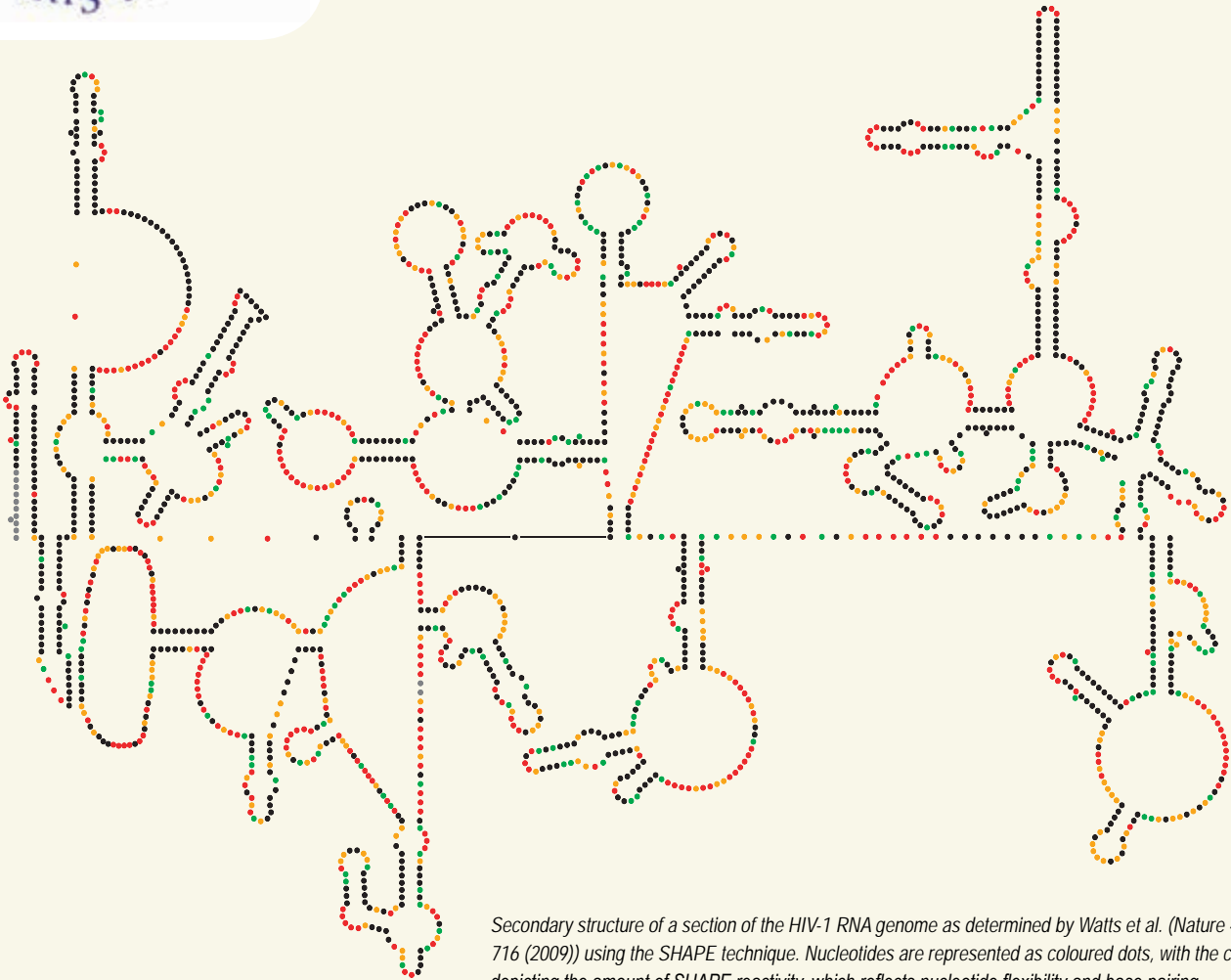




The British Paediatric Surveillance Unit 30th anniversary report

*Facilitating childhood rare disease research for over
30 years*



*Secondary structure of a section of the HIV-1 RNA genome as determined by Watts et al. (Nature 460, 711–716 (2009)) using the SHAPE technique. Nucleotides are represented as coloured dots, with the colours depicting the amount of SHAPE reactivity, which reflects nucleotide flexibility and base pairing.
Reference: Al-Hashimi HM. Structural biology: Aerial view of the HIV genome. Nature 2009 Aug 6;460(7256): 696-698. doi:10.1038/460696a*

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This report is available for download at www.rcpch.ac.uk/bpsu/30yearreport

Message from HRH Princess Anne



The British Paediatric Surveillance Unit (BPSU) was launched in 1986 and has facilitated research into uncommon childhood infections and disorders and importantly monitors emerging infections. No one could have predicted how effective its simple methodology of monthly reporting of rare disease by paediatricians would become.

As Patron of the Royal College of Paediatrics and Child Health, I am delighted to support this initiative which has been a major contributor to improving the lives of children with rare disease in the UK and across the world. With the support of the College, Public Health England, and UCL Institute of Child Health, the BPSU can be justly pleased with its achievements. This collaboration has enabled the UK to become a leader in rare disease surveillance and monitoring.

In the UK alone, there are nearly one million children living with a rare disease. The work of the BPSU, supported by gene mapping, is vital in addressing these alarming statistics.

As this 30th anniversary report highlights, the need remains for sound knowledge on the natural history of such diseases and I wish the BPSU continued success over the next 30 years and beyond.

A handwritten signature in dark ink, appearing to read 'Anne', with a long, sweeping horizontal line extending from the end of the signature.

Foreword from the Chief Medical Officer of England



*Professor Dame Sally Davies,
Chief Medical Officer for England*

From its outset, the BPSU has been at the forefront of gathering evidence that has been used to monitor and influence the nation's child health policies. The unique methodology for collecting clinical data on a national basis has been replicated across the world. An important remit of the BPSU has been to respond rapidly to public health emergencies and this has been demonstrated time and again. At its launch it was gathering evidence on the newly emerging conditions such as AIDS/HIV. Unbroken surveillance of AIDS/HIV has led the UK to become a world leader in the field of AIDS/HIV epidemiology. The BPSU highlighted the impact that the introduction of HIV antenatal screening has had on mother to child transmission rates. At the height of the bovine spongiform encephalopathy crisis the BPSU was there to help by assessing the likely impact of variant Creutzfeldt-Jakob disease (vCJD) in the child population.

The Unit has monitored newly introduced vaccines, their impact and efficacy. More recently the BPSU confirmed that there was no association between H1N1 vaccine and Guillain-Barré/Miller Fisher syndrome. This April saw the UK become the first country in the world to introduce congenital Zika syndrome surveillance, this could not have been achieved so rapidly without the expertise of the BPSU and Public Health England.

I have only touched on some of the achievements of the BPSU, which in its small and quiet way, contributes hugely to the health of the nation's children, and for that we are all grateful.

I have no doubt that the Unit will be making a major contribution in the field of rare disease for a long time to come.

Message from the BPSU Chair



*Dr Richard Reading,
Norfolk and Norwich University Hospitals*



British Paediatric Surveillance Unit Report Card

NOTHING TO REPORT April 2016 (1604)
CODE No []

Specify in the box the number of cases seen

<input type="checkbox"/>	HIV Infection & Perinatal HIV Exposure
<input type="checkbox"/>	Progressive Intellectual & Neurological Deterioration
<input type="checkbox"/>	Congenital Rubella
<input type="checkbox"/>	Nutritional Rickets
<input type="checkbox"/>	Type 2 Diabetes < 17 years of age
<input type="checkbox"/>	Acute Rheumatic Fever
<input type="checkbox"/>	Behçet's Syndrome
<input type="checkbox"/>	Visual Impairment & Blindness (excl RQI)
<input type="checkbox"/>	ADHD Transition Between Children's & Adult Services
<input type="checkbox"/>	Female Genital Mutilation < 16 years of age
<input type="checkbox"/>	Pierre Robin Sequence
<input type="checkbox"/>	Congenital Zika Syndrome

Orange Reporting Card

It is an honour and a pleasure to introduce the 30th anniversary report from the BPSU.

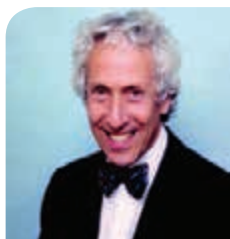
The BPSU was founded in 1986 arising from the vision of an inspirational group of paediatricians, epidemiologists, public health specialists and financial backers from the voluntary and private sector with an interest in rare childhood diseases and disorders. However, the success of the BPSU would not have been possible without the enthusiasm and engagement of paediatricians from across the United Kingdom and the Republic of Ireland who have embraced the idea of an active surveillance methodology, returning their 'Orange Card' every month. Since 1986 the BPSU has been in continuous business, facilitating over 100 surveillance studies, contributing to important public health priorities, health policy decisions and clinical practice. The founders of the BPSU can hardly have predicted the enduring success of their simple but robust active surveillance system.

