

NOTTINGHAM  
CLINICAL  
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UNIT

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Annual Report  
2016

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## 1

# WELCOME

Welcome to the 2016 annual report for the Nottingham Clinical Trials Unit. An early highlight this year was publication, in the New England Journal of Medicine, of the results of one of our first studies, the 35/39 trial. This trial recruited women aged over 35 years and compared a policy of induction of labour at 39 weeks gestation with a policy of awaiting spontaneous labour. Overall 619 women participated, and there were no clear differences between the groups in the proportion of women who had a caesarean section, or the proportion with short-term adverse maternal or neonatal outcome. This trial helps fill an important gap in the evidence. Although it was not intended to assess differences in neonatal outcome and so was not powered to do so, it is further evidence that induction of labour using modern methods may not increase the risk of caesarean section.

August saw the launch of our Strategic Development Fund award from the University. This award includes nine new posts, six academic and three administrative, three of which we have now appointed to. Exciting news is that Jane Daniels will be joining us in April 2017 as Professor of Clinical Trials. Jane is currently Deputy Director of the Birmingham Clinical Trials Unit, and has a particular interest in women's health trials. We are delighted she will be joining us and look forward to working with her.

Many of you who have worked with the unit over the last 10 years will know Diane Whitham. Having worked closely with Diane since my arrival in 2011, it is a particular pleasure to announce that she has been appointed as Associate Professor in Clinical Trials. Diane takes up her new post in March 2017. The third appointment is that Charlotte Curnow has taken up the post of Assistant Unit Manager, a much needed new role which will strengthen administrative support as the unit grows.

In September we heard that Nottingham had been awarded £23 million for a National Institute of Health Research Biomedical Research Centre, which is fantastic news. The new Centre will launch in April 2017 and will focus on internationally competitive translational research in gastrointestinal and liver disease, hearing loss and tinnitus, respiratory disease, musculoskeletal disease, and mental health and technology. Imaging is a cross cutting theme within the BRC. Our Strategic Development Fund award is particularly timely as it offers unique opportunities for new collaboration, and will help us build expertise and capacity to collaborate on translational studies with colleagues in the BRC.

It has not been all good news this year, as on a dark February evening Alan Montgomery, our Professor of Medical Statistics, was involved in an accident whilst heading home on his motor bike. The bike did not survive the accident, thankfully Alan did. However, his right lower leg has needed the full expertise of our excellent Nottingham trauma and orthopaedic teams. He is now on the mend, and getting back involved in the unit's work. My personal thanks to the many people who have supported Alan and the unit during a challenging time.

**Lelia Duley**

Director, Nottingham Clinical Trials Unit

# 2 RANDOMISED TRIALS

## 2.1 Cancer

**POsitive Sentinel NOde: adjuvant therapy alone versus adjuvant therapy plus Clearance or axillary radiotherapy. A randomised trial in women with early stage breast cancer (POSNOC)**

Chief Investigator: **Amit Goyal**, Derby Teaching Hospitals NHS Foundation Trust

Each year over 48,000 women are diagnosed with breast cancer in the UK. Currently women having surgical treatment for early breast cancer also have the first one or two lymph glands (sentinel nodes) in their armpit (axilla) removed, an early procedure called sentinel node biopsy. For about a quarter of women, the breast cancer has spread to these sentinel nodes. Currently, these women are offered axillary treatment. This is either a second operation to remove all the axillary lymph glands (axillary node clearance) or axillary radiotherapy. The women also receive adjuvant therapy (chemotherapy, hormone therapy, local radiotherapy of breast or chest wall). Outcome is now very good following adjuvant therapy, and so routine axillary treatment which has unavoidable adverse effects may no longer be needed. Axillary treatment is associated with lymphoedema and other long term complications such as numbness, pain and shoulder stiffness. These arm problems can be upsetting and difficult to cope with and are often irreversible.

This trial aims to assess whether adjuvant therapy alone is no worse than (non-inferior to) adjuvant therapy plus axillary treatment for women with early stage breast cancer who have macrometastases in one or two axillary lymph nodes. The primary outcome is axillary recurrence within 5 years. The planned sample size is 1900 women. Recruitment began in the UK in July 2014, and extended to Australia and New Zealand in 2016.

**Contact:** Shabina Sadiq  
**Funding:** NIHR Health Technology Assessment, National Health and Medical Research Council (Australia)  
**Status:** Recruiting  
**Publications:** 2012-18

## 2.2 Eyes

**A randomised controlled Trial of standard and low dose Avastin® for Neovascular macular Degeneration in the East Midlands (TANDEM)**

Chief Investigator: **Alexander Foss**, Nottingham University Hospitals NHS Trust

Wet, or neovascular age-related, macular degeneration causes severe sight loss in older people. It is a common condition, with about 25,000 newly affected people each year in the UK. Treatment with Lucentis® (Ranibizumab) or Eyelea® (Aflibercept) is now recommended best practice. Although they prevent sight loss in 90% of patients with wet macular degeneration when given as injections into the eye, Lucentis® and Eyelea® are both quite expensive. Another drug, which has similar properties to Lucentis® is Avastin® (Bevacizumab). Avastin® is currently licensed for colorectal cancer therapy but can also be used for wet macular degeneration, and is a cheaper alternative to Lucentis®.

This is a factorial trial comparing standard versus low-dose Avastin®, and monthly versus two-monthly review intervals. Recruitment closed on 31 October 2016 with a total of 812 participants and follow-up will continue until 31 March 2017. The primary outcome is time to treatment failure.

**Contact:** Beki Haydock  
**Funding:** NHS England and Care Commissioning Groups  
**Status:** Follow Up  
**Publications:** 2015-5

## 2.3 Infection

### Gentamicin in the Treatment of Gonorrhoea (G-TOG)

Chief Investigator: **Jonathan Ross**, University Hospitals Birmingham  
NHS Foundation Trust

Currently the antibiotic ceftriaxone is used to treat gonorrhoea, but there is evidence that with increasing antibiotic resistance it is becoming less effective over time, and will stop curing patients with gonorrhoea within the next few years.

Many currently available antibiotics do not work against gonorrhoea, and there is an urgent need to find an alternative treatment which is effective and safe. Gentamicin was used in the past in the UK to treat gonorrhoea, and laboratory testing suggests that it remains effective against gonorrhoea. It is currently being used as treatment for gonorrhoea in some developing countries.

This randomised trial is comparing gentamicin with the current standard treatment ceftriaxone to assess whether gentamicin is a safe and effective alternative treatment for gonorrhoea. The primary outcome is clearance of gonorrhoeae at all infected sites confirmed by swab testing two weeks after treatment.

Recruitment commenced in October 2014 across 15 sexual health centres in the UK and closed in November 2016 having met the target of 720 participants. Follow up will complete in early 2017.

**Contact:** Sukhwinder Thandi  
**Funding:** NIHR Health Technology Assessment  
**Status:** Follow up  
**Publications:** 2014-33; 2016-14

## 2.4 Mental Health

### Psycho-Education and Problem Solving therapy for adults with personality disorder (PEPS trial)

Chief Investigator: **Mary McMurrin**, The University of Nottingham

Personality disorders are conditions in which an individual experiences difficulties in terms of how they think, perceive, feel or relate to others. People with personality disorder may have problems which can include negative feelings such as distress, anxiety, worthlessness or anger; avoiding other people and feeling emotionally disconnected; having difficulty managing negative feelings without self-harming (for example, abusing drugs and alcohol or taking overdoses), and having difficulty maintaining stable and close relationships. Social problem-solving therapy is a potential strategy that may benefit people with personality disorders.

