LONDON'S GLOBAL UNIVERSITY

UCL

2019 Report

Better lives for women and babies across the world

15th ANNIVERSARY

Celebrating 15 Years of UCL EGA Institute for Women's Health

Our Vision

Better lives for women and babies across the world

Our Mission

To bring together the expertise of clinicians and researchers from a diverse range of disciplines so that they can deliver excellence and innovation in research, clinical practice, education and training in order to make a real and sustainable difference to women's and babies' health locally, nationally and worldwide.

Elizabeth Garrett Anderson

Elizabeth Garrett Anderson was a pioneer of women's rights in medicine and society. Born in 1836, she made history in 1865 by becoming the first woman to become a doctor in the UK despite vigorous opposition from the medical establishment. She was also Britain's first woman mayor and an early suffragette. She fought tirelessly for women to have access to high quality health care and for the right of women to practise medicine. In 1872, at the age of 36, she founded the first British hospital for women in London – which became the Elizabeth Garrett Anderson Hospital after her death. In 2008 the hospital's maternity and neonatal services moved to the new UCLH Elizabeth Garrett Anderson Wing.

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Director's Report

I am delighted to welcome you to our 15th anniversary report of the Elizabeth Garrett Anderson Institute for Women's Health.

Professor Anna David, Director (2018)

Why an Institute for Women's Health?

Traditionally, women's health care has been confined to obstetrics and gynaecology, and has failed to take into account all the health issues affecting women and their babies. There are differences in the factors that determine health and the burden of ill-health for women and men, and the dynamics of gender in health have long been overlooked. The Institute was formed in 2004 to address this disparity.

Women's health is the future of human generations. The lack of knowledge about age related decline in fertility has led us to develop a taskforce on fertility education. Through Institute work on preconception healthcare, the vital importance of getting fit for pregnancy is now recognized, and we study how pregnancy can reveal the potential for pathology in older women, such as diabetes and stroke. The Institute also champions improving reproductive choice through novel delivery of family planning advice. We pioneer less invasive treatment of pelvic pathology such as endometriosis and fibroids. Our teams are researching risk-reducing surgery for ovarian cancer and our initiatives are showing that ovarian cancer can be detected years earlier by looking for DNA fragments in the bloodstream. In 2019 threats to women's health comes from all directions, including gender violence, lack of choice in planning their families, and environmental changes. Now more than ever, women's health requires an Institute such as this to provide a broad holistic approach to medicine, improving outcomes for women and their babies.

The Life-Course Approach

When appointed as Director in 2018 one of my key aims was to foster collaboration between research and clinical colleagues. With this aim in mind we have modelled this 15 year anniversary report on the Life-Course of women, from pregnancy and newborn health through adolescence and fertility, screening and cancer prevention and on to a healthy menopause. When viewed across this trajectory of women's health, the breadth and depth of all that we do within the Institute comes to life. Along the way, we research, educate and deliver on our promise of better lives for women and babies across the world. Our annual meeting in 2018 was attended by over 200 delegates from across the university and hospital, and our 15 year meeting in June 2019 was even more successful.

Achievements and Innovations

The Institute Education team has successfully delivered on three new courses in the last two years significantly enhancing our education portfolio. This includes a brand new intercalated BSc for medical students at UCL and external institutions, an MSc in Women's Health, that covers the physical, mental, social, cultural, legal and ethical aspects of women's health and a new MRes to provide a more in depth research period for Masters' students.

Our new Centre for Prenatal Therapy was launched in February 2018. This initiative is a collaboration between the EGA Institute for Women's Health and UCL Great Ormond Street Institute of Child Health, with Great Ormond Street Hospital and UCLH providing core clinical expertise. Through the appointment of KU Leuven's Jan Deprest as Professor of Fetal Surgery, the Centre is bringing innovative prenatal therapy such as open fetal surgery for spina bifida to the UK for the first time. Congratulations go to all the team who recently won the BMJ 2019 Clinical Leadership of the Year award.

On the clinical side Donald Peebles has continued as Clinical Director for the UCLH Division of Women's Health supported by Natilla Henry as Head of Midwifery. UCLH successfully implemented an electronic patient healthcare record in 2019 which promises to provide an exciting new era of research into big data in maternity. Women's Health also played an important role in the Care Quality Commission continuing Good rating of the UCLH, with outstanding practice in maternity and gynaecology services.

Appointments and Promotions

We welcome to the Institute some exciting new appointments. Associate Professor and Consultant Obstetrician Dimitris Siassakos is an expert in intrapartum care, stillbirth and bereavement care both nationally and internationally. He leads a new research group on Perinatal Care and Operative Birth and also takes on the important role of Integrated Clinical Academic Training Lead for the Institute supporting our junior doctors through their clinical academic career path. In addition, Mr Neill Patani has been appointed as Consultant Oncoplastic Breast Surgeon at UCLH and Honorary Senior Lecturer at UCL where he is exploring how breast cancer metabolism can be targeted for novel management strategies. Dr Jacqueline Nicholls is appointed as Associate Professor in Health Law. As well as teaching on our new MSc in Women's Health she is researching informed consent in maternity care, and the implications of the Montgomery ruling in 2015 which was a landmark case for medical litigation in the UK. Finally congratulations to Dr Suzy Buckley who has been appointed as the new Vice-Dean for Equality, Diversity and Inclusion in the UCL Faculty of Population Health Sciences, within which Faculty the Institute is situated.

Great news in 2018 was that Simon Waddington and Rezan Kadir were both promoted to Professor. Simon who has led the Gene Transfer Technology group for many years plays a major role in the outstanding development and clinical translation of genetic therapies at UCL. Rezan is an internationally renowned expert on the impact and management of bleeding disorders in women's health. The Institute was delighted that both Simon and Rezan's work has been recognised by these well-deserved awards.

Institute staff speak out and write regularly on social media about issues to do with women's health. Highlights over the last two years include Martin Widschwendter talking to BBC Two's Trust Me I'm a Doctor programme about better prevention of women's cancer and Joyce Harper appearing twice on BBC Sunday Morning Live discussing fertility and genome editing.

You can keep abreast of activities within the Institute for Women's Health on our Facebook page and our Twitter account. www.facebook.com/ucl.ega.ifwh @UCL_IfWH

Professor Ian Jacobs
Founding Director (2004)

Congratulations to all involved in the EGA Institute for Women's Health on this 15th anniversary.

I have wonderful memories of moving to UCL to set up the Institute in 2004, of talented highly collegiate colleagues, of exciting meetings to plan the strategy and objectives of the Institute and of the shared sense of purpose in implementing our plans over the initial 7 years.

It has been good to see the progress and impact of the Institute since then and I know that even greater things will follow in the future. The need for progress in women's health across the world is even greater than when the Institute was founded and the extraordinary array of expertise in the Institute team at UCL has a major role to play.

Good luck with the next phase of the Institute and my very best wishes, Ian

Institute Impact

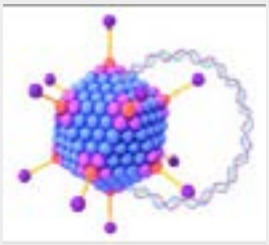
The Institute for Women's Health has had a major impact over the last 15 years on the health of women and their babies.

The Institute was the only university department in the UK awarded the Athena SWAN Gold Award in 2017. Athena SWAN is a national charter mark which encourages the advancement of gender equality in higher education and research, especially in science, technology, engineering, maths and medicine (STEMM)

The Centre for Prenatal Therapy performed the first open fetal surgery for spina bifida in the UK. The team from UCLH, Great Ormond Street Hospital (GOSH), UCL Institute for Women's Health, UCL GOS Institute of Child Health (ICH) in collaboration with KU Leuven, Belgium recently won the 2019 BMJ Clinical Leadership Award in recognition.

UKCTOCS: Lead by the Institute, the UK Collaborative Trial of Ovarian Cancer Screening is the largest ever randomised controlled trial in ovarian cancer screening, recruiting 200,000 women.

Contraception Choices website. This website, developed by the Institute and the E-Health Unit at UCL, has been chosen as the lead website for contraception advice on NHS Choices – www.contraceptionchoices.org.



The Gene Transfer Technology Group in collaboration with clinicians from GOSH-ICH have set up a pathway from bench to bedside to develop genetic therapies to treat life-threatening inherited childhood diseases including urea cycle diseases, Gaucher's Disease, Dravet Syndrome and Dopamine Transporter Deficiency Syndrome and to work with patient charities to deliver therapy.

EPICure
Population based studies of survival and later health status after extremely premature birth

The EPICure studies are important national studies that have driven national policy and changed attitudes towards children and adults born extremely premature.

UCLH Neonatal unit is the regional specialist centre for the care of very sick and premature babies with excellent long term follow up and outcome measures.

The EVERREST project is developing a novel maternal gene therapy to treat severe early onset fetal growth restriction. The team have performed the largest natural history study of this untreatable condition, providing improved counselling for affected couples about mother and baby outcomes.

EVERREST

First baby tested for breast cancer gene BRCA1 before implantation born in UK. The UCL Centre for PGD was the first to perform preimplantation genetic diagnosis for families who carry mutations the BRCA1 gene in the UK. After a public consultation a licence for BRCA gene testing was granted by the Human Fertilisation and Embryology Authority (HFEA). In collaboration with the Centre Reproductive and Genetic Research, the first baby was born in 2009.

Approximately 7000 women have been recruited to the FORECEE trial. FORECEE (Female Cancer Prediction Using Cervical Omics to Individualise Screening and Prevention) aims to develop personalised risk prediction and prevention for common female cancers.

