

# Centre for Women's Health Research Annual Report 2015



## Neonatology



## Physiology

## Perinatal Pharmacology



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## Introduction

Professor Zarko Alfirovic



When Prof Dame Sally Davies opened our Centre in 2013, we set the bar extremely high – our mission has been to make significant contributions to women’s health globally through excellence in research and clinical care. In our efforts to meet the expectations of the University of Liverpool, Liverpool Women’s Hospital and our patients, we have worked tirelessly to generate ever more grant income, publish more papers and engage with the scientific community by speaking at international meetings. We have also endeavoured to involve public and patients in our activities to ensure maximum dissemination and impact of our achievements. All these efforts have left very little or no time to step back and take a ‘helicopter view’ of our Centre.

Towards the end of 2015 we asked, with a heavy heart, each of our research groups to provide a one page summary of their accomplishments. We knew that this was yet another thing to do in their busy academic life. Eventually, when our Tracey Ricketts expertly put all of them together, by the way none of the groups managed to stick to one page only, this fantastic document emerged. Clearly, we have every right to be very proud of it.

Personally, I wish to thank all of our staff for their hard work, commitment, enthusiasm and particularly for the smiles and laughter in our corridors. Please disseminate this report to all your friends and colleagues worldwide and let’s make sure that our 2016 report is at least as impressive as this one.

## Cochrane Pregnancy and Childbirth

Cochrane is an international, not-for-profit and independent organization dedicated to making healthcare research readily available to consumers, clinicians and policy-makers worldwide. We search for clinical trials of interventions relevant to pregnancy and childbirth and use the trial evidence to produce summaries of evidence. These summaries are high quality systematic reviews and are published monthly as part of the Cochrane Library.

Pregnancy and Childbirth was the first of one of 53 Cochrane Review Groups producing evidence for healthcare. Our group prepares and updates systematic reviews of all treatments related to pregnancy and childbirth and up to 30 days following childbirth, as well topics related to breast feeding. We also maintain an extensive database of randomised controlled trials relevant to the scope of our group.

Our editorial team manages a portfolio of around 600 Cochrane systematic reviews. We support the work of over 1200 review authors from 51 countries to keep these reviews current. It was great for us to meet up with some of our authors, referees and consumers at our contributors' meeting during the Cochrane Colloquium in Vienna during October 2015.

*PCG contributors' meeting – Vienna 2015*



During 2015 we published 107 articles (92 full reviews and 17 protocols). We now have a total of 583 full reviews and 84 protocols published in the Cochrane Library. Around a quarter of our published outputs from 2015 involved members of the Centre for Women's Health Research.

During 2015 we have worked closely with national and international guideline developers to provide good quality evidence for healthcare decision-making. Work on our NIHR Cochrane Programme Grant is going well – this project involves preparing Cochrane reviews needed to inform NICE/RCOG guidelines for breech presentation, multiple pregnancy, labour induction and diabetes in pregnancy. In November 2015 the WHO published their guideline for interventions to improve preterm birth outcomes. We prepared evidence for the scoping of this guideline and updated 21 Cochrane Pregnancy and Childbirth systematic reviews which contributed to the evidence base for the final recommendations in the guideline. We also prepared 18 reviews to inform another guideline, WHO recommendations for prevention and treatment of maternal peripartum infections, published in September 2015. Finally, we have produced a suite of 54 reviews to form the evidence base for the upcoming WHO Antenatal Care guideline, and many of our reviews are also featured in the WHO Reproductive Health Library.



## Endometrial Proliferative Disease Research Group

The overarching strategy for the endometrial research group is to develop a comprehensive, interconnected research program examining common, yet different aspects of the two endometrial proliferative diseases; endometriosis and endometrial cancer.

We have published the first papers on the role of telomerase in endometriosis and the first report on characterisation of a human endometrial epithelial progenitor population.

Furthermore, we have just published the first validated clinically applicable scoring system “Liverpool endometrial steroid quick score” to assess endometrial cancers for steroid responsiveness.

These are all significant findings in the field.

Our current work involves developing further specific projects examining the common themes to endometriosis and endometrial cancer that largely include: stem/progenitor cells, metastasis, telomerase and hormonal regulation.

### Scientific meetings

Seminar on endometrial cancer studies;  
Regional collaborative meetings (Lancaster/  
Manchester);  
March 2015  
August 2015

Endometriosis Network Meeting (Edinburgh/  
Oxford/ Birmingham)  
Sept 2015

### Other outputs

The Wellbeing of Women’s Clinical Research Training Fellowship was awarded to Dr Nicola Tempest (2015-2018) ‘Analysis of human endometrial epithelial stem cells and their niche in health and disease by lineage labelling’.

*SRI, Annual Scientific Meeting, San Francisco, USA, presidential Award 2015 to Dr Eve Bunni*



MPhil graduates 2015, University of Liverpool  
Eve Bunni  
Veda Avula

MRes graduates 2015, University of Liverpool  
Kishen Popat  
Sarah Dodd  
Pratiksha Patel  
Misha Patel  
Olayisade Ajibola-Taylor



## Posters

### SRI 2015, San Francisco

Bunni E, Kamal AM, Valentijn A, Drury J, Hapangama DK. Differences in Phenotypic Features and Hormone Responsiveness between Healthy Eutopic Endometrium and Tubal Epithelium in Women – Functional Relevance in Gynaecological Disease

Valentijn AJ, Saretzki G, Tempest N, Critchley HO, Hapangama DK. Human endometrial epithelial telomerase is important for epithelial proliferation and glandular formation with potential implications in endometriosis.

Tempest N, McGuinness N, Hapangama D. Is Manual rotation an advanced operative obstetrics delivery method with a place in contemporary practise?

### ESHRE 2015, Lisbon

Mathew D, Drury JA, Valentijn AJ, Vasieva O, Hapangama DK. In silico, in vitro and in vivo analysis identifies a potential role for steroid hormone regulation of FOXD3 in endometriosis-associated genes.

### BGCS, 2015, Newcastle

C Parkes<sup>1</sup>, A Valentijn<sup>1</sup>, R Barraclough<sup>2</sup>, D Barraclough<sup>3</sup> and D Hapangama<sup>1</sup>. A Panel of metastasis inducing proteins are differentially expressed in 3 endometrial cancer cell lines.