This study evaluated the effectiveness of Psycho-Education and Problem Solving (PEPS) therapy compared with usual care for adults with personality disorder. The primary outcome was social functioning at 13 months, assessed by the Social Functioning Questionnaire. The trial completed in October 2014. Results indicate that PEPS therapy plus usual treatment was no more effective than usual treatment alone on the primary outcome or any secondary outcomes.

**Contact:** Florence Day  
**Funding:** NIHR Health Technology Assessment  
**Status:** Published  
**Publications:** 2011-1; 2016-7

## 2.4 Mental Health Cont

### Lamotrigine versus inert placebo in the treatment of borderline personality disorder: the LABILE trial

Chief Investigator: **Mike Crawford**, Imperial College London

People with borderline personality disorder experience rapid and distressing changes in mood, poor social functioning and have high rates of suicidal behaviour. Several small scale studies suggest that mood stabilisers may produce short-term reductions in the symptoms of borderline personality disorder. These studies have not been large enough to reliably assess clinical and cost-effectiveness.

The aim of this trial is to investigate the effect of adding lamotrigine to usual care for people with borderline personality disorder on their mental health, social functioning, and quality of life. The study will also assess the effect on suicidal behaviour, prescribing of anti-psychotic and other psychotropic medication, and side effects of lamotrigine. The trial includes an economic evaluation.

**Contact:** Alan Montgomery  
**Funding:** NIHR Health Technology Assessment  
**Status:** Analysis and reporting  
**Publications:** 2015-16

### Expanding care for perinatal women with depression (EXPONATE trial)

Chief Investigator: **Oye Gureje**, University of Ibadan, Nigeria

Depression is common among women during the perinatal period and is associated with long-term adverse consequences for the mother and infant. In Nigeria, as in many other low- and middle-income countries, perinatal depression usually goes unrecognised and untreated.

The aim of EXPONATE is to test the effectiveness and cost-effectiveness of an intervention package for perinatal depression delivered by community midwives in primary maternal care in which physician support and enhanced patient compliance are implemented using mobile phones.

**Contact:** Alan Montgomery  
**Funding:** Grand Challenges Canada  
**Status:** Analysis and reporting

### A stepped care intervention for depression in primary care (STEP CARE trial)

Chief Investigator: **Oye Gureje**, University of Ibadan, Nigeria

Depression constitutes a significant public health burden and is associated with a high level of individual suffering. Insufficient human and material resources impede the provision of adequate care for people with depression in low- and middle-income countries. To bridge this treatment gap, it is essential to integrate the treatment of depression into the primary health care system.

The aim of this study is to evaluate the clinical and cost effectiveness of a care package for care delivered mainly by non-medical Primary Health Care workers with supervision and support from physicians and specialists.

**Contact:** Alan Montgomery  
**Funding:** MRC/DFID/Wellcome Trust Joint Global Health Trials scheme  
**Status:** Analysis and reporting  
**Publications:** 2015-26; 2015-49

## 2.5 Musculoskeletal

### Nottingham Gout Treatment Trial Phase 2: trial of a nurse-lead package of care

Chief Investigator: **Michael Doherty**, The University of Nottingham

Gout is often said to be the most painful form of arthritis. Symptoms include intensely painful, red, hot and swollen joints. Gout is most common in men and rarely affects women before the menopause. Prevalence increases with age. Of all the forms of arthritis, gout is understood the best. This has led to a range of therapies to treat acute attacks and control the condition. People with gout are usually managed in primary care, but their care is not always optimal.

This trial to assess whether, for patients with untreated or under-treated gout, nurse led care is effective and cost-effective compared with usual general practitioner-led care. Estimated sample size is initially 724 participants, but this was subsequently revised to 512 participants. The primary outcome is serum uric acid within the therapeutic range (<360 µmol/L) at two years. Recruitment was from March 2013 to October 2014, in total 517 participants were recruited.

**Contact:** Lelia Duley  
**Funding:** Arthritis Research UK  
**Status:** Follow up

### Needle fasciotomy versus limited fasciectomy for treatment of Dupuytren's contractures of the fingers: a feasibility study to investigate the acceptability and design of a multicentre randomised trial (HAND-1)

Chief Investigator: **Tim Davis**, Nottingham University Hospitals NHS Trust

Dupuytren's contractures are fibrous cords under the skin in the palm of the hand. These contractures are painless but cause one or more fingers to gradually and irreversibly curl into the palm, resulting in loss of hand function. Standard treatment is surgery to either remove or divide the contractures, allowing the finger to straighten again. The most common operation is to remove the contracture (limited fasciectomy): the fibrous cords preventing the finger(s) from straightening are cut out through a long skin incision in the hand. The alternative procedure is to divide the contracture with a needle (needle fasciotomy): a needle is put through the skin and sawing movements used to divide the fibrous cords. There is no clear evidence of the comparative benefits and risks of these two quite different surgical procedures for Dupuytren's contractures.

The HAND-1 study aims to assess the feasibility and acceptability to patients and clinicians of conducting a large randomised trial assessing the comparative clinical and cost effectiveness of needle fasciotomy versus limited fasciectomy for Dupuytren's contractures of fingers. Recruitment took place from November 2015 to September 2016 at three sites, and a total of 71 participants were randomised. Participant follow-up is planned to continue until February 2017.

**Contact:** Ellie Harrison  
**Funding:** NIHR Research for Patient Benefit  
**Status:** Follow Up

## 2.6 Oral and Gastrointestinal

### Systematic Evaluation of Aspirin and Fish Oil polyp prevention trial (seAfOod)

Chief Investigator: **Mark Hull**, University of Leeds

Colorectal cancer develops over a number of years from tumour initiation and benign adenoma (or polyp) growth, followed by transformation into malignant adenocarcinoma. Currently colorectal cancer prevention is aimed at detection and removal of asymptomatic colorectal polyps. Polyp removal does reduce bowel cancer risk, but does not prevent all cases of bowel cancer.

This factorial trial is assessing the effects of eicosapentaenoic acid (fish oil) and/ or aspirin for people with colorectal polyps attending for colonoscopic surveillance in the NHS Bowel Cancer Screening Programme. 709 participants were recruited between Nov 2011 and June 2016, follow-up is due to complete in June 2017. The primary outcome is recurrent polyp/s at surveillance colonoscopy.

**Contact:** Kirsty Sprange  
**Funding:** NIHR Efficacy and Mechanism Evaluation  
**Status:** Follow-up  
**Publications:** 2013-6

### “Follow-on” rifaximin for the prevention of relapse of clostridium-associated diarrhoea: a randomised trial (RAPID)

Chief Investigator: **Robin Spiller**, The University of Nottingham

Clostridium difficile infection is the main cause of antibiotic associated diarrhoea. It mainly affects frail and elderly hospitalised patients, although more recently a rising incidence of a more virulent strain has been associated with infection in younger patients and those in the community. It is characterised by a high incidence of recurrent infection, which can have debilitating consequences for already weakened patients. There are few well designed randomised trials in this condition, and treatment is largely based on experience and consensus opinion.

This trial is comparing rifaximin with placebo to reduce relapse for people who have had successful treatment of clostridium difficile. 151 participants were recruited between January 2013 and March 2016. The primary outcome is relapse within 12 weeks.

**Contact:** Alan Montgomery  
**Funding:** NIHR Research for Patient Benefit  
**Status:** Analysis and Reporting



## 2.7 Pregnancy and Childbirth

### Induction of labour at 39 weeks versus expectant management for nulliparous women over 35 years of age (35/39 Trial)

Chief Investigator: **Jim Thornton**, The University of Nottingham

In the UK, the average age at childbirth is increasing, with 20% of women now giving birth over 35 years of age. These women are at higher risk of perinatal death, and of pregnancy complications. Obstetric intervention increases with maternal age. Thirty eight per cent of nulliparous women over 35 years give birth by Caesarean section, rising to 50% for women over 40 years.