4C forecee
Four cancers One test

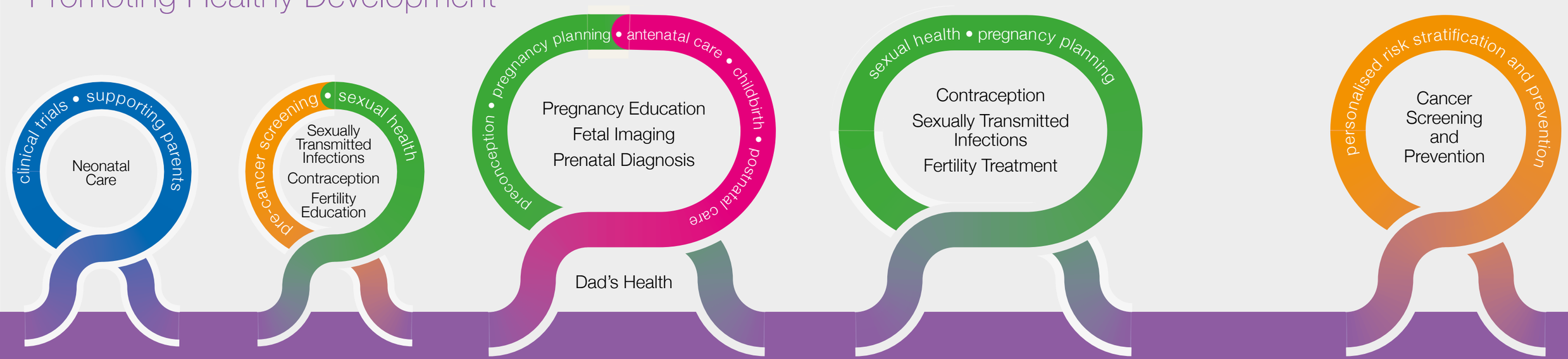
£82,000,000 of grant funding received at the Institute for Women's Health

The Life Course and the Institute for Women's Health

The diagram outlines a woman's healthy development through her life as a purple banner and her typical health care needs across the life course above. At the Institute for Women's Health, we strive to protect healthy development, responding promptly to departures from health below the banner and restoring health whenever possible throughout the life course.

Neonatology | Reproductive Health | Maternal and Fetal Medicine | Women's Cancer

Promoting Healthy Development



Restoring Health

Healthy Early Development

The Institute focuses on providing better lives for babies through minimising harm and providing novel treatment options for newborn babies that are directed at improving long term outcomes following premature birth, brain injury and genetic conditions.

The neurobiology of pain in the newborn

J Meek, M Fitzgerald, L Fabrizi, L Jones, K Whitehead and M Laudiano-Dray

Pain is an unfortunate but common experience for newborn babies in hospital. Premature babies in particular often experience multiple painful procedures every day over weeks and months, during a vulnerable period of brain development. Our group, a collaboration between Professor Fitzgerald's internationally recognised lab at UCL (Neuroscience, Physiology and Pharamology) and the clinical team on the Neonatal Unit at UCLH has pioneered methods of measuring cortical responses to noxious stimulation (including clinically required blood tests such as the heel lance) in the newborn.

Under the leadership of Professor Maria Fitzgerald and Dr Lorenzo Fabrizi we have investigated the neurobiology of pain in premature and term born infants who are in patients at UCLH. We have developed techniques using electroencephalogram (EEG), near infrared spectroscopy (NIRS) and fMRI to improve our understanding of the effects of prematurity and multiple painful and sensory experiences on the developing brain. Dr Fabrizi has set up a collaboration with academics and clinicians from King's College London and St Thomas' Hospital.

We have recently demonstrated that the pattern of responses to noxious stimuli changes with maturation and that the distribution of the responses over the cortex is gender dependent, even from birth. We have investigated neurovascular coupling using simultaneous EEG and NIRS. In a groundbreaking experiment we found that babies with high baseline cortisol measurements have larger cortical responses to noxious stimulation, but that this response is dissociated from the baby's facial and behavioural response. This implies that the use of clinical pain scores is limited, and will underestimate the extent of a baby's experience if the baby is already stressed.

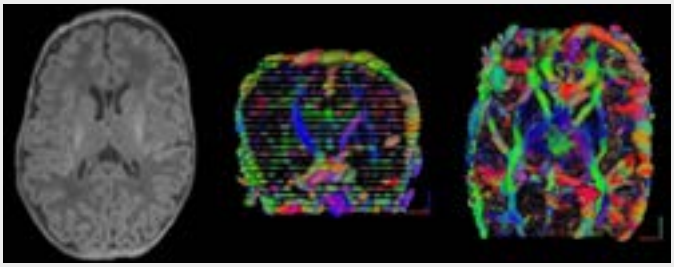
We are currently investigating the evolving connectome, how this is affected by a baby's pain history and how interventions such as kangaroo mother care can improve a baby's experience on the Neonatal Unit, and ultimately their outcome.

Neonatal MRI and MRS

G Kendall, S Mitra, N Marlow, N Robertson

Neonatal Magnetic Resonance Imaging (MRI) at UCLH has changed dramatically over the last 15 years. We have transitioned from in house designed and built magnets, coils and pods in which babies were imaged to commercial magnets and a state-of-the-art MR incubator to allow the safe imaging of smaller and babies with more complex illnesses. This has both allowed a better understanding of the conditions affecting individual babies and allowed individualisation of care. Much of what was considered research 10 years ago has moved into routine clinical practice for diagnostics and prognostication. One example is our routine use of magnetic resonance spectroscopy in babies with hypoxic ischemic brain injury. These techniques which were first used in neonates in the 1980s at UCL/UCLH defined the mechanisms of brain injury and allowed the development of clinical interventions including therapeutic hypothermia.

The strong collaboration with the Department of Medical Physics at UCL allowed the development of novel MR sequences to better delineate pathology and help plan clinical care. The use of 4D Arterial Spin Labelling (ASL) to measure the speed of blood flow through a vein of Galen malformation (a large arterio-venous shunt within the brain) is one example of how collaboration between neonatal medicine, radiology, medical physics and teams from Great Ormond Street Hospital and Institute of Neurology can develop new approaches to diagnostics and plan the timing and nature of interventions.



Optical monitoring in perinatal brain injury

S Mitra, I Tachtsidis, N Robertson

The UCL Baby Brain Study

Perinatal brain injury leads to significant mortality and morbidity. Despite progress in neonatal neurology over the last few decades, there is still an urgent need for an early real-time cot side biomarker to improve our understanding of the background pathophysiology and outcome prognostication in neonatal intensive care.

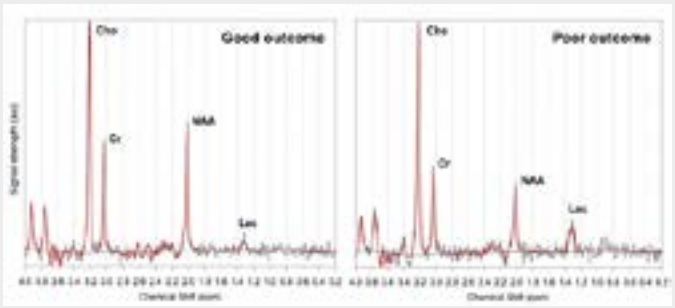
In collaboration with Dr Ilias Tachtsidis in the Department of Medical physics and Biomedical Engineering in UCL, we developed a novel broadband near infrared spectroscopy (BNIRS) instrument that can monitor real time changes in cerebral mitochondrial oxidative metabolism (changes in cytochrome c oxidase concentration (oxCCO)), cerebral oxygenation and haemodynamics. We have now monitored more than 100 infants in the neonatal intensive care unit in UCLH since 2014 using BNIRS and demonstrated that oxCCO monitoring can identify infants with poor outcome early at the cot side following neonatal encephalopathy. Background metabolic changes in the developing brain in real time during seizures were also described for the first time using cot side monitoring. Our group was selected this year to showcase the research work in the Royal Society Summer Science Exhibition.

Broadband NIRS monitoring in the neonatal intensive care in UCLH.

Magnetic resonance imaging biomarkers of neonatal encephalopathy

S Mitra, G Kendall, N Robertson

MRI is the imaging modality of choice for the assessment of injury pattern, severity and prognostication in neonatal encephalopathy (NE). It was important to review the MR biomarkers following introduction of cooling treatment as a standard of care in 2010. In a cohort of 55 term infants admitted between February 2012 and August 2014 to NICU in University College London Hospital for therapeutic hypothermia, thalamic Lac/NAA on 1H MRS at 3T MRI within first 2 weeks of life accurately predicted 2-year motor, cognitive and language outcome.



Lac/NAA peak area ratio >=0.39 on thalamic 1H MRS indicates poor outcome after hypothermia following neonatal encephalopathy.

Melatonin for Birth Asphyxia (MELBA)

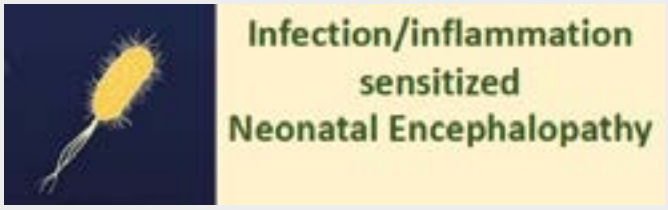
N Robertson, K Martinello, I Lingam, A Avdic-Belltheus, C Meehan, X Golay

In 2013, a research collaboration agreement was set up between N Robertson, UCL Business and Chiesi Pharmaceuticals S.p.A. to develop a novel melatonin formulation, with excipients safe for babies. This research collaboration (£1.6m) resulted in a series of studies defining the safety and optimal dose and therapeutic window for melatonin as an adjunct to therapeutic hypothermia for babies with neonatal encephalopathy (MELBA 1,2 & 3 studies). Orphan Drug Designation was obtained from the European Medicines Agency (EMA) for Melatonin as a Treatment for Neonatal Encephalopathy.

Infection-sensitized neonatal encephalopathy

N Robertson

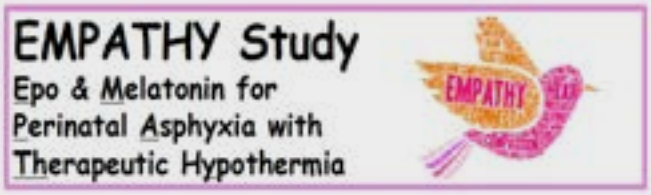
With Medcial Research Council (MRC) funding, we have developed an inflammation sensitized model of birth asphyxia which is relevant for low resource settings. With this model we can assess effective therapies in babies with infection/ inflammation co-existing with neonatal encephalopathy.



