NOTTINGHAM CLINICAL TRIALS UNIT

NOTTINGHAM CLINICAL TRIALS UNIT

Annual Report 2018

CONTENTS

1 WELCOME

Welcome to the 2018 annual report for the Nottingham Clinical Trials Unit.

The Unit began the year by celebrating 10 years since gaining UKCRC registered status. The event, held in Nottingham's Albert Hall, also marked the retirement of Lelia Duley and Diane Whitham from the Unit. Attendees enjoyed a varied programme of talks about the Unit's research over the years. Taking time to recognise the impact that our research has on the lives of patients and carers is extremely valuable for everyone associated with the Unit.

We continue to make new appointments as part of the University's Strategic Development Fund investment in the Unit: Dr Chris Partlett as Assistant Professor of Medical Statistics and Clinical Trials from the University of Oxford, and Dr Caroline Rick as Associate Professor of Clinical Trials from Birmingham Clinical Trials Unit. Attracting experienced clinical trialists to the Unit, and developing the skills and expertise of our existing staff, is a key part of continuing to grow Nottingham's reputation as a centre of excellence in clinical trials research.

We enjoyed success with our NIHR funding applications in 2018. We have strengthened existing research relationships and formed new ones, and everyone is hugely excited at the prospect of our new trials starting in 2019. More details of all these new studies will be included in future reports, but a highlight is GBS3, a study of screening for Group B Streptococcus (GBS) in pregnancy led by Professor Jane Daniels and Dr Kate Walker. The study is unlike any other in NCTU's portfolio for a number of reasons: the sample size is 320,000 women from 80 maternity units cluster randomised to either universal testing or risk-based screening for GBS, and all outcome data will come from central NHS sources. The study presents new challenges, but trials that use data directly retrieved from electronic records offer enormous potential for efficiency and we intend to be at the forefront of developing trials using routine data.

Some of our studies have reported main results in high profile publications: RAPID in Gut and SEAFOOD in the Lancet. The FAST trial, reported in the New England Journal of Medicine, tested a temporary quadrupling of dose of inhaled glucocorticoids as part of a self-management plan for adults and adolescents with asthma. The study recruited 1922 participants, with the quadrupling group experiencing fewer severe asthma exacerbations than controls. A challenging study to complete, the high quality of the trial is testament to the hard work of the research team.

Nationally, the profile of NCTU among trial managers has risen by becoming the coordinating centre for the UK Trial Managers' Network. The UKTMN offers a forum to promote best practice in effective management and delivery of clinical trials, and is working towards providing a professional accreditation scheme for trial managers.

All of our work represents a huge collaborative effort of patients, researchers, clinicians, and methodologists working together to deliver the highest quality research. Thank you all, I hope you enjoy reading our 2018 report.

Alan Montgomery
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 or breast of 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 finished on 31 October 2016 with a total of 812 randomised participants. The primary outcome is time to treatment failure.

Contact: Beki Haydock
Funding: NHS England and Care Commissioning Groups
Status: Analysis and reporting
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 increasing evidence that this antibiotic 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 a treatment in some developing countries.

This randomised control 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 a total of 15 sexual health centres in the UK. The trial hit its recruitment target of 720 participants in November 2016. The results of the trial were accepted for publication in 2018 and are expected to be published early 2019.

Contact: Clare Brittain / Sukhy Thandi
Funding: NIHR Health Technology Assessment
Status: Awaiting publication
Publications: 2014-33; 2016-14

Metronidazole versus lactic acid for treating bacterial vaginosis (VITA)

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

Bacterial vaginosis (BV) is a common condition in women which causes a discharge from the vagina, often with an unpleasant fishy smell. The exact cause of BV is not known but it is associated with a change in the type of bacteria in the vagina; specifically a reduction in 'lactobacilli' and an increase in 'anaerobic bacteria'.

Oral metronidazole is currently recommended as first line therapy in the UK national BV treatment guidelines. However, BV comes back again in about a third of women, who then require repeated courses of this antibiotic treatment.

The objective of this randomised control trial is to determine if lactic acid gel (a non-antibiotic treatment) is better than metronidazole for the symptomatic resolution of recurrent bacterial vaginosis.

The VITA study opened to recruitment in October 2017 and is now recruiting participants from 16 sexual health centres across the UK. A further 9 centres are due to open to recruitment by the end of January 2019.

The study aims to recruit 1900 women with recurrent BV. To-date, 330 participants have been randomised.

Contact: Sukhy Thandi / Clare Brittain
Funding: NIHR Health Technology Assessment
Status: Recruiting

2.4 Mental health

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 stabilizers 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.

