to the study was fewer than expected from previous reports,¹⁻³ however this may change if additional cases are confirmed.

The underlying causes of microcephaly included genetic disorders and congenital infections, but no cases of Congenital Zika Syndrome were identified. Although most children had been discharged from hospital and were living at home with their families, at least half had one or more neurodevelopmental abnormalities, including epilepsy, vision and hearing problems. Once data collection and analysis has been

completed, comparison will be made with similar international surveillance studies currently underway in Australia and Canada, and with routine reporting systems, such as the National Congenital Anomaly and Rare Disease Registration System (NCARDS).

Acknowledgements

We would like to thank Anna Horn and Helen Peters at UCL Great Ormond Street Institute of Child Health for their hard work in supporting the questionnaire mailouts and study administration, and Steve Rose (formerly at Sense) and Dr Suzanne Kelleher (Consultant Developmental Paediatrician, Ireland) for their help in setting up the study.

Funding

This study has been funded with a grant from Great Ormond Street Hospital Children's Charity (GOSHCC).

Public patient engagement

Sense (<https://www.sense.org.uk>) – a national service-providing organisation for children and families with sensory impairments.

Contact (formerly Contact a Family, <https://www.contact.org.uk>) – a charity supporting families of children living with a disability.

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Visual impairment and blindness

Key points

- Initial and 12 month follow-up data collection are complete.
- 351 notifications were received from the BPSU, of which 190 were confirmed cases.
- Cerebral visual impairment (visual loss as a result of insult to the visual pathways and cortex) continues to be the major cause of SVI/BL in the UK.



Professor Jugnoo Rahi

Summary

Most children living in the UK with visual impairment or blindness are likely to be affected from birth or infancy and will experience a significant lifelong impact on their development, education, social and emotional wellbeing. The aim of this second British Childhood Visual Impairment and Blindness Study (BCVIS2) was to determine the incidence, causes, mode/context of detection, associated factors, management and short-term health and social outcomes of all-cause childhood visual impairment. All children aged ≤18 years diagnosed during a 13-month period as being severely visually impaired or blind were identified through their clinicians using national active surveillance independently but concurrently through the BPSU and the British Ophthalmological Surveillance Unit (BOSU). There was simultaneous identification of those children with visual impairment (i.e. less severe impairment) through BOSU as these children were unlikely to be seen by a paediatrician. The merged dataset encompasses the full spectrum of visual disability.

Methodology

Data capture used a dual surveillance methodology using the BOSU in addition to the BPSU, to identify cases of visual impairment (VI) as well as severe visual impairment and blindness (SVI/BL); details of the study protocol are available at <http://www.rcpch.ac.uk/bpsu/bcvis>

Surveillance period

October 2015 – October 2016 (inclusive).
Follow-up period: Follow-up questionnaire at 12 months after initial diagnosis, ending in October 2017.

Analysis

Three hundred and fifty-one case of severe visual impairment or blindness (SVI/BL) have been reported through the BPSU, of which 190

have been confirmed. There were 159 ineligible notifications; of these 11 were duplicate reports, 83 error reports and 53 were non-responders (did not return the initial questionnaire).

Children born with low birth weight (33%, n=43), from ethnic minorities (non-White: 29%, n=52) and in the most deprived socio-economic group (bottom quintile of IMD; 28% n=52) are over-presented in children with SVI/BL compared to the general UK child population (children aged 18 years of less).

Prematurity (born <37 weeks: 28%, n=47) and admission to a NICU/SCBU (51%, n=86) was more frequent in children with SVI/BL compared to the general UK infant population (all live births in 2016).

Table 6: Age at diagnosis of SVI/BL

Age diagnosed with poor vision	n=190	%
<1 year	114	60
1-4 years	47	25
5-14 years	20	11
15 years	1	<1
Unknown date of diagnosis	8	4

The visual pathways and cortex are the leading anatomical site (57%, n=108) affected in SVI/BL (cerebral visual impairment). Optic nerve disorders (primarily optic nerve hypoplasia and optic nerve atrophy) and retinal disorders were affected in 31% (n=59) and 23% (n=44) of 190 BPSU confirmed cases respectively.

Disorders caused by insults occurring in the prenatal period (62%) predominate SVI/BL, with perinatal and childhood causes resulting in SVI/BL in 14% and 13% of cases respectively. The remaining 11% of children had SVI/BL caused by an insult in either the prenatal or perinatal period.