Epo and Melatonin for Perinatal Asphyxia with Therapeutic Hypothermia (EMPATHY). 2017-2019 (MRC funding)

N Robertson, K Martinello, I Lingam, A Advic-Belltheus, C Meehan, X Golay

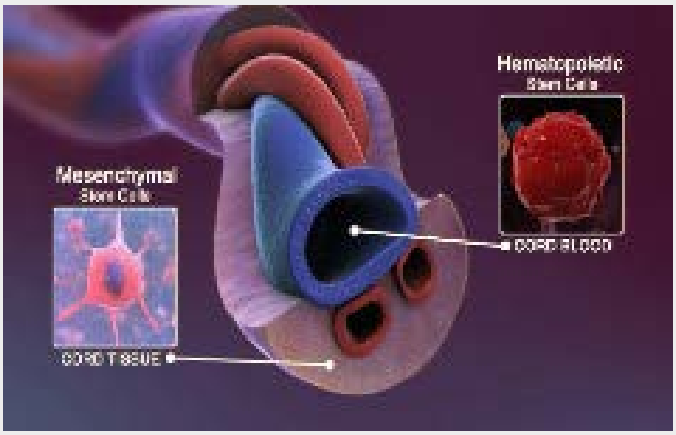
The Neonatal Neuroprotection Group studied a cocktail of therapies for neonatal encephalopathy – Erythropoietin (Epo), Melatonin and Therapeutic Hypothermia, alone or combined. The study focuses on both early and late neuroprotection and the chance of early Melatonin to target oxygen free radicals and Epo started after cooling to induce regeneration and repair.



Mesenchymal Stem Cells (MSC) to Protect and Repair the Brain after Perinatal Hypoxia Ischaemia

N Robertson, M Lowdell

We have investigated the potential of MSC to protect the brain after a hypoxic ischemic insult. 30 million MSC obtained from the Centre for Cell, Gene and Tissue Therapeutics at UCL were delivered either intravenously or intranasally following hypoxia ischemia in our model. We saw protection with the intranasally administered cells in terms of improved brain energy levels, reduced cell death in the white matter and improved recovery of the EEG. We will move on to larger studies of safety and efficacy with the aim to translate to clinical trials in neonatal encephalopathy.



Remote ischemic post conditioning (RIPostC) as a therapy for neonatal encephalopathy

N Robertson, D Yellon

Simple, low tech interventions are urgently required to improve outcomes in babies with neonatal encephalopathy (NE). In low resource settings where NE incidence is up to 10 times higher than developed world settings, therapeutic hypothermia may not be safe and effective; other therapies that do not require venous access and intensive care support are likely to be effective and sustainable.

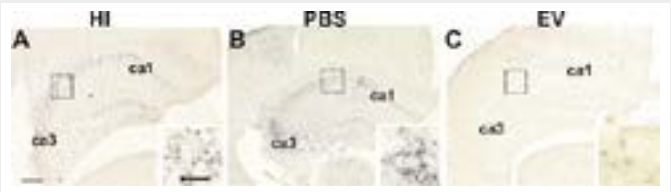
Remote ischemic postconditioning (RIPostC) is the application of a transient and brief ischemic stimulus to a distant site from the organ that has been exposed to severe HI and has been found to reduce brain injury in various animal models. Clinical trials in adults with stroke are on-going and show promise for RIPostC as a safe and effective therapy after stroke. We showed protection of the brain white matter in a neonatal model of HI with RIPostC given at 10 mins after HI; protection was seen in brain biochemistry, surviving white cells and overall reduced cell death and inflammation. We are focusing on the therapeutic window of RIPostC as a possible intervention for brain protection applicable to all settings.

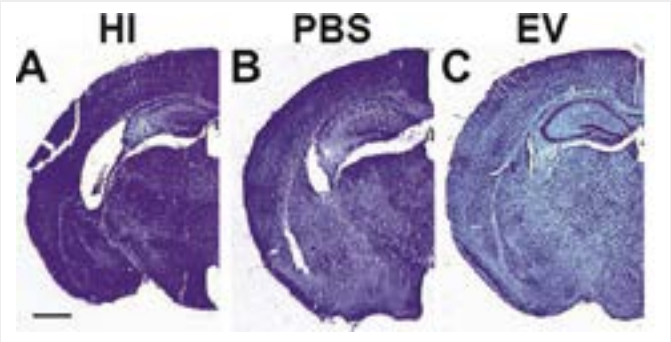
Treating perinatal brain injury

C Sisa, S Kholia, J Naylor, M Herrera Sanchez, S Bruno, M Deregibus, G Camussi, J Inal, S Lange, E Rocha-Ferreira, X Fontana, L Thei, R Buckle, M Christou, S Hompoonsup, N Gostelow, D Peebles, M Hristova

Birth asphyxia is a leading cause of disability and death in newborns, and currently there is no effective treatment to guarantee the complete recovery of the baby. Therefore, research in drug development for neonatal hypoxic ischaemic encephalopathy (HIE) is an urgent need for the public healthcare. We have found neuroprotective effects of stem cell-derived extracellular vesicles in a murine model of asphyxia induced brain injury.

In a mouse model of birth asphyxia we found that cell-specific STAT3-deletion significantly reduced brain damage markers, while systemic STAT3-inhibition reduced them to a more moderate degree. Our results suggest that STAT3 is a crucial factor in birth asphyxia and its removal in some cell types, and, to some extent, systemic inhibition reduces inflammation and tissue loss. Overall, the protective effects of STAT3 inactivation make it a possible target for a therapeutic strategy in neonatal HI.





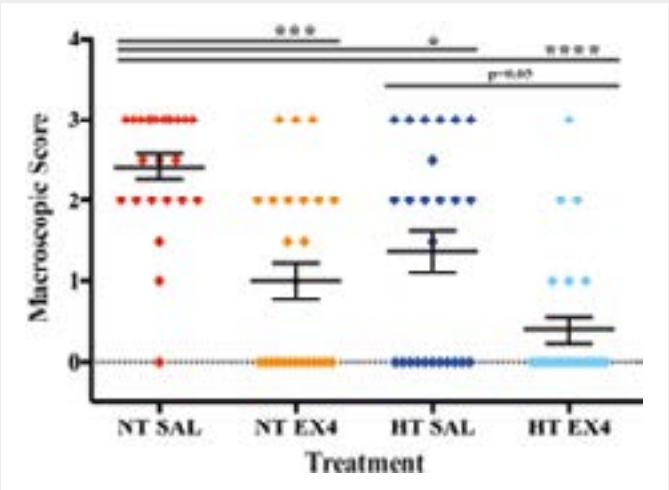
Histochemical overview of TUNEL+ cell death (top panel) and Cresyl-Violet stain (bottom panel) in the ipsilateral forebrain of control (HI, A), vehicle- (PBS, B), and extracellular vesicle-treated (EV, C) animals. Intranasal application of stem cell-derived extracellular vesicles following hypoxia ischaemia significantly reduces TUNEL+ cell death and volume loss at 48h.

Neuroprotective exendin-4 enhances hypothermia therapy in a model of hypoxic-ischaemic encephalopathy. Brain 2018

E Rocha-Ferreira, L Poupon, A Zelco, A Leverin, S Nair, A Jonsdotter, Y Carlsson, C Thornton, H Hagberg, A Rahim

Neonatal mortality accounts globally for almost 50% of total deaths in children under the age of 5. The three main risk factors are prematurity, birth asphyxia and infections. Survivors are at a high risk of developing lifelong neurological neurodisabilities, including cerebral palsy. Currently, there are no treatments available for preterm birth and subsequent brain haemorrhage. Cooling is the only treatment available for term birth asphyxia, but it is only available in high income countries, and over 50% of treated newborns still suffer adverse effects. Furthermore, cooling has been shown to be ineffective and even harmful in the presence of antenatal infection, which is highly prevalent in low resource settings. This has resulted in an unmet urgent need for development of brain protective strategies in neonates born preterm or suffering from birth asphyxia with and without infection that is applicable globally in both high and low resource settings.

Exendin-4 is a small peptide drug approved by the FDA in 2005 and EMA in 2006 for the treatment of type 2 diabetes mellitus, with ongoing clinical trials for Alzheimer's and Parkinson's diseases (NCT01971242 and NCT01255163). We have recently shown that exendin-4 protects the neonatal brain from birth-asphyxia injury, and also enhances hypothermia neuroprotection.



The EPICure Studies

N Marlow, A Gibson, K Costello, J Morris, E Draper, J Stocks, E Hennessy, S Johnson, D Wolke, J Beckman, A Melbourne, H O'Reilly, L McCormack, E Suonpera, A Fahy, M Bernardi, Y Ni, C Logon, R Lancaster, J Trickett, J Larsen, J Okell, J Hurst

The EPICure Studies are population-based studies of survival and later health status in extremely preterm infants. The IfWH hosts the Research Centre for these studies which originally commenced with a population study in 1995 and a second study in 2006 enrolling births before 26 weeks of gestation in 1995 (EPICure) and before 27 weeks in 2006 (EPICure2) (www.epicure.ac.uk). Since 2005 these studies have been supported by a programme grant from the Medical Research Council. These important studies are continuing to inform health policy in the care of extremely preterm infants today. The research teams also work with International colleagues to provide comparative information and individual patient analyses which increase the power of our studies. Two EPICure studies have recently been completed:

EPICure@19

This study evaluated the original 1995 cohort at 19 years of age. We invited all participants to a 2 day assessment at UCL and have been able to determine outcomes over the whole of childhood for this group. Key findings have been how stable measures made at 6 and 11 years are, how some of the psychological morbidity has tended to lessen with age and how well the group are doing as they settle into employment and higher education. We have shown exciting information on the childhood trajectories of several important outcomes.

EPICure2@11

EPICure2@11 has just completed the assessments of a sample of 200 children born before 27 weeks of gestation in 2006. Most were done at schools. These data will tell us the extent to which the improvements in outcomes we saw at 3 years of age have persisted.

The Preterm Development Project

N Marlow, M de Haan, S Johnson, S Ourselin

The Preterm development project is a longitudinal collaboration between neonatology (Marlow), developmental cognitive neuroscience (de Haan, Johnson) and Engineering (Ourselin). We have been following in detail the development of a group of very preterm children from birth through to school age. We have evaluated a whole range of infancy measures of executive function that appear to be only weak predictors of later function and are now studying how these cognitive processes differentiate into school age. We will detail differences in preterm development from this perspective and how it links into school attainment.