This report highlights the BPSU's achievements over the past 30 years. While it is rightly a celebration of the impact the BPSU has had on health policy, child public health and clinical practice, the emphasis throughout this report reflects the BPSU philosophy of looking forward, identifying opportunities and possible developments to improve the working of the Unit. It might be rash to predict another 30 years of success, but not unrealistic.

It is worth reflecting on the identity of the BPSU – what exactly is it? The office staff, the medical advisers, the Scientific Committee, the Governance Board, the paediatricians of the five countries, the administrative and information systems that underpin the collection of surveillance data, the parents and voluntary organisations that support us so actively, the scientific teams that run the studies? Of course it is all of these, but more. It is the metaphysical notion that this activity can and should be done. That active surveillance for rare childhood disorders is an obligation and a privilege we are all a part of. It is this idea of the BPSU as a philosophical concept rather than a concrete body, which is the best indicator of its likely success for the future.

I would like to thank everyone who has contributed to this report, whether by writing a piece or simply by supporting or collaborating with the BPSU over the years. I hope you enjoy reading this report, and may the next 30 years be as successful as the last.

Past & present faces



Left to right:
Prof David Baum;
Sir Cyril Clarke; Dr
Spence Galbraith. Sir
Peter Tizard, Dr Sue
Hall



Left to right:
Dr Richard Reading;
Prof Catherine Peckham;
Dr Christopher Verity;
Prof Euan Ross;
Prof Alan Colver;
Prof Alan Emond;
Prof Mike Preece.



Left: Children
Nationwide Medical
Research Fund -
trustees/guests circa
1986.

National rare disease surveillance



The BPSU offers a robust methodology that has made national rare disease surveillance accessible to researchers and clinicians. In its early years the BPSU was supported by the Thomas Bailey Trust and the Children Nationwide Research Fund (now WellChild). The Department of Health (DoH) supported the Unit between 1997 and 2012. More recently the BPSU has received grants from its partners - Public Health England (PHE), UCL Institute of Child Health (UCL-ICH), and the Royal College of Paediatrics and Child Health (RCPCH), with support from Great Ormond Street Children's Charity and from the Scottish Government.

The BPSU also receives contributions from research teams using the BPSU system, who in themselves may be funded by patient support groups and/or through educational grants from commercial companies. Long-term surveillance of HIV, congenital rubella and vCJD is funded through the DoH and PHE. Through its collaborations with the National Screening Committee, the BPSU has received contributions for facilitating the surveillance of congenital adrenal hyperplasia, congenital hypothyroidism, Group B streptococcal disease and medium chain acyl Co-A dehydrogenase deficiency (MCADD) as well as several others.

The BPSU is proud that its methodology has been replicated by other specialties in the UK. The BPSU is working actively with some of these units to maximise case ascertainment.

BPSU facts: Did you know...?

- 107 rare conditions/events studied
- 500 individual researchers involved as collaborators
- Monthly response rates >90%
- Questionnaire response rates >80%
- 810 clinicians reported in 1986, now ~3,500 reporting clinicians
- >30,000 rare disease cases reported
- >200 original journal articles
- >300 scientific presentations

British Ophthalmological Surveillance Unit (BOSU) (<http://bit.ly/28Rv28Z>) was formed in 1997 to investigate the incidence and clinical features of rare eye conditions. The BPSU has worked with BOSU on a number of studies; for example childhood visual impairment and blindness, and congenital cataracts.

The UK Obstetric Surveillance System (UKOSS) (www.npeu.ox.ac.uk/ukoss) was launched in February 2005. The system is designed to survey a range of rare conditions in pregnancy. The BPSU has collaborated with UKOSS on studies such as Group B streptococcal disease.

The Child and Adolescent Psychiatry Surveillance System (CAPSS) (www.rcpsych.ac.uk/capss) was launched in 2009 with joint surveillance with the BPSU on early onset eating disorders. Since then CAPSS have collaborated with the BPSU on several further studies including conversion disorder, gender identity disorder and ADHD transition.

About the BPSU

Aims of the BPSU

- 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 less common disorders.
- Respond rapidly to public health emergencies.

What we do

Over the last 30 years the BPSU has acted as a facilitator for those research teams wishing to carry out national surveillance on rare childhood conditions and disorders. The BPSU provides a unique platform for the study of rare childhood diseases and supports the following activities:

- National disease surveillance
- Education for clinicians, families and students
- Policy and advocacy
- International collaboration
- Research into rare diseases and their impacts on families, clinicians and health services

How we do it

Each month an electronic card with a list of disorders is sent to ~3,500 paediatric consultants in the UK and the Republic of Ireland. Clinicians return the 'Orange Card' notifying the BPSU if they have seen any cases or have 'nothing to report'. If the clinician has seen a case their details are passed on to the investigators who will then contact the said clinician with a short questionnaire. It is important to note that BPSU studies, with appropriate approvals, use data from patient records but do not involve any direct contact by investigators with individual patients; individual patient consent is not sought. If a patient (or legal guardian) wishes to dissent from research, their data will not be used in BPSU studies.

Over 90% of clinicians in receipt of an Orange Card return the reporting card every month and of those who have reported cases, over 80% return notification questionnaires. Up to 12 different rare conditions can be studied simultaneously and data on demographics, diagnosis, clinical management and outcomes is collected. The results of which have had a major impact on the health of the nation's children.



Richard Lynn,
BPSU Scientific Coordinator



Key partners & leaders



Dr Jacqueline Cornish *National Clinical Director, Children, Young People and Transition to Adulthood*

"In recent times the impact of rare disease on affected children and families has come to the fore. The 2013 *UK Strategy for Rare Diseases* referenced the work of the BPSU and the continuing need to improve the epidemiology and understanding of the natural history of these conditions. With the support of the BPSU and similar units, the UK is now a leader in rare disease diagnostic research. Evidence produced by the BPSU has contributed to guideline development and service evaluation. The Unit has raised awareness of rare childhood conditions amongst clinicians and the public, and has been an advocate for the 'patient's voice'. The BPSU punches above its weight and so may it continue to do so. Congrats on your 30th birthday!"



Professor John Newton *Chief Knowledge Officer, Public Health England, Chair of the BPSU Governance Board*

"From the time it was set up this internationally regarded collaboration has been quietly but effectively protecting the health of children in the UK and Ireland from a wide range of rare but serious illnesses. The knowledge generated by the BPSU has also indirectly benefited countless children across the world."



Professor Neena Modi *President, Royal College of Paediatrics and Child Health*

"I am delighted to congratulate the BPSU on this 30th year milestone. Many individuals and organisations have contributed to its success, but none more so than the many consultant paediatricians across the UK and Republic of Ireland who diligently return the Orange Card every month and supply clinical information on reported cases. I would like to thank them all; without their active engagement, the BPSU would not have been able to deliver the many insights over the past 30 years that have been so important to child health.

As RCPCH President, a clinician, and head of a research group, I am well aware of the many challenges faced by paediatrics. To tackle these requires vision and adaptation to change. The BPSU has been a national and international beacon in supporting rigorous, high quality studies. I look forward to the continued success of the BPSU over the coming years in continuing to help address the many pressing child health issues that confront the nation."



Professor Rosalind Smyth *Director of the UCL-Institute of Child Health*

"The BPSU is an exemplar of what a national body of professionals, in this case the RCPCH, can achieve. It has single-handedly harnessed the observations and insights of paediatricians in addressing important questions about rare conditions in children. The benefits have been profound."



Professor Euan Ross *Co-founder of the BPSU*

"Good ideas need a little financial lubrication but above all they need people who are able to use them to good effect. Sir Peter Tizard, former President of the British Paediatric Association, used his charisma to outwit doubters. His friend Sir Cyril Clarke knew of a trust fund. The trustees donated enough seed money to get the BPSU germinating, and look at how we have grown."

Rare Disease Day tea party events

Alex and mum with Earl Howe,



Thines speaking at BPSU's Rare Disease Day tea party in 2015



Young people of the Alström Syndrome UK presenting their T-KASH transition resource.

Public & patient engagement

The BPSU is committed to ensuring that public and patient engagement (PPE) is embedded in all of its work. Two lay representatives, Jane Sutton and Madeleine Wang, are appointed to the Scientific Committee and provide expert guidance to research teams. Whenever the BPSU holds events it now includes an aspect of PPE, often directly engaging with children and young people.