Ninety percent of children had an additional major systemic disorder or impairment (SVI/BL plus). Children with SVI/BL plus were more likely to have cerebral visual impairment compared to children

Figure 12: Reporting sources for SVI/BL confirmed reports

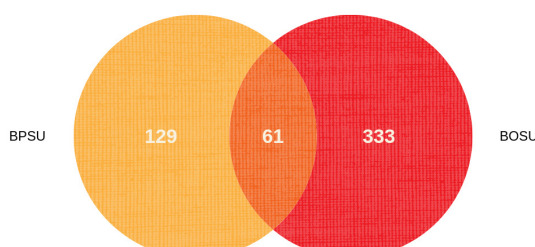
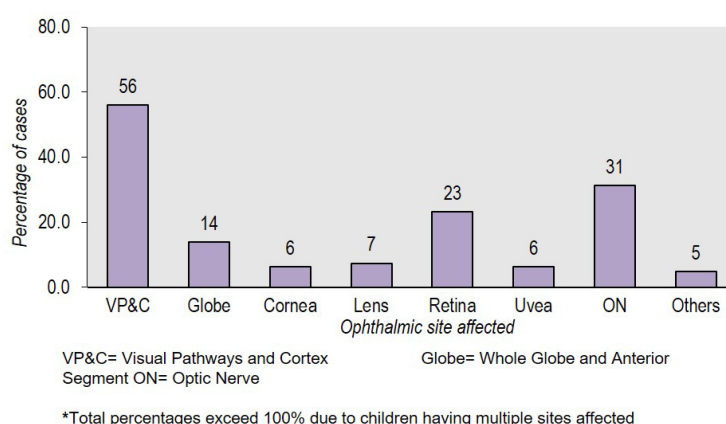


Figure 13: Ophthalmic sites affected in cases of SVI/BL reported through BPSU* n=190



with isolated visual loss (odds ratio: 5.5 ,p=0.01, 95% CI: 1.5- 20.4).

Of the 190 confirmed cases, 96% of children were reported also to be under the care of an ophthalmologist (n=183).

Thirteen per cent of children with SVI/BL at initial notification reported through BPSU were registered as sight impaired (SI) and 32% registered severely sight impaired (SSI).

Discussion

Analysis of cases of SVI/BL indicates a heterogeneous population, with most children diagnosed under the age of one year.

Children newly diagnosed with SVI/BL in the U.K are still a vulnerable population, with children from ethnic minorities and from the most deprived socioeconomic group over-represented compared to the general child population.

In addition, SVI/BL is also a clinically complex group, with the vast majority (over 80%) of children diagnosed with at least one major non-ophthalmic disorder or impairment.

Cerebral visual impairment (CVI) is one of the leading causes of SVI/BL in high and middle income countries.^{1,2} In line with this finding, our study confirms that in the UK, CVI continues to be the major cause of SVI/BL in children. Disorders originating from the pre and perinatal period still predominate SVI/BL.

Findings from BCVIS2 will provide the evidence base for advocacy for health, social and educational services for visually impaired children and their families, enabling visual disability to be placed in the broader context of child health, particularly by offering an understanding of the

social determinants of childhood visual disability, so as to inform policy. In undertaking the study, a unique resource will be created – a representative inception cohort of children spanning the spectrum of visual disability in whom long term clinical, social and educational outcomes of current and emerging interventions can be determined.

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2. Solebo AL, Teoh L, Rahi J. Epidemiology of blindness of children. Archives of Disease in Childhood. 2017 102; 853-857

Funding

This study is funded by Fight for sight (<http://www.fightforsight.org.uk>).

Public and patient engagement

Royal National Institute of Blind People.
Web: <https://www.rnib.org.uk/>

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Appendix - Publications 2018 -2019

Attention deficit hyperactivity disorder

1. Eke H, Ford T, Newlove-Delgado T, Price A, Young S, Ani C, Sayal K, Lynn RM, Paul M, Janssens A. Transition between child and adult services for young people with attention-deficit hyperactivity disorder (ADHD): findings from a British national surveillance study. *The British Journal of Psychiatry* 2019 Jun 4:1-7.

BPSU

2. Lynn RM, Reading R. A report from the British Paediatric Surveillance Unit Ascertainment Group. *Archives of Disease in Childhood* 2019. In press

Congenital Zika syndrome

3. Oeser C, Aarons E, Emond A, Heath PT, Johnson K, Khalil A, Knight M, Ladhani S, Lynn RM, Morgan D, O'Brien P, Tuffnell D, Pebody R. Surveillance of Congenital Zika Syndrome in England and Wales: Methods and Results of five surveillance systems. *Epidemiology and Infection* 2019. In press

Eating disorders

4. Petkova H, Simic M, Nicholls D et al. Incidence of anorexia nervosa in young people in the UK and Ireland: a national surveillance study. *BMJ open*, 9(10), p.e027339.

Elevated blood lead levels

5. Ruggles R et al. Surveillance of Elevated Blood Lead in Children (SLiC) - A British Paediatric Surveillance Unit analysis. *Public Health England* 2018 Online https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/751982/SLiC_final_report_v3.pdf

Enterovirus and parechovirus meningitis

6. Kadambari S, Braccio S, Ribeiro S, et al Enterovirus and parechovirus meningitis in infants younger than 90 days old in the UK and Republic of Ireland: a British Paediatric Surveillance Unit study *Archives of Disease in Childhood* 2019;104:552-557.

Kawasaki disease

7. Tulloh RMR, Mayon-White R, Harnden A, Lynn RM et al Kawasaki disease: a prospective population survey in the UK and Ireland from 2013 to 2015. *Archives of Disease in Childhood* 2019 Jul;104(7):640-646.

HIV infection & vertical HIV exposure

8. Rasi V, Cortina-Borja M, Peters H, Sconza R, Thorne C. Surveillance of congenital anomalies following exposure to Raltegravir or Elvitegravir during pregnancy in the UK and Ireland, 2008-2018. *JAIDS* 2018.

9. Peters H, Thorne C, Tookey PA, Byrne L. National audit of perinatal HIV infections in the UK, 2006-2013: what lessons can be learnt? *HIV Medicine* 2018.

10. Favarato G, Townsend C, Bailey H, Peters H, Tookey P, Taylor G, Thorne C. Protease inhibitors and preterm delivery: another piece in the puzzle. *AIDS* 2018.

Progressive intellectual and neurological deterioration

11. Verity C, Winstone AM, Will R, Powell A, Baxter P, de Sousa C, Gissen P, Kurian M, Livingston J, McFarland R, Pal S, Pike M, Robinson R, Wassmer E, Zuberi S. Surveillance for variant CJD: should more children with neurodegenerative diseases have autopsies? *Archives of Disease in Childhood* 2019;104:360-365.

Type 2 diabetes

12. Candler TP, Mahmoud O, Lynn RM, Majbar AA, Barrett TG, Shield JPH. Treatment adherence and BMI reduction are key predictors of HbA1c 1 year after diagnosis of childhood type 2 diabetes in the United Kingdom. *Pediatr Diabetes*. 2018 Dec;19(8):1393-1399.

Appendix - Presentations 2018-2019

HIV infection and vertical HIV exposure

1. Francis K, Thorne C, Horn A, Peters H. Successes and emerging challenges in prevention of vertical HIV transmission in the UK and Ireland. British HIV Association conference, Bournemouth 2019.
2. Peters H, Francis K, Sconza R, Horn A, Thorne C. Children's HIV Association (CHIVA), London 2019.
3. Peters H, Francis K, Sconza R, Thorne C. Breastfeeding, vertical HIV transmission and implications for accurate monitoring: data from the UK and Ireland. International Workshop on HIV Pediatrics, Amsterdam 2018.
3. Rasi V, Cortina-Borja M, Peters H, Sconza R, Thorne C. Assessing the influence of BHIVA guidelines on trends in antiretroviral use in pregnancy in the UK and Ireland in 2005-2016. British HIV Association (BHIVA). Edinburgh 2018.
4. Peters H, Byrne L, Tookey P, Webb S, Thorne C. Audit of perinatally acquired HIV in UK-born infants 2014-2017. British HIV Association (BHIVA). Edinburgh 2018.
5. Rasi V, Peters H, Cortina-Borja M, Thorne C. Raltegravir in pregnancy: patterns of use and birth outcomes in the UK and Ireland. Conference on Retroviruses and Opportunistic Infections (CROI). Boston, USA 2018.
6. Collins J, Chappell E, Peters H, Francis K, Thorne C, Judd A. The cascade of care for children with HIV in the UK and Ireland in 2015. Children's HIV Association (CHIVA) Conference. London 2018.
7. Peters H, Francis K, Horn A, Thorne C. The cascade of care for children with HIV in the UK and Ireland in 2015. Children's HIV Association (CHIVA) Conference. London 2018.

Nutritional rickets

8. Shaw N, Pall K, Leoni M, Lynn R et al. Vitamin D deficiency nutritional rickets presenting to secondary care in children (<16 Years) – A United Kingdom surveillance study. 9th International Conference on Child Bone Health, 22-25 June; Salzburg, Austria 2019.

Progressive intellectual and neurological deterioration

9. Verity C, Powell A, Winstone AM. The changing clinical spectrum of Aicardi-Goutières syndrome in UK children (poster presentation); 45th BPNA Annual Scientific Meeting; 23 - 25 January; Liverpool 2019.
10. Powell AE. Has SSPE disappeared from the UK? Findings from the PIND Study. 45th BPNA Annual Scientific Meeting; 23 - 25 January; Liverpool 2019.
11. Winstone AM, Powell A, Will R, Verity C. No evidence of variant Creutzfeldt-Jacob disease in undiagnosed UK children with neurodegenerative disease (poster presentation); Public Health England Annual Conference 11 Sep - 12 September; Coventry 2018

Visual impairment and blindness

12. Poster presentation at Royal College of Ophthalmology Congress 2018 May 22, Liverpool
13. Poster presentation at ARVO Annual Conference 2018, April 29, Honolulu, USA
14. Oral presentation at VIEW (QTVI professional association) Conference 2018, March 15, Birmingham.

Membership of Scientific Committee 2018

Dr Shamez Ladhani	Chair
Dr Lamiya Samad	Medical Advisor (non-infectious disease), UCL Great Ormond Street Institute of Child Health
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Dr Simon Nadel	Consultant in Intensive Care
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