PDP
UCH Preterm Development Project

Parents and Neonatal Decisions (PND)

N Marlow, P Drew, C Shaw, K Gallagher, N Aladangady, K Connabeer, T Morris

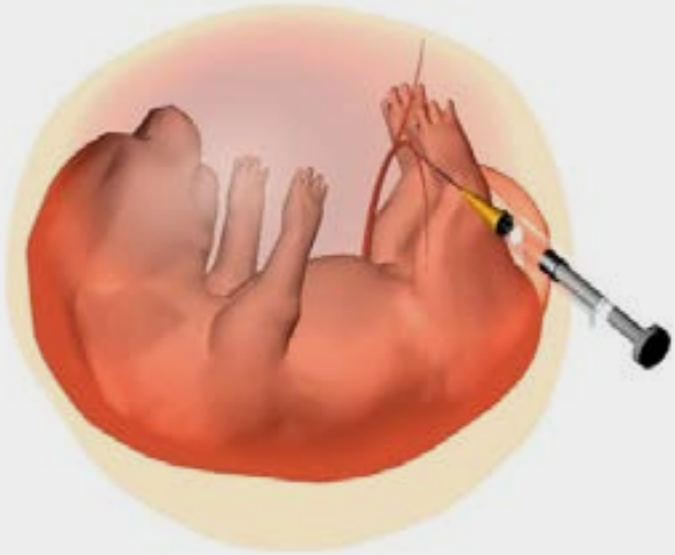
Parents and Neonatal Decisions (PND) is part of a study to evaluate what happens when doctors recognise serious brain injury in newborn babies. Withdrawing Life Sustaining Treatment (WiLST) was developed by Marlow working with Alagandagy at Homerton Hospital to determine how often challenging decisions are made. As a result of this PND has been recording and analysing conversations between doctors and parents to improve the way these decisions are made (Marlow, working with Stokoe (Loughborough) and Drew (York). We have run our first educational workshop from this work and are planning further training with the Stillbirth and Neonatal Death Society (SANDS) at present. Separate studies into how doctors introduce unexpected news and how pain is described are underway.

Parents & neonatal decisions

Gene therapy for neurological disorders

R Privolizzi, M Tijani, A Rahim, M Kurian, S Waddington, J Ng

Our work has been focusing on the development of gene therapy for untreatable childhood neurological disorders. We are developing adeno-associated viral vectors aimed towards clinical application for childhood movement disorders and stroke. The main research focus is studying viral vector tropism and expression efficiency modified by capsid and promoters to target the central nervous system in vivo for different neurological disease application. We validate clinically translatable gene therapy designs in relevant cell and animal models of childhood neurological disease. We received the British Society for Gene and Cell Therapy (BSGCT) Fairbairn Award and MRC Developmental Pathway Funding Scheme (DPFS) translational grant towards developing clinically applicable gene therapy for Dopamine transporter deficiency syndrome with Professor Kurian and Dr Rahim. We received a UCL Impact PhD studentship for Riccardo Privolizzi to develop novel CNS gene therapy promoters with Synpromics Ltd and work closely with their promoter design team and research scientist Dr Maha Tijani. GFP immunohistochemistry of novel CNS promoters in mouse brain sections (Tijani, Privolizzi et al 2019)

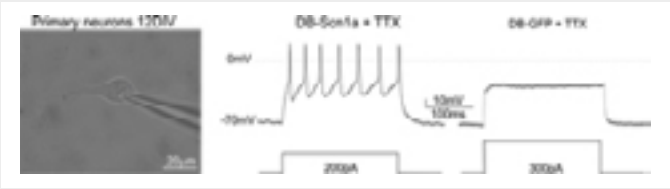


Delivery of gene therapy to a fetal mouse

Gene Therapy for Inherited Epilepsies

J Antinao Diaz, M Berti, S Schorge, G Lignani, S Waddington, J Counsell, R Karda

We have been developing gene therapy for the inherited lethal childhood-onset epilepsy, Dravet Syndrome. Our team has been evaluating different viral vector strategies in two mouse models of this disease and we collaborate closely with Stephanie Schorge (UCL School of Pharmacy) and Gabriele Lignani (UCL Institute of Neurology). We received an MRC DPFS, and SPARKS grant to fund the studies of our PhD student, Juan Diaz, and a third grant, as Principle Investigator, co-funded by SPARKS/GOSH and Dravet Syndrome. Our aim is to bring gene therapy for Dravet Syndrome to the clinic in the next 5-10 years.

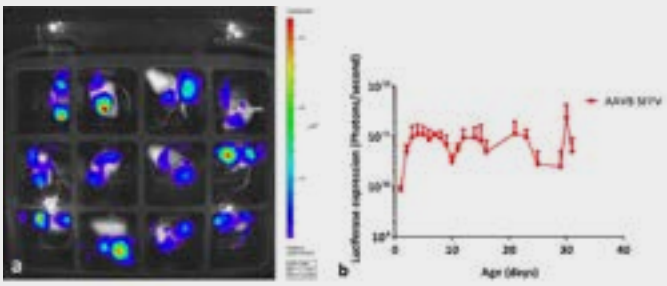


Action potentials in neurons after gene delivery of corrected copies of the gene which is mutated in Dravet Syndrome patients

Gene Transfer for Bioluminescence Imaging

S Waddington, S Buckley, T McKay, A Rahim, N Suff, D Perocheau, N Palomar Martin, E Henckaerts, M Hughes, J Delhove, R Karda

In a parallel we have been developing light-emitting biosensors to address the aims of the National Centre for Reduction, Refinement and Replacement towards improving animal welfare in research. Using this technology we are able to monitor physiological and pathological processes in conscious, freely-moving mice in a non-invasive way.



Non-invasive bioluminescence imaging in conscious, freely-moving mice

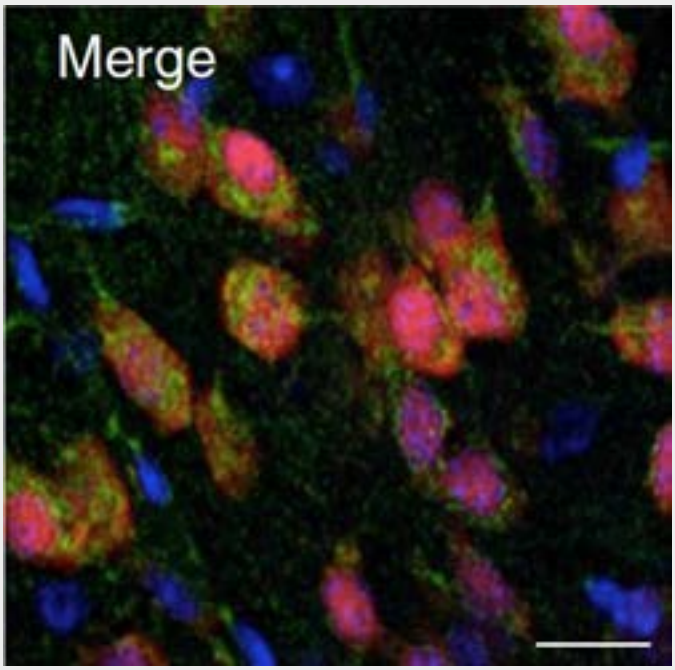
Developing gene therapy for multi-organ diseases: the success of argininosuccinic aciduria

J Baruteau, D Perocheau, J Hanley, M Lorvellec, E Rocha-Ferreira, R Karda, J Ng, N Suff, J Diaz, A Rahim, M Hughes, B Banushi, H Prunty, M Hristova, D Ridout, A Virasami, S Heales, S Howe, S Buckley, P Mills, P Gissen, S Waddington

Over the last decade, clinical success of gene therapy have been achieved for hemoglobinopathies, immunodeficiencies, inherited clotting disorders, retinal blindness or spinal muscular atrophy. These approaches were focussing on a single organ target. However various inherited diseases present with multi-organ involvement, which has not been successfully treated by gene therapy.

Argininosuccinic aciduria is an inherited disease caused by argininosuccinate lyase (ASL) deficiency. This disease presents defective ureagenesis with hyperammonaemia and a systemic disease, especially a neurological disease with neurocognitive deficiency, behavioural difficulties and epilepsy. A gene therapy mediated by adeno-associated viral vectors (AAV) was developed to successfully target cerebral neurons and hepatocytes after systemic injections in neonatal ASL deficient mice. This corrected the impaired urea cycle in the liver and the neuronal nitric oxide metabolism enabling a dramatic improvement of the neurological disease. This provided a proof-of-concept of the ability of AAV gene therapy to sustainably treat multi-organ diseases and various metabolic cycles after an unique systemic administration.

This work has enabled seminal pathophysiological findings in argininosuccinic aciduria highlighting a neuronal disease with oxidative/nitrosative stress, independent of hyperammonaemia. This is leading to a better understanding in the role of ASL in neuronal physiology, neuroinflammation, neurodevelopment and neurodegeneration. Other delivery systems (i.e. exosomes, mRNA, protein-mediated delivery) are now being considered to target the liver and the central nervous system.



Nitrosative stress in cortical neurons of ASL deficient mice. Immunostaining of nitrotyrosine (green), NeuN (red) and DAPI (blue). Scale bar 500µm

Healthy Sexual Development

Awareness of fertility is vital to our future generations. The Institute works to ensure that young people are empowered to have healthy sexual development, and to help those where gynaecological development is dysfunctional. We aim to improve sexual and reproductive health (SRH) care through research, training, service enhancement and empowerment through knowledge transfer.