Avula V, Kamal A, Parikh C, DeCruze SB, Taylor S, Drury J, Hapangama DK. Endometrial epithelial expression of 3-mercaptopyruvate sulfurtransferase (3-MPST) is lost with abnormal endometrial proliferation and may play a role in endometrial carcinogenesis.

Kamal AM, Bulmer JN, DeCruze SB, Stringfellow HF, Martin-Hirsch P, Hapangama DK. Androgen receptors are acquired by healthy postmenopausal endometrial epithelium and their subsequent loss in endometrial cancer is associated with poor survival.

### ESGO, 2015, Nice

Kamal A, DeCruze SB, Stringfellow HF, Martin-Hirsch P, Hapangama DK. Up regulation of AGR2 is an early step in low grade endometrial carcinogenesis and progression.

Popat K, Kamal A, Valentijn A, Hapangama DK. Dyskerin protein expression is negatively correlated with cell proliferation in endometrioid endometrial cancer and is regulated by oestrogen.

Mathew D, Kamal A, Hapangama DK. EXPLORING THE ROLE OF AGR-2 IN ENDOMETRIAL CANCER, A BIOINFORMATICS APPROACH

Patel P, Bennett D, Drury J, DeCruze SB, Martin-Hirst P, Stringfellow H, Hapangama DK. MAP4K4: A POTENTIAL PROGNOSTIC AND THERAPUETIC MARKER FOR ENDOMETRIAL CARCINOMA

Draper H, Kamal A, Valentijn AJ, McSweeney L, DeCruze SB, Martin-Hirst P, Stringfellow H, Hapangama DK. Nuclear SOX9 is down-regulated in endometrial cancer: a potential prognostic marker.



## Global Women's Health – Sanyu Research Unit

The Sanyu Research Unit is based at the University's Department of Women's and Children's Health, and directed by Andrew Weeks, Professor of International Maternal Health. Formed in 2011, the unit is dedicated to improving maternity care worldwide, particularly in poorer settings. The unit is named after Edith Sanyu, a woman who died from obstructed labour in Uganda at the time that this unit was founded. Although not well known herself, she represents the many voiceless who suffer daily through lack of resources for maternal and child health.

Sanyu aims to generate sustainable improvements in maternal and infant health. The goal is to develop and evaluate low cost technologies for clinical care that will have a direct impact on mothers all over the world.

Professor Weeks' overseas research is centred mainly in Uganda and India. In 2013 Sanyu's African research unit was opened adjacent to Mbale Regional Referral Hospital in Mbale, Eastern Uganda. The Sanyu Africa Research Institute (SAfRI) offers expertise in undertaking clinical trials. Lead by its Executive Director, James Ditai, this Unit has delivered a number of research studies. It is currently involved in the AIMS and the Babygel studies, as well as running trials of its own and in association with research teams in Melbourne and London.

### Current Sanyu research studies

#### **Third stage of labour:**

PPH Butterfly (1<sup>st</sup> stage – development study)  
UK (£320K – National Institute of Health Research (NIHR) i4i)

PPH Butterfly (2<sup>nd</sup> stage – clinical testing study)  
UK (£850K – NIHR i4i)

#### **Induction of labour:**

INFORM (India) – Comparison of two methods of inducing labour in Nagpur, India (£611k – MRC)

#### **Public Health Obstetrics:**

AIMS– Antibiotic Use in Miscarriage Surgery (Uganda, led by University of Birmingham) (£268k – MRC)

Babygel – Use of alcohol based hand rub to prevent infection in neo-nates (Uganda) (£150k –MRC)

#### **Postgraduate Students**

The Sanyu Unit also supports three students undertaking PhDs:

- Dr Abiola Aiyenigba - “The Management of Psychological Morbidities associated with Infertility within African populations”
- Dr Achier Akol - Study on classifications of retained placenta  
Part I study: Factors and outcomes associated with various forms of retained placenta  
Part II study: A Prospective Study of the Diagnostic Role of Ultrasound amongst Women with Retained
- Mrs Angela Hancock “Exploring clinical recognition of excessive maternal blood loss following childbirth”

#### **Academic Clinical Research Fellow**

Dr Robbie Kerr – his research focuses on extending the use of the PPH Butterfly to low resource settings. He has also co-ordinated an international team of experts advising the Brighton Collaboration (an international team of researchers seeking to develop good practice in maternity vaccination trials funded by the Gates Foundation and WHO) on the definition of post-partum haemorrhage.



## Recent Awards

In September 2015 Professor Weeks lead an application into the NIHR for 3 years funding to undertake clinical testing of the PPH Butterfly.

This is a follow-on study from the initial development study of the actual device. This device will be used in the management of post-partum haemorrhage. A multi-disciplinary team from the University of Liverpool, other Universities, the NHS and Industry developed the device from conceptual idea to working prototype.

In January 2016 the NIHR notified the team of its success in this application and the Award will commence in April 2016. The device will initially be tested on women experiencing PPH in the Liverpool Women's Hospital. If shown to be effective it is hoped that it can be rolled out across the UK and globally.

The PPH Butterfly was a finalist in the UK Plastics awards and winner of the NIHR NW Coast Academic Health Science Network Innovation of the Year 2015.



Professor Andrew Weeks  
Director



Dot Lambert  
Unit Manager



Caroline Cunningham  
Research Midwife



James Ditai  
SAfRI Director

## Scientific meetings

Sanyu African Research Institute (SAfRI) – Board of Trustees Meeting, Kampala, Uganda (January 2015)

SAfRI Annual Review, Mbale, Uganda (January 2015) Keynote speaker

Academic meeting (RCOG) (January 2015) – Keynote speaker

INFORM meeting, Nagput (January 2015)

Empower Study meeting, Edinburgh (February 2015)

GLOW conference (February 2015)

BJM conference (March 2015) – Keynote speaker

Katherine Twinning Event (June 2015) – Keynote speaker

ITM Research Day (July 2015)

Cord Clamping meeting, Nottingham (September 2015)

BMJ conference, Manchester (October 2015) – Keynote speaker

FIGO, Vancouver, Canada (October 2015) – Keynote speaker

PPH meeting, Sheffield (20 November 2015) – Keynote speaker

Annual Professional Development Conference (RCOG) (November 2015) – Keynote speaker

LWH “Great Day” (18 December 2015) – Keynote speaker





## Harris-Wellbeing Preterm Birth Research Centre

The Harris-Wellbeing Preterm Birth Research Centre opened April 2015. The Centre investigates treatments using a personalised medicines approach, addressing women who have experienced or are at risk of preterm birth.