This trial investigated the effect of adding lamotrigine or placebo to usual care for people with borderline personality disorder on their mental health, social functioning, and quality of life. The study also assessed the effect on suicidal behaviour, prescribing of anti-psychotic and other psychotropic medication, and side effects of lamotrigine. Results indicate no evidence of any differences between lamotrigine and placebo on the primary or any secondary outcomes.

Contact: Alan Montgomery
Funding: NIHR Health Technology Assessment
Status: Published
Publications: 2015-16, 2017-27; 2018-10

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
Publication: 2015-57

A stepped care intervention for depression in primary care (STEPCARE trial)

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

Depression constitutes a significant public health burden and is associated with 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 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

Promoting Independence in Dementia (PRIDE): A Feasibility Randomised Controlled Trial

Chief Investigator: **Martin Orrell**, University of Nottingham

Dementia is a national priority in the UK. Over 800,000 older people in the UK have dementia which can lead to social exclusion, loss of identity and loss of independence due to deterioration in cognition and activities of daily living, the double stigma of age and dementia and the reduced capacity for social participation.

The PRIDE Programme aims to promote independence for people with dementia by investigating how social and lifestyle changes may reduce risk of dementia, and understanding the social impact of dementia, in order to develop and evaluate an effective social intervention to enhance independence and quality of life for people with mild dementia and the friends and family that support them. The present study is a feasibility randomised controlled trial (RCT) of the PRIDE social intervention for living well with dementia to determine the feasibility and inform the design of a large multi-centre randomised control trial.

The trial is recruiting in 6 sites and target is to recruit 75-80 participants by the end of June 2019.

Contact: Aisha Shafayat
Funding: ESRC and NIHR programme
Status: Recruiting

STAndardised DIagnostic Assessment for children and adolescents with emotional difficulties (STADIA): a multi-centre randomised controlled trial

Chief Investigator: **Kapil Sayal**, University of Nottingham

This research focuses on children and adolescents with significant levels of emotional difficulties (such as anxiety or depression) who have been referred to Child and Adolescent Mental Health Services (CAMHS) for specialist help. The trial will investigate whether the use of a standardised diagnostic assessment (SDA) tool helps with the assessment and diagnosis process in CAMHS. The effectiveness and cost-effective of this approach will be evaluated. Specifically, the research will explore whether the SDA tool makes a difference to rates of diagnosis and whether this better helps children and their family access appropriate treatment. Follow-up will continue for 12 months to assess the impact on the children's emotional difficulties, day-to-day functioning and quality of life.

Recruitment is due to commence in May 2019.

Contact: Florence Day
Funding: NIHR HTA programme
Status: Set-Up

2.5 Musculoskeletal

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

Chief Investigator: **Michael Doherty**, 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 investigated whether, for patients with untreated or under-treated gout, nurse led care is effective and cost-effective compared with usual general practitioner-led care. 517 participants were recruited. More patients receiving nurse-led care had serum uric acid within the therapeutic range (<360 µmol/L) at two years than those receiving usual care.

Contact: Lelia Duley
Funding: Arthritis Research UK
Status: Published
Publications: 2018-18

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 aimed 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 was completed in July 2017.

Contact: Eleanor Harrison
Funding: NIHR Research for Patient Benefit
Status: Reporting
Publications: 2017-24

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 assessed 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 into the trial. The trial completed in June 2017. The primary outcome is recurrent polyp/s at surveillance colonoscopy. The seAFOod Polyp Prevention Trial found no evidence of an effect of either eicosapentaenoic acid (fish oil) or aspirin on polyps at 12 month surveillance colonoscopy in patients deemed 'high risk' in the NHS Bowel Cancer Screening Programme.

Contact: Kirsty Sprange/Aisha Shafayat
Funding: NIHR Efficacy and Mechanism Evaluation
Status: Published
Publications: 2013-6, 2015-48, 2018-19

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

Chief Investigator: **Robin Spiller**, 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 compared rifaximin with placebo to reduce relapse for people who had successful treatment of clostridium difficile. 151 participants were recruited between January 2013 and March 2016. The primary outcome is relapse within 12 weeks. Recurrence within 12 weeks was 30% (18/61) among participants allocated to placebo compared with 16% (11/69) among those allocated to rifaximin, a difference of 14% (95% CI −28% to 1%).

Contact: Alan Montgomery
Funding: NIHR Research for Patient Benefit
Status: Published
Publications: 2018-16

2.7 Pregnancy and childbirth

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

Chief Investigator: **Lelia Duley**, 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 was at one year, and for children at age two years (corrected for gestation at birth) and all follow-up was completed by August 2017. Results showed that a large trial on timing of cord clamping in very preterm is feasible. The results also indicated that delaying cord clamping may possibly help more babies to survive, but the findings are uncertain and can only be confirmed with data from a much larger trial.