Female Genital Cutting

S Creighton, L Liao

Clinicians from UCLH have made a major contribution to the National and International debate on Female Genital Cutting (FGC). The work is led by Lih-Mei Liao and Sarah Creighton and falls into three broad categories:

- Differences in Sex Development (DSD/Intersex)
- Female Genital Cosmetic Surgery (FGCS)
- Female Genital Mutilation (FGM)

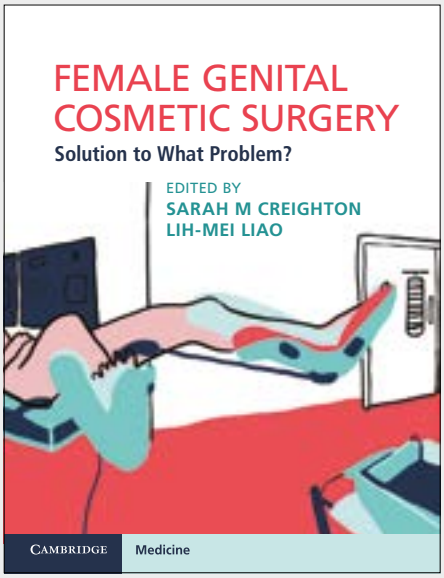
This work has been ongoing since the inception of the IfWH and highlights of the past five years are as follows:

Differences of Sex Development (DSD/Intersex)

Early research at UCLH into adult outcomes of infant and childhood feminising surgery for atypical genitalia confirmed that early surgery has psychosocial ramifications and damages adult sexual function. Infant and childhood genital surgery for DSD is now recognised as a human rights violation. This development has influenced the body of ground breaking psychosocial research involving the UCLH team led by Professor Katrina Roen (University of Oslo) and Professor Peter Hegarty (University of Surrey). The research is now at different stages of dissemination. Meanwhile our editorial in the BMJ in 2015 "Parental choice on normalising cosmetic genital surgery: between a rock and a hard place" highlighted the need for non-surgical management pathways. In 2018 NHS England established a working party to develop integrated multidisciplinary care and a policy on infant genital surgery. Several experts from UCLH are involved, including Gerry Conway (endocrinologist), Sarah Creighton, Lih-Mei Liao and Dan Wood (adolescent urologist).

Female Genital Cosmetic Surgery (FGCS)

The development of female genital cosmetic surgery (FGCS) into an industry raises ethical, medical and psychosocial concerns. In 2012 Sarah Creighton and Lih-Mei Liao were involved in developing two UK guidances. In 2017 Louise Williams (clinical nurse specialist) and Hazel Learner (clinical fellow) were awarded a grant to produce an information resource to educate girls and young women on vulval appearance diversity "So what is a vulva anyway". In March 2019 a new book edited by Sarah Creighton and Lih-Mei Liao "FGCS: Solution to What Problem?" interrogates the cultural and economic drivers of FGCS, helps researchers to reformulate their questions, and provide social, psychological and educational solutions for girls and women with genital appearance concerns.



Female Genital Mutilation (FGM)

In 2014 Sarah Creighton and Deborah Hodes (paediatrician) established the UK's first and only clinic for girls with FGM or suspected FGM. This unique clinic has allowed publication of the first data on FGM practices in migrant communities. We demonstrate that FGM occurs less frequently than expected given the population. This has led to cautious optimism about abandonment of FGM in the UK. Our editorial in the BMJ in 2019 "Tackling FGM in the UK: current response is disproportionate" highlights the poor treatment of innocent families suspected of FGM and calls for a change in strategic response.

Research into Use of Contraception

J Stephenson, J Bailey, A Gubijev, A Blandford, A Copas, P d'Souza, S Oliver.

CONTRACEPTION choices

The SRH group has conducted some key studies to improve women's choice of contraceptive options.

We did a randomised trial with 500 women to compare the acceptability of tailored versus standard pill regimens over one year. A tailored regimen involves fewer pill free days and reduces the amount and frequency of bleeding compared with the standard regimen. The findings are reported in National Clinical Guidance on Combined Hormonal Contraception (FSRH 2018) as evidence supporting wider use of tailored regimens. We developed and evaluated an interactive website to improve informed choice of contraceptive method, and then conducted a randomised trial to test its impact in a clinic population of women aged 15-30 years. Despite the benefits of contraception, we know that myths, misunderstandings and concerns still abound.

Contraception Choices (www.contraceptionchoices.org), provides information on the effectiveness, benefits and side effects of a range of contraceptive methods, and addresses common concerns using clearly presented text, interactive graphics, and videos. The site features the What's Right for Me? interactive tool to help women choose a method of contraception tailored to their preferences.

The feedback from over 414 (90%) of the women who used the website was strikingly positive: *"I feel very well educated thanks to the website – I wish someone had explained about all the different choices years ago."*

"It's what I've always looked for, a clear way to compare methods of contraception and find the best for you, with in-depth information about how they work"

The website also helped women to be better prepared before appointments with doctors and nurses: *"It has left me more informed and help me make a decision. It also allowed me to have more of a say when I saw my GP about my options."*

Adolescent gynaecology – hormone treatment

M Davies, C Brain

During the last 5 years we have built up a joint service for adolescents between paediatric endocrinology and reproductive medicine. We see teenagers transitioning to adult services, all of whom require hormone treatment. Many of them have not entered puberty and we monitor their growth and development on oestrogen therapy, which has a huge impact on their emotional and social well-being. There is little evidence on the best method for induction of puberty and bids for funding for comparative trials have not so far been successful. We are collaborating with the European Society of Paediatric Endocrinology to try to set up prospective observational studies.

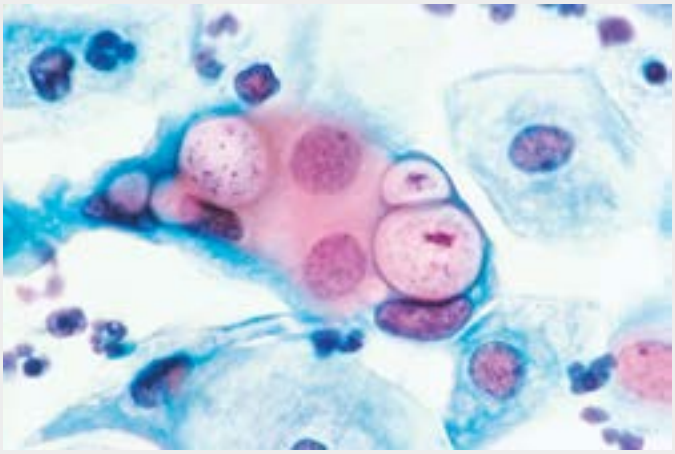
Improving the National Chlamydia Screening Programme

J Stephenson, S Dave

National Chlamydia Screening Programme

Chlamydia is one of the most common sexually transmitted infections (STIs) in the UK. Research by the UCL Institute of Women's Health into the effectiveness of chlamydia screening resulted in changes to the National Chlamydia Screening Programme in England. Through systematic review of available evidence (2009), we recommended focusing chlamydia testing within sexual health and primary care services rather than screening low-risk groups. These changes, together with related efficiencies, were expected to save the NHS £40 million per year. The current National Chlamydia Screening Programme has made changes in line with our recommendations.

"Finding and treating chlamydia infection in asymptomatic women is a good thing, but there is no clear evidence that population-based screening reduces long term complications (ectopic pregnancy or infertility)." Quote from Judith Stephenson plenary debate at the STI and AIDS World Congress in Vienna 2013.



Chlamydia in a cervical smear preparation

BRCA UNITE (Uniting researchers and BRCA mutation carriers to advance our understanding of hereditary cancer)

M Widschwendter and BRCA Team

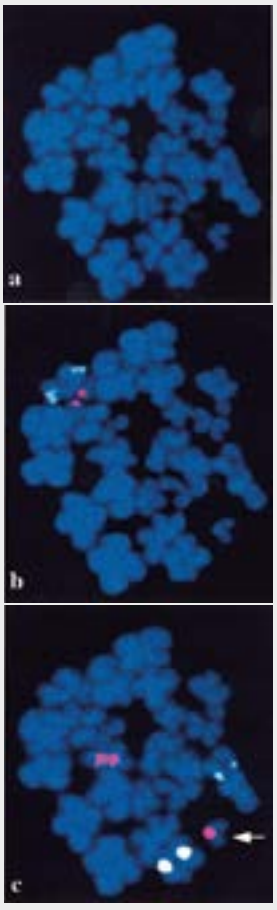
BRCA UNITE (www.brcaunite.org), aims to build upon the ethos of BRCA PROTECT by further characterising those cellular non-autonomous factors that may impact on organs at risk of tumour development. Identifying these potential biological triggers may help with the development of "cancer neutralising" preventive strategies as an alternative to invasive risk-reducing surgery. This innovative research project aims to prospectively follow women over an entire menstrual cycle in order to understand the interplay between hormonal changes, immune function and gut microbiome. To date, no study has taken such a holistic approach to further our understanding of the BRCA gene mutation. At present we are focusing on women with the BRCA1 or 2 gene mutation and wild type controls who are negative for BRCA1 and BRCA 2 gene mutations (siblings, cousins, those with similar backgrounds) to act as controls, as the BRCA mutation subset are at a significantly increased risk of developing breast and ovarian cancer. The rationale behind the name of the study 'BRCA UNITE' was based on the ethos of a true collaboration between researchers and members of the BRCA community, uniting to advance our understanding of hereditary cancers. In parallel we generated the concept of 'BRCA Champions', who would be members of the BRCA community, all with different stories and journeys, and who would also be advocates and supportive members of the research community and support those taking part in the study.

When do chromosome errors arise in oocytes?

J Delhanty, S Sen Gupta, H Ghevaria

Oogenesis (egg formation) is an error prone process in humans. Most errors affect the final stages of egg maturation, just before it is released from the ovary. As women age the risk of an oocyte with abnormal chromosomes (aneuploidy) increases because by then the egg is an 'old' cell.

We have applied molecular cytogenetic techniques and most recently next generation sequencing to study the DNA of oocytes to find out exactly when errors occur. This has shown that a significant amount of aneuploidy is in fact already present in oocytes in the early embryo, leading to a high risk of chromosomally abnormal eggs irrespective of the mother's age. This provides an explanation for why some chromosomally abnormal babies are born to younger women. In future we plan to investigate how the woman's genes affect this early aneuploidy.



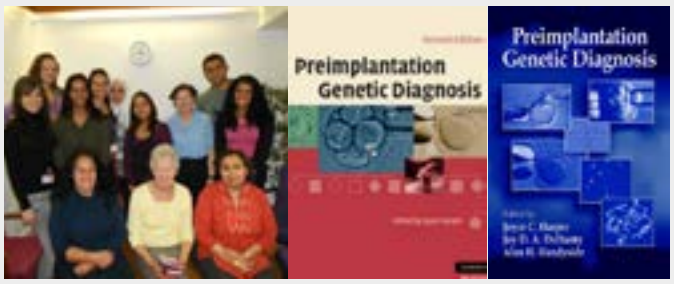
Direct examination of chromosomes from a mature oocyte using fluorescent microscopy. There should be one copy of each chromosome; a) is the counterstain on its own showing all the chromosomes. b) analysis of the chromosomes with probes for chromosome 13(green) and 21(red). Each chromosome consists of two halves (chromatids) so the fluorescent spots are seen in duplicate. c) is a re-analysis of the same oocyte with probes for chromosomes 16 (red), 18 (green) and X (gold). Overall this oocyte is normal for chromosomes 13, 21,18 and X. The arrow identifies an additional chromatid for chromosome 16.