This includes developing risk assessments for early pregnancy, understanding the effectiveness of different preterm labour drugs and facilitating better and safer use of preventative therapies.

### **Workstream 1: Genomic and metabolomic approach to spontaneous preterm birth (sPTB) phenotyping**

Workstream 1 is in its recruitment phase. The original plan was to recruit 150 women at high risk of sPTB to the study, with samples taken at 16 and 20 weeks of pregnancy. At each time point samples are taken of urine, blood, vaginal swabs and cervical length. Currently there are 50 women recruited to the study, with an additional 129 in a pilot study (bloods and cervical length only). The target date for completion is August 2017.

The team have discussed a validation cohort with large biobanks, such as Baby Biobank. However there were insufficient samples available for validation work. Therefore a low risk cohort is additionally being collected at Liverpool Women's Hospital following an ethical amendment to the research. We have currently recruited 47 low risk controls, the aim is to recruit 250 low risk controls in total.

Following collaboration with Professor Chris Probert, University of Liverpool, we are now collecting stool samples for a project examining "Volatile Organic Compounds" (VOC). The aim is to look for potentially modifiable signatures of inflammation in high risk women.

From preliminary pilot work, novel serum biomarkers have been identified as potential candidates for added predictive value of preterm birth. We have submitted an application to SCOPE biobank for sPTB samples matched with 2:1 low risk controls for validation work of these markers.

Feasibility DNA/RNA extraction work and analysis on the pilot cohort will begin in the next few months at the University of Liverpool Wolfson Centre for Personalised Medicine.

Dr Laura Goodfellow, Clinical Research Fellow, commenced her 2 year post at the Harris Centre supporting current recruitment and working on vaginal microbiome research with collaboration from Professor Van De Wiggert. Her aim is to secure PhD funding to develop her work and combine the research findings of this cohort with Dr Angharad Care's work on blood biomarkers and layers of "omics" data to ultimately analyse pathophysiological pathways of spontaneous preterm birth.



## Workstream 2: Developing better tocolytics

### **Combination tocolytic therapy with Magnesium sulphate**

We have secured funding for a PhD student, Blessing Osaghae, to undertake some of the work described in workstream 2. Our first focus was to look the potency of magnesium sulphate (Mg) and which tocolytics in combination with Mg would be the most promising for treating threatened preterm birth. This is because Mg is given for fetal neuroprotection whilst a tocolytic is given to reduce uterine contractions and delay delivery. We have used our mouse model of term pregnancy to examine this.

Firstly, the effects of Mg were investigated in the presence and absence of oxytocin to reflect the hormonal milieu surrounding labour. Similarly to human myometrium, we find a large shift in the potency of Mg in inhibiting myometrial contractions in the presence of oxytocin. That is, it is less potent in the presence of oxytocin than in its absence. This may point to why Mg is not an effective tocolytic *in vivo*.

We therefore next investigated the combination of Mg plus the oxytocin receptor antagonist atosiban which is one of the first line tocolytics in use in the UK in cases of threatened preterm labour and thus is likely to be used when Mg is given for neuroprotection. We find that the combination is more effective than either tocolytic alone.

We are currently investigating the combination of indomethacin plus Mg as well as examining other specific gestational time points which would considered to be 'preterm' in the mouse.

### **Oxytocin and vasopressin receptor signalling in the uterus**

The oxytocin receptor (OTR) and vasopressin receptors of which there are three subtypes (V1aR, V1bR and V2R) share high sequence homology. In addition, the native hormones, oxytocin and vasopressin can each activate all 4 receptor subtypes creating significant cross-talk between the two signalling systems.

We are collaborating with a peptide chemist (Dr Muttenthaler, University of Queensland, Australia) and are using custom-designed receptor-specific peptides to elucidate the different contributions of each of the 4 receptors to human uterine contraction and oxytocin receptor signalling. Our goal is to aid the design of better tocolytics focussed at inhibiting oxytocin-driven contractions in preterm labour.



*Harris-Wellbeing Inaugural Preterm Birth Conference (18 & 19/09/2015) - Liverpool*



### Workstream 3: Evaluating current preventative strategies by research synthesis – global approach

Nancy Medley was appointed as Research Fellow in Evidence Synthesis in October 2015.

The first project underway for the evidence synthesis work stream is a descriptive overview of all Cochrane systematic reviews of interventions to prevent spontaneous preterm birth. In collaboration with the World Health Organization (Dr Joshua Vogel), our author team has registered a study title and submitted a protocol for publication with Cochrane Pregnancy & Childbirth. The proposed overview of systematic reviews will provide interested clinicians and consumers an entry into the current evidence base in the Cochrane library for key interventions to prevent spontaneous preterm birth. The overview will map the effectiveness of these interventions, assess the quality of the evidence reported and locate gaps in the knowledge base in the Cochrane library. The overview will also stimulate the updating of selected literature searches and Cochrane systematic reviews for priority interventions to prevent spontaneous preterm birth.

We are also involved in the updating of several Cochrane systematic reviews relevant to preterm birth, including reviews of cervical cerclage in singleton pregnancy, cervical pessary for prevention of preterm birth in multiple pregnancy and antenatal corticosteroids for the prevention of respiratory distress.