Contact: Lindsay Armstrong-Buisseret
Funding: NIHR Programme Grants for Applied Research
Status: Main results published, follow-up ongoing
Publications: 2011-3; 2012-12; 2013-13; 2013-14; 2014-13; 2014-17; 2015-13; 2015-17; 2015-31; 2015-43; 2015-50; 2017-10; 2017-16; 2017-19

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**, 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 in not clamped immediately. Finally, potential barriers to recruitment in a randomised trial are being explored in a qualitative study in Uganda.

Contact: Eleanor Mitchell
Funding: MRC/DFID/Welcome 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. Other neonatal outcomes include small for gestational age, length of stay in hospital, duration of respiratory support and number of dependency days on the neonatal unit.

Over a period of approximately 9 months, 216 participants were recruited in total at 8 sites and follow-up of those participants is continuing.

Contact: Lindsay Armstrong-Buisseret
Funding: NIHR Clinician Scientist Fellowship
Status: Recruitment closed, trial in follow-up
Publications: 2015-38; 2018-17

2.8 Rehabilitation

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

Chief Investigator: **Roshan das Nair**, University of Nottingham

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 evaluated a group memory rehabilitation programme for adults, including military personnel, who have had a traumatic brain injury. The study compared group based memory rehabilitation plus usual care with usual care alone and recruited 328 participants. The primary outcome is an assessment of memory at six months. Follow-up was completed in December 2016 and the final report is currently in press.

Contact: Florence Day
Funding: NIHR Health Technology Assessment
Status: Main report in press
Publications: 2015-2

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

Chief Investigator: **Nadina Lincoln**, 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. Recruitment completed on time in March 2017 with a total of 449 randomised participants. Follow-up was completed in March 2018 and the final report is currently in press.

Contact: Florence Day
Funding: NIHR Health Technology Assessment
Status: Main report in press
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, 2017-18

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

Chief Investigator: **Dr Tim Harrison**, 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 compared a self-management plan which included a temporary fourfold increase in inhaled corticosteroid with the same plan without an increase in inhaled corticosteroid when the participants' asthma control deteriorates. A total of 1922 participants were recruited from 207 sites (primary and secondary care) across the UK. The trial showed that the patients in the 'fourfold' group experienced fewer severe asthma exacerbations than patients following a self-management plan only.

Contact: Beki Haydock
Funding: NIHR Health Technology Assessment
Status: Published
Publications: 2016-11; 2018-12; 2018-20

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**, Skanes 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. Recruitment to the trial took place from August 2013 to May 2017 at sites in the UK, Sweden and Denmark. A total of 595 patients were consented, and 269 of these went on to be randomised. Participant follow-up is completed and trial has been published.

Contact: Aisha Shafayat
Funding: Reapplix
Status: Published
Publications: 2018-23

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

Chief Investigator: **Kim Thomas**, 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 at the time of commissioning the trial, the evidence supporting their use was limited. The trial objectives were to: 1) assess whether silk therapeutic clothing, when used in addition to standard eczema care, reduced 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 was eczema severity, as assessed by research nurses who were 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 centres, and follow-up was completed in December 2015. Primary analysis included 282/300 (94%) children (n = 141 in each group). There was no evidence of any difference between the groups in EASI score averaged over all follow-up visits.

Contact: Eleanor Harrison
Funding: NIHR Health Technology Assessment
Status: Published
Publications: 2015-14, 2017-8, 2017-6; 2018-1

Barrier Enhancement for Eczema Prevention (BEEP)

Chief Investigator: **Hywel Williams**, 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. A sub-study has been incorporated into the trial to explore whether the use of daily emollients may also help to prevent or reduce the severity of food allergy. The trial has successfully completed the two year follow-up period with an overall retention rate of 86.8% (1210 of 1394 recruited children). Primary outcome results will be published in 2019 and long term follow up continues until December 2021.

Contact: Rachel Haines
Funding: NIHR Health Technology Assessment
Status: Long Term Follow up
Publications: 2017-14

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

Chief Investigator: **Jonathan Batchelor**, King's College Hospital NHS Foundation Trust and 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 recruited 517 adults and children over the age of 5 between May 2015 and September 2017 across the UK with non-segmental vitiligo, with at least one patch of vitiligo which has shown to be active in the past 12 months. Participants treated their vitiligo patches with ointment and a light therapy unit at home, for a period of 9 months. Participants were then followed up by post for a period of 12 months, primarily to assess the maintenance of any treatment response.

The follow-up stage of the trial ended on 31 December 2018 and the results of the trial are now being analysed. Results will be made available to the public in Autumn 2019.