UCL Centre for Pre-implantation Genetic Diagnosis

J Delhanty, J Harper, S Sen Gupta

There have been a number of world 'firsts' for the UCL group:

- First clinical cases of pre-implantation genetic diagnosis (PGD) for embryo sexing by fluorescence in situ hybridisation (FISH) to avoid X-linked disease.
- Abnormalities due to chromosome translocations first diagnosed by FISH in embryonic cells for PGD.
- First case of a 'cancer gene' (for colon cancer) diagnosed in embryos for PGD.
- First cases of PGD for a Breast/ovarian cancer gene (BRCA1), Retinoblastoma, Neurofibromatosis 1 & 2 and several other 'cancer genes' in UK

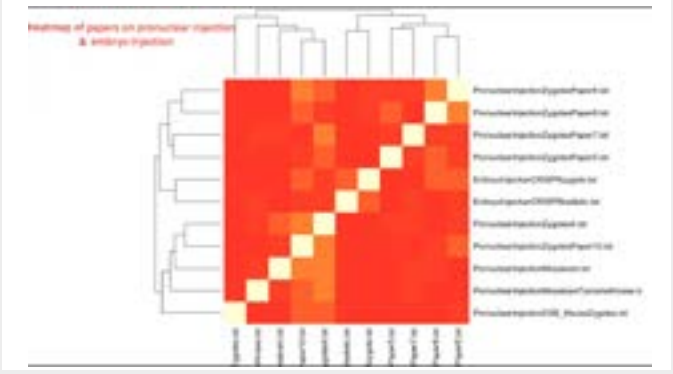


From 1998 until early 2015 the team performed PGD clinical cases for a known genetic condition and pre-implantation genetic screening (PGS) cases for chromosome abnormalities in infertile couples.

Treatment Cycles started	545	(PGD 350 PGS 195)
Deliveries	154	
Twins	16	
Babies	170	All healthy

All cycles received a diagnosis and there were no misdiagnoses.

During this time we received approximately 1250 referrals. Until the advent of NHS England in April 2013 there was no core funding for PGD, and applications were made on a case by case basis. Since 2015 the service has been carried out by commercial companies, allowing many more couples to be able to start a pregnancy knowing that their baby will not be affected by the genetic disorder that is in their family. As a result, the IfWH team closed their service, but the legend of our innovative service lives on as so many of the world's experts were trained at UCL.



ESHRE PGD Consortium

J Harper, S Sengupta

After Joyce Harper wrote two reports on the global status of preimplantation genetic diagnosis (PGD) in 1994 and 1996, the world leaders in PGD felt it was important to continue this work and in 1997, Joyce was co-founder of the European Society of Human Reproduction and Embryology PGD Consortium. As chair and deputy chair of the consortium, Joyce led on projects including writing guidelines, position statements, annual data reports and organising workshops. Sioban SenGupta joined the steering committee and was instrumental in setting up the external quality assessment scheme. In 2017 the consortium held a celebration of the first 20 years in Brussels.

First meeting of ESHRE PGD Consortium 1997

Celebration in 2017

Analysis of Guide Design Algorithms for CRISPR Genome Editing in preimplantation embryos; Reassessing Mosaicism and Off-Target Editing

H O'Neill

Genome editing (CRISPR-Cas9 or Base Editing) is a revolutionary tool which allows DNA or RNA to be altered at directed loci in the genome with ease and efficiency. The advances in genome editing coupled with assisted reproductive technologies and genomics lend themselves to germline therapy and the correction of genetic disorders in embryos.

In order for this to reach the clinic, significant and rigorous testing must be carried out to ensure that edits are controllable, reproducible and that mosaicism is avoided. Our research focuses on the delivery of components of CRISPR, assessing the accuracy of edits and measuring mosaicism in edited murine preimplantation embryos.

We are also using in-silico based methods to analyse RNA-guide design algorithms to predict mosaicism and machine learning to allow for global examination of accurate protocols for precision.

Children by Choice and Healthy Pregnancy

The Institute aims to help women on their journey to having a family if they choose to do so. We research pregnancy planning and how to optimise preconception health. We are developing novel therapies for pregnancy diseases such as pre-eclampsia, preterm birth and fetal growth restriction, so as to improve the health of mothers and their babies. Our research also provides new opportunities for the primary prevention of future disease in mother, father and offspring in later life.

Preconception Health and Measurement of Pregnancy Planning

J Hall, G Barrett, J Stephenson, D Patel, B Grace, B Howden

Our compelling research into the importance of the preconception period for future health, and vision for improving health before pregnancy, has generated new definitions of the preconception period and driven national policy in this area, including the Chief Medical Officer (CMO) for England's 2015 annual report on women's health and Public Health England's 2018 launch of 'making the case for preconception care'.

A truly 'high' point was a 3-day meeting in the Lake District (2016) of transdisciplinary experts with mandatory fell walk! This collaboration resulted in a series of papers in the Lancet on preconception health and the formation of the UK Preconception Partnership, a group of experts and stakeholders, to translate research into policy and practice.

Members of the Sexual & Reproductive Health Research Group atop a Lakeland fell (from left to right: Dilisha Patel, Judith Stephenson, Bola Grace and Mary Barker).

Our research into the measurement of pregnancy planning is also world leading. We developed the London Measure of Unplanned Pregnancy (LMUP), a simple, validated score of the 'plannedness' of a pregnancy. We have shown that the LMUP is valid across many countries and in Malawi we found that it predicts maternal post-natal depression and possibly stillbirth. Our pilot study for including the LMUP in London maternity services will pave the way for its use in all maternity services in England.

In the next 15 years, we hope that:

- Throughout health care, conversations about planning and preparing for pregnancy are routine, rather than rare.
- National policies support better health before pregnancy, for example, through mandatory fortification of flour with folic acid, a healthier food environment and education in schools.
- That our work serves to hold governments and other agencies to account to deliver interventions to improve preconception health.
- That we can measure the impact of these changes nationally on the extent of pregnancy planning (LMUP), and on pregnancy and birth outcomes.

Expectant Management of Ectopic Pregnancy

D Mavrelos, H Nicks, W Hoo, E Jauniaux and D Jurkovic

Tubal ectopic pregnancy is a common condition affecting 3% of first pregnancies. While this can be a life threatening condition requiring surgery, up to a third of women can be treated conservatively avoiding surgery and keeping their Fallopian tube.


Editorial

Working with Mr Davor Jurkovic we have published work on the safety and efficacy of a new protocol to manage ectopic pregnancy expectantly. This work, demonstrating expectant management as a safe alternative option for women with tubal ectopic pregnancy, has been incorporated in latest RCOG and NICE guidance and is likely to have helped a number of women to avoid life changing surgery and removal of a Fallopian tube.

One-stop gynaecology Clinics

D Jurkovic, M Memtsa, E Sawyer, A Donaldson, A Jamil, K Schramm, Y Sana, M Otify, L Farahani, N Nunes, G Ambler, J Ross

UCLH has for a number of years offered one-stop services for women with problems in early pregnancy, acute gynaecological conditions and those needing urgent assessment because of suspected gynaecological cancer. These clinics are consultant-led, supported by clinical fellows, and provide ultrasound imaging combined with medical diagnosis and management. The benefits are rapid turn-around times, good clinical outcomes and improved patient experience. Examples of where this approach has led to research that changes clinical management are: a randomised control trial looking at the use of methotrexate, a widely used treatment in women requesting conservative management with an ectopic pregnancy compared with expectant management alone. This study concluded that expectant management was safe and that methrotrexate conferred no additional benefit

VESPA

D Jurkovic, M Memtsa

VESPA – a Health Research Authority supported study led by Davor Jurkovic (UCLH Gynaecology Consultant) has looked at variations in the organisation of Early Pregnancy Assessment Units (EPAUs) in the UK and their effects on clinical, service and patient-centred outcomes.

Prenatal diagnosis and prevention services for haemoglobin disorders

M Petrou, B Modell, M Darlison, A Schuh, A Cutts, D Vavoulis, S Henderson

UCL was key to research and implementation of prevention services for haemoglobin disorders starting from 1976. The team have trained more than 50 health professionals from different countries in the prevention of haemoglobin disorders and now train three international trainees every year under the Thalassaemia International Federation (TIF) Renzo Galanello Fellowship programme. They collaborate within the UCL WHO Collaborating Centre for Community Control of Hereditary Disorders: producing information materials for haemoglobinopathies which is used globally in genetic counselling.

Working with a team from Oxford University (AS,AC,DV,SH), research has developed non-invasive prenatal diagnosis of monogenic autosomal recessive disorders with a particular focus on sickle cell anaemia. The aim is to implement the method into routine antenatal care after a period of offering this test in parallel with invasive prenatal diagnosis.

Mary Petrou is working with teams in Pakistan and Bangladesh to develop culturally sensitive prevention programmes of premarital screening, genetic counselling and prenatal diagnosis. Her research is studying the knowledge, perceptions and social implications of thalassaemia in Bangladesh and the views of at risk couples towards prenatal diagnosis and termination of pregnancy.

The Institute also donated equipment to Dhaka Children's Hospital to be used in screening for carriers of thalassaemia.

With colleagues and thalassaemia patients at the International thalassaemia workshop in Dhaka, Bangladesh, January 2019

The placenta and early pregnancy

E Jauniaux, D Jurkovic

Eric Jauniaux and his team have worked for over 30 years on placental organogenesis, physiology and the pathophysiology of placental-related disorders of pregnancy. In collaboration with Pr GJ Burton (University of Cambridge) and Pr B Gulbis (Universite Libre de Bruxelles), we have demonstrated that one of the essential roles of the primitive placenta is to protect the developing fetus from the effects of free radicals. We also showed how inadequate placentation leads to pregnancy complications such as miscarriage and preeclampsia. We have made several ground-breaking discoveries on how the placental circulation establishes and the role of alternative transfer pathways inside the first-trimester gestational sac. Recently we demonstrated the importance of secondary yolk-sac transfer. Our work has changed anatomy teaching around the world and has been integrated in the last 3 editions of the classic textbook Gray's Anatomy.