### Scientific meetings attended

Angharad Care - **PROMPT meeting** (10/07/2015) – Paris

Angharad Care - **PREBIC - 2015 Annual Scientific Meeting and Workshops** (8-10 May 2015) - Florence, Italy

Zarko Alfirovic and Andrew Sharp - **14th World Congress in Fetal Medicine** (21-25/06/2015) – Crete

Angharad Care - **PROMPT meeting** (10/07/2015) – Paris

Blessing Osaghae - **European Young Physiology Symposium** (26-29/08/2015) - Lithuania

Blessing Osaghae - **Federation of European Physiologist Society main meeting** (26-29/08/2015) - Lithuania

Angharad Care - **PREIS meeting** (9-11/09/2015) – Florence, Italy

**Harris-Wellbeing Inaugural Preterm Birth Conference** (18 & 19/09/2015) – Liverpool

Nancy Medley - **Cochrane Collaboration Annual Meeting** (October 2015) – Vienna



## Other Outputs

### Harris-Wellbeing Inaugural Preterm Birth Conference (18 & 19/09/2015) - Liverpool

120 attendees  
4 Keynote speakers  
31 presentations

Dr Angharad Care – **Speaker at the Wellbeing of Women Volunteer Conference** — 22 October 2015

Dr Andrew Sharp – **Promotion to Senior Lecturer** – January 2016

N Medley, A Care and A Sharp - **Attended a Cochrane workshop** on how to write clinical evidence in plain language to improve the readability and understanding of evidence summaries – February 2016

S Wray “**Supporting women in childbirth and research**” Research Professional 10/12/2015

Z Alfirevic, S Wray, A Weeks, S Arrowsmith, A Sharp, A Care, N Medley and T Ricketts – **Attendance at the Centre for Women's Health Research Day**, Liverpool Women's Hospital, University Department—1 December 2015

## Social Media

Facebook page created—received x2—5\* reviews and 90 likes

[Harris-Wellbeing Facebook](#)

Twitter account created-32 followers  
[Harris-Wellbeing \(@WellbeingHarris\) on Twitter](#)

## Public Engagement

PPI (Public & Patient Involvement) - group meetings 28/03/2015 and 03/10/2015—15 patient group members.

## Oral Presentations, Posters & Abstracts

Harris-Wellbeing Inaugural Preterm Birth Conference (Liverpool) 18 & 19/09/2015

- Angharad Care, Using Systems Biology for the Stratification of Women Attending Preterm Labour Clinic – *Oral Presentation, abstract*
- Sarah Arrowsmith, Examining the role of vasopressin receptors (AVPRs) in myometrial contraction – implications for effective tocolysis – *Oral Presentation, abstract*
- Blessing Osaghae, MgSO<sub>4</sub> in combination with other tocolytics: a promising treatment for threatened preterm birth - *Oral Presentation, abstract*

European Young Physiology Symposium, (26-29 Aug 2015) - Lithuania

- Blessing Osaghae, 'MgSO<sub>4</sub> inhibits uterine contraction' - Oral presentation, abstract

Federation of European Physiologist Society main meeting (26-29 Aug 2015) – Lithuania



- Blessing Osaghae 'Magnesium inhibits spontaneous and oxytocin induced contractions' – poster presentation, abstract (Prize winning presentation)



## Neonatology

The Neonatal group conducts research to improve access to high quality medicines for babies and children. This includes clinical studies (12 medicines in the past 7 years) and development of methodologies as well as leading global initiatives to integrate medicines research and disseminate good practice.

### Research

This is built around a number of national and European collaborations including the FP7 following projects:

- TINN (Treat Infections in Neonates)
- TINN2 (Treat Infections in Neonates)
- NEOCIRC (Dobutamine for NEONatal CIRCulatory failure defined by novel biomarkers)
- NEOVANC (Treatment of late onset bacterial sepsis caused by vancomycin susceptible bacteria in neonates and infants aged under three months)

Completed projects that continue to yield results are the MRC / ERA-NET-funded European Study of Neonatal Excipient Exposure and Paediatric Accelerator Mass Spectrometry Evaluation Research Study.

Each of these projects has led to continued publications and on-going work, including novel methodologies such as:

- <sup>14</sup>C labelled *micro-dosing* which has been presented to regulators and industry across Europe
- excipient assays which have been used in clinical studies that have influenced regulatory guidance
- novel work with Prof William Hope bridging between laboratory, clinical and animal study to optimise dosing regimens of antibiotics in neonates.

### Current Research Fellows and PhD students:

- Virginia Ramos Martin is working on optimising dosage regimens of glycopeptides in children
- Jennifer Duncan is studying the health economics of age inappropriate formulations
- Helen Hill is studying optimal dosing regimens of ciprofloxacin in neonates
- Charalampos Kotidis is studying biomarkers following birth at extreme prematurity

### Network Building

Dr Turner continues to play a major role in developing networks across Europe and globally. This work includes:

- Chair of the European Network of Paediatric Research at the European Medicines Agency (EnprEMA)
- Co-Director of the International Neonatal Consortium, which is developing novel ways to study medicines in neonates: <http://c-path.org/programs/inc/>
- Member of the Co-ordinating Committee and Work Group lead of the Paediatric Trials Consortium which is developing a business case for a global paediatric clinical trials network: <http://c-path.org/programs/ptc/>

All these activities have involved presentations to hospitals, learned societies, companies and regulators across Europe, America and Asia.

## Scientific Co-ordination of Global Research in Paediatrics (GRiP)

During 2015 Dr Turner developed the European Paediatric Clinical Trials Research Infrastructure which was submitted to the European Strategic Forum for Research Infrastructure which is developing Europe's research infrastructure roadmap. This application was highly rated and will be recognised as a complimentary research infrastructure in the 2016 Infrastructure Roadmap. Efforts are on-going to integrate paediatric research infrastructure with other infrastructures across Europe and North America.

## Posters

Virginia Ramos Martin

**Pharmacodynamics of Vancomycin for Coagulase-Negative Staphylococcal Infection: Experimental Basis for Optimal Use in Neonates.** 55<sup>th</sup> Interscience Conference on Antimicrobial Agents and Chemotherapy. 17-21 September, 2015, San Diego, CA, USA [Poster]

Charalampos Kotidis

**Haemodynamics in preterm infants with Patent Ductus Arteriosus (HAPI-PDA study): A feasibility study.** 23<sup>rd</sup> Northern Cardiovascular Research Group Meeting – Newcastle upon Tyne, 21<sup>st</sup> April 2015 C. Kotidis, N. Subhedar, M. Weindling, M. Turner. Haemodynamics in preterm infants with Patent Ductus Arteriosus (HAPI-PDA study): A feasibility study

## Scientific meetings

NEOVANC Consortium Meeting Paris 23 January 2015

Neonatal & Research Midwife National Delivery Meeting Birmingham 11 February 2015 M.Turner

Enpr-EMA Neonatology Meeting, London, 17 March 2015 M Turner

Enpr-EMA Meeting, London, 28—29 May 2015 M Turner

NEOVANC Consortium Meeting Talinn, 8—9 June 2015 M Turner

24th Biennial Meeting of the International Perinatal Collegium, Napa, California 12—16 July 2015 C. Kotidis

TINN Consortium Meeting, London, 28 August 2015, M.Turner

jENS (joint European Neonatal Societies 1st Congress in Budapest 16-20 September 2015 M.Turner, C Kotodis

Neonatal Society Autumn Meeting 2015, 5th November 2015 M.Turner, C Kotodis A. Weindling

RAINBOW Meeting Berlin 24 November 2015 M. Turner

## Knowledge Exchange

Dr Turner has engaged with a number of companies to provide neonatal input to drug development programmes. These companies include Chiesi, Shire, Grunenthal and Janssen. This provides useful case studies to develop research infrastructure and to apply lessons learnt from research activities.