This trial compared a policy of induction of labour at 39 weeks gestation for women aged over 35 years with a policy of awaiting spontaneous onset of labour. The primary outcome was Caesarean section. The study also assessing the feasibility of conducting a larger trial to assess the comparative effects on perinatal mortality and serious neonatal morbidity. Overall, 619 women participated. There were no significant differences between groups in the proportion of women who had caesarean section, or the proportion with short-term adverse maternal or neonatal outcome.

**Contact:** Jim Thornton  
**Funding:** NIHR Research for Patient Benefit  
**Status:** Complete.  
**Publications:** 2012-17; 2016-6

### Immediate versus deferred cord clamping for preterm birth before 32 weeks gestation, a pilot randomised trial (Cord Pilot Trial)

Chief Investigator: **Lelia Duley**, The University of Nottingham

Preterm birth is the most important single determinant of adverse outcome in terms of survival, quality of life, psychosocial and emotional impact on the family, and costs for health services. In the UK one in every 70 babies is born before 32 weeks gestation (very preterm). For very preterm infants, the umbilical cord is usually clamped immediately at birth and the baby taken to a resuscitaire at the side of the room. Deferring cord clamping will allow blood flow between the placenta and baby to continue for a few minutes after birth. The net flow is known as 'placental transfusion'. If cord clamping is deferred, initial care and stabilisation of the baby will be at the bedside. There is promising evidence that deferring cord clamping at very preterm birth may be beneficial, but stronger evidence is needed about the effects on serious morbidity, mortality and disability-free survival.

This pilot trial is comparing cord clamping within 20 seconds with clamping after at least two minutes, for births before 32 weeks gestation. The aim is to assess the feasibility of conducting a large randomised trial in the UK. Recruitment was from March 2013 to February 2015. Overall 261 women/baby pairs were recruited at eight sites. Follow up for women is at one year, and for children at age two years (corrected for gestation at birth).

**Contact:** Lindsay Armstrong-Buisseret  
**Funding:** NIHR Programme Grants for Applied Research  
**Status:** Follow up  
**Publications:** 2011-3; 2012-12; 2013-13; 2013-14; 2014-13; 2014-17; 2015-13; 2015-17; 2015-31; 2015-43; 2015-50

## 2.7 Pregnancy and Childbirth *Cont*

### Feasibility of conducting a randomised trial evaluating timing of cord clamping for preterm births in low and middle income countries (i-Cord)

Chief Investigator: **Lelia Duley**, The University of Nottingham

An estimated 15 million babies are born before preterm (before 37 gestation weeks) each year, of whom more than 1 million die following complications of being born too early. Preterm birth is more common in low and middle income countries. Almost two thirds of preterm births occur in sub-Saharan Africa and South Asia. Inequalities in survival around the world are stark. For example, of infants born at 28 to 32 weeks gestation in high income countries 95% survive, compared with 30% in low income countries.

This study aims to assess feasibility of a large randomised trial comparing alternative policies for timing of cord clamping for births between 28 and 34 weeks gestation (or 1–2 kg birthweight). A prospective audit of births at five hospitals in Uganda (2 sites), Kenya, India and Pakistan is assessing current practice for timing of cord clamping and for neonatal care in the delivery room, and the proportion of births which can be correctly identified as being at this gestation. A separate study in India is assessing the volume and duration of umbilical flow at preterm birth if the umbilical cord is not clamped immediately. Finally, potential barriers to recruitment in a randomised trial are being explored in a qualitative study in Uganda.

**Contact:** Lelia Duley  
**Funding:** MRC/DFID/Wellcome Trust Joint Global Health Trials scheme  
**Status:** Analysis and reporting

### Do tests of placental function improve outcome for women with reduced fetal movements at 36 weeks gestation, or later? The REMIT-2 trial

Chief Investigator: **Alexander Heazell**, University of Manchester

In the UK, 1 in 220 babies are stillborn (born with no signs of life after 24 weeks of pregnancy). This is a higher proportion than in many other high income countries. Forty percent of babies who are stillborn die after 36 weeks of pregnancy and have no lethal structural abnormality. These deaths are tragedies for the families. If babies at risk of stillbirth could be identified and delivered early, lives could be saved.

An association between the mother noticing reduced fetal movements and subsequent stillbirth has been documented for over 40 years. For women reporting reduced fetal movements at 36 weeks or later, standard care varies but usually includes assessment of the fetal heart rate with cardiotocography, and assessment of fetal growth and wellbeing by ultrasound scan and umbilical artery doppler. The aims of this trial are to assess whether using tests to measure placental function may improve pregnancy outcome, compared with standard care for women at or near term (at least 36 weeks gestation); and if so to assess the feasibility of a large multicentre trial. The primary neonatal outcome is a composite measure which includes perinatal death, five minute Apgar score <7, umbilical artery pH <7.05 or admission to the neonatal intensive care unit for at least 48 hours, presence of hypoglycaemia, hypothermia, seizures or complications of fetal growth restriction, use of therapeutic cooling, respiratory support and number of dependency days. The sample size is 750 women.

**Contact:** Lindsay Armstrong-Buisseret  
**Funding:** NIHR Clinician Scientist Fellowship  
**Status:** Set up  
**Publications:** 2015-38

## 2.8 Rehabilitation

### Community in-reach and care transition (CIRACT trial)

Chief Investigator: **Opinder Sahota**, Nottingham University Hospitals NHS Trust

With the proportion of acute medical emergencies contributed by older people significantly rising in the last 5 years from 9.5% to 14% and is expected to increase significantly over the next 10 years. The trial aimed to reduce the length of hospital stay and re-admission and to improve health-related quality of life for unplanned hospital admission for people over the age of 70 years by delivery of the Community in-reach and care transition (CIRACT) service as compared to traditional hospital based rehabilitation (THB-Rehab). The primary outcome was hospital length of stay from admission to discharge from the general medical elderly care ward. Follow up of participants was to day 91 post discharge date. The sample size was 240 participants; which was achieved in July 2014. The trial showed that the CIRACT service as a complex intervention did not reduce major hospital length of stay nor short-term readmission rates compared to the THB-Rehab service; however, a modest (<2.3 days) but worthwhile effect cannot be excluded.

**Contact:** Alan Montgomery  
**Funding:** NIHR Health Services and Delivery Research  
**Status:** Published  
**Publications:** 2015-11; 2016-10

### Rehabilitation of memory following traumatic brain injury: a randomised trial (ReMemBrin trial)

Chief Investigator: **Roshan das Nair**, Nottingham University Hospitals NHS Trust

Memory problems are common following traumatic brain injury. These can not only be persistent, but may be debilitating and difficult to treat. The effectiveness of cognitive rehabilitation following brain injury has been assessed in randomised trials, which have mainly focused on attention, executive functions, and visual neglect. Memory rehabilitation has not been sufficiently researched, however.

This trial is evaluating a group memory rehabilitation programme for adults, including military personnel, who have had a traumatic brain injury. The study is comparing group based memory rehabilitation plus usual care with usual care alone. Estimated sample size is 312 participants. The primary outcome is an assessment of memory at six months. Recruitment closed at the end of December 2015 with a total of 328 randomised participants. The final follow-up was completed in December 2016. Analysis and reporting is currently underway.

**Contact:** Florence Day  
**Funding:** NIHR Health Technology Assessment  
**Status:** Reporting  
**Publications:** 2015-2

### Cognitive Rehabilitation for Attention and Memory for people with Multiple Sclerosis (CRAMMS)

Chief Investigator: **Nadina Lincoln**, The University of Nottingham

Around two thirds of people with Multiple Sclerosis experience difficulties paying attention, learning, remembering new things and planning tasks. This can be distressing for the individual and their families and friends. Small scale trials suggest that cognitive rehabilitation may be effective to improve memory in people with MS. However, large randomised controlled trials have not been performed.

This trial is assessing whether a group cognitive rehabilitation programme plus usual care is associated with reduced impact of MS on quality of life, compared to usual care alone. The primary outcome is the psychological impact of MS on everyday life 12 months after randomisation. Estimated sample size is 400 participants, to be recruited from 4 sites. Recruitment opened in March 2015 and the recruitment target was reached in March 2017. Follow-up is due to be completed by the end of March 2018.

**Contact:** Florence Day  
**Funding:** NIHR Health Technology Assessment  
**Status:** Follow-up  
**Publications:** 2016-15

## 2.9 Respiratory

### Double-blinded randomised trial of early low dose steroids in patients admitted to hospital with influenza infection during a pandemic (ASAP)

Chief Investigator: **Wei Shen Lim**, Nottingham University Hospitals NHS Trust

An influenza pandemic occurs when a new strain of influenza virus emerges which is different from other currently circulating strains of the virus. This means that few people have any protection against the new virus, and so the virus can infect people easily. The virus therefore spreads on a worldwide scale and infects a large proportion of the population. In contrast to the regular seasonal epidemics of influenza, these pandemics occur irregularly, with the 1918 Spanish flu the most serious pandemic in recent history. There are currently no markers that will predict the pathogenicity or spread of a potential pandemic strain. Therefore, any plans for a future pandemic need to be flexible and take account of different possible scenarios from mild to severe.

Corticosteroid use in influenza is widespread, non-systematic and controversial. During the last pandemic in 2009, corticosteroid use during hospital admission was reported in various cohort studies and non-randomised studies but there are no randomised trials of the use of corticosteroids for patients with pandemic, avian or seasonal influenza infection.

This trial will assess the effects of adding a five-day course of dexamethasone (a corticosteroid), started within 24 hours of hospital admission, to standard care. Participants will be adults hospitalised with an influenza-like illness during the pandemic. Estimated sample size is 2,200 participants. The primary outcome is admission to intensive care unit or death, within 30 days of hospital admission. During a pandemic, the aim is to activate the trial within four weeks during the first wave of the pandemic, and to complete recruitment in six weeks. Results would then inform clinical practice and health policy during the second wave.

The trial is now set up, with full regulatory approval, and has been hibernated. During hibernation the trial will be reviewed annually to ensure it remains ready to activate rapidly when required.

**Contact:** Garry Meakin  
**Funding:** NIHR Health Technology Assessment  
**Status:** Hibernation  
**Publications:** 2013-20; 2015-7; 2015-53

### Clinical and cost-effectiveness of temporarily quadrupling the dose of inhaled steroid to prevent asthma exacerbations: a pragmatic randomised trial (FAST)

Chief Investigator: **Tim Harrison**, The University of Nottingham

Asthma is a common chronic condition. Acute exacerbations of asthma cause considerable morbidity, and account for a large component of the NHS-associated costs of asthma as they lead to high levels of emergency healthcare use. Asthma self-management plans could potentially improve asthma control, reducing exacerbations requiring oral corticosteroids and emergency healthcare as well as time away from work.

Although written self-management plans are recommended for all patients with asthma, many patients are not provided with one. Reasons for this include a lack of time and confusion about what to include in the plan when asthma control is deteriorating but before the need for oral corticosteroids.

This trial compares a self-management plan which includes a temporary fourfold increase in inhaled corticosteroid with the same plan without an increase in inhaled corticosteroid when the participants' asthma control deteriorates. 1922 participants were recruited from 11 secondary care sites with a further 197 primary care research GP practices with follow-up scheduled to finish on 31st January 2017. The primary outcome is the time to first asthma exacerbation, requiring the use of oral steroids, or an unscheduled healthcare consultation for asthma.

**Contact:** Beki Haydock  
**Funding:** NIHR Health Technology Assessment  
**Status:** Follow Up  
**Publications:** 2016-11

## 2.10 Skin and wound healing

### LeucoPatch® in the management of hard to heal diabetic foot ulcers

**Chief Investigators:** UK - **Frances Game**, Derby Teaching Hospitals NHS Foundation Trust;  
Sweden - **Magnus Löndahl**, Skane University Hospital;  
Denmark - **Lise Tarnow**, Nordsjaellands Hospital

Diabetic foot ulcer is a common and severe complication of diabetes mellitus and despite improved outcomes remains the dominating reason for non-traumatic leg amputations in most western countries. LeucoPatch® is produced from the patient's own venous blood by centrifugation, the final product comprising of a thin circular plug composed predominantly of fibrin with living platelets and leucocytes. The number of plugs used is determined by the size of the individual wound.

This trial sets out to demonstrate whether the application of LeucoPatch® used in conjunction with usual care is superior to usual care alone. The primary outcome will be percentage of ulcers healed within 20 weeks. The required sample size is 269 participants. The study opened to recruitment in August 2013, and is expected to continue until May 2017. Recruitment is at 35 sites in the UK, Sweden and Denmark.

**Contact:** Eleanor Harrison  
**Funding:** Reapplix  
**Status:** Recruiting

### Bullous pemphigoid steroids and tetracyclines study (BLISTER)

**Chief Investigator:** Hywel Williams, University of Nottingham

Bullous pemphigoid is an autoimmune skin disorder characterised by large blisters, which can cause considerable pain and distress. It may be acute or chronic, and is most common in people over 70 years of age.

This study is comparing the antibiotic doxycycline (a tetracycline) with prednisolone (a corticosteroid) for treatment of bullous pemphigoid. Both drugs are given as a single daily oral dose. The primary outcomes are blister control at six weeks, and severe or life threatening events at one year. The trial recruited from 57 sites, 50 in the UK and 7 in Germany. Recruitment closed having reached target accrual of 256 patients in September 2013.

**Contact:** Beki Haydock  
**Funding:** NIHR Health Technology Assessment  
**Status:** Submitted for publication  
**Publications:** 2012-7

### Fibreglass casts in the management of ulcers of the heel in diabetes (HEELS)

**Chief Investigator:** William Jeffcoate, Nottingham University Hospitals NHS Trust

Up to 15% of people with diabetes develop chronic ulceration of their foot, and this is most common among the elderly. Two-thirds of foot ulcers heal within 12 months, but of these 40% will recur within 12 months. Lightweight fibreglass heel casts are used for heel ulcers in the belief that they improve healing and reduce pain and discomfort. These casts take 15 minutes to mould to the heel, are applied over the primary wound dressing, and held in place with an outer dressing. They can be worn inside shoes, and need to be replaced on average every three weeks.

This trial is comparing usual care plus fibreglass heel casts with usual care alone for the management of ulcers of the heel in diabetes. The primary outcome is ulcer healing at 24 weeks. Recruitment closed in September 2014 having reached target accrual of 509 participants.

**Contact:** Lucy Bradshaw  
**Funding:** NIHR Health Technology Assessment  
**Status:** Submitted for publication  
**Publications:** 2012-14; 2014-6

## 2.10 Skin and wound healing *Cont*

### Randomised controlled trial of silk therapeutic clothing for the long-term management of eczema in children (CLOTHES)

Chief Investigator: **Kim Thomas**, The University of Nottingham

Eczema is a chronic, inflammatory skin condition that impacts on the quality of life of patients and their families. Some types of clothing can cause irritation to the skin, and current guidelines recommend the use of loose cotton clothing, and the avoidance of wool and other rough fibres next to the skin. In response to this need, new clothing products have become available in recent years, and these are now marketed as having beneficial effects in the treatment of eczema.