Contact: Garry Meakin
Funding: NIHR Health Technology Assessment
Status: Analysis and Reporting
Publications: 2016-2; 2018-13

2.11 Hearing

Feasibility of conducting a multi-centre randomised controlled trial to assess the effectiveness and cost-effectiveness of digital hearing aids in patients with tinnitus and hearing loss (HUSH)

Chief Investigator: **Magdalena Sereda**, National Institute for Health Research Nottingham Biomedical Research Centre

Tinnitus is a major problem affecting 10-30% of adult population. About 20% of people with tinnitus experience symptoms that negatively affect quality of life (including sleep disturbances, hearing difficulties, difficulties with concentration, social isolation and emotional difficulties including anxiety, depression, irritation or stress) and require clinical intervention. It is estimated that tinnitus prevalence in people with hearing loss is as high as 70-85%. The incidence of clinically bothersome tinnitus increases with increasing age. In the UK the most common management strategy for tinnitus is education and support combined with some form of sound therapy. Treatment is however variable between clinics. While all clinics tend to provide education and support, the additional management strategies (i.e. provision of devices) depends very much on individual clinical decisions.

Although hearing aids are prescribed primarily to overcome hearing loss, they may also be effective for tinnitus. Hearing aids can amplify environmental sounds and mask or provide distraction from tinnitus. They can reduce listening effort and improve communication which can reduce stress and anxiety, commonly associated with tinnitus.

A definitive trial comparing the outcomes and costs of digital hearing aids combined with education and support compared with education and support without hearing aid is needed. However before this can be performed a feasibility trial is needed to provide data which may inform the design and conduct of a future trial. The findings of the definitive trial will ultimately be used to facilitate evidence-based NHS commissioning, facilitate evidence-based clinical practice in audiology and support equity of care in a way that provision of hearing aids for tinnitus will be informed by high-quality research evidence.

The HUSH trial opened to recruitment in October 2018 in five trusts across England and Wales. Recruitment will run for 12 months.

Contact: Jennifer White
Funding: NIHR Research for Patient Benefit (RFPB)
Status: Recruitment

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**, 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: Alan Montgomery
Funding: British Heart Foundation and NIHR Health Technology Assessment programme
Status: Published
Publications: 2015-42; 2016-13, 2017-25, 2018-35

Tranexamic acid for hyperacute primary IntraCerebral Haemorrhage (TICH 2)

Chief Investigator: **Nikola Sprigg**, 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: Analysis and reporting
Publications: 2016-5; 2018-14

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

Chief Investigator: **Philip Bath**, 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
Publications: 2018-36

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, 2017-29

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 produced a narrative review of the ethical issues. The review was relatively novel, combining approaches across the disciplinary divide between philosophy and social science. The aim was to identify the ethical challenges and potential solutions, in order to inform the design and conduct of future trials. The project was led by Chris Megone (University of Leeds).

Contact: Lelia Duley
Funding: NIHR Programme Grants for Applied Research
Status: Published
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 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. This questionnaire was 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: Lelia Duley
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 minimizing 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 mangers, Trial Management Groups (TMG) and Trial Steering Committees (TSC). This study uses 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. Methods include focus groups of stakeholders and literature searching, a Delphi survey and a consensus meeting.

Contact: Alan Montgomery
Funding: NIHR CTU Support Funding Call for Efficient and Innovative Methodology
Status: Analysis and reporting
Publications: 2018-24; 2018-25

4.3 Recruitment and retention

We conduct SWATs (Studies Within a Trial) to investigate methods to improve trial recruitment and retention. These include embedded randomised trials of multi-media website interventions to enhance recruitment and a factorial embedded trial to evaluate two interventions to enhance retention of participants and collection of outcome data at follow up.

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 have 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. In an NIHR Doctoral Fellowship with three components; (1) A systematic review, (2) A cost-effectiveness analysis and (3) A statistical simulation study, we will address the question: What are the costs and benefits of adjudicating outcomes in stroke trials?

Contact: Pete Godolphin
Funding: NIHR Doctoral Research Fellowship
Status: Ongoing
Publications: 2018-22

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 trial 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**, 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: Analysis and reporting
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, 2016-17, 2017-10, 2017-16, 2017-19

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: Follow-up

6 RECENT PUBLICATIONS

The Unit's full publication list is available at: **nottingham.ac.uk/nctu/publications/publications.aspx**

2018-36: Bath PM, Scutt P, Appleton JP, Dixon M, Woodhouse LJ, Wardlaw JM, Sprigg N. Baseline characteristics of the 1149 patients recruited into the Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial-2 (RIGHT-2) randomised controlled trial. journals.sagepub.com/doi/10.1177/1747493018816451