PPE is fundamental to the operation of the BPSU. Patient support groups are not directly involved in the data collection process, however, the BPSU asks that research teams engage effectively with patient representatives throughout the life-cycle of a study. As part of its approval criteria the BPSU requires that research groups publish a public information leaflet. This is available on the BPSU website and accessible to the wider public. It is ethically important to do this because the studies use information from medical notes without patient consent. PPE ensures greater transparency and accountability of the BPSU methodology. The public information leaflets are written in plain English for ease of understanding and often include links to other resources, including contact details for support groups.

Examples of PPE achievement:

- The BPSU is affiliated to Rare Disease UK (RDUK), the leading national rare disease patient advocacy organisation.
- With RDUK, introduced and funded a national Rare Disease Day tea party event bringing together patient groups, clinicians, and researchers.
- Presented work at a variety of events organised by patient support networks.
- Produced an educational pack for researchers on how to involve patients and the public in research.
- Supported young people to produce and launch a podcast on 'living with a rare disease'.

The BPSU have been really helpful, the Kawasaki Disease study that they facilitated, which Kawasaki Support Group UK part funded, to obtain figures of Kawasaki in the UK is just the latest. To have a body where things can be discussed and started in regard to childrens health is a vital need for all of our children, healthy or not."

Sue Davidson, Kawasaki Disease Support Group

"We were very influenced by the families and buoyed up by the fact that they were so supportive of what we were planning to do."

Researcher

Patient stories

Gary, age 26, Kawasaki Disease – mum's experience

In February of 1992 my wonderful, happy two year-old son Gary became desperately unwell and seemed to baffle all the medics. He was eventually diagnosed with Kawasaki Disease. Life has never been the same. We had to 'pop' 45 miles away to Birmingham Children's Hospital for a heart scan because, 'occasionally', this illness might affect it. Well it did, massively - he had three aneurysms. After a very long month in hospital we got to go home.

The effect on us all was incredible, we had to deal with all the medical things (which was like learning a new language), but more than that we had to cope with a very different little boy. All in all it turned our lives upside down.

After a few months I got very frustrated by the standard answer of 'we don't know' to questions about the illness and Gary's future. After trawling the library (the internet was not really that active then) for articles and buying a medical directory to help me with the terminology, I wrote to anyone who contributed to the academic papers. I managed to get quite a good response which I took to Gary's doctors.

I read an article about Contact a Family (www.cafamily.org.uk) and got in touch with them. Two other mums had done the same. We arranged to meet and after that meeting the Kawasaki Support Group UK (www.kssg.org.uk) was formed!

For the last 22 years we have done everything we possibly can to raise awareness of the illness and to get the latest information together. Mostly though, we have let other parents know about us and that they are not alone. We now have over 1,500 members in the UK, a closed Facebook group, I collate statistics, we have a yearly newsletter and a family get together. I am extremely proud of what we have achieved.

More than anything Gary knows that I have done everything I can to find out about this illness and to help others. I am incredibly proud of my son, he still has one aneurysm just sitting there but with yearly check-ups and an excellent adult cardiologist (finding one of those who know about the transfer from paediatric to adult care is another story), he is doing fine.



Gary

"The BPSU's methodology has enabled us to collect population data and has allowed an analysis of that data to be disseminated to the wider paediatric community. This has achieved the aims of education and helped us to improve care for the children of the UK and Ireland."

Professor Robert Tulloh, investigator on the BPSU Kawasaki study

Policy & advocacy

"Those founders of the BPSU probably never imagined the resultant impact findings would have on national health policy."

Professor John Newton, Chief
Knowledge Officer,
Public Health England

Clinical and public health policy impacts of BPSU studies

- Supported public health prevention strategies through informing or supporting vaccination programmes such as rubella, varicella, and haemophilus influenzae B.
- Monitoring newly emerging disease such as vCJD, *E.coli* 0157, congenital Zika syndrome, and AIDS/HIV.
- Data on accidents and injuries have informed injury prevention strategies related to drowning and near drowning, accidental poisoning, shaking baby syndrome, abdominal injuries, and Munchausen syndrome by proxy.
- Drug safety and monitoring; for example exchange blood transfusion issues, anaphylaxis following immunisation, Reye syndrome and aspirin warning, fatal adverse drug reactions, Guillain-Barré/Miller Fisher syndrome following H1N1 vaccination.
- Informed National Screening Committee policy; for example MCADD, Group B streptococcal, congenital adrenal hyperplasia, and congenital hypothyroidism.

Supporting national action on rare disease

The BPSU, with other national rare disease organisations, have been strong advocates for the need to expand and develop research in the field. The Unit contributed to the *Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy*. This document informed the British government's response to EU directives on rare disease and the development of the *UK Strategy for Rare Diseases*, published in 2013. Through its work with PHE, the BPSU has collated evidence on newly emerging and re-emerging disease.

Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy:

<http://www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf>

The UK Strategy for Rare Diseases:

<https://www.gov.uk/government/publications/rare-diseases-strategy>

Advocacy

BPSU advocates on behalf of children and families affected by rare diseases through collaboration with RDUK, hosting their annual general meeting and having representation on RDUK's Management Board. In addition, the BPSU and RDUK host a national UK Rare Disease Day event. In 2016 this event was held in collaboration with Birmingham Children's Hospital and involved the young people of Alström Syndrome UK, Hear My Voice Youth Forum who presented their newly designed transition resources, known as T-KASH (Transition-Knowledge And Skills in Health). This resource is aimed at young people / families and professionals. For more information visit www.alstrom.org.uk/news/t-kash-launches-today.

"The Sir Peter Tizard Bursary provides a unique opportunity to work with a team of experts, gain experience in clinical epidemiology and establish a further understanding of a rare but potentially distressing and life-threatening condition."

Dr Yim Yee Mathews

"Winning the Bursary allowed me to pursue my interest in thyroid disease and in turn brought a great number of other opportunities and connections which helped direct my career."

Dr Scott Williamson

"The Bursary was great for me. It gave me an introduction to research, the support to formulate my question and develop my ideas. I got the opportunity to present internationally and I have helped another successful application subsequently. It was the building block for a career long interest in research."

Dr Tom Dawson

Sir Peter Tizard Bursary published papers:

Williamson S, Greene SA. Incidence of thyrotoxicosis in childhood: a national population based study in the UK and Ireland. *Clinical Endocrinology* 2010;72(3):358-363

Adalat S, Dawson T, Hackett SJ, et al. Toxic shock syndrome surveillance in UK children. *Arch Dis Child*. 2014 Dec;99(12):1078-82

Education for clinicians & researchers

Clinicians

The BPSU provides educational resources for clinicians by:

- Producing research and management guidance on surveillance project development.
- Publishing BPSU results in reports, academic journals and on the web.
- Distributing surveillance protocols to ~3,500 paediatricians and specialists, providing information about diagnosis, treatment and outcomes for each of the rare conditions being studied.
- Collaborating on the development of e-learning modules.
- Holding educational conferences/symposia on rare diseases.
- Presenting at paediatric and public health conferences in the UK and abroad.

BPSU studies have informed the development of new clinical resources; for example the diabetes guideline development for diabetic ketoacidosis, the redrafting of meningitis guidance, the review of diagnostic criteria for early-onset eating disorders, and the development of vitamin K prophylaxis policy.

Researchers

The BPSU supports clinicians in training who wish to undertake research into rare childhood conditions. The Sir Peter Tizard Bursary was launched in 2003 and was named after the first chair of the BPSU Scientific Committee. This competitive bursary comes with a financial stipend and expert guidance over the life of the project. To date twelve individuals have benefited from this scheme, some of whom have moved on to supervise other aspiring researchers wishing to use the BPSU reporting scheme. The collaborative nature of the BPSU has helped to increase the research capacity within the NHS.

Many clinicians have gained postgraduate awards through their involvement in BPSU facilitated studies and have been afforded the opportunity to present and publish nationally and internationally.



Left: Dr Shamez Ladhani receiving his award from Professor Sir Alan Craft, then President of the RCPCH, for his study on imported Malaria.

"The Sir Peter Tizard Bursary was my first exposure to epidemiology and surveillance. The experience I gained has been instrumental in developing my career in leading the surveillance of preventable infections at PHE."

Dr Shamez Ladhani

"I am extremely honoured to receive the Sir Peter Tizard Bursary. It has been paramount in developing my knowledge and skills in epidemiological and surveillance research that I will utilise throughout my paediatric career."

Dr Lizzie Starkey

"Working with the BPSU team has provided me with an unparalleled opportunity to investigate a rare disease which otherwise would not have been possible. A real gem of an organisation!"

Dr Mary Salama



Right: Dr Lizzie Starkey receiving her award from Professor John Newton, Chief Knowledge Officer, PHE, for her forthcoming study on accidental poisonings.

BPSU through the ages

June 1986

- BPSU card launches with 7 conditions to 800 consultant paediatricians
- The UK is the first nation to undertake systematic surveillance of newly emerging condition HIV

1992-97

- HiB vaccination efficacy monitored

1999

- Kasia operation limited to three centres following review of the BPSU Biliary atresia outcome evidence

1990

- Acute flaccid paralysis study confirm UK free of wild polio
- BPSU card response rate consistently above 90%

1995

- Congenital cataract study is the first to involve ophthalmologists

1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001

1988

- First of several studies on HUS confirming link with E.coli 0157 and demonstrating improving mortality rates
- First of a series of studies monitoring the changes of management on the rates of VKDB
- BPSU secures 7 year funding from the Research Fund of Children Nationwide (now WellChild)

1994

- BPSU launches its website

1998

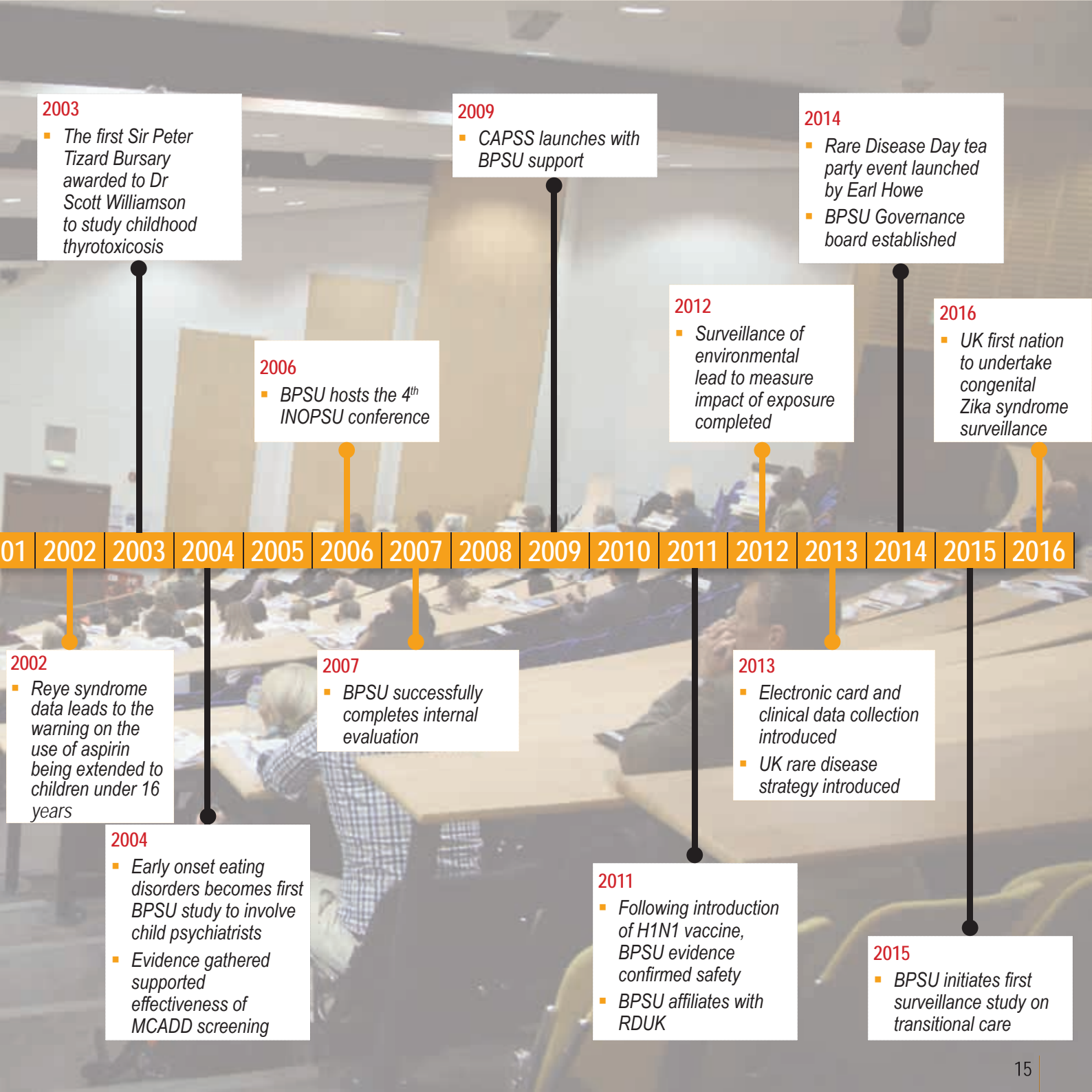
- BPSU secured funding from the Department of Health to last 14 years

1991

- Chemistry set poisoning – data leads to change in EU legislation on packaging

1997

- UK is the first country to survey vCJD
- BPSU is a founding member of INoPSU



2003

- The first Sir Peter Tizard Bursary awarded to Dr Scott Williamson to study childhood thyrotoxicosis

2009

- CAPSS launches with BPSU support

2014

- Rare Disease Day tea party event launched by Earl Howe
- BPSU Governance board established

2006

- BPSU hosts the 4th INOPSU conference

2012

- Surveillance of environmental lead to measure impact of exposure completed

2016

- UK first nation to undertake congenital Zika syndrome surveillance

01 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016

2002

- Reye syndrome data leads to the warning on the use of aspirin being extended to children under 16 years

2007

- BPSU successfully completes internal evaluation

2013

- Electronic card and clinical data collection introduced
- UK rare disease strategy introduced

2004

- Early onset eating disorders becomes first BPSU study to involve child psychiatrists
- Evidence gathered supported effectiveness of MCADD screening

2011

- Following introduction of H1N1 vaccine, BPSU evidence confirmed safety
- BPSU affiliates with RDUK

2015

- BPSU initiates first surveillance study on transitional care

Anorexic at the age of 6

By Julia Whitham
Health Correspondent

More and more girls - and boys - have eating disorders before their teens

CHILDREN as young as six are suffering from eating disorders, a shocking study reveals.

In the space of a year, doctors have seen thousands of six-year-olds with problems such as bulimia and anorexia nervosa. Most of them will be referred to hospital for treatment, but some may be too young to be treated.

The disorder, characterised by self-induced vomiting and/or refusal to eat, is a serious condition which can lead to severe physical and mental health problems. Experts believe the condition has risen in prevalence since the mid-1990s.

One, which doctors worry will increase as the years pass, is the fact that the disorder is also affecting boys. In the past, it was thought to be a condition of girls only.

There have been at least 10 cases of anorexia in boys aged 10 to 12 years in the last 12 months, according to a study by the Royal Free Hospital in London.

At one time, it was thought that the disorder was confined to girls aged 10 to 12 years, but now it is being seen in boys as young as six.

The study, by the British Paediatric Association, is the first to show that the disorder is not confined to girls.

Health authorities in London, including paediatricians and child psychiatrists, have been alerted to the fact that the disorder is also affecting boys. In the past, it was thought to be a condition of girls only.

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Screening urged to cut toxoplasma toll

THE INDEPENDENT
Doubts cast on screening for foetal infection

BPA NEWSLETTER
March 1997

Inside this issue:

- Keeping members in touch
- National study will examine routine CDH screening risk
- Hip screening project starts



CURRENT PROBLEMS
in Paediatrics

SYMPOSIUM ON 14 APRIL 1997

Aspirin and Reye's syndrome in children up to and including 15 years of age

The new guidelines on children aged 15 years and under, published in the British Medical Journal, recommend that aspirin should not be given to children under 16 years of age.

These guidelines are a result of a review of the evidence on the link between aspirin and Reye's syndrome, a rare but serious condition which can be fatal.

The review found that there is a clear link between aspirin and Reye's syndrome, and that the risk of Reye's syndrome is increased in children who are given aspirin for viral infections.

The guidelines recommend that aspirin should not be given to children under 16 years of age, and that parents should be warned of the risk of Reye's syndrome if their child is given aspirin.

The guidelines also recommend that aspirin should not be given to children who are recovering from a viral infection, and that parents should be warned of the risk of Reye's syndrome if their child is given aspirin.

The guidelines also recommend that aspirin should not be given to children who are recovering from a viral infection, and that parents should be warned of the risk of Reye's syndrome if their child is given aspirin.

PRIVATE EYE

"BEEF SAFE" - GUMMER



32 • newsworld.co.uk

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INSIGHT

30 years of research into childhood rare diseases

As the British Paediatric Surveillance Unit (BPSU) approaches its 30th year, many of the principles on which the Unit was founded remain today



Michelle Wright: Over the last 30 years the BPSU has been tracking childhood rare diseases in the UK

Over 30 years on, the principles on which the BPSU was founded remain today. The Unit was set up in 1967 to monitor the incidence of rare diseases in children in the UK. It was founded on the principles of surveillance, research, and education.