The therapeutic silk garments included in this trial are available on prescription through the NHS, but the trial evidence supporting their use is currently limited. The trial objectives are to: 1) assess whether silk therapeutic clothing, when used in addition to standard eczema care, reduces eczema severity in children over a period of six months, 2) estimate the within trial cost-effectiveness of silk therapeutic clothing with standard care, compared to standard care alone, from an NHS and a family perspective. The primary outcome is eczema severity, as assessed by research nurses who are blinded to participant group allocation.

Recruitment took place from November 2013 to May 2015. 300 children with moderate to severe eczema were recruited from five sites, and follow-up was completed in December 2015.

**Contact:** Eleanor Harrison  
**Funding:** NIHR Health Technology Assessment  
**Status:** Submitted for publication  
**Publications:** 2015-14

### Barrier Enhancement for Eczema Prevention (BEEP)

Chief Investigator: **Hywel Williams**, The University of Nottingham

Eczema is a common skin problem affecting 16% to 30% of children in the UK, and around 20% worldwide. The onset of eczema usually occurs in infancy, and generally dry skin is one of the first abnormalities in babies who eventually develop the condition. It is thought that skin barrier dysfunction (dry skin and increased trans-epidermal water loss) could be a primary event in the development of eczema and atopy. Emollient therapy has been shown to improve skin barrier function by providing lipids to the stratum corneum (the outermost layer of skin), in turn improving skin hydration by trapping in water. Early and regular use of emollient could lead to a potential improvement in skin barrier function.

The primary objective of this trial is to determine whether advising parents to apply emollient to their child's skin daily for the first year of life, in addition to best practice infant skin care advice, can prevent or delay the onset of eczema in high-risk children, when compared with a control group who are given the best practice infant skin care advice only. Recruitment began in November 2014 and finished on 19th November 2016 with a total of 1395 participants randomised.

**Contact:** Rachel Haines  
**Funding:** NIHR Health Technology Assessment  
**Status:** Follow up

## 2.10 Skin and wound healing *Cont*

### Home Interventions and Light Therapy for the Treatment of Vitiligo (HI-Light)

Chief Investigator: **Jonathan Batchelor**, Derby Hospitals NHS Foundation Trust and The University of Nottingham

Vitiligo causes loss of pigment on the skin and white patches appear in the affected areas. This condition affects around 1% of the population worldwide, and patients with vitiligo can experience problems such as shame, depression, and low self-esteem due to the appearance of their skin. There is no cure for vitiligo, as the cause of the condition is not understood. Treatment options for small areas of vitiligo are limited; small patches are sometimes treated with topical corticosteroid ointments. Narrowband Ultraviolet B light therapy (NB-UVB) may also be offered as a treatment, but it involves frequent visits to hospital and is mainly used for widespread vitiligo. Hand-held NB-UVB light units are available to use in the home on small patches of vitiligo, though these are not available on the NHS. Previous vitiligo research suggests that combination therapies (topical steroid and light therapy) may prove more effective in the treatment of the condition than either therapy alone, though the efficacy of these combined treatments has yet to be established.

The objective of this trial is to provide information on the comparative effectiveness and safety of topical corticosteroids (mometasone furoate 0.1% ointment) versus (i) home-based NB-UVB light, and (ii) the combination of topical corticosteroids and home-based NB-UVB light for early and limited vitiligo in adults and children. The trial aims to recruit 440 adults and children over the age of 5 across the UK who have non-segmental vitiligo, and at least one patch of vitiligo which has shown to be active in the past 12 months. Participants will be asked to treat their vitiligo patches with ointment and a light therapy unit at home, for a period of 9 months. Recruitment began in May 2015 and is planned to close at the end of February 2017.

**Contact:** Garry Meakin  
**Funding:** NIHR Health Technology Assessment  
**Status:** Recruiting  
**Publications:** 2016-2

## 2.11 Stroke

### Visual Cue Training to improve walking and turning after stroke: a pilot study (VCT trial)

Chief Investigator: **Kristen Holland**, University of Salford

Following stroke, a major goal of rehabilitation is retraining in walking. Even if the ability to walk is regained, problems with slow speed and lack of balance are common. Up to half of stroke survivors discharged into the community will fall, and a large proportion of these falls occur during walking and turning. Given the importance of vision in the control of walking and evidence indicating varied practice of walking improves mobility outcomes, this study aims to examine the feasibility and preliminary efficacy of varied walking practice in response to visual cues, for the rehabilitation of walking following stroke.

This three arm pilot trial is comparing (i) visual cue training plus standard rehabilitation with walking and turning practice; (ii) treadmill based visual cue training; and (iii) standard rehabilitation alone. The sample size was 60 participants. Fifty six participants took part, and thirty four completed treatment and follow-up assessments. Adherence to the treatments was good with 16 treatments being provided over a median of 8.4, 7.5 and 9 weeks for T-VCT, O-VCT, and UC respectively. No adverse events were reported. Post treatment improvements in walking speed, symmetry, balance and functional mobility were seen in all treatment arms.

**Contact:** Diane Whitham  
**Funding:** NIHR Research for Patient Benefit  
**Status:** Published  
**Publications:** 2013-35; 2015-55

## 2.12 Trials Co-ordinated by the Nottingham Stroke Trials Unit *Nottingham Clinical Trials Unit collaborates with the Nottingham Stroke Trials Unit, led by Philip Bath, on several large multicentre trials.*

### Safety and efficacy of intensive versus guideline antiplatelet therapy in high-risk patients with recent ischaemic stroke or transient ischaemic attack: a randomised trial (TARDIS)

Chief Investigator: **Philip Bath**, The University of Nottingham

The highest risk time for recurrence is immediately after stroke or transient ischaemic attack. Existing prevention strategies (such as antithrombotic drugs, lowering lipids or blood pressure lowering, and carotid endarterectomy) reduce, but do not abolish, further events. Dual antiplatelet therapy is superior to aspirin monotherapy. Triple antiplatelet therapy has already been shown to improve outcome for patients with coronary disease.

This international trial compares triple therapy (aspirin, dipyridamole and clopidogrel) with guideline antiplatelet therapy (combined aspirin and dipyridamole or clopidogrel) given for one month. Target sample size is 4,100 patients. The primary outcome is stroke severity at 90 days assessed using the modified Rankin Scale.

**Contact:** Lelia Duley  
**Funding:** British Heart Foundation and NIHR Health Technology Assessment  
**Status:** Recruitment stopped, currently in closedown  
**Publications:** 2015-42; 2016-13

### Tranexamic acid for hyperacute primary IntraCerebral Haemorrhage (TICH 2)

Chief Investigator: **Nikola Sprigg**, The University of Nottingham

There is currently no effective treatment for stroke associated with intracerebral haemorrhage. Tranexamic acid is an antifibrinolytic drug, which reduces mortality in trauma patients who are bleeding, and is most effective if given early.

This trial is comparing intravenous tranexamic acid with placebo for patients who are within eight hours of acute primary intracerebral haemorrhagic stroke. Estimated sample size is 2,000 participants. Recruitment opened in March 2013.

**Contact:** Lelia Duley  
**Funding:** NIHR Health Technology Assessment programme  
**Status:** Recruiting  
**Publications:** 2016-5

### Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial-2 (RIGHT-2)

Chief Investigator: **Philip Bath**, The University of Nottingham

This trial is assessing the safety and efficacy of transdermal glyceryl trinitrate, a nitric oxide donor, and of the feasibility of a multicentre ambulance-based stroke trial. Total sample size is 850 participants. Recruitment opened in September 2015. The primary outcome is death/dependence/independence: 7-level modified Rankin Scale (mRS) 90 days after stroke.