More recent research on invasive placental disorders such as placenta accreta has led to the development of an international classification. Eric was lead developer for the RCOG Green Top Guidelines on placenta praevia, placenta accreta and vasa praevia and for the FIGO guidelines on the diagnosis and management of placenta accreta spectrum disorders. Eric is now working with the NHS England specialised working group on service specifications for maternity care for women diagnosed with abnormally invasive placenta.

3D image of the early embryo in the uterus

Training room on labour ward

D Peebles

We have launched a training room on the labour ward; bringing training to the clinical area and creating opportunities for an MDT approach. Initial focus has been on the design and implementation of exercises that support the development of skills and understanding in the estimation of blood loss and the management of the 2nd stage. This is to provide immediate opportunities for learning and a timely response to lessons learned from local incidences, as well as recent results from the survey of 2nd stage management. Initial findings show that 3rd/4th degree tear rates have reduced from 5% to 2%.

Driving national screening standards for fetal medicine including NIPT and NIPD

P Pandya

As Chair of the Fetal Anomaly Screening Programme (FASP) Advisory Group, Public Health England (PHE) Pran Pandya is centrally involved in developing and implementation for national standards in screening for trisomy 21, 18, 13 and fetal anomalies at 18-20 week anomaly scan. He lead at a national level the implementation of non-invasive prenatal testing (NIPT) to screen for Trisomy 21, 18 and 13, and was centrally involved in developing the pathway, e-learning, advice to parliament, ethical review (Nuffield Council), inclusion of twins and QA. NIPT will result in 5000 fewer invasive procedures in England every year and fewer miscarriages.

Under his leadership of the major congenital heart defects (CHD) sub-group at FASP the group have implemented the 3 Vessel Trachea (3VT) view into routine ultrasound in all Trusts in England. National detection rates are up from 40% to 64%. Pran is also working with the National Congenital Anomaly Register Committee, Public Health England national audit to cover all of England. The data is being used to improve screening performance e.g. defining geographical variation and targeting resources to improve performance.

Transverse view of the fetal heart at 20 weeks showing the three vessel and trachea view

Women's Health Psychological Services (WHPS)

LM Liao

The goal of the Women's Health Psychological Services (WHPS) is to increase care users' capacity to: 1) reduce psychological distress and incapacity associated with gynaecological and fetal-maternal-neonatal complications and 2) maximise function, goal engagement and quality of life. We do this via advance psychological interventions that are clearly linked to research evidence and/or recognisable psychosocial frameworks. Seeded initially by research interests of academic clinical psychologists at UCL in the 1980s, and developed by NHS clinical psychologists from the 1990s, the current multi-professional staff share the longest history in the UK for delivering psychological care in Women's Health. Currently, services exist for gynaecological specialties (gynaecological oncology, reproductive medicine, diverse sex development, female genital mutilation) and fetal-maternal-neonatal medicine. In the past 15 years, the group has moved from a sprinkling of part-time counsellors and psychologists with unclear roles and responsibilities to a single department that produces regular audits, promotes learning, trains medical and midwifery staff, and reports to the clinical director and divisional manager via the consultant clinical psychologist. Embedded in our research-rich division, individual WHPS staff hold track records of academic outputs and professional contributions to national care standards. WHPS is more than just a therapy service. As biomedicine advances, the need for psychosocial understandings of process, outcome and dilemma will grow. We see this, and we are ready for new challenges as they emerge.

Some WHPS staff work closely with maternity care providers

Guided Instrumentation for Fetal Therapy and Surgery (GIFT-Surg)

R Aughwane, Y Kunpalin, B Dromey, A Sacco, R Napolitano, A David, D Peebles, J Deprest, R Wimalasundera, G Attilakos

GIFT-Surg is a 7 year Wellcome Trust and EPSRC funded collaborative project that aims to improve the outcomes of fetal surgery and intervention through development of new technologies. Engineers from UCL Centre for Medical Image Computing and UZ Leuven, Belgium, and clinicians within the Institute of Women's Health and UCL Great Ormond Street Institute of Child Health are working together to understand the challenges faced by surgeons working in this restrictive environment, and develop creative solutions.

Progress this last year has been made in optimising a needle tracking system to improve accuracy of ultrasound guided interventions, advanced computer training systems to ensure surgeons are adequately skilled before performing procedures, and automatic segmentation of Magnetic Resonance Imaging. There is a thriving patient public engagement group which guides the group.

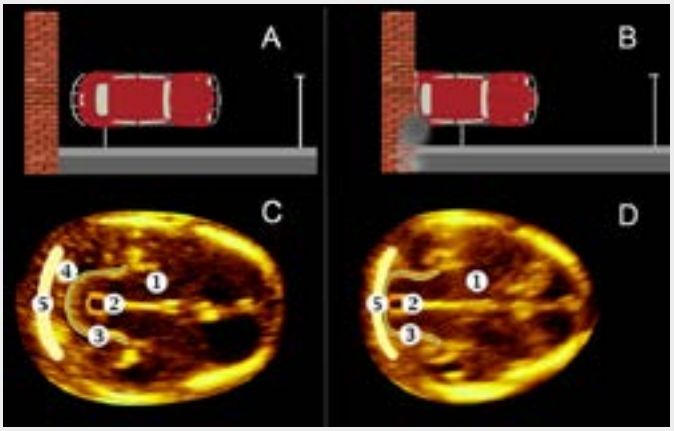
Photo from the GIFT-Surg Patient Public Engagement Group (PPIAG).

Fetal surgery for spina bifida around the world

A Sacco, J Deprest, A David

Over the last 18 months we have evaluated global availability of fetal surgery for myelomeningocoele/open spina bifida in collaboration with the International Society for Prenatal Diagnosis (ISPD). Since the publication of the MOMS randomized control trial in 2011 that showed fetal surgery improved neonatal outcomes, there has been a rapid expansion in centres offering surgery. Two-thirds offer open fetal surgery only but some are now offering fetoscopic repair. The map is available on the ISPD website through the Fetal Surgery Special Interest Group (SIG) co-chaired by Anna David and Lynn Simpson from Columbia USA.

Fetal surgery for spina bifida around the world. Images by Myrthe Boymansm, reproduced with permission from the Fetal Medicine Unit, UZ Leuven, Belgium.



Crash Sign: A new First Trimester Sonographic Marker of Spina Bifida

F Ushakov, A Sacco, T Everett, A David, P Pandya

We have described a new first trimester sonographic sign associated with fetal spina bifida with collaborators from Moscow regions Research Institute of Obstetrics and Gynecology, Medical-Genetics Department, Moscow, Russia (Elena Andreeva), and University of Medicine and Pharmacy Craiova, Romania (Stefania Tudorache). The "crash sign" is seen where there is posterior displacement and deformation of the mesencephalon against the occipital bone in the axial sonographic view of the fetal head.

12-13 weeks ultrasound images of the mesencephalon in a normal fetus (left) and its posterior displacement and deformation against the occipital bone in a fetus with open spina bifida (right): the "crash sign". (1) thalami, (2) aqueduct, (3) mesencephalon, (4) arachnoid space, (5) occipital bone.

The EVERREST project: developing a treatment for fetal growth restriction

A David, R Spencer, J Dyer, C Rossi, K Maksym, Y Ginsberg, T Weissbach, C Heppolette, D Peebles, N Marlow, A Huertas-Ceballos, L Ingram, J Okello and the EVERREST consortium

Fetal growth restriction (FGR) is an untreatable condition affecting up to 8% of all pregnancies. Babies born from growth restricted pregnancies are not only at increased risk of perinatal death and complications such as cerebral palsy, but there are long term consequences for their health which include diabetes and cardiovascular disease. When severe and early onset, the affected babies stop growing in the womb and are extremely small, often less than 500g. Some even die in the womb. There is no treatment.

The EVERREST project, led by the Institute and funded by the European Commission has been bringing a completely new therapy to the clinic over the last 6 years. This aims to increase maternal blood flow to the placenta by delivering an adenovirus vector gene medicine containing the Vascular Endothelial Growth Factor (VEGF) to the uterine arteries. In pre-clinical FGR pregnancies the maternal growth factor gene medicine safely increases fetal growth and birthweight. What is most promising is that relatively small increases in fetal growth and gestational age at delivery are associated with major improvements in survival and morbidity.

The EVERREST consortium found no ethical and regulatory concerns about the therapy and patients welcomed a treatment. An observational study of severely affected pregnancies at four academic health science centres has defined the inclusion and exclusion criteria for the trial. It has also improved our understanding of the disease and outcomes. The drug product has been manufactured and two reproductive toxicology studies found that it had a good safety profile. The project has a thriving patient group who met for the second time in November 2018 to review the results and guide clinical trial application. Regulatory submission to start the first-in-woman clinical trial is ongoing.

The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007–2013) under grant agreement no. 305823

Baby Abigail was born 12 weeks early with severe early onset fetal growth restriction. She weighed just over half her expected weight. Sadly she died at just 10 ½ months old and will always be missed. © The Times. All Rights Reserved.

EVERREST Patient Group meeting: Parents and children who are part of EVERREST Prospective Study on early onset severe fetal growth restriction.

Paris Descartes/UCL Collaboration in Fetal Growth Restriction

G Friedlander, G Hart, A David, S Hillman, O Morel, J Okell, L Salomon, D Siassakos, J Sibiude, V Tsatsaris, D Vaiman, D Williams, E Zaba-Taieb, J Zeitlin, R Aughwane, R Napolitano, N Marlow, R Spencer

The UCL-Paris Descartes Collaborative was launched in 2017 to take advantage of the synergy of research in fetal growth restriction across the two universities. The first symposium was held at the Résidence de France in London where a Memorandum of Understanding was signed to set up a medical student exchange program between the two universities. Over 50 clinicians, scientists and clinical academics attended from the two universities for an exciting program to showcase research in pregnancy, fetal growth restriction and neonatal outcomes.