## Future Work

The neonatal team will contribute to the development of personalised perinatal medicine and promote the availability of high quality **medicines** for babies and children.



Charalampos Kotidis

## Perinatal Pharmacology

As the newest research group in The Centre for Women's Health Research it is important for us to have a vision of where we want to be in the future and explain how we feel we can build upon the successes of our previous work.

The aim of this research group is to use targeted approaches to deliver safe effective medicines for mothers and their babies.

We have several studies currently in process and many more in the early stages of development.

We have now established the Perinatal Pharmacology Group with members from Obstetrics, Neonatology and Paediatrics with close collaboration with experts from Pharmacology, Pharmacogenetics, Nanomedicine, Chemistry, Physiology, Nuclear Magnetic Resonance and Mass Spectrometry. Group meetings will occur monthly.

### Current Research Studies

#### STRIDER

The STRIDER study is an NIHR/MRC funded project studying the effect of treatment with the nitric oxide promotor sildenafil on growth restricted fetuses. It is a randomised controlled trial of sildenafil versus placebo assessing clinical efficacy, cardiovascular, placental and angiogenic effects.

The CI is Professor Zarko Alfirevic and Principal Investigator in Liverpool is Dr Andrew Sharp.



The trial is run over 20 sites throughout England and Scotland and has been recruiting above expectations with >100 women currently enrolled. The trial is due to complete recruitment at the end of August 2016.

Follow up studies to assess offspring at age 2.5years have just been submitted for funding.

#### EARTH

The EARTH Study is a prospective cohort Study funded by Wellbeing of Women. EARTH will investigate the mechanisms of platelet response to aspirin. 'Aspirin resistance' describes a state of insufficient suppression of platelet activation despite aspirin treatment. In Cardiology and Stroke research aspirin resistance has been linked to an increased risk of heart attacks, stroke and death. The study will assess the relationship between laboratory platelet activation tests in 'high risk' women taking aspirin and any association with pregnancy complications (pre-eclampsia, fetal growth restriction, fetal death).

Assessment of genetic factors and compliance with aspirin will also be performed. Further discussions regarding pk modelling techniques have also begun with pharmacology.

The study started in January 2014 and recruitment is now complete.

A further aspirin resistance project has been included in the current BRC personalised medicine grant application.



## Current Research Studies

### Nanomedicine

Developing novel nanomedicine strategies for the prevention of preterm birth. This study, in collaboration with Professor Owen (nanomedicine) and Professor Rannard (chemistry), will determine whether nanomedicine delivered tocolytics can be applied to human preterm labour. An initial grant application for chemical nanoparticle formation techniques will be submitted in March 2016.

This study is led by Dr Sharp and Dr Arrowsmith (physiology).

This project is currently in the short list for inclusion in the nanomedicine cross-cutting theme for the upcoming £20million BRC personalised medicine grant application headed by Professor Sir Munir Pirmohamed.

### Magnesium

Initial discussions have been between Prof Alfirovic, Dr Sharp, Dr Turner and Dr Kotidis about investigating the role of magnesium in improving neonatal outcomes from preterm birth. Whilst preterm babies <34 weeks have less cerebral palsy when treated with magnesium prior to birth the exact mechanism remains unclear. Initial studies will investigate the potential relationship between antenatal magnesium and early neonatal magnesium levels. Further studies may aim to identify the exact mechanism and markers of response to allow personalisation of care.

### Breast Milk Pharmacology

Initial project discussions and audits with Dr Hawcutt (paediatrics) and Dr Waitt (pharmacology) will be developed over the next 6 months into a project for a scholar programme student in September 2016.

## Funding Awards and Applications

- Biomedical Research Centre – Preterm labour Nanomedicine Technologies and aspirin resistance have been selected for inclusion in the second round of projects put forward for the £20+million BRC application for personalised care. Decision early/mid 2016.

- Dr Kate Navaratnam – Research Training Fellowship from Wellbeing of Women (£199,810), March 2014.



- £5000 from Jon and Katie Dutton (CfWHR PPI group), generously donated to the EARTH Study, allowing maternal cardiovascular assessments to be performed.
- 50% matched funding (£7500) from University of Liverpool Technology Directorate to undertake a pilot assessment of Nuclear Magnetic Resonance spectrometry assessment of salicylic acid from maternal blood and urine as a marker of compliance, using EARTH Study samples.
- Application to National Institute for Health for \$100,000 funding for a genome wide association study (GWAS) using maternal DNA from the EARTH study.

## Poster Presentations

'Assessment of platelet activation and the mechanism of action of aspirin in pregnancy', RCOG Annual Academic Meeting 21-23/01/15, RCOG, London.

'Assessment of platelet activation and the mechanism of action of aspirin in pregnancy', Institute of Translational Medicine Research day 2015, University of Liverpool.

## Patient and Public Involvement

In 2015 we established a patient and public involvement group for the Centre for Women's Health Research, including participants and their families involved with the EARTH study.

We have invited individuals with experience of pre-eclampsia, intrauterine growth restriction and stillbirth. We will continue to develop this group and involve members in each step of the research design, funding applications, fundraising and ethical approvals.

It is anticipated that significant PPI involvement will be a part of future nanomedicine studies/applications due to the nature of the research.

## Collaborations

Professor Owen and Professor Rannard (UoL) to develop novel nanomedicine techniques for tocolytic drug delivery to prevent preterm birth.

Professor Papageorgiou (St. Georges/Oxford), Dr Johnstone (Manchester), Dr Khalil (St. Georges), Professor Baker (Leicester) and Professor Sebire (UCH/GOSH) to continue STRIDER study and to develop follow up studies (STRIDER).

Professor Robson (University of Newcastle) and Professor McAuliffe (University College Dublin) to validate cohort using whole genome sequencing (EARTH).