**Contact:** Alan Montgomery  
**Funding:** British Heart Foundation  
**Status:** Recruiting



# 3 SYSTEMATIC REVIEWS

## 3.1

### Contribution to the Cochrane Pregnancy and Childbirth Group

The Cochrane Pregnancy and Childbirth Group was the first review group within the Cochrane Collaboration, and remains the largest with over 600 published reviews and protocols. The unit contributes to this group as Editor (Lelia Duley), and Review Author (Lelia Duley, Jim Thornton) for over 30 reviews. The topics covered by these Cochrane Reviews include prevention and treatment of hypertensive disorders of pregnancy, care during childbirth, and diagnosis of gestational diabetes.

**Contact:** Lelia Duley  
**Status:** Ongoing  
**Publications:** 2009-8; 2011-4; 2011-8; 2012-2; 2012-5; 2012-6; 2012-12; 2012-16; 2013-3; 2013-4; 2013-8; 2013-9; 2013-15; 2014-13; 2014-31; 2014-32; 2015-3; 2015-38; 2015-46

## 3.2

### Ethics issues in recruitment of sick and preterm infants to randomised trials

Recruitment of preterm or sick infants to trials requires approaching parents at a particularly difficult time, often with a tight timescale for making a decision. This raises challenges for obtaining informed consent to such research, especially issues regarding competence, understanding, time and voluntariness for parents reaching a decision. On the other hand if the problem of consent is not successfully addressed, this risks becoming an 'orphan' area of research. Following a systematic search, this review will produce a narrative review of the ethical issues. The review is relatively novel, combining approaches across the disciplinary divide between philosophy and social science. The aim is to identify the ethical challenges and potential solutions, in order to inform the design and conduct of future trials. The project is led by Chris Megone (University of Leeds).

**Contact:** Lelia Duley  
**Funding:** NIHR Programme Grants for Applied Research  
**Status:** Analysis and reporting  
**Publications:** 2014-30; 2015-40; 2016-9

### 3.3

## Prospective meta-analysis of alternative strategies for placental transfusion at very preterm birth

Internationally, the meta-register of controlled trials lists a growing number of planned or ongoing trials of timing of cord clamping that include preterm births. This project has formed a collaborative group of these trialists, which has developed and agreed the protocol for a prospective meta-analysis. The review has been registered with Prospero (CRD42013004405) the international prospective register of systematic reviews (see <http://www.crd.york.ac.uk/prospero/>). As the trials scheduled to be part of this meta-analysis are due to be completed at different times, the analysis plan will include at least two cycles of analysis. The first collaborators' meeting for trialists took place in April 2015. The project is in collaboration with Lisa Askie, William Tarnow-Mordi and John Simes, at the University of Sydney.

**Contact:** Lelia Duley  
**Funding:** NIHR Programme Grants for Applied Research  
**Status:** Set up

# 4 IMPROVING THE QUALITY AND EFFICIENCY OF TRIALS

## 4.1

### Site identification and selection

Careful site selection methods and tools, such as questionnaires, have evolved to become “best” practice in the commercial and non-commercial clinical trials setting. However, there is little evidence of the value of such strategies, and there is no generally accepted model or tool to use when identifying potential sites and deciding which to include in a trial.

The Nottingham Clinical Trials Unit developed a simple template site selection questionnaire in 2010. This includes both generic questions about research experience and capacity and study specific questions based on requirements of the trial protocol. These questionnaires were piloted in five multi-centre trials in the UK. This study aimed to evaluate the performance of an SSQ developed by the Nottingham Clinical trials Unit (NCTU), using data on key metrics collected from five randomised controlled trials. Data analysis to comparing the average number of days taken to recruit the first participant and follow-up data on the % average monthly recruitment ratio (actual/target) has been performed and submitted for publication.

We have also conducted a survey of Chief Investigators for trials funded by the National Institute for Health Research, and of UK Trial Managers’ Network members, to describe strategies in current use for identifying and selecting trial sites for randomised trials.

**Contact:** Diane Whitham  
**Status:** Analysis and reporting  
**Publications:** 2013-16; 2015- 54; 2015-56

## 4.2

### Performance Metrics

There are numerous variables we can measure in trial management to assess site performance. However, key performance metrics should provide meaningful information that can be compared within and between sites. A standardised set of clear and easily accessible data summaries would allow the timely identification and resolution of potential problems, so minimising their impact and improving the efficient delivery of the trial.

The aim of the project is to improve the conduct and efficiency of trials by agreeing a standardised set of performance metrics for the monitoring and reporting of site performance in multicentre trials, and developing a standardised tool for presenting these metrics to trial managers, Trial Management Groups (TMG) and Trial Steering Committees (TSC). This will be achieved through a mixed method approach to develop the key performance metrics, benchmark indicators that will trigger action, and standardised reporting for monitoring site performance in ongoing trials. A Delphi survey will be conducted to determine key performance metrics, informed by focus groups of stakeholders and literature searching. The final key metrics will be agreed at a consensus workshop.

**Contact:** Diane Whitham  
**Funding:** NIHR CTU Support Funding Call for Efficient and Innovative Methodology  
**Status:** Set-up

## 4.3

### Recruitment and retention

We are conducting a number of SWATs (Studies Within a Trial) to investigate methods to improve trial recruitment and retention. These include two embedded randomised trials of multi-media website interventions to enhance recruitment into the seAFood and HiLight trials. These studies are both part of the MRC-funded Systematic Techniques for Assisting Recruitment to trials (START) study.

A further study embedded in the BEEP trial is evaluating two interventions to enhance retention of participants and collection of outcome data at follow up. This study has a factorial design, and assesses the effects of SMS notification before sending questionnaires and of timing of a voucher payment.

**Contact:** Alan Montgomery  
**Status:** Ongoing

## 4.4

### Adjudication in clinical trials

#### Adjudication in stroke trials

Central adjudication in clinical trials involves the review of trial data by independent assessors in order to standardise outcome assessment and reduce bias. Adjudication may be conducted by one individual or a panel of experts, usually blinded to treatment allocation whenever possible. However, this procedure can be time consuming and expensive, and may or may not alter the classification of site-reported events. Currently there is a lack of evidence to guide when an adjudication committee should be used in a clinical trial.

Working in collaboration with the Stroke Trials Unit, we conducted secondary analyses of a large stroke trial to investigate the impact that adjudication of stroke type, and adjudication of serious adverse events, had on the trial results. We submitted an application for an NIHR Doctoral Fellowship with three components; (1) A systematic review, (2) A cost-effectiveness analysis and (3) A statistical simulation study. The fellowship is intended to address the question: What are the costs and benefits of adjudicating outcomes in stroke trials? This application was successful and a systematic review investigating how adjudication impacts on the trial results of stroke trials is underway.

**Contact:** Pete Godolphin  
**Funding:** NIHR Research Methods Fellowship  
**Status:** Ongoing

#### Adjudication of neonatal cranial ultrasound scans

There is substantial variation between individuals in reporting the findings of cranial ultrasound scans. This could have important implications for clinical trials that use diagnoses assessed by cranial ultrasound as an outcome measure. Trials of timing of cord clamping at very preterm birth have suggested there may be an effect on intraventricular haemorrhage, which in these trials was a diagnosis based on cranial ultrasound scan. However, these trials have not reported clearly how the ultrasound data were collected and assessed. Often a mix of people will conduct and report the scans, and both the quality of the scans and their interpretation is variable in clinical practice.

This study aimed to provide standardised, independent adjudication of the cranial ultrasound scans for babies recruited to the Cord Pilot Trial, and to allow assessment of the intra- and inter-observer reliability of the scan interpretation.