The Unit has been successful in its mission, and has been able to identify many rare diseases in children. It has also been able to provide information on the incidence of these diseases, and to provide advice on the management of these diseases.

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ASPIRIN LINK TO KILLER BRAIN BUG

MEDICAL experts aspirin to be restrict of a link with a de They say warning people up to 20 not Aspirin bottles is "possible association

Child diseases aid for paediatricians

By Our Social Services Correspondent

A unique reporting system to allow paediatricians to find cases, and the possible causes of rare but serious childhood illnesses such as acquired immune deficiency syndrome (Aids) and Reye's syndrome, is to begin operation shortly.

The system will also allow information to be gathered more quickly on possible side-effects of treatments. For example, it will almost certainly be used to assess any serious side-effects from the new generation of whooping cough vaccines that are due to go on trial soon.

The British Paediatric Sur-

so, the unit hopes to acquire data more quickly and comprehensively than now.

Dr Susan Hall, senior lecturer at the Institute of Child Health, who is the unit's medical co-ordinator, said yesterday: "Instead of paediatricians being bombarded with requests to report different types of rare cases to eight or 10 centres we hope the unit will be able to provide a central registry."

"The individual researchers can then get in touch for details of the cases in which they are interested. We believe this system is unique."

The idea came out of the

respondent der 12. But no senagers. In the both age groups. y the British its to a link with ases of Reye's is linked to are reported in

Selected themes & impacts



Mental Health

The epidemiology of rare paediatric mental health conditions is very much a poor relation in the field of epidemiology. The Faculty of Child and Adolescent Psychiatry at the Royal College of Psychiatrists, with the support of the BPSU, addressed this by developing a new system to involve child psychiatrists in disease surveillance activity.

Early onset eating disorders (5-13 yrs): The study sought to identify young children aged 5 to 13 who presented with significant weight loss and associated psychological and medical complications. Case notifications were received from both paediatricians and psychiatrists.

Key findings: 208 cases were reported over a 24 month period. Incidence of 3.01/100,000; 37% met the criteria for anorexia nervosa; 1.4% for bulimia nervosa; and 43% for eating disorder not otherwise specified. Food avoidance, fear of weight gain, preoccupation with bodyweight and shape were seen in >50% of cases. At one year, 73% were reported to have improved, 6% worse and 10% unchanged.

Selected publications:

Hudson LD, Nicholls DE, Lynn RM, Viner RM. Medical instability and growth of children and adolescents with early onset eating disorders. *Arch Dis Child*. 2012 Sep;97(9):779-84.

Lynn R, Viner RM, Nicholls DE. Ascertainment of Early Onset Eating Disorders: A Pilot for Developing a National Child Psychiatric Surveillance System. *Child Adolesc Ment Health* 2011;17:109–12.

Nicholls DE, Lynn R, Viner RM. Childhood Eating Disorders: A British National Surveillance Study. *Br J Psychiatry*. 2011 May; 198(5):410.

Madden S, Morris A, Zurynski YA, Kohn M, & Elliott EJ (2009). Burden of eating disorders in 5-13-year-old children in Australia. *The Medical Journal of Australia*, 190, 410–414.

Study impacts: Demonstrated that prospective surveillance involving child psychiatrists was possible, paving the way for the creation of the Child and Adolescent Psychiatry Surveillance System (CAPSS). Since CAPSS launched in 2009 collaborative studies on conversion disorder, gender identity disorder and ADHD transition have taken place.

Data on early onset eating disorders was used to develop guidelines for these early year cases. Previously, such information was missing from the National Institute for Health and Care Excellence guidelines.

This data has provided a valuable contribution to the debate on the definition of eating disorders among young children. Evidence from which contributed to the revision of diagnostic classification produced in DSM-5 criteria for those with eating disorders.

An international comparison of the incidence, diagnosis and outcomes of early onset eating disorders is being facilitated by the International Network of Paediatric Surveillance Units, with data available from the Australian and Canadian surveillance units.

Selected themes & impacts (continued)

Vaccines and other conditions

The BPSU has been at the forefront of supporting national vaccine policy through the monitoring of newly introduced vaccines such as MMR, Haemophilus influenzae B (HiB), and H1N1. The BPSU has also facilitated many non-infectious studies, the data from which has led to changes in health policy and clinical policy.

Guillain-Barré/Miller Fisher syndrome (GBS/MFS): In 2009, following the spread of swine flu from Mexico to Europe, the H1N1 vaccine was introduced in the UK. A previous outbreak in 1976 in the lead-up to a national immunisation programme in the USA was discontinued following reports of GBS/MFS in some of those who were vaccinated. The BPSU fast-tracked surveillance to monitor the incidence of these conditions following the vaccines introduction.

Key findings: Very few cases of GBS/MFS were reported. Of those, the majority were temporally associated with a variety of previous infections. There is little association with H1N1 influenza vaccination or seasonal flu vaccination.

Study impacts: The vaccine was declared safe to use.

Reye's syndrome: Reye's syndrome can cause serious liver and brain damage. If not treated promptly it may result in permanent brain injury or death.

Key findings: Monitored the change in incidence of Reye's syndrome following the introduction in 1986 of the warning of aspirin use in children <12 years.

Study impacts: The recommendation that aspirin use warning should be extended to teenagers <16 years was approved by the Medicines and Healthcare products Regulatory Agency.

Sudden unexpected postnatal collapse (SUPC): SUPC of a healthy newborn infant is a rare event which carries a high risk of mortality and significant neurodisability in survivors.

Key findings: 50% of infants die and the majority of survivors suffer severe neurological damage.

Study impact: Recommendations resulted in the creation of a new national guideline for the investigation of infants suffering a SUPC within the first seven days of life.



Selected publications:

Verity C, Stellitano L, Winstone AM et al. Pandemic A/H1N1 2009 influenza vaccination, preceding infections and clinical findings in UK children with Guillain-Barré syndrome. *Arch Dis Child*. 2014 Jun;99(6):532-8

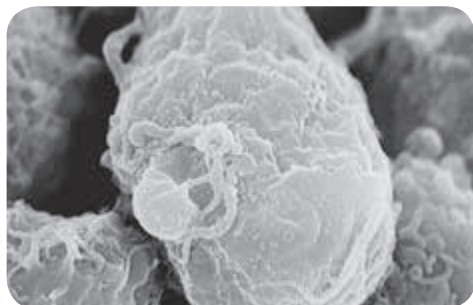
Erlewyn-Lajeunesse M, Hunt LP, Heath PT, Finn A. Anaphylaxis as an adverse event following immunisation in the UK and Ireland. *Arch Dis Child* 2012; 97:487-490

Hall SM, Lynn RM. The disappearance of Reye's syndrome - A public health triumph. Letter of response. *The New Engl J Med* 1999; 341 No. 11: 845

Beecher JC, Bhushan SS et al. Unexpected collapse in apparently healthy newborns - a prospective national study of a missing cohort of neonatal deaths and near-death events. *Arch Dis Child Fetal Neonatal Ed*. 2012 Jan;97(1):F30-4

Selected themes & impacts (continued)

C. Goldsmith



Scanning EM of HIV, grown in cultured lymphocytes. Virons are seen as small spheres on the surface of the cell.

Screening - Infectious disease

The early 1990's saw the establishment of the National Screening Committee. The National Screening Committee was established to make decisions regarding screening for many conditions and to consider the value of existing programmes. The BPSU has provided data to help decide whether to perform national screening for congenital infections such as HIV, congenital rubella, Group B streptococcal disease, congenital syphilis, toxoplasmosis and neonatal herpes.

HIV infection and perinatal HIV exposure: Since 1986 the BPSU has been the cornerstone of paediatric HIV surveillance in the UK and the Republic of Ireland. Together with active obstetric HIV surveillance, this comprises a complete, continuous and comprehensive dataset of all pregnancies in women with diagnosed HIV infection, their infants, and all resident children diagnosed with HIV since 1989. For further information contact the National Study of HIV in Pregnancy and Childhood (www.ucl.ac.uk/nshpc).

Key findings: There are now around 1,200 births to mothers living with HIV annually in the UK, with a mother to child transmission rate of less than 0.5%. Annual paediatric diagnoses have declined from 100-150 per year in 2000-2003 to <50 since 2012. Most children with HIV are born abroad (~75% since 2012).

Study impacts: BPSU data has provided evidence for recommendations for the monitoring, screening and treatment of HIV, contributed to modelling studies, and informed long-term planning and commissioning of services for the paediatric population living with HIV.