Professor Lian, Dr Phelan and Professor Khoo (UoL) to refine Nuclear Magnetic Resonance and Mass Spectrometry methods for the assessment of compliance with low-dose aspirin (EARTH).

## Physiology

### The Myometrial Research Group

Preterm labour, dysfunctional labour and post-partum haemorrhage are all clinical conditions associated with abnormal uterine function which can have devastating health consequences for both mother and fetus.

The overarching aim of our research is to understand the physiology of the myometrium (smooth muscle of the uterus) so that we can better understand and treat its pathophysiology.

The research undertaken by the Liverpool Myometrial Research Group is directed towards identifying the key cellular and molecular mechanisms underlying myometrial contraction, including those governing its excitability, as well as exploring current and novel pharmacological tools and treatments to modulate its activity.

### Current research studies

Tocolytic efficacy and designing better tocolytic regimens for the treatment of preterm labour.

The molecular pharmacology of oxytocin and vasopressin receptor signalling in the uterus.

The contribution of the uterine environment and its role in abnormal uterine function.

The role of dyslipidaemia on uterine contractility.

This year we have published a number of findings including identifying a novel mechanism whereby repetitive, transient episodes of hypoxia increase uterine contractions during labour (Alotaibi et al., PNAS) as well as others (see below).

One of our first year PhD Students, Blessing Osaghae won two prizes this year for her work on magnesium sulphate and uterine function (see picture).



Another of our PhD students, Dr Seham Alsaif won first prize at the annual meeting of UK Gulf states students in Leeds for her work on visfatin and contractility (see picture).



## Scientific meetings

**Society of Reproductive Investigation**, San Francisco, USA Invited Oral Presentation— 'Tocolytic efficacy in multiple pregnancy', S Arrowsmith (March 2015)

**European Young Physiology Symposium (FEPS)**, Lithuania- Oral presentation, 'MgSO<sub>4</sub> inhibits uterine contraction' B Osaghae, S Arrowsmith and S Wray (August 2015)

**Federation of European Physiologist Society** main meeting, Lithuania.

**Inaugural Harris-Wellbeing preterm birth conference**

- Oral presentation 'MgSO<sub>4</sub> in combination with other tocolytics: a promising treatment for threatened preterm birth' B Osaghae, S Arrowsmith and S Wray

- Oral presentation 'The role of vasopressin receptors and myometrial contraction: Implications for tocolysis.' S Arrowsmith, S Wray and M Muttenthaler (September 2015)

**Turkish Physiological Society, Gallipoli** - Susan Wray - Keynote Speaker

## Other outputs

**BSc Hons. Graduates, University of Liverpool 2015:**

**Chloe Jones**

**Jessica Melia**

**MRes. Graduates, University of Liverpool 2015:**

**Sarah Dodd**

*Royal College of Obstetricians and Gynaecologists, Trainee meeting, London (December 2015) – Poster "Could combination tocolytic therapy be the future from preterm birth?"*

**Daniel Newman**

**Olayisade Ajibola-Taylor**

*Royal College of Obstetricians and Gynaecologists, Trainee meeting, London (December 2015) – Poster "Examining the Role of Vasopressin Receptors (AVPRs) in myometrial contraction – Implications for effective tocolysis"*

## Posters

**Society of Reproductive Investigation, San Francisco, USA** 'Re-examining the importance of vasopressin receptors in myometrial contraction', **S Arrowsmith, S Wray** and M Muttenthaler

**Abstract published—***Reprod Sci* (2015) Vol 22 No.3 (suppl):332S [S106].

**ITM Research Day—**'Novel mechanisms for modulating contractility' (Prize winning presentation) *Wray Group*, presented by *B Osaghae* (July 2015)

**Federation of European Physiologist Society main meeting**

- 'Magnesium inhibits spontaneous and oxytocin induced contractions' (**Prize winning presentation**) **B Osaghae, S Arrowsmith and S Wray** (August 2015)
- 'The effect of adipokines on uterine contractility' (Presentation) and 'The effect of visfatin on uterine contractility' (Poster) **S Alsaif** (August 2015)

## Patient and Public Involvement (PPI)

In 2013 we established a patient and public involvement group for the Centre for Women's Health Research, including participants and their families involved with current research studies.

We have invited individuals with experience of preterm birth, pre-eclampsia, intrauterine growth restriction and stillbirth. We are continuing to develop this group and involve members in each step of the research design, funding applications, fundraising and ethical approvals.

Some of the PPI group have also raised funds for the Liverpool Women's Charity. We work closely with the Charity to foster this relationship and to encourage funding into ongoing research. Two of the group members are lay representatives on the trial steering committee for RECAP – a feasibility clinical trial investigating preventative therapies for women at risk of preterm birth.

Our PPI group's main interest is in experiences of pregnancy and pre-term birth issues.



We currently meet two to three times a year. Our group meetings usually take place on a Saturday morning/lunch time; we include a light lunch and facilities for childcare. At the meeting in October the group discussed and amended a number of draft study documents.

The last meeting also created an opportunity for the University of Liverpool, Liverpool Women's Hospital and the parent representative of a special interest group to work together in the promotion of World Prematurity Day on 17 November. This is an international awareness day for premature birth and the issues surrounding it. This is in its 5th year and one of the main activities associated with it is the purple illumination of buildings.

The University of Liverpool, Active Learning Laboratory supported World Prematurity Day by illuminating their building in purple.



It is anticipated that PPI involvement will be a part of all future Women's Health studies and applications.

### University of Liverpool Team involved:

**Professor Zarko Alfirevic** Dr Med, PhD, FRCOG  
Professor of Fetal and Maternal Medicine

**Dr Andrew Sharp** BSc, PhD, MBBS, MRCOG  
Senior Lecturer in Obstetrics and Gynaecology

**Dr Angharad Care** BSc, MBBS, MRCOG  
Academic Clinical Fellow

**Dr Kate Navaratnam**  
Wellbeing of Women Research Training Fellow

**Kim Hall**  
PA to Professor Zarko Alfirevic

**Tracey Ricketts**  
Harris-Wellbeing Preterm Birth Centre, Research Co-ordinator

# List of Publications 2015

## Cochrane Pregnancy & Childbirth

PCG Cochrane reviews published January-December 2015 that include members of the CfWHR

Farrar D, Duley L, **Medley N**, Lawlor DA. **Different strategies for diagnosing gestational diabetes to improve maternal and infant health**. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD007122. DOI: 10.1002/14651858.CD007122.pub3.

Buppasiri P, Lumbiganon P, Thinkhamrop J, Ngamjarus C, Laopaiboon M, **Medley N**. **Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes**. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD007079. DOI: 10.1002/14651858.CD007079.pub3.

Catling CJ, **Medley N**, Foureur M, Ryan C, Leap N, Teate A, Homer CSE. **Group versus conventional antenatal care for women**. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD007622. DOI: 10.1002/14651858.CD007622.pub3.

Cluver C, Gyte GML, Sinclair M, **Dowswell T**, Hofmeyr GJ. **Interventions for helping to turn term breech babies to head first presentation when using external cephalic version**. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD000184. DOI: 10.1002/14651858.CD000184.pub4.

Begley CM, Gyte GML, Devane D, McGuire W, **Weeks A**. **Active versus expectant management for women in the third stage of labour**. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD007412. DOI: 10.1002/14651858.CD007412.pub4.

Hofmeyr GJ, Kulier R, **West HM**. **External cephalic version for breech presentation at term**. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD000083. DOI: 10.1002/14651858.CD000083.pub3.

**Alfirevic Z**, Stampalija T, **Medley N**. **Fetal and umbilical Doppler ultrasound in normal pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD001450. DOI: 10.1002/14651858.CD001450.pub4.

Bricker L, **Medley N**, Pratt JJ. **Routine ultrasound in late pregnancy (after 24 weeks' gestation)**. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD001451. DOI: 10.1002/14651858.CD001451.pub4.

**Dowswell T**, Carroli G, Duley L, Gates S, Gülmezoglu AM, Khan-Neelofur D, Piaggio G. **Alternative versus standard packages of antenatal care for low-risk pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD000934. DOI: 10.1002/14651858.CD000934.pub3.

Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, **Dowswell T**. **Daily oral iron supplementation during pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD004736. DOI: 10.1002/14651858.CD004736.pub5

Hofmeyr GJ, Kulier R, **West HM**. **Expedited versus conservative approaches for vaginal delivery in breech presentation**. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD000082. DOI: 10.1002/14651858.CD000082.pub3

Hutton EK, Hofmeyr GJ, **Dowswell T**. **External cephalic version for breech presentation before term**. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD000084. DOI: 10.1002/14651858.CD000084.pub3

Zhou K, **West HM**, Zhang J, Xu L, Li W. **Interventions for leg cramps in pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD010655. DOI: 10.1002/14651858.CD010655.pub2

Nabhan AF, **Aflaifel N**. **High feedback versus low feedback of prenatal ultrasound for reducing maternal anxiety and improving maternal health behaviour in pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD007208. DOI: 10.1002/14651858.CD007208.pub3

Grivell RM, **Alfirevic Z**, Gyte GML, Devane D. **Antenatal cardiotocography for fetal assessment**. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD007863. DOI: 10.1002/14651858.CD007863.pub4

Matthews A, Haas DM, O'Mathúna DP, **Dowswell T**. **Interventions for nausea and vomiting in early pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD007575. DOI: 10.1002/14651858.CD007575.pub4

Peña-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, **Dowswell T**. **Intermittent oral iron supplementation during pregnancy**. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD009997. DOI: 10.1002/14651858.CD009997.pub2.

Smyth RMD, **Aflaifel N**, Bamigboye AA. **Interventions for varicose veins and leg oedema in pregnancy.** Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD001066. DOI: 10.1002/14651858.CD001066.pub3.

Allred SK, Takwoingi Y, Guo B, Pennant M, Deeks JJ, **Neilson JP**, **Alfirevic Z.** **First trimester serum tests for Down's syndrome screening.** Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD011975. DOI: 10.1002/14651858.CD011975.

Bricker L, Reed K, Wood L, **Neilson JP.** **Nutritional advice for improving outcomes in multiple pregnancies.** Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD008867. DOI: 10.1002/14651858.CD008867.pub3.

Dodd JM, **Dowswell T**, Crowther CA. **Reduction of the number of fetuses for women with a multiple pregnancy.** Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD003932. DOI: 10.1002/14651858.CD003932.pub3.

Dodd JM, **Dowswell T**, Crowther CA. **Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes.** Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD005300. DOI: 10.1002/14651858.CD005300.pub4.

**Sharp AN**, **Alfirevic Z.** **Vasodilators for treating intrauterine growth restriction (Protocol).** Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD011978. DOI: 10.1002/14651858.CD011978.

Mbuagbaw L, **Medley N**, Darzi AJ, Richardson M, Habiba Garga K, Ongolo-Zogo P. **Health system and community level interventions for improving antenatal care coverage and health outcomes.** Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD010994. DOI: 10.1002/14651858.CD010994.pub2.

Allred SK, Guo B, Takwoingi Y, Pennant M, Wisniewski S, Deeks JJ, **Neilson JP**, **Alfirevic Z.** **Urine tests for Down's syndrome screening.** Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD011984. DOI: 10.1002/14651858.CD011984.

**Neilson JP.** **Fetal electrocardiogram (ECG) for fetal monitoring during labour.** Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD000116. DOI: 10.1002/14651858.CD000116.pub5.

Whitford HM, Wallis SK, **Dowswell T**, Renfrew MJ. **Breastfeeding education and support for women with multiple pregnancies (Protocol).** Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD012003. DOI: 10.1002/14651858.CD012003.

## Endometrial Proliferative Disease Research Group

**Mathew D**, **Drury JA**, **Valentijn AJ**, Vasieva O, **Hapangama DK.** **In silico, in vitro and in vivo analysis identifies a potential role for steroid hormone regulation of FOXD3 in endometriosis-associated genes.** Hum Reprod. 2015 (In Press)

**Kamal AM**, Bulmer JN, DeCruze SB, Stringfellow HF, Martin-Hirsch P, **Hapangama DK.** **Androgen receptors are acquired by healthy postmenopausal endometrial epithelium and their subsequent loss in endometrial cancer is associated with poor survival.** British Journal of Cancer, 2015 (In Press)

**Hapangama DK**, Bulmer JN. **Pathophysiology of heavy menstrual bleeding.** Womens Health (Lond Engl). 2015, In Press.

**Valentijn AJ**, Saretzki G, **Tempest N**, Critchley HO, **Hapangama DK.** **Human endometrial epithelial telomerase is important for epithelial proliferation and glandular formation with potential implications in endometriosis.** Hum Reprod. 2015 Dec;30(12):2816-28

Biswas Shivhare S, Bulmer JN, Innes BA, **Hapangama DK**, Lash GE. **Menstrual cycle distribution of uterine natural killer cells is altered in heavy menstrual bleeding.** J Reprod Immunol. 2015 Nov;112:88-94

**Tempest N**, Navaratnam K, **Hapangama DK.** **Management of deliveries when malposition of the fetal head complicates the second stage of labour.** The Obstetrician & Gynaecologist 2015 Oct;17(4): 273-80.