**Contact:** Lucy Bradshaw  
**Funding:** NIHR Programme Grants for Applied Research  
**Status:** Analysis and reporting

# 5 OTHER RESEARCH

## 5.1

### Improving quality of care and outcome at very preterm birth

Chief Investigator: **Lelia Duley**, The University of Nottingham

This five-year programme includes five work packages, with 10 projects. These projects include a James Lind Alliance Priority Setting Partnership for Preterm Birth, qualitative work exploring the experiences of parents at the time of preterm birth, developing and evaluating a new trolley to support providing initial neonatal care at the bedside, a systematic review of ethics issues in recruitment of preterm and sick infants to randomised trials, the Cord Pilot Trial, and a prospective meta-analysis.

The programme was developed by, and is being conducted by, partners from a wide range of institutions, including: Jane Abbott and Zoe Chilvers (Bliss); Susan Ayers (University of Sussex); Jon Dorling and Jim Thornton (University of Nottingham); David Field (University of Leicester); Gill Gyte (National Childbirth Trust); William McGuire (University of York); Chris Megone (University of Leeds); Sam Oddie (Bradford Teaching Hospitals NHS Foundation Trust); Sandy Oliver (Institute of Education, University of London); John Simes (University of Sydney); Andrew Weeks (University of Liverpool); and Bill Yoxall (Liverpool Women's Hospital NHS Trust).

**Contact:** Lelia Duley  
**Funding:** NIHR Programme Grants for Applied Research  
**Status:** Ongoing  
**Publications:** 2012-12; 2013-1; 2013-7; 2013-8; 2013-9; 2013-10; 2013-11; 2013-12; 2014-17; 2014-21; 2014-22; 2014-29; 2014-30; 2015-12; 2015-13; 2015-17; 2015-31; 2015-40; 2015-43

## 5.2

### Journeying through Dementia (JtD)

Chief Investigator: **Gail Mountain**, Bradford University

Dementia is a national priority; approximately 820,000 people in the UK have a diagnosis. Approx. two thirds of people with dementia live in the community, with half of these requiring some form of support to maintain independent living. There is a growing body of evidence to demonstrate how individuals with dementia can be supported to use self-management based techniques (sometimes in combination with other interventions such as occupational therapy).

Journeying through Dementia (JtD) is a pragmatic, two-arm, parallel group, individually randomised controlled trial, intended to determine the benefit of an occupational therapy based self-management intervention compared to usual care for people in the early stages of dementia. This intervention has been designed to improve the quality of life for people in the early stages of dementia by promoting self-efficacy and assisting them to continue to participate in life and maintain their independence. The content of the intervention was developed in consultation with people with dementia. The primary outcome measure is the DEMQOL at 8 months post randomisation. Estimated sample size is 486 participants.

**Contact:** Kirsty Sprange  
**Funding:** NIHR Health Technology Assessment  
**Status:** Recruitment

# 6 RECENT PUBLICATIONS

## The Unit's full publication list is available at:

<http://www.nottingham.ac.uk/nctu/publications/publications.aspx>

2016-16: Thomas KS, Batchelor JM, Bath-Hextall F, Chalmers JR, Clarke T, Crowe S, Delamere FM, Eleftheriadou V, Evans N, Firkins L, Greenlaw N, Lansbury L, Lawton S, Layfield C, Leonardi-Bee J, **Mitchell E**, Nankervis H, Norrie J, Nunn A, Ormerod AD, Patel R, Perkins W, Ravenscroft JC, Schmitt J, Simpson E, Whitton ME, Williams HC. A programme of research to set priorities and reduce uncertainties for the prevention and treatment of skin disease. Programme Grants for Applied Research 4 (18) doi:10.3310/pgfar04180.

2016-15: Lincoln NB, das Nair R, **Bradshaw L**, Constantinescu CS, Drummond AER, **Erven A**, **Evans AL**, Fitzsimmons D, **Montgomery A**, Morgan M. Cognitive Rehabilitation for Attention and Memory in people with Multiple Sclerosis: study protocol for a randomised controlled trial (CRAMMS) *Trials* 16:556 doi: 10.1186/s13063-015-1016-3.

2016-14: **Brittain C**, **Childs M**, **Duley L**, Harding J, **Hepburn T**, **Meakin G**, **Montgomery A**, **Tan W**, Ross JDC. Gentamicin versus ceftriaxone for the treatment of gonorrhoea (G-TOG trial): study protocol for a randomised trial. *Trials* doi: 10.1186/s13063-016-1683-8.

2016-13: Bath P, Appleton JP, Beridze M, Christensen H, Dineen RA, **Duley L**, England TJ, Hepinstall S, James M, Krishnan K, Markus HS, Pocock S, Ranta A, Robinson TG, Flaherty K, Scutt P, Venables GS, Woodhouse LJ, Sprigg N. Baseline characteristics of the 3096 patients recruited into the 'Triple Antiplatelets for Reducing Dependency after Ischemic Stroke' trial. *International Journal of Stroke* doi:10.1177/1747493016677988.

2016-12: Wilkes S, Williams H, Ormerod A, Craig F, Greenlaw N, Norrie J, **Mitchell E**, Mason J, Thomas K, on behalf of the United Kingdom Dermatology Clinical Trials Network STOP GAP team. Is speed of healing a good predictor of eventual healing of pyoderma gangrenosum? *Journal of the American Academy of Dermatology* doi:10.1016/j.jaad.2016.07.049.

2016-11: **Skeggs A**, McKeever TM, **Duley L**, **Mitchell E**, **Bradshaw L**, Mortimer K, Walker S, Parrot S, Wilson A, Pavord I, Brightling C, Thomas M, Price D, Devereux G, Higgins B, Harrison T, **Haydock R**. FourFold Asthma Study (FAST): a study protocol for a randomised controlled trial evaluating the clinical cost-effectiveness of temporarily quadrupling the dose of inhaled steroid to prevent asthma exacerbations. *Trials* doi:10.1186/s13063-016-1608-6.

2016-10: Sahota O, Pulikottil-Jacob R, Marshall F, **Montgomery A**, Tan W, Sach T, Logan P, Kendrick D, Watson A, Walker M, Waring J. The Community In-reach Rehabilitation and Care Transition (CIRACT) clinical and cost-effectiveness randomisation controlled trial in older people admitted to hospital as an acute medical emergency. *Age and Ageing* doi: 10.1093/ageing/afw149.

2016-9: Megone C, Wilman E, Oliver S, **Duley L**, Gyte G, Wright J. The ethical issues regarding consent to clinical trials with pre-term or sick neonates: a systematic review (framework synthesis) of the analytical (theoretical/philosophical) research. *Trials* 17:443 doi:10.1186/s13063-016-1562-3.

2016-8: Thomas KS, Ormerod AD, Craig FE, Greenlaw N, Norrie J, **Mitchell E**, Mason JM, Johnston GA, Wahie S, Williams HC, on behalf of the UK Dermatology Clinical Trials Network's STOP GAP Team. Clinical outcomes and response of patients applying topical therapy for pyoderma gangrenosum: A prospective cohort study. *American Academy of Dermatology* doi:10.1016/j.jaad.2016.06.016.

2016-7: McMurrin M, Crawford MJ, Reily J, Delport J, McCrone P, **Whitham D**, **Tan W**, Duggan C, **Montgomery A**, Williams HC, Adams CE, Jin H, Lewis M, **Day F**. Psychoeducation with problem-solving (PEPS) therapy for adults with personality disorder: a pragmatic randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of a manualised intervention to improve social functioning. *Health Technol Assess* 20 (52) doi:10.3310/hta20520.

2016-6: Walker KF, Bugg GJ, Macpherson M, McCormick C, Grace N, Wildsmith C, **Bradshaw L**, **Smith G**, **Thornton JG** for the 35/39 Trial Group. Randomised trial of labour induction in women 35 years of age or older. *N Eng J Med* 374 813-822 doi:10.1056/NEJMoa1509117.