2018-35: Bath PM, Woodhouse LJ, Appleton JP, Beridze M, Christensen H, Dineen RA, Flaherty K, **Duley L**, England TJ, Havard D, Heptinstall S, James M, Kasonde C, Krishnan K, Markus HS, **Montgomery AA**, Pocock S, Randall M, Ranta A, Robinson TG, Scutt P, Venables GS, Sprigg N. Triple versus guideline antiplatelet therapy to prevent recurrence after acute ischaemic stroke or transient ischaemic attack: the TARDIS RCT. journalslibrary.nihr.ac.uk/hta/hta22480#/abstract

2018-34: Wilson MJA, MacArthur C, Hewitt CA, Handley K, Gao Smith F, Beeson L, **Daniels JP**. Remifentanil intravenously administered patient-controlled analgesia (PCA) versus pethidine intramuscular injection for pain relief in labour: a randomised controlled trial. sciencedirect.com/science/article/pii/S0140673618317173?via%3Dihub

2018-33: Denny E, Weckesser A, Jones G, Bibila S, **Daniels JP**, Bhattacharya S. Women's experiences of medical treatment for endometriosis and its impact on PRE-EMPT trial participation: A qualitative study. pilotfeasibilitystudies.biomedcentral.com/articles/10.1186/s40814-018-0358-5

2018-32: Khan KS, Tryposkiadis K, Tirlapur SA, Middleton LJ, Sutton AJ, Priest L, Ball E, Balogun M, Sadhev A, Roberts T, Birch J, **Daniels JP,** Deeks JJ. MRI versus laparoscopy to diagnose the main causes of chronic pelvic pain in women: a test-accuracy study and economic evaluation. njl-admin.nihr.ac.uk/document/download/2021073

2018-31: Lissauer D, Wilson A, **Daniels JP**, Middleton L, Bishop J, Hewitt C, Merriel A, Weeks A, Mhango C, Mataya R, Taulo F, Ngalawesa T, Chirwa A, Mphasa C, Tambala T, Chiudzu G, Mwalwanda C, Mborna A, Qureshi R, Ahmed I, Gulmezoglu M, Oladopo OT, Mbaruku G, Chibwana J, Watts G, Simon B, Ditai J, Tom CO, Acam JF, Ekunait J, Uniza H, Iyaku M, Anyango M, Zamora J, Roberts T, Gorantitis I, Desmond N, Coomarasamy A. Prophylactic antibiotics to reduce pelvic infection in women having miscarriage surgery - The AIMS (Antibiotics in Miscarriage Surgery): study protocol for randomised controlled trial. trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2598-3

2018-30: Vincent K, Baranowski A, Bhattacharya S, Birch J, Cheong Y, Cregg R, **Daniels JP**, Hewitt CA, Macfarlane GJ, Middleton L, Szubert W, Tracey I, Williams ACC, Horne AW. GaPP2, a multicentre randomised controlled trial of the efficacy of gabapentin for the management of chronic pelvic pain in women: study protocol. bmjopen.bmj.com/content/bmjopen/8/1/e014924.full.pdf

2018-29: Khan KS, Moore PAS, Wilson MJ, Hooper R, Allard S, Wrench I, Beresford L, Roberts TE, McLoughlin C, Geohegan J, **Daniels JP**, Catling S, Clark VA, Ayuk P, Robson S, Gao-Smith F, Hogg M, Lanz D, Dodds J on behalf of the SALVO study group. Cell salvage during Caesarean Section: A Pragmatic Multicentre Randomised Controlled Trial (SALVO) journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002471

2018-28: Rachaneni S, Middleton L, Sajja A, Balogun M, **Daniels J**, Latthe P, Deeks J, Reproducibility of the transvaginal sonographic assessment of bladder wall thickness. sciencedirect.com/science/article/pii/S0301211517305213?via%3Dihub

2018-27: Horne AW, Vincent K, Cregg R, **Daniels JP**. Is gabapentin effective for women with unexplained chronic pelvic pain: bmj.com/content/358/bmj.j3520

2018-26: Verghese TS, Middleton LJ, **Daniels JP**, Deeks JJ, Latthe PM. The impact of urodynamics on treatment and outcomes in women with an overactive bladder: a longitudinal prospective follow-up study. link.springer.com/content/pdf/10.1007 %2Fs00192-017-3414-4.pdf

2018-25: **Walker KF, Turznski J, Whitham D, Montgomery AA, Duley L**. Monitoring performance of sites within multicentre randomised trials: a systematic review of performance metrics. ncbi.nlm.nih.gov/pmc/articles/PMC6192157/

2018-24: **Whitham D, Turzanski J, Bradshaw L**, Clarke M, Culliford L, Duley L, Shaw L, Skea Z, Treweek SP, **Walker K**, Williamson PR, **Montgomery AA**. Development of a standardised set of metrics for monitoring site performance in multicentre randomised trials: a Delphi study. ncbi.nlm.nih.gov/pmc/articles/PMC6192223/