**Tempest N**, Navaratnam K, **Hapangama DK.** **Does advanced operative obstetrics still have a place in contemporary practice?** Curr Opin Obstet Gynecol. 2015 Apr;27(2):115-20

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Weeks AD, Watt P, Yoxall CW, Gallagher A, Bewley S, Odd D, Burleigh A, Fisher T, Heuchan AM, Duley L. **Innovation in immediate neonatal care: development of the Bedside Assessment, Stabilisation and Initial Cardiorespiratory Support (BASICS) Trolley.** *BMJ Innovations* 2015;1:53–58.

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Sharma G, Mathai M, Dickson KE, Weeks A, Hofmeyr GJ, Lavender T, Day L, Mathews J, Fawcus S, Simen-Kapeu A, de Bernis L. **Quality care during labour and birth: a multi-country analysis of health system bottlenecks and potential solutions.** *BMC Pregnancy and Childbirth* 2015, 15(Suppl 2):S2.

Weeks AD, Ditai J, Ononge S, Faragher B, Frye LJ, Durocher J, Mirembe FM, Byamugisha J, Winikoff B, Alfirevic Z. **The MamaMiso study of self-administered misoprostol to prevent bleeding after childbirth in the community: A placebo-controlled randomised trial.** *BMC Pregnancy and Childbirth* 2015;15:219.

Hancock A, Weeks AD, Lavender T. **Is accurate and reliable blood loss estimation the 'crucial step' in early detection of postpartum haemorrhage? An integrative review of the literature.** *BMC Pregnancy and Childbirth* 2015, 15:230.

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Narayanan RP, Weeks A, Quenby S, Rycroft D, Hart A, Longworth H, Charnley M, Abayomi J, Topping J, Carter J, Turner MA, Wilding JPH. **Fit for Birth - the effect of maternal weight changes in obese pregnant women on maternal and neonatal outcomes: a prospective cohort study.** *Clin Obes* 2016 Feb;6(1):79-88. doi: 10.1111/cob.12129



## Harris-Wellbeing Preterm Birth Centre

Publications recognising Harris-Wellbeing Preterm Birth Centre

**Arrowsmith S**, Neilson J, Bricker L and **Wray S**. **Differing *in vitro* potencies of tocolytics and progesterone in myometrium from singleton and twin pregnancies.** *Reprod Sci*. 2015

Alotaibi M, **Arrowsmith S & Wray**. **Hypoxia-induced force increase (HIFI) is a novel mechanism underlying the strengthening of labor contractions, produced by hypoxic stresses.** *PNAS*, 2015

Attah F, Hellinger R, Sonibare M, Moody J, **Arrowsmith S, Wray S**, Gruber C. **Ethnobotanical survey of *Rinorea dentata* (Violaceae) used in South-Western Nigerian ethnomedicine and detection of cyclotides.** *Journal of Ethnopharmacology* (accepted Dec 2015).

Article

**Professor Susan Wray “Supporting women in childbirth and research”** Research Professional 10/12/2015

<https://www.researchprofessional.com/0/rr/funding/insight/2015/12/Top-PI-Susan-Wray--Supporting-women-in-childbirth-and-research-.html>

## Neonatology

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Nellis G, Metsvah T, Varendi, H, Toompere, K Lass, J, Mesek, I, Nunn, AJ, Turner, MA and Lutsar, I. **Potentially harmful excipients in neonatal medicines: a pan-European observational study** (2015). *Archives of Disease in Childhood*. ISSN 0003-9888

Whitby T, McGowan P, Turner MA, Morgan C. **Concentrated parenteral nutrition solutions and central venous catheter complications in preterm infants** *Arch Dis Child Fetal Neonatal Ed*. 2015 May;100(3):F250-2

Metsvaht T, Nellis G, Varendi H, Nunn AJ, Graham S, Rieutord A, Storme T, McElnay J, Mulla H, Turner MA, Lutsar I. **High variability in the dosing of commonly used antibiotics revealed by a Europe-wide point prevalence study: implications for research and dissemination.** *BMC Pediatr*. 2015 Apr 16;15:41

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## Perinatal Pharmacology

Navaratnam K, Alfirevic Z. **Low dose aspirin and pregnancy: How important is aspirin resistance?** Accepted for publication *British Journal of Obstetrics and Gynaecology*. A mini-commentary has been commissioned.

Sharp A, Alfirevic Z. **Vasodilators for the treatment of Intrauterine growth restriction (Protocol).** *Cochrane Database of Systematic Reviews* 2015, Issue 11. Art. No.:CD011978. DOI:10.1002/14651858.CD011978

Sharp A, Navaratnam K, Abreu P, Alfirevic Z. **Short versus standard mifepristone and misoprostol regimen for second and third trimester termination of pregnancy for fetal anomaly.** *Fetal Diagnosis and Therapy* 2015

## Physiology

**Arrowsmith S, Neilson J, Bricker L and Wray S. Differing in vitro potencies of tocolytics and progesterone in myometrium from singleton and twin pregnancies.** *Reprod Sci*. 2015

Alotaibi M, **Arrowsmith S & Wray S. Hypoxia-induced force increase (HIFI) is a novel mechanism underlying the strengthening of labor contractions, produced by hypoxic stresses.** *PNAS*, 2015

Attah F, Hellinger R, Sonibare M, Moody J, **Arrowsmith S, Wray S**, Gruber C. **Ethnobotanical survey of *Rinorea dentata* (Violaceae) used in South-Western Nigerian ethnomedicine and detection of cyclotides.** *Journal of Ethnopharmacology* (accepted Dec 2015).

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