Congenital Rubella (CR): Surveillance commenced in 1971 to monitor the impact of rubella vaccine in the prevention of congenital rubella. Active surveillance began in 1990 through the BPSU.

Key findings: 71 cases have been reported since 1990, but very few in the last decade. Most cases are now imported.

Study impacts: Tracked decline in CR births, and the changing demographics of affected mothers and babies, both before and after vaccine strategy moved from selective to mass immunisation. Evidence has been used to measure the impact of changes in policy, and to inform antenatal screening policy on rubella susceptibility screening. This led to the cessation of antenatal screening in April 2016.

Selected publications:

Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Trends in management and outcome of pregnancies in HIV-infected women in the United Kingdom and Ireland, 1990-2006. *BJOG* 2008;115:1078-86

French CE, Cortina-Borja M, Thorne C, Tookey PA. Incidence, patterns, and predictors of repeat pregnancies among HIV-infected women in the United Kingdom and Ireland, 1990-2009. *J AIDS* 2012; 59:287-93

Townsend CL, Byrne L, Cortina-Borja M, Thorne C, de Ruiter A, Lyall H, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. *AIDS*. 2014;28(7):1049-1057

Tookey PA, Peckham CS. Surveillance of congenital rubella in Great Britain, 1971-96. *BMJ* 1999; 318:769-70

Selected themes & impacts (continued)

Screening - Metabolic

With the ability to screen more easily for metabolic disease there has been pressure to offer screening for a multitude of metabolic conditions. BPSU studies have supplied evidence on incidence, natural history, cost-effectiveness and outcomes which have informed decisions on whether or not screening should be recommended. Data from the medium chain acyl Co-A dehydrogenase deficiency (MCADD) and congenital adrenal hyperplasia studies amongst others, have helped formulate national screening policy.

Medium chain acyl co-A dehydrogenase deficiency: MCADD is a recessive disease defined by progressive metabolic crisis and collapse with fasting (vomiting, infection or surgery). Two studies have been undertaken; one in 1994 and the other in 2004.

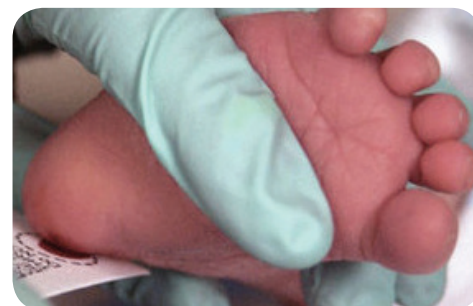
Key findings: In the 1994 study the median age of diagnosis was 14 months; incidence of 0.5/10,000; 28% mortality; 10% of survivors had neurological impairment. In 2004, an incidence rate of 1/10,000 births with a 28% mortality was identified. The BPSU study, combined with the six centre screening pilot, confirmed that newborn screening reliably identifies affected children before they are likely to develop symptoms.

Study impacts: Following the 1994 study a recommendation was made to the National Screening Committee to pilot screening. In February 2007, the Secretary of State for Health, Patricia Hewitt MP announced that screening for MCADD was to be added to newborn bloodspot screening in England in a phased roll-out during 2007/8 and 2008/9. Early detection enables parents to use simple measures to avoid fasting and thereby reduce the chances of severe illness or death.

Congenital adrenal hyperplasia (CAH): CAH is a group of inherited conditions present at birth where the adrenal gland is larger than usual. In CAH the body is missing an enzyme that stimulates the adrenal gland to release the cortisol hormone. A BPSU study was undertaken in 2007 as there was uncertainty about disease burden.

Key findings: 5/100,000 live births; <50% boys recognised compared to 90% for girls by 14 days of age.

Study impacts: The study highlighted that the test accuracy is poor and showed no evidence of improvement in mortality. BPSU data informed the recommendation to not introduce screening.



Bloodspot screening

Selected publications:

Pollitt RJ, Leonard JV. Prospective surveillance study of medium chain acyl-CoA dehydrogenase deficiency in the UK. *Arch Dis Child* 1998;79:116-119

Leonard JV, Dezateux C. Newborn screening for medium chain acyl CoA dehydrogenase deficiency. *Arch Dis Child* 2009;94:235-238

Oerton JM, Khalid JM et al. Newborn screening for medium chain acyl-CoA dehydrogenase deficiency in England: prevalence, predictive value and test validity based on 1.5 million screened babies *J Med Screen* 2011;18:173-181

Khalid JM, Oerton JM, Dezateux C, et al. Incidence and clinical features of congenital adrenal hyperplasia in Great Britain. *Arch Dis Child* 2012;97:101-06

Knowles RL, Khalid JM, Oerton JM, et al. Late clinical presentation of congenital adrenal hyperplasia in older children: findings from national paediatric surveillance. *Arch Dis Child* 2014;99:30-34

Patient stories

Rosie, age 20, Rett syndrome - mum's experience

Imagine being told your daughter, who you thought was normal but perhaps a bit slow to progress, had a rare and devastating neurological disorder that would leave her needing lifelong 24/7 care. Well that was me 20 years ago. Rosie was 14 months old and very much like other babies of that age, although she was quite floppy, did odd things with her hands, and was not weight bearing. Just before her first birthday, she screamed solidly and inconsolably for 24 hours. The next day she was a different child. Different because she had lost the ability to do some of the things she had been able to do 24 hours before. Like finger feeding, getting on to all fours and picking a cup up.



Rosie and mum

Our lives changed as we realised our precious first child had Rett syndrome; a complex neurological disorder that almost exclusively affects females. We were terrified, numb, unbelieving. As we looked at Rosie, we were aware from others that by age 10 she may be non-verbal, have feeding difficulties, mobility problems, possibly no purposeful use of her hands, and a catalogue of medical problems including epilepsy.

But if we were terrified, how did that feel for Rosie? It is only now that we know so much more about her condition that we can begin to consider how life was changing for her. How scared, vulnerable, and anxious she must have felt. Looking at Rosie now I can only feel a huge amount of positivity about who she is, the journey she has taken me on and the amazing people I have met along the way. A particular thanks goes out to Rett UK (www.rettuk.org), for whom I am now CEO, the charity that not only supported me in those early days, but also provided me with the tools and knowledge to ensure that Rosie lives as full a life as she does.

Rett syndrome strikes indiscriminately. This could be your daughter or grand-daughter that is affected. Rett UK have provided life-changing access to support. They have provided the tools and knowledge to ensure Rosie lives a full a life as she can."

Rosie's mum

Selected themes & impacts (continued)

Treatment variation

Over many years BPSU studies have produced evidence to help determine best practice. This evidence has been used to develop or update clinical guidelines and have informed changes in service provision. The vitamin K deficiency bleeding (VKDB) study reviewed the impact of differing prophylaxis regimen. The biliary atresia study identified failings in management and its impact on clinical outcomes. Both led to policy changes.

Vitamin K deficiency bleeding: VKDB is an uncommon, potentially severely handicapping or fatal condition caused by vitamin K (VK) deficiency in early life.

Key findings: Four studies have been undertaken between 1990 and 2008. The incidence of VKDB and the associated morbidity and mortality rates fell significantly between 1994 and 2002. VK prophylaxis protects almost all babies if given intramuscularly or by multi-dose oral regimens. Investigating prolonged jaundice identifies liver disease and VK deficiency. The incidence of VKDB might be halved if all parents consented to VK prophylaxis.

Study impacts: The National Institute for Health and Care Excellence were made aware that 31% of UK paediatric units deviated from their 2006 guidance and that the existing guidance should be reviewed to reflect new data and treatment options. Awareness of VKDB and the effectiveness of prophylaxis have improved considerably.

Biliary atresia: Biliary atresia is a childhood disease of the liver in which one or more bile ducts are abnormally narrow, blocked, or absent. It can be congenital or acquired. If left untreated the condition is fatal.

Key findings: 93 cases were confirmed. Survival rates were higher in units that had greater than five cases per year. Children with biliary atresia should be managed in surgical centres with a caseload of more than five annually.

Study impacts: Following a DoH review, services were concentrated in three centres across the UK. Reviews since have shown that overall survival rates following surgery continue to be higher than they were previously.



Selected publications:

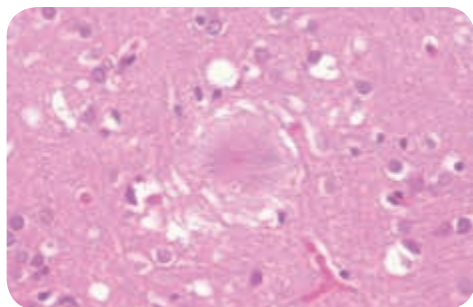
McNinch A, Tripp J. Vitamin K deficiency bleeding in Great Britain and Ireland: British Paediatric Surveillance Unit Surveys, 1993-94 and 2001-02; *Arch. Dis. Child.* 2007 Sep;92(9):759-66

Busfield A, Samuel R, McNinch A, Tripp J. Vitamin K deficiency bleeding after NICE guidance and withdrawal of Konakion Neonatal: British Paediatric Surveillance Unit study, 2006-2008. *Arch Dis Child* 2013;98:41-47

McKiernan PJ, Baker AJ, Kelly DA. The frequency and outcome of biliary atresia in the UK and Ireland. *Lancet* 2000; 355: 25-29

McKiernan PJ, Kelly DA. The BPSU study of biliary atresia outcome after 8 years. *Journal of Paediatric Gastroenterology and Nutrition* 2003; 36(4): 529

Selected themes & impacts (continued)



Florid plaque vCJD x400 haemotoxylin eosin stain

Emerging and re-emerging infectious disease

The ability of the BPSU to respond rapidly to emerging public health concerns has meant that it stands out against other passive surveillance systems. Even as the Unit was being developed, the condition known as AIDS/HIV was emerging. The BPSU is well equipped to respond and monitor newly emerging diseases, the most recent example being the emergence of the Zika virus infection and its association with microcephaly.

Progressive Intellectual and Neurological Deterioration (PIND): Following the rise of bovine spongiform encephalopathy in the late 1980's concern grew that the public could be affected. In 1996, following reports of what was to be called variant vCJD, surveillance of PIND commenced.

Key findings: 190 different neurodegenerative disorders have been diagnosed of which there have been four confirmed and two probable cases of paediatric vCJD. No case of vCJD have been identified since 2000.

Study impacts: Contamination of blood products, surgical instruments, and theoretically via vertical transmission has led the DoH to the view that surveillance should continue for the foreseeable future. The UK now has the largest and most comprehensive dataset on children with neurodegenerative disorders yielding invaluable clinical and epidemiological information on a range of conditions.

Haemolytic Uraemic Syndrome (HUS): The BPSU has undertaken three HUS studies. The third was fast tracked following concern over a large outbreak in Europe in the months leading-up to the London Olympics in 2012.

Key findings: The first study in 1986 confirmed the *E.coli* 0157 link with HUS. Scotland was identified as having the highest known incidence rate. Peak incidence of HUS is in children <5 years of age, where mortality is at its highest.

Study impacts: The study confirmed that *E.coli* 0157 infection can be transmitted via many routes; incidence rates were not falling but improved treatment has reduced mortality rates.

Selected publications:

Verity CM, Nicoll A, Will RG, Devereux G, Stellitano L. Variant Creutzfeldt-Jakob disease in UK children: a national surveillance study. *Lancet* 2000;356:1224-7

Devereux G, Stellitano L, Verity CM, Nicoll A, Rogers P. Variations in neurodegenerative disease across the UK: findings from the national study of Progressive Intellectual and Neurological Deterioration (PIND). *Arch Dis Child* 2004; 89:8-12

Milford DV, Taylor CM, Guttridge B, Hall SM, Rowe B, Kleanthous H. Haemolytic uraemic syndromes in the British Isles 1985–8: association with verocytotoxin producing *Escherichia coli*. Part 1: clinical and epidemiological aspects. *Arch Dis Child*.1990;65:716–21

Lynn RM, O'Brien SJ, Taylor CM, Adak GK, Chart H, Cheasty T, et al. Childhood Haemolytic Uraemic Syndrome, United Kingdom and Ireland. *Emerg Infect Dis* 2005; 11:590-96

Messages from clinicians & stakeholders

"As one of the "grandparents" of the BPSU, I am proud and delighted that 30 years later it continues to make a major contribution to child health. Its methodology has been adopted by other specialties and countries – in particular Australia, who themselves recently celebrated their 20th Australian Paediatric Surveillance Unit anniversary. Two other "grandparents" were Dr Martin Bellman and Dr Spence Galbraith (then Director of the Public Health Laboratory Service, Communicable Disease Surveillance Centre). Spence's enthusiastic adoption of Martin's proposal for a Reye's syndrome surveillance scheme laid the foundations of the BPSU."

Dr Susan Hall, BPSU founder coordinator



Dr Susan Hall with cheetah

"The BPSU has been a key partner for RDUK. The insights this partnership have generated have been invaluable, informing the advocacy and campaigning work of RDUK with the scientific rigour and health care excellence of the BPSU. Recognising the importance of listening to the voice of patients has been a key element in building rigour into the work of both organisations. Interactions with patients and other young people, culminating in the annual BPSU tea party on Rare Disease Day, has ensured that we are realistic and robust in the work we do together."

Alastair Kent OBE, CEO Rare disease UK

"The BPSU's work has impacted on policy and practice for 30 years, not only directly but via the large number of sister surveillance units that have applied the same methodology, allowing international collaborations to flourish. As the chair of one of the BPSU's youngest siblings, I am immensely grateful to the support that we have received and the enormous amount that have learnt from our paediatric colleagues and am delighted that so many of our child and adolescent psychiatry studies are run jointly with the BPSU."

Professor Tamsin Ford, Chair of CAPSS



CAPSS executive committee

"I have been involved with five studies through the BPSU. It is undoubtedly a major resource for research in rarer conditions. The BPSU team are thorough and extremely helpful. Not only do the studies establish incidence but allow hypothesis generation for future studies."

Professor Julian Hamilton-Shield, Professor in Diabetes and Metabolic Endocrinology, University of Bristol

"The BPSU has been a fantastic innovation, copied around the world and by other medical specialties. Since 1986 over 100 rare diseases have been studied providing valuable insights into incidence and natural history. As a practising paediatrician I have been a beneficiary of all 100 and having led one of these studies, I can testify to the hard work involved by reporting paediatricians. As a past President of the RCPCH I have been proud to work in partnership with the BPSU."

Professor Terence Stephenson, Chair of the General Medical Council



Professor Terence Stephenson

International activities



Following the success of the BPSU, sister units have adopted and adapted the BPSU's methodology. In 1992 surveillance units were established in the Netherlands and Germany, and in 1994 and 1995 respectively units were formed in Wales and Switzerland. The European led initiative also acted as the stimulus for the development of units in Canada, Australia and Portugal and several other countries. As of 2016 there are 12 national units.

Importantly, the BPSU is a founding member and driving force in the establishment of the International Network of Paediatric Surveillance Units (INoPSU) in 1998. INoPSU aims to facilitate the sharing of information and multi-national collaboration through the use of shared protocols and data. In so doing, INoPSU has supported international collaboration in the study of rare childhood diseases. Collectively, INoPSU member units conduct surveillance in a population of over 46 million children. More than 12,000 clinicians contribute data on rare conditions each month and over 300 conditions have been studied.

Examples of impacts on public health policy and clinical practice include:

- Acute flaccid paralysis surveillance confirms absence of wild or vaccine-related poliovirus; contributes to WHO eradication program.
Units: Australia, Canada, New Zealand, Switzerland, UK
- Congenital rubella surveillance supports childhood rubella vaccination programmes and the need for targeted vaccination for susceptible women including immigrants, women who have not received the rubella vaccination, either pre-conception or post-partum to prevent significant birth defects.
Units: Australia, Canada, Netherlands, New Zealand, Switzerland, UK
- Early onset eating disorders (<13 years) surveillance confirmed the need for pre-adolescent diagnostic criteria and early recognition, and evidence-based treatment.
Units: Australia, Canada, Netherlands, UK
- Haemolytic uraemic syndrome surveillance described geographic variation in the conditions aetiology, highlighting the need for new diagnostic tests. Supported preventative measures through education; hygiene recommendations for family friendly farms, new legislation on safe food production, and the monitoring of water supplies.
Units: Australia, Canada, Latvia, New Zealand, Portugal, Switzerland, UK
- Vitamin K deficiency bleeding surveillance confirmed that most cases are late onset and related to underlying liver disease; and that a high proportion of cases receive no prophylaxis or an incomplete vitamin K prophylaxis at birth.
Units: Australia, Canada, Germany, Netherlands, New Zealand, Switzerland, UK

Selected publications:

Elliott E, Nicoll A, Lynn R, Marchessault V, Hirasing R (INoPSU Secretariat), on behalf of INoPSU members. An international network of paediatric surveillance units: A new era in monitoring uncommon diseases of childhood. *Paediatrics and Child Health*; 2001 6: No 5 250-59



2011 INoPSU meeting, Switzerland

"Congratulations to BPSU on 30 years of paediatric surveillance. The BPSU had a vision and put it into reality. They have come a long way despite many hurdles, financial, political, organisational and others and are still going strong today. They have inspired many other countries to follow their lead and develop a surveillance network generating scientific data to enhance paediatric public health policy.

Thanks BPSU!"

Mirjam Maeusezahl,
INoPSU Convenor

"Congratulations to the BPSU on 30 years of successful surveillance for rare childhood conditions! You have contributed important knowledge to improve child health outcomes. Your leadership and innovation is valued and respected by national paediatric surveillance units across the world. Best wishes from the APSU and we look forward to ongoing collaboration. Keep up the great work!"

Yvonne Zurynski, Director of Research,
Australian Paediatric Surveillance Unit

Looking forward

This is a time of rapid change in disease epidemiology related to globalisation and developments in scientific knowledge. Great strides are being made in genetic diagnosis and the treatment of rare disease. The strength of the BPSU is its ability to describe the epidemiology and natural history of a rare disease. This puts the BPSU in a unique position to exploit new opportunities, respond to emerging threats and adapt to changing public expectations.

The BPSU now has a robust governance structure embedding the roles of the three parent bodies of PHE, UCL-ICH, and the RCPCH. This guarantees the longer term security of the BPSU, and allows us to achieve financial sustainability by seeking a wider range of funding. This coupled with more efficient processes, increased flexibility and system development puts the BPSU in a strong position going forward. Collaboration, communication and public engagement are a particular focus.



Collaboration

- **Other UK surveillance units:** Work with the Royal College of Psychiatrists has already helped the BPSU broaden its remit to include health service research and those involving health economics.
- **Government advisory bodies:** The BPSU will continue to work in support of the National Screening Committee and the Joint Committee on Vaccination and Immunisation.
- **Public health bodies of the four UK countries and the Republic of Ireland:** Ebola and the flu pandemic are examples of how a rapid mobilisation of epidemiological and translational research are central to the global response to public health crises. The utility of the BPSU was evidenced most recently when the Unit became the first paediatric surveillance system in the developed world to undertake surveillance for congenital Zika syndrome.
- **Supporting the new UK National Congenital Anomaly and Rare Disease Registration Service (NCARDRS):** The BPSU will be helping to validate the new system.
- **Rare disease translational research:** The rapid advances in genome technology and knowledge are opening up many opportunities for rare disease research and developments in treatment. The BPSU offers unparalleled opportunities for epidemiological research on phenotypes. The interaction between genotype and phenotype at a population level is an essential step in the translation of basic science into public health and clinical practice. Changing ethical and legal frameworks may provide the BPSU with the opportunity for more work at the interface between genetic research and disease surveillance. One example of this being the BPSU work with the Birmingham based Translational Research Consortium on type 2 diabetes phenotyping.
- **International surveillance units:** Collaborative and comparative studies are now being encouraged and this can be seen through the sharing of protocols.

Communication, dissemination and public engagement

Communication, dissemination and public engagement are increasingly important to the work of the Unit, both in relation to conditions which have been the subject of BPSU studies and also in relation to rare disease activities more generally. The BPSU has communicated its work in a number of ways, for example:

- **Hosting and contributing to conferences and dissemination events:** Throughout 2016 the BPSU have held a number of workshops and symposia, culminating in a 'Paediatric Rare Disease Conference' to mark the Unit's 30th anniversary.
- **Expanding opportunities for rare disease education and training:** In collaboration with study investigators, the BPSU is taking a leading role in developing e-learning packages and organising educational events for clinicians.
- **Active patient and public engagement (PPE):** Ensuring that active PPE is embedded in all of the work of the BPSU, from study design to dissemination of research findings.
- **Public health advocacy:** BPSU facilitated research has influenced public health and health service policy. The BPSU is adopting a more active role, building policy and dissemination strategies into BPSU study proposals, supporting research teams in implementing policy change as a consequence of their findings, and engaging more actively with public health and policy groups.
- **Website:** The BPSU is developing an easily accessible website for the public, media, clinicians and allied healthcare professionals.

Finally, on behalf of the BPSU, our thanks go out to all of the clinicians who faithfully return their Orange Card each and every month. Without their active engagement in the reporting scheme all of the successes that the BPSU has contributed to over the last 30 years - its role in assessing the efficacy of vaccines, its rapid response to public health emergencies, informing clinical management guidelines, would not have been possible. Thank you!

Encouraging lay dissemination of findings of BPSU research

Dr Julie-Claire Becher, who ran surveillance on sudden unexpected postnatal collapse, has disseminated her research to families on the WellChild website and produced guidelines for hospitals - <https://www.wellchild.org.uk/what-we-do/research/>. The study into Group B streptococcal disease have also published their results on the Group B Strep Support group website <http://gbss.org.uk/latest-news/group-b-streptococcal-disease-in-uk-irish-infants-less-than-90-days-of-age/>

"It is a matter of pride for this country that the innovative and scrupulous epidemiology of the BPSU has been emulated by several countries in Europe and beyond."

Professor Sir Liam Donaldson, Chief Medical Officer (September 2011)

Conditions undertaken 1986 - 2016

Haemolytic uraemic syndrome 1, Haemorrhagic shock and encephalopathy syndrome, Kawasaki disease 1, Neonatal herpes, **Reye's syndrome**, Subacute sclerosing panencephalitis, X-linked anhydrotic ectodermal dysplasia, AIDS/HIV, Lowe syndrome, Drowning-near drowning, Galactosaemia, Insulin dependent diabetes mellitus in under 15, Haemorrhagic disease of the newborn, Higher order births, Congenital toxoplasmosis, Acute rheumatic fever, **Measles Mumps Rubella**, meningococcal meningitis, Rett syndrome, Chemistry set poisoning, Acute flaccid paralysis, Androgen insensitivity syndrome, Haemophagocytic lymphohistiocytosis, Insulin dependent diabetes <5, Long term parenteral nutrition, Juvenile dermatomyositis, Munchausen by proxy syndrome/Non accidental poisoning, **Haemophilus influenzae b**, Vitamin K deficiency bleeding 2, **Biliary atresia**, Congenital dislocation of the hips, Congenital syphilis 1, Neonatal necrotising enterocolitis, Medium chain acyl CoA dehydrogenase deficiency 1, Adverse neonatal outcomes of deliver-labour in water, Transient-permanent neonatal diabetes, Pyridoxine dependent seizures, Cerebral oedema following DKA, Congenital cataracts, Neonatal meningitis 1, **Haemolytic uraemic syndrome 2**, Hepatitis C Virus, Congenital brachial palsy, Fatal / severe allergic reaction to food, Subdural haematoma & effusion, Inflammatory bowel disorder, Encephalitis in early childhood, Visual impairment and blindness 1, Group b streptococcal disease 1, Stroke and cerebrovascular disease, **Vitamin K deficiency Bleeding 3**, Congenital cytomegalovirus, Thrombosis in childhood, Internal abdominal injuries due to abuse, Fatal severe adverse drug reactions, Congenital toxoplasmosis, Varicella - severe complications, Invasive fungal infections, Hyperbilirubinemia, Langerhans cell histiocytosis, Tuberculosis, Neonatal herpes simplex virus 2, **Medium chain acyl CoA dehydrogenase deficiency 2**, Thyrotoxicosis, **Non type 1 diabetes**, Early onset eating disorders, Methicillin-resistant Staphylococcus aureus, Scleroderma, Malaria, Fetomaternal alloimmune thrombocytopenia, Vitamin k deficiency bleeding 4, Genital herpes, Idiopathic intracranial hypertension, Congenital adrenal hyperplasia, **Intussusception in children under 12 months**, Anaphylaxis following immunisation, Conversion disorder, Sudden unexpected postnatal collapse, Toxic shock syndrome, Severe Neonatal Hyponatraemia, CNS Demyelination, Guillain-Barré/ Miller Fisher syndromes, Congenital syphilis, gonorrhea, syphilis, chlamydia & trichomonas, Chylothorax, **Raised blood lead levels**, Glutaric Aciduria 1, Neonatal meningitis 2, End stage renal failure, Congenital hypothyroidism, Autoimmune Addison's disease, Hypocalcaemia seizures due to Vitamin D deficiency, Haemolytic uraemic syndrome 3, **Gender identity disorder**, Surgically ligated patent ductus arteriosus, Kawasaki disease 2, Acute pancreatitis, Acute hepatitis, Group B streptococcal disease 2, Enterovirus and Parechovirus meningitis, Exchange blood transfusion, Congenital rubella, **HIV infection & perinatal exposure**, Progressive intellectual neurological deterioration, Congenital hypothyroidism, Acute pancreatitis, Acute hepatitis, **Rickets presenting to secondary care**, Acute rheumatic fever 2, Behcet's disease, Visual impairment and blindness 2, Attention deficit hyperactivity disorder transition, **Female genital mutilation**, Pierre Robin Sequence, **Congenital Zika syndrome**

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