2018-23: Game F, Jeffcoate W, Tarnow L, Jacobsen JL, **Whitham DJ, Harrison EF**, **Ellender SJ**, Fitzsimmons D, Londahl M. LeucoPatch system for the managment of hard-to-heal diabetic foot ulcers in the UK, Denmark and Sweden: an observer-masked, randomised controlled trial. sciencedirect.com/science/article/pii/S2213858718302407?via%3Dihub

2018-22: **Godolphin PJ, Hepburn T**, Sprigg N, Walker L, Berge E, Collins R, Gommans J, Ntaios G, Pocock S, Prasad K, Wardlaw JM, Bath PM, **Montgomery AA**. Central masked adjudication of stroke diagnosis at trial entry offered no advantage over diagnosis by local clinicians: Secondary analysis and simulation. sciencedirect.com/science/article/pii/S2452054818301170

2018-21: **Godolphin PJ, Montgomery AA**, Woodhouse LJ, Bereczki D, Berge E, Collins R, Diez-Tejedor E, Gommans J, Lees KR, Ozturk S, Phillips S, Pocock S, Prasad K. Central adjudication of serious adverse events did not affect trials safety results: Data from the Efficacy of Nitric Oxide in Stroke (ENOS) trial. journals.plos.org/plosone/article?id=10.1371/journal.pone.0208142

2018-20: McKeever T, Mortimer K, **Bradshaw L, Haydock R**, Pavord I, Higgins B, Walker S, Wilson A, Price D, Thomas M, Devereux G, Brightling C, Renwick C, Parrott S, **Mitchell E, Duley L**, Harrison T. Temporarily quadrupling the dose of inhaled steroid to prevent asthma exacerbations: FAST. journalslibrary.nihr.ac.uk/hta/hta22700#/abstract

2018-19: Hull MA, **Sprange KE, Hepburn T, Tan W, Shafayat A**, Rees CJ, Clifford G, Logan RF, Loadman PM, Williams EA, **Whitham D, Montgomery AA**. Eicosapentaenoic acid and aspirin, alone and in combination, for the prevention of colorectal adenomas (seAFOod Polyp Prevention trial): a multicentre, randomised, double-blind, placebo-controlled, 2 x 2 factorial trial. thelancet.com/journals/lancet/article/PIIS0140-6736(18)31775-6/fulltext

2018-18: Doherty M, Jenkins W, Richardson H, Sarmanova A, Abhishek A, Ashton D, Barclay C, Doherty S, **Duley L**, Hatton R, Rees F, Stevenson M, Zhang W. Efficacy and cost-effectiveness of nurse-led care involving education and enagagment of patients and treat-to-target urate-lowering strategy versus usual care for gout: a randomised controlled trial. thelancet.com/journals/lancet/article/PIIS0140-6736(18)32158-5/fulltext

2018-17: **Armstrong-Buisseret L, Mitchell E, Hepburn T, Duley L, Thornton JG**, Roberts TE, Storey C, Smyth R, Heazell AEP. Reduced fetal movement intervention Trial-2 (ReMIT-2): protocol for a pilot randomised controlled trial of standard care informed by the result of a placental growth factor (PlGF) blood test versus standard care alone in women presenting with reduced fetal movement at or after 36+0 weeks gestation. trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2859-1

2018-16: Major G, **Bradshaw L**, Boota N, **Sprange K**, Diggle M, **Montgomery AA**, Jawhari A, Spiller RC on behalf of RAPID Collaboration Group. Follow-on RifaAximin for the Prevention of recurrence following standard treatment for Infection with Clostridium Difficile (RAPID): a randomised placebo controlled trial. gut.bmj.com/content/gutjnl/early/2018/09/25/gutjnl-2018-316794.full.pdf

2018-15: Askie L, **Duley L**. Associations between the timing and dosing of aspirin prophlyaxis and term and preterm pre-eclampsia. ebm.bmj.com/content/early/2018/06/07/bmjebm-2018-110931.full

2018-14: Sprigg N, Flaherty K, Appleton JP, Al-Shahi Salman R, Bereczki D, Beridze M, Christensen H, Ciccone A, Collins R, Czlonkowska A, Dineen RA, **Duley L**, Egea-Guerrero JJ, England TJ, Krishnan K, Laska AC, Law ZK, Ozturk S, Pocock SJ, Roberts I, Robinson TG, Roffe C, Seiffge D, Scutt P, Thanabalan J, Werring D, Whynes D, Bath PM. Tranexamic acid for hyperacute primary IntraCerebral Haemorrhage (TICH-2): an international randomised placebo-controlled, phase 3 superiority trial. sciencedirect.com/science/article/pii/S0140673618310330X?via%3Dihub

2018-13: **Haines RH**, Thomas KS, **Montgomery AA**, Ravenscroft JC, Akram P, Chalmers JR, **Whitham D, Duley L**, Eleftheriadou V, **Meakin G, Mitchell EJ, White J**, Rogers A, Sach T, Santer M, **Tan W**, **Hepburn T**, Williams HC, Batchelor J. Home interventions and light therapy for the treatment of vitiligo (HI-Light Vitiligo Trial): study protocol for a randomised controlled trial. bmjopen.bmj.com/content/8/4/e018649

2018-12: McKeever T, Mortimer K, Wilson A, Walker S, Brightling C, Skeggs A, Pavord I, Price D, **Duley L**, Thomas M, Bradshaw L, Higgins B, **Haydock B, Mitchell E**, Devereux G, Harrison G. Quadrupling Inhaled Glucocorticoid Dose to Abort Asthma Exacerbations. nejm.org/doi/full/10.1056/NEJMoa1714257

2018-11: Coghill N, Garside L, **Montgomery AA**, Feder G, Horwood J. NHS health checks: a cross-sectional observational study on equity of uptake and outcomes. bmchealthservres.biomedcentral.com/articles/10.1186/s12913-018-3027-8

2018-10: Crawford MJ, Sanatinia R, Barrett B, Cunningham G, Dale O, Ganguli P, Lawrence-Smith G, Leeson V, Lemonsky F, Lykomitrou G, **Montgomery AA**, Morriss R, Munjiza J, Paton C, Skorodzien I, Singh V, **Tan W**, Tyrer P, Reily JG. The Clinical Effectiveness and Cost Effectiveness of Lamotrigine in Borderline Personality Disorder: A Randomized Placebo-Controlled Trial. ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2018.17091006

2018-9: Stynes S, Konstantinou K, **Ogollah R**, Hay EM, Dunn KM: Clinical diagnostic model for sciatica developed in primary care patients with low back-related leg pain: journals.plos.org/plosone/articleid=10.1371/journal.pone.0191852

2018-8: Konstantinou K, Dunn KM, **Ogollah R**, Lewis M, van der Windt D, Hay EM: Prognosis of sciatica and back-related leg pain in primary care: the ATLAS cohort. thespinejournalonline.com/article/S1529-9430(17)31148-8/

2018-7: Burroughs H, Bartlam B, Ray M, Kingstone T, Shepherd T, **Ogollah R**, et al. A feasibility study for NOn-Traditional providers to support the management of Elderly People with Anxiety and Depression: The NOTEPAD study Protocol. ncbi.nlm.nih.gov/pmc/articles/PMC5842638/

2018-6: Quicke JG, Foster NE, Croft PR, **Ogollah RO**, Holden MA. Change in physical activity level and clinical outcomes in older adults with knee pain: a secondary analysis from a randomised controlled trial. ncbi.nlm.nih.gov/pmc/articles/PMC5816451/

2018-5: Stynes S, Konstantinou K, **Ogollah RO**, Hay EM, Dunn KM. Novel approach to characterising individuals with low back-related leg pain: cluster identification with latent class analysis and 12-month follow-up. insights.ovid.com/pubmed?pmid=29319608

2018-4: **Ogollah RO**, Konstantinou K, Stynes S, Dunn KM. Determining one-year trajectories of low back related leg pain in primary care patients: growth mixture modelling of a prospective cohort study. onlinelibrary.wiley.com/doi/abs/10.1002/acr.23556

2018-3: **Duley L**, Gillman A, Duggan M, Belson S, Knox J, McDonald A, Rawcliffe C, Simon J, Sprosen T, Watson J, Wood W. What are the main inefficiencies in trial conduct: a survey of UKCRC registered clinical trials units in the UK. trialsjournal.biomedcentral.com/articles/10.1186/s13063-017-2378-5

2018-2: Chatters R, Newbould L, **Sprange K**, Hind D, Mountain G, Shortland K, Powell L, Gossage-Worrall R, Chater T, Keetharuth A, Lee E, Woods B. Recruitment of older adults to three preventative lifestyle improvement studies. trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2482-1

2018-1: Wake EV, Batchelor J, Lawton S, Thomas KS, **Harrison EF**, Cowdell FC. The views of children and young people on the use of silk garments for the treatment of eczema: a nested qualitative study within the CLOTHing for the relief of Eczema Symptoms (CLOTHES) randomized controlled trial. onlinelibrary.wiley.com/doi/10.1111/bjd.15909/abstract

7 ADVISORY GROUP AND STEERING GROUP

7.1 Advisory group

Professor Mike Clarke
(Chair) Director, All Ireland Hub for Trials Methodology Research

Professor Janet Darbyshire
Emeritus Professor of Epidemiology, University College London

Professor Philip Bath
Professor of Stroke Medicine, University of Nottingham, and Chair of NCTU Steering Group

Professor Tony Avery
Professor of Primary Health Care, University of Nottingham, and Dean of the School of Medicine

Alison McDonald
Senior Trial Manager, CHaRT at the University of Aberdeen.

Professor Peter Sandercock
Professor of Medical Neurology & Honorary Consultant Neurologist at the University of Edinburgh

Amanda Roberts
Lay PPI Representative

Barbara Preston
Lay PPI Representative

Professor Kerry Hood
Professor of Trials & Director of the UKCRC Registered Centre for Trials Research, Cardiff University

7.2 Steering group

Philip Bath
(Chair) Professor of Stroke Medicine

Maria Koufali
Managing Director, Nottingham University Hospitals NHS Trust

Sarah Armstrong
Director of Research Design Service, East Midlands

Tony Avery
Dean of the School of Medicine

Richard Deeley
Head of Commercial Finance, Faculty of Medicine and Health Sciences

Avril Drummond
Professor of Healthcare Research

Frances Game
Consultant Diabetologist and Clinical Director of R&D, Derby Teaching Hospitals NHS Foundation Trust

Jonathan Hollands
Head of Research Operations, School of Medicine

Kim Thomas
Professor of Applied Dermatology Research

Wei Shen Lim
Consultant Respiratory Medicine

David Rowbotham
Director of Clinical Research Network East Midlands

Professor Martin Orrell
Director of the Institute of Mental Health

8 STAFF LIST

Rob Allen
Trial Coordinator

Lindsay Armstrong-Buisseret
Trial Manager

Brian Barnes
Data Manager

Sarah Bellis
Unit Administrator

Melanie Boulter
Quality Assurance Manager

Lucy Bradshaw
Medical Statistician

Clare Brittain
Senior Trial Manager

Monica Crone
Data Coordinator

Charlotte Curnow
Unit Manager

Florence Day
Trial Manager

Jane Daniels
Professor of Clinical Trials

Wendy Daunt
Unit Coordinator

Gurmit Dhanjal
Trial Coordinator

Sharon Ellender
Clinical Trials Monitor

Alex Erven
Quality Assurance Officer

Lisa Evans
Data Administrator

Matthew Foster
Data Administrator

Charlotte Gidman
Data Coordinator

Pete Godolphin
Doctoral Research Fellow

Louisa Gray
Trial Coordinator

Rachel Haines
Senior Trial Manager

Ellie Harrison
Trial Manager

Beki Haydock
Trial Manager

Jessica Haywood
Data Administrator

Trish Hepburn
Senior Medical Statistician

Julie Jones
Trial Coordinator

Alexia Karantana
Clinical Associate Professor in Hand Surgery

Mickey Lewis
Trial Coordinator

Faye Martin
Unit Administrator

Chien May
Database Systems Developer

Garry Meakin
Trial Manager

Aneesa Mehmood
Trial Administrator

Sebastian Moody
Trial Administrator

Eleanor Mitchell
Assistant Professor of Clinical Trials

Alan Montgomery
Professor of Medical Statistics and Clinical Trials, and Unit Director

Reuben Ogollah
Associate Professor of Medical Statistics

Mara Ozolins
Medical Statistician

Chris Partlett
Assistant Professor of Medical Statistics and Clinical Trials

Chris Rumsey
Database Systems Developer

Shabina Sadiq
Trial Manager

Aisha Shafayat
Trial Manager

Dan Simpkins
Senior Data Manager

Kirsty Sprange
Senior Trial Manager

Richard Swinden
Trial Coordinator

Wei Tan
Medical Statistician

Stella Tarr
Data Coordinator

Sukhwinder Thandi
Trial Manager

Jim Thornton
Professor of Obstetrics and Gynaecology

Julie Turzanski
Research Fellow

Natalie Wakefield
UKTMN Manager

Kate Walker
Clinical Assistant Professor in Obstetrics and Gynaecology

John Watson
Trial Coordinator

Keith Whitaker
Database Systems Developer

Jennifer White
Trial Coordinator

Diane Whitham
Associate Professor in Clinical Trials

University of Nottingham
UK | CHINA | MALAYSIA

NOTTINGHAM CLINICAL TRIALS UNIT

Nottingham Clinical Trials Unit
Nottingham Health Science Partners
C Floor, South Block
Queen's Medical Centre
Nottingham
NG7 2UH
UK

t: +44 (0)115 823 1600
f: +44 (0)115 919 4430