2016-5: Sprigg N, Robson K, Bath P, Dineen R, Roberts I, Robinson T, Roffe C, Werring D, Al-Shahi Salman R, Pocock S, **Duley L**, England T, Whyne D, Ciccone A, Laska AC, Christensen H, Ozturk S, Collins R, Bereczki D, Egea-Guerrero JJ, Law ZK, Czlonkowska A, Seffige D, Beredzie M on behalf of the TICH-2 Investigators. Intravenous tranexamic acid for hyperacute primary intracerebral haemorrhage: Protocol for a randomised, placebo controlled trial. *International Journal of Stroke*. doi: 10.1177/1747493016641960.

2016-4: Sailsbury C, O'Cathain A, Thomas C, Edwards L, Gaunt D, Dixon P, Hollinghurst S, Nicholl J, Large S, Yardley L, Fahey T, Foster A, Garner K, Horspool KA, Man MS, Rogers A, Pope K, **Montgomery A**. Telehealth for patients at high risk of cardiovascular disease: pragmatic randomised controlled trial. *BMJ* 353 doi: 10.1136/bmj.i2647.

2016-3: Sailsbury C, O'Cathain A, Edwards L, Thomas C, Gaunt D, Hollinghurst S, Nicholl J, Large S, Yardley L, Lewis G, Foster A, Garner K, Horspool KA, Man MS, Rogers A, Pope K, Dixon P, **Montgomery A**. Effectiveness of an integrated telehealth service for patients with depression: a pragmatic randomised controlled trial of a complex intervention. *Lancet Psychiatry* 3 (6) 515-525 doi: 10.1016/S2215-0366(16)00083-3.

2016-2: Batchelor JM, **Tan W**, Tour S, Yang A, **Montgomery AA**, Thomas KS. Validation of the Vitiligo Noticeability scale: a patient reported outcome measure of vitiligo treatment success. *Br J Dermatol* 174 (2) 386-394 doi:10.1111/bjd.14208.

2016-1: Edwards L, Sailsbury C, Horspool K, Foster A, Garner K, **Montgomery AA**. Increasing follow-up questionnaire response rates in a randomised controlled trial of telehealth for depression: three embedded controlled studies. *Trials* 17:107 doi:10.1186/s13063-016-1234-3.

2015-56 **Coleby D**, **Whitham D**, **Duley L**. Can site performance be predicted? Results of an evaluation of the performance of a site selection questionnaire in five multicentre trials. *Trials* 2015,16 (Suppl 2):P176.

2015-55 Hollands K, Pelton T, Wimperis A, **Whitham D**, **Tan W**, Jowett S, Sackley C, Wing A, Tyson S, Mathias J, Hensman M, M van Vliet P. Feasibility and Preliminary Efficacy of Visual Cue Training to Improve Adaptability of Walking after Stroke: Multi-Centre, Single-Blind Randomised Control Pilot Trial. *PLOS One* Oct 2015 doi. org/10.1371/journal.pone.0139261.

2015-54 **Whitham D**, **Duley L**, **Coleby D**. Site identification and selection: current practices within the trial manager's network and NIHR chief Investigators. *Trials* 2015, 16 (Suppl 2): P175.

2015-53: **Brittain C**, **Meakin G**, **Childs M**, **Duley L**, Lim WS. Conducting a randomised trial during an influenza pandemic: an example of a trial set up and 'hibernated' ready to activate and recruit within 4 weeks. *Trials* 2015, 16(Suppl 2):O14.

2015-52: Morris JM, Roberts CL, Bowen KR, Patterson JA, Bond DM, Alger CS, **Thornton JG**, Crowther C, on behalf of the PPRoMT Collaboration. The Preterm Pre-labour Rupture of the Membranes close to Term (PPRoMT) randomised trial; immediate delivery increases neonatal morbidity. *Lancet*. 2015;11 doi:10.1016/50140-6736(15)00724-2.

2015-51: Walker KW, Bugg GJ, Macpherson MBM, McCormick C, Grace N, Wildsmith C, **Bradshaw L**, **Smith GCS**, **Thornton JG** on behalf of the 35/39 trial group. A randomised trial of labour induction for women aged 35 or over. *New Engl J Med*. DOI: 10.1056/NEJM09/1509117.

2015-50: **Duley L**, Drife JO, Soe A, Weeks AD. Clamping of the umbilical cord and placental transfusion. RCOG Scientific Impact Paper No. 14. 2015. <https://www.rcog.org.uk/globalassets/documents/guidelines/scientific-impact-papers/sip-14.pdf>.

2015-49: Gureje O, Oladeji BD, Araya R, **Montgomery AA**. A cluster randomised clinical trial of a stepped care intervention in primary care (STEP CARE) – study protocol. *BMC Psychiatry* 2015; 7:148 doi:10.1186/s12888-015-0542-6.

2015-48: **Sprange K**, **Mitchell E**, **Hull M**, **Bumphrey G**. No drug, no trial? Think again! *Trials*. 2015;16(Suppl 2):P201. Doi:10.1186/1745-6215-16-S2-P201.

2015-47: **Sprange K**, Mountain G, Shortspiller K, Craig C, Blackburn D, Bowie, P, Harkness K, Spencer M. Journeying through Dementia, a community-based self-management intervention for people aged 65 years and over: a feasibility study to inform a future trial. *Pilot and Feasibility*. 2015;1(1):1-14. Doi:10.1186/s40814-015-0039-6.

2015-46: Dowswell T, Carroli G, **Duley L**, Gates S, Gulmezoglu AM, Khan-Neelofur D, Piaggio G. Alternative versus standard packages of antenatal care for low-risk pregnancy. *Cochrane Database Systematic Reviews* 2015;7:CD000934.



2015-45: Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, Stewart G, Tierney JF on behalf of the PRISMA-IPD Development Group (**Duley L, member**). Preferred reporting items for a systematic review and meta-analysis of individual participant data: The PRISMA-IPD Statement. *JAMA* 2015 313: 1657-1665. Doi:10.1001/jama.2015.3656.

2015-44: Treweek S, Altman D, Bower P, Campbell M, Chalmers I, Cotton S, Craig P, Crosby D, Davidson P, Devane D, **Duley L**, Dunn J, Elbourne D, Farrell B, Gamble C, Gillies K, Hood K, Lang T, Littleford R, Loudon K, McDonald A, McPherson A, Nelson A, Norrie J, Ramsay C, Sandercock P, Shanahan D, Summerskill W, Sydes M, Williamson P, Clarke M. Making randomised trials more efficient: report of the first meeting to discuss the Trial Forge platform. *Trials* 2015 16:261 doi:10.1186/s13063-015-0776-0.

2015-43: Sawyer A, Ayers S, Bertullies S, Thomas M, Weeks AD, Yoxall CE, **Duley L**. Providing immediate neonatal care and resuscitation at birth beside the mother: parents' views, a qualitative study. *BMJ Open*. 2015;5(9):e008495 doi:10.1136/

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## 7

# ADVISORY GROUP AND STEERING GROUP

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## 8

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<b>Sharon Ellender</b> Clinical Trials Monitor	<b>Mickey Lewis</b> Trial Coordinator	<b>Julie Turzanski</b> Research Fellow
<b>Alex Erven</b> Clinical Trials Facilitator	<b>Faye Martin</b> Secretary/Administrator	<b>Natalie Wakefield</b> Trial Administrator
<b>Amy Evans</b> Trial Manager	<b>Chien May</b> Database Systems Developer	<b>Sarah Walker</b> Data Coordinator
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<b>Steve Fowkes</b> Database Systems Developer	<b>Pat Morris</b> Trial Administrator	<b>Phillip Whitehead</b> Research Fellow
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