Launch of cooperation between Université Paris Descartes (UPD) and UCL at the Résidence de France, London, May 2017

Prof. Graham Hart (Dean of UCL Faculty of Population Health Sciences, Geoffrey Sockett (Vice President for International Relations, UPD), Prof. Anna David (Head of UCL Dept. of Maternal-Fetal Medicine), Prof. Gérard Friedlander (Dean of the Faculty of Medicine, UPD), Prof. Vassilis Tsatsaris, (Hôpital Cochin – APHP and UPD).

In November 2018 the 2nd Joint Symposium took place in Paris, bringing together specialists from both universities. Projects exploring placental MR imaging, recurrent stillbirth from Chronic Histiocytic Intervillositis and neonatal outcomes after fetal growth restriction.

Quantifying placental perfusion using the novel "DECIDE" Magnetic Resonance Imaging algorithm

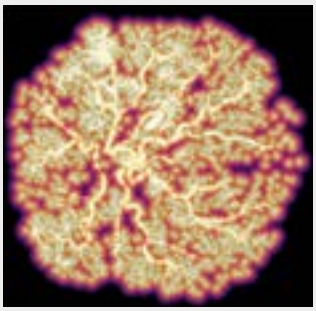
A Melbourne, R Aughwane, M Sokolska, D Owen, G Kendall, D Flouri, A Bainbridge, D Atkinson, J Deprest, T Vercauteren, A David, S Ourselin

Working with physicists and engineers from UCL Department of Medical Physics and Biomedical Engineering and UCLH Medical Physics staff at IfWH have developed a novel Magnetic Resonance Imaging (MRI) method that separates fetal and maternal flow characteristics of the placenta using a 3-compartment model. This splits placental fluid flow into fast and slowly circulating fluid pools, and a tissue pool in between. The images provide a novel MRI model of placental perfusion and fetal blood oxygen saturation with the potential for a non-invasive way of measuring fetal oxygenation, an important tool in understanding fetal wellbeing.

Building effective networks

Dr Roz Aughwane, the PhD student researching the DECIDE algorithm, has also produced some beautiful images of the placenta winning several international competitions.

Exchange of oxygen and food between mum and baby occurs in the placenta. This vibrant image, generated from 3D micro-CT and customised analysis software, shows the distance to the nearest exchanging vessel. The placenta effectively distributes the blood, ensuring a large surface area for exchange and an efficient vascular network.



Winner of International Federation of Placenta Association (IFPA) Image Competition 2017

Placental Pop-Art

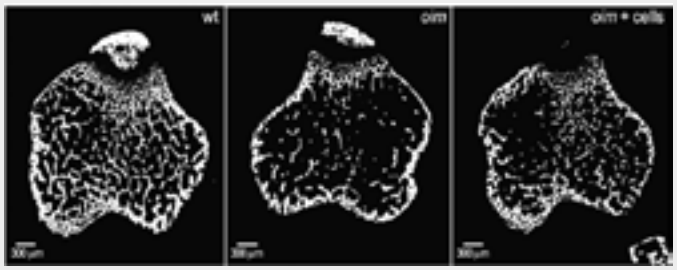
Placentas are fantastically diverse in shape and appearance, but each one of these examples in our montage successfully supported a new life; our simple colour palette reflects how diversity can arise whilst providing this vitally important life-creating role.

Placental Pop-Art was featured widely in the press having come second in the Weird and Wonderful Category of Engineering and Physical Sciences Research Council (EPSRC) Image Competition 2018, and appeared on BBCs QI programme.

Counteracting bone fragility with amniotic fluid stem cell (AFSC)

R Sagar, A Ranzoni, D Moschidou, M Corcelli, T Arnett, A David, F Van Dijk, PV Guillot

Bone fragility can develop in response to a number of different factors, including menopause, ageing, reduced motility and even low gravity, but it can also result from genetic mutations in the genes encoding type I collagen or involved in its biosynthesis and folding. This is the case for the brittle bone disease osteogenesis imperfecta (OI), which is a genetic disease that starts to manifest before birth and results in infants suffering from multiple fractures and skeletal deformities in response to osteoblast malfunction. Over the last 5 years, we have established the ability of human amniotic fluid stem cell (AFSC) transplantation into an experimental model of severe OI (oim model) to decrease fracture rate through the improvement of bone structural quality and normalisation of bone remodelling.



Our research now focuses on (i) understanding the molecular mechanisms of OI progression, (ii) developing in vitro human bone-on-chip models, (iii) using genome editing to develop personalised cell therapy and (iv) developing cell-free therapies to overcome the pitfalls associated with the transplantation of live cells.

The BOOSTB4 trial: Boost Brittle Bones Before Birth

R Sagar, A David, P Guillot

The BOOSTB4 trial is an innovative clinical trial which aims to investigate mesenchymal stem cell transplantation as a prenatal treatment for Osteogenesis Imperfecta (OI). The primary outcome of the trial is the safety of stem cell infusion in pregnant women and their babies with OI. The secondary outcome is efficacy, in particular, investigating if the number of fractures and chronic pain can be reduced and growth can be improved.

The trial is led by Dr Cecilia Götherström at the Karolinska Institutet in Sweden, whilst Professor Anna David leads the team at the IfWH and the UK arm of the study. Consortium members have successfully received funding from both the Swedish Research Council and the European Union's Horizon 2020 research and innovation programme. Together with extensive laboratory investigation, work to date has focussed on developing a robust clinical trial protocol and ensuring the suitability of patient facing materials.

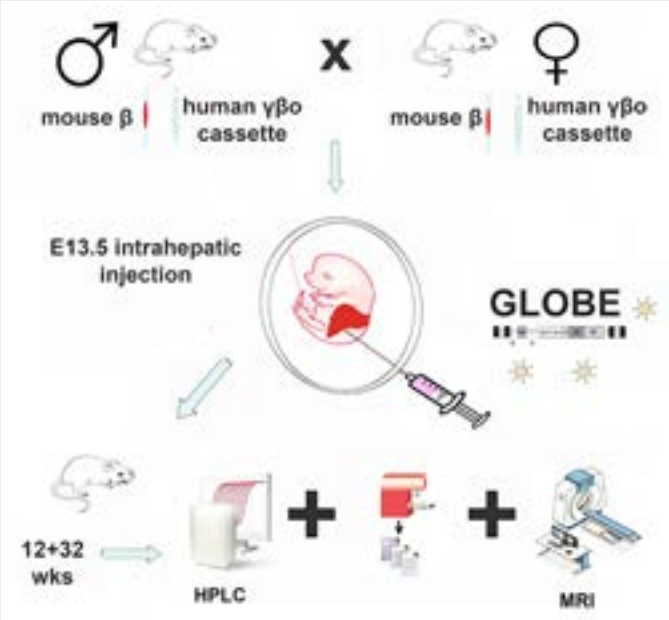
As part of regulatory approvals, we performed a systematic review of all in utero stem cell transplantation procedures performed to date and showed that in general, the procedure has a low complication rate. By February 2019, we had received regulatory and ethical approvals to start the trial in both the UK and Sweden, with recruitment anticipated to start in late 2019. Looking forwards to the next 15 years, we hope that a successful study will enable us to develop the stem cell infusion as a future prenatal treatment for OI.

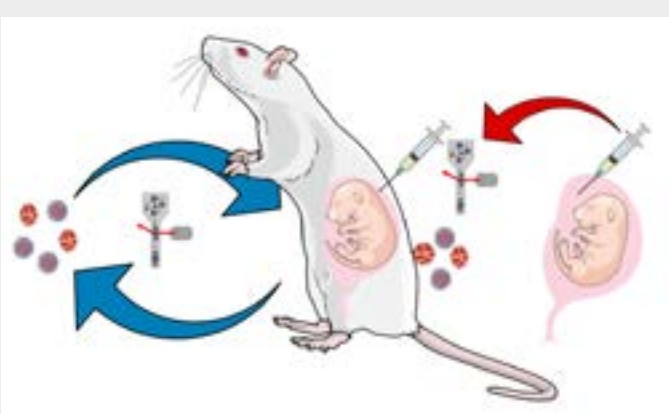
The BOOSTB4 Consortium team members

In utero gene and stem cell therapy to treat congenital blood disorders

P Shangaris, N Bakhamis, S Waddington, A David with collaborators P Loukogeorgakis, S Subramaniam, M Blundell, S Eaton, D Ramachandra, A Thrasher, P De Coppi, D Stuckey and M Antoniou

Diseases which are inherited through families, such as those affecting the genes in red blood cells eg thalassemia, are not very common, but can have a serious effect on health. We are investigating whether correction of the faulty red blood cell gene in the developing baby whilst still in the womb could correct or reduce the problem before the baby is born. We tested out if in utero gene therapy (IUGT) to the fetal liver, with the corrected gene might cure the disease before birth. In a pre-clinical study we found that this treatment increased haemoglobin levels and red cells similar to the normal controls. We also showed that transplanting self-stem cells (autologous) had higher levels of engraftment after in utero delivery compared to non-self cells (allogeneic). These types of prenatal therapy may be a promising approach to treat congenital blood disorders and might be offered as a third option to parents to be, who currently have a difficult decision – either to terminate or continue with the pregnancy.





Fetal therapy and interventions for complicated monochorionic pregnancies.

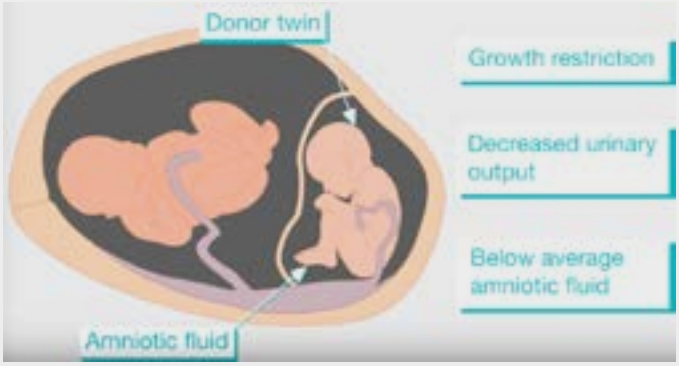
G Attilakos, R Wimalasