Vol 33 No 1 June 2016

# BPSU

**The British Paediatric Surveillance Unit** (BPSU) is part of the Research & Policy Division of the Royal College of Paediatrics and Child Health

**Editor**
Richard Lynn
BPSU Scientific Coordinator

Tel: 020 7092 6173/4
Fax: 020 7092 6001
Email: bpsu@rcpch.ac.uk
Website: www.rcpch.ac.uk/bpsu

Inside this issue





# BPSU Bulletin

## Congenital Zika syndrome surveillance commences

A study on congenital Zika syndrome commenced this April for 13 months. Such was the concern over the implications of Zika virus infection for travelers that the BPSU in conjunction with the Public Health England (PHE) have fast tracked the application to mount surveillance on the condition. The study is being led by Dr Richard Pebody, Head of Respiratory Disease Department at PHE and aims to identify all babies with microcephaly or neurological abnormalities born in the UK and Ireland to mothers who have travelled to countries with active Zika transmission. An associated study is also being undertaken through the UK Obstetric Surveillance System. The study is part of a wider collaboration with our sister surveillance Units in Australia, Canada and New Zealand. Dr Richard Reading has been quoted as saying:

Dr Richard Pebody

"*Following an increase in Zika virus infection, many more cases of microcephaly and other abnormalities of the brain have been seen in Brazil amongst infants than would be expected. This has led to significant concern from health care professionals across the world that this rise is related to increased rates of Zika virus infection amongst women during pregnancy.*"

"*To address such concerns, the UK and Ireland will be the first nations to introduce systematic surveillance of this newly emerging condition, referred to as congenital Zika syndrome. Using the BPSU, the study aims to identify how many babies are born in the UK with microcephaly or neurological abnormalities requiring investigation whose mothers have travelled to a country with active Zika transmission. To put rapidly into place such a monitoring system demonstrates the ability of the UK public health agencies and the BPSU to respond to such an emerging threat and is a testament to the dedication of the staff that have made this possible.*"

**Clinicians are asked report:** All infant ≤ 6 months of age with a head circumference > 2 standard deviations below the mean for gestational age and sex (i.e. below the 2nd centile) or any neurological abnormality requiring investigation whose mother has travelled to a country with active Zika transmission during pregnancy or in the three months prior to conception.

**Exclusion Criteria:** Travel only to countries without reported Zika transmission (Please check on: http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-countries-with-transmission.aspx)

Since autumn 2015, 42 countries worldwide have reported cases of Zika virus infections. An increase in cases with malformations of the brain has also been reported in French Polynesia, where an outbreak of Zika virus has previously occurred.

So far in the UK, two babies, whose mothers were resident in countries with no active Zika transmission but with a travel history to Brazil during pregnancy, microcephaly and abnormalities of the brain have been reported, Zika virus infection was subsequently confirmed by laboratory tests. Almost 1.4 million UK residents travel to South and Central America and the Caribbean on average each year, 25% of those are women of child bearing age who, if pregnant, are at risk of being infected with the Zika virus and of transmitting it to their unborn baby.

The study protocol information and a lay public information guide which can be distributed in your ward/clinics is available form is available www.rcpch.ac.uk/bpsu/zika.

**Patient support:** Microcephaly Support Group

**For contact:** Dr Clarissa Oeser, Public Health England, 61 Colindale Avenue, London NW9 5EQ

**Email:** clarissa.oeser@phe.org,uk **Tel:** 0208 327 6729

**Supported by Public Health England, Royal College of Paediatrics and Child Health, and UCL-Institute of Child Health with support from GOSH Children's Charity**

# Study updates

Dr Priscilla Julies

**Nutritional Rickets –second surveillance year approved.** The Nutritional Rickets Presenting to Secondary Care, BPSU study aims to review the incidence and clinical management of rickets in the UK and Republic of Ireland in children aged 0-16 years. The study is being led by Dr Priscilla Jules from Royal Free in conjunction with the RCPCH Research and Policy division. The project went live on 1st March 2015 and ,unlike the traditional method of paper based BPSU data collection methodology, this project uses an online clinical questionnaire and reporting system.

A total of 149 cases were notified (from March 2015 to 2nd March 2016) of which 59 (40%) have been confirmed as cases, 77 (52%) are reporting errors and data on 31 (20%) is still awaited. The number of case reports was expected to be higher (approx. 100-300) and there is concern that either under ascertainment may be occurring or, perhaps more likely, the incidence is not as high as first thought. Confirmation of this through a second year of surveillance aims to strengthen/disprove the view that the level of incidence is truly lower than expected.

Of the confirmed cases 26 (54%) are male; 55 (93%) are under the age of 5. Ethnic breakdown is described in Figure 1

Of particular interest is that 90% of cases were not taking supplements at diagnosis 88% still followed-up in secondary care and there appears to be variable treatment regimens despite published guidance.

Please do report any cases of children 0-16 years arising since March 1st 2015 presenting with either clinical or radiological rickets as defined by the case definition.

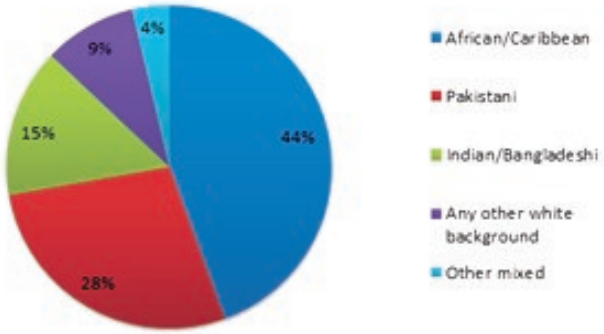


**Figure 1: Ethnic breakdown**

**The case definition is :**

**Clinical Rickets with any of the following:**
Leg deformity (bowing or knock-knees)/Swollen wrists or knees or ankles or ribs (Rachitic Rosary) AND 25OHVitamin D <25nmol/L with one or more abnormalities of serum calcium, alkaline phosphatase, phosphate, parathyroid hormone.

**OR**

**Radiological Rickets with widening, cupping, splaying of metaphysis (of any long bone) AND 25OHVitamin D <25nmol/L**

**Exclusion Criteria:**

- Vitamin D dependent rickets e.g. 1α-hydroxylase deficiency - vitamin D resistant rickets e.g. familial or X-linked hypophosphataemic rickets.
- Rickets associated with other chronic diseases e.g. malabsorption, liver disease, chronic renal disease
- Metabolic bone disease of prematurity (infants whose corrected age is < 3 months at presentation, who were born < 36 weeks gestation and weighing <1.5kg

The study protocol information and a lay public information guide which can be distributed in your ward/clinics is available form is available at www.rcpch.ac.uk/bpsu/RKT . For further information on the study contact karina.pall@rcpch.ac.uk

**Congenital Rubella Screening to end but BPSU surveillance continues**

Following a review of evidence by the UK National Screening Committee rubella susceptibility screening in England ceased from 1 April 2016 (further information available at https://www.gov.uk/government/news/rubella-susceptibility-screening-in-pregnancy-to-end-in-england). The health agencies in the devolved nations of Wales, Scotland and Northern Ireland are reviewing their guidance.

In spite of the cessation of antenatal screening, BPSU surveillance of congenital rubella will continue. Though rubella is no longer freely circulating in the UK population and the few cases that do present are generally imported from broad, BPSU surveillance is an important tool to monitor the condition and the circumstances of any congenital rubella births particularly in light of the changed policy.

## Study update

**ADHD Transition study to continue:** This study commenced in November 2015 and in the first instance was expected to last 7 months. This has now been extended to 13 months due to the fewer than expected case reports. This may reflect the true incidence of the issue or under ascertainment; the extension will allow investigation of both. A 9 month follow-up will also be undertaken. The study is being led by Professor Tamsin Ford of Exeter University Medical School and aims to provide recommendations to improve service delivery and provision for young people with ADHD thus improving young peoples health at a key life stage and beyond.

Thank you very much to those that have notified us of a case and returned the questionnaires. To date we have had 126 case notifications from the BPSU. Of those notifications, 64 questionnaires have been returned, of which 51 are eligible and confirmed cases. The psychiatrists have reported 111 cases, returned 45 questionnaires of which 38 are eligible cases.

If you think you have wrongly notified us of a case, please do complete **section C** of the questionnaire and return it to us. This enables us to keep our records up-to-date and close the case.

This study explores a rare event, rather than a rare condition. On the contrary, the group we are targeting have a rather "common" condition. We appreciate that many of you reporting these cases have a high caseload and are snowed under with all sorts of requests. No question this study adds to that pressure. However, it is hoped that this study will shed a light on the woeful situation that contributes to the pressure that clinicians work under. Without the data, we cannot be nearly as effective; so, please contact us to discuss a more manageable strategy to collect the necessary data.

There is still some confusion over the eligibility criteria. To clarify:

- Young person with ADHD on medication for the ADHD
- Young person within 6 months of the age boundary for your service (whatever age that may be; usually 18 but some area services stretch from 16-25)
- The first time you have reported this case to BPSU

To help clinicians keep track of the information they have provided to us, we will now be sending 'receipt emails'. If you returned a questionnaire prior to 15th March you won't have received one; if for any reason we haven't received a questionnaire you have returned though, we will send you a reminder for it via email.

The study protocol information and a lay public information guide which can be distributed in your ward/clinics is available form is available www.rcpch.ac.uk/bpsu/ADHD

For further information, please contact; Professor Tamsin Ford: t.j.ford@exeter.ac.uk Web: www.medicine.exeter.ac.uk/catchus/

## Tizard bursary

The winner of the **Sir Peter Tizard Bursary 2015-16** was Hanna Lythgoe, a clinical research fellow at Alder Hey Hospital, Liverpool.

Hanna wishes to investigate Juvenile-onset Systemic Lupus Erythematosus (JSLE) or 'childhood lupus' . In accepting the award Hanna stated that *"the study will provide data from across the UK and ROI that will be of great importance in delivering national healthcare services that meet the needs of children and young people with JSLE. It will facilitate prospective evaluation of new classification criteria which may improve early detection of JSLE in children and young people. Through defining patterns of care it will allow us to assess our current situation against those proposed within the European SHARE guidelines, helping us to develop plans to improve service provision that is targeted to where it is required. This will ensure that children and young people across the UK have access to specialist and multi-disciplinary care with timely access to treatment."*

The BPSU team will be working with Hanna and her supervisor Professor M.W. Beresford, Director, UK Experimental Arthritis Treatment Centre (EATC) for Children to produce the project protocol with the aim of starting this study later in the year.

The candidates for this year's award were of such quality that several were encouraged to re-submit their applications through the normal BPSU process and we are hopeful that, if funding can be identified, that they also will be able to commence soon.

The call for the next Bursary will go out around July, but you can visit the www.rcpch.ac.uk/bpsu/bursary for further details or contact the BPSU office.

# BPSU news

**30 years of collaboration with the RCPCH and its members.** To celebrate its 30 year association with the RCPCH and its members the BPSU held a half day symposia at the RCPCH annual conference on the afternoon of Wednesday 27th April. Presentations were received from Professor Paul Health on the changing patterns in the epidemiology of meningitis; on dealing with public health emergencies from Dr Chris Verity; a key note speech from Dr David Elliman on the dilemmas surrounding screening; as well as presentations from distinguished speakers on nutritional rickets, lead toxicity, diabetes in childhood rare psychiatric conditions and involving patients and public in research. The symposium is free to all those who have registered for the day with the RCPCH so do come along.

Chair and former Chairs of the BPSU (*from left to right*): Dr Reading, Professor Peckham, Dr Verity, Professor Ross, Professor Colver

# BPSU on the road

Since the last newsletter, the BPSU has been out and about publicising its work. Excellence in Paediatrics asked the BPSU to host their rare disease session at their London conference last December. The attendees were predominately from overseas and were not familiar with BPSU which gave Dr Richard Reading an opportunity to present the work of the BPSU and that of the International Network of Paediatric Surveillance Units. Dr Chris Verity presented the work of the PIND study and Dr Pat Tookey discussed surveillance of HIV and congenital rubella. Feedback was such that the BPSU have been asked to organise a session on rare metabolic disease at this years London conference in December 2016.

As part of its 30th anniversary, the BPSU hosted a rare diseases in paediatrics conference at the University of Birmingham in February. The event was a great success with nearly 150 delegates attended from across a wide range of interest groups including patients and carers, healthcare professionals, researchers, industry and policy-makers.

The conference was opened by Professor John Newton, Chief Knowledge Office to PHE and chair of the BPSU Governance Board explored the theme of 'rare diseases in paediatrics – from birth to transition' and centred on the child's journey from diagnosis through transition and end of life care. Spread over three sessions delegates heard presentations the first of which explored the theme of improving and speeding-up diagnosis and examined the advances in genomics, how it will facilitate early rare disease diagnosis prenatally, antenatally and soon after birth. The second explored the theme of research into practice and looked at specific BPSU studies and how findings of clinical research can be translated into real practice to benefit children and their families living with rare disease. The third session examined the importance of supporting older children and adolescents through their transition into adult care and the challenges faced. Further details and access to the slide presentations can be found at www.rcpch.ac.uk/bpsu/rdc16.

From feedback, 88% rated the event as excellent or above average and 95% rated the education as good to excellent. 64% visited stands from the sponsors and the charities. Suggested themes for future BPSU conferences include genetic / genomic research developments and their implications for clinical practice; recent advances in treatment and difficulties faced by rare disease research. There was also interest in the BPSU holding more regional events (90%). We are aware that time and cost can influence whether one attends such events so for the first time the BPSU sought sponsorship for this event in order to subsidise fees and in doing so managed to cover its costs. Thanks goes to our main sponsor Alexion, and also SOBI, Pfizer, Genzyme, Biomarin and OpenApp.

The BPSU annual Rare Disease Day tea party, sponsored by Diurnal, rounded off the event. The tea party has established itself on the calendar as one of the main events for UK rare disease activities. This year the event was organised in conjunction with Birmingham Children's Hospital for their rare disease week. At this year's tea party, the young people of Alstrom Syndrome UK, Hear my Voice Youth Forum (HMV) presented their newly designed transition resources. The resources known as T-KASH (Transition-Knowledge And Skills in Health) are aimed at young people/ families and professionals. They consist of ten logos and a visual map, which can be used in any setting e.g. Hospital, GP, Health Centre to signify that adolescent health care is more than just a consultation about a medical condition's. The message is that young people, with long term health conditions, have full and active lives. Find out more at www.rcpch.ac.uk/bpsu/rarediseaseday16


The Unit is aiming to put on further celebratory events in conjunction with our partners, so do look out for details. If you have ideas for themes for events or you wish to support holding a regional BPSU event please do get in contact with BPSU office.

# Publications

I Simms, PA Tookey, BT Goh, H. Lyall, B Evans, CL Townsend, H Fifer, C Ison, The Incidence of congenital syphillis in the United Kingdon: February 2010 to January 2015. BJOG 2016; DOI: 10.1111/1471-0528.13950.

LA Stellitano, A Winstone, MS van der Knaap, CM Verity. Leukodystrophies and genetic leukoencephalopathies in childhood: a national epidemiological study. Dev Med Child Neurol 2016 Feb 11. Epub 2016 Feb 11.

L Samad, M Cortina-Borja, Sutcliffe AG, S Marven, JC Cameron, HE Bashir, R Lynn, B Taylor. National hospital data for intussusception: Data linkage and retrospective analysis to assess quality and use in vaccine safety surveillance. Vaccine. 2016 Jan

# Reports and Analysis

**Analysis:** For the period June to November 2016 Orange Card return rates stand at 90.8% (Table 1). There have been some significant shifts in response rates over the last 6 months, with South-East Thames response rate falling from their high response rates of 93% in May 2015 to 89.6% in November 2016. On the other end of the scale, North Scotland's responses rates of 97.4% are the UK's top responding region - congratulations to North Scotland!!!

As always, if you are experiencing any problems with the electronic orange card, do get in touch with the BPSU team.

**Table 1 - % Regional Response Rates June-November 2016**

| Region | % retd | rank |
|---|---|---|
| EAngl | 95.4% | 2 |
| Mersey | 90.4% | 15 |
| NET | 86.4% | 19 |
| NScot | 97.4% | 1 |
| NWest | 87.5% | 18 |
| North | 92.0% | 8 |
| NIre | 89.4% | 17 |
| NWT | 90.7% | 14 |
| Oxfrd | 91.9% | 11 |
| RIre | 85.0% | 20 |
| SET | 89.6% | 16 |
| SScot | 92.3% | 7 |
| SWest | 91.9% | 10 |
| SWT | 92.0% | 9 |
| Trent | 91.6% | 12 |
| Wales | 92.5% | 6 |
| Wessx | 93.1% | 5 |
| WMids | 90.9% | 13 |
| WScot | 93.4% | 3 |
| Yorks | 93.3% | 4 |
| **Average** | **90.8%** | |

**Table 2: All cases reported and follow ups to 14.03.2016**

| | | VALID | | IN-VALID | | | | (as % of total) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Condition | Start | C | R | D | E | X | TOTAL | C&R | D&E | X |
| HIV | 1986 | 8,307 | 115 | 851 | 777 | 1,451 | 11501 | 73 | 14 | 13 |
| CR | 1990 | 81 | 12 | 39 | 65 | 0 | 197 | 47 | 53 | 0 |
| PIND | 1997 | 2195 | 0 | 513 | 1244 | 61 | 4013 | 55 | 44 | 2 |
| SYP | 2010 | 52 | 0 | 35 | 27 | 16 | 130 | 40 | 48 | 12 |
| KAW | 2013 | 481 | 0 | 99 | 111 | 190 | 881 | 55 | 24 | 22 |
| HEP | 2014 | 69 | 0 | 8 | 32 | 4 | 113 | 61 | 35 | 4 |
| GBS | 2014 | 509 | 0 | 107 | 53 | 142 | 811 | 63 | 20 | 18 |
| EPM | 2014 | 378 | 0 | 23 | 69 | 68 | 538 | 70 | 17 | 13 |
| EBT | 2014 | 106 | 0 | 25 | 5 | 24 | 160 | 66 | 19 | 15 |
| RKT | 2015 | 68 | 0 | 3 | 43 | 49 | 163 | 42 | 28 | 30 |
| T2D | 2015 | 35 | 0 | 4 | 5 | 87 | 131 | 27 | 7 | 66 |
| BEH | 2015 | 18 | 0 | 3 | 9 | 43 | 73 | 25 | 16 | 59 |
| ARF | 2015 | 0 | 0 | 0 | 1 | 39 | 40 | 0 | 3 | 98 |
| VIB | 2015 | 37 | 0 | 0 | 33 | 66 | 136 | 27 | 24 | 49 |
| FGM | 2015 | 2 | 0 | 0 | 8 | 3 | 13 | 15 | 62 | 23 |
| ADHD | 2015 | 36 | 0 | 0 | 22 | 43 | 101 | 36 | 22 | 43 |
| PRS | 2016 | 0 | 0 | 0 | 0 | 47 | 47 | 0 | 0 | 100 |
| **Total** | | **12374** | **127** | **1710** | **2504** | **2333** | **19048** | **66** | **22** | **12** |

| | |
|---|---|
| HIV | Human immunodeficiency virus in childhood |
| CR | Congenital rubella |
| PIND | Progressive intellectual & neurological deterioration |
| SYP | Congenital syphilis |
| HUS | Haemolytic uraemic syndrome |
| KAW | Kawasaki Disease |
| HEP | Acute Symptomatic Hepatitis |
| GBS | Group B streptococcal disease |
| EPM | Enterovirus and parechovirus meningitis |
| EBT | Exchange blood transfusion |
| RKT | Nutritional Rickets |
| T2D | Type 2 Diabetes |
| BEH | Behcet's syndrome |
| ARF | Acute rheumatic fever |
| VIB | Visual impairment & blindness |
| FGM | Female genital mutilation |
| ADHD | ADHD transition |
| PRS | Pierre Robin sequence |

C/R = confirmed/already known

D = duplicate

E = reporting error or revised diagnosis

X = status not yet reported to BPSU by investigator

ALL DATA IS PROVISIONAL & CONTINUALLY BEING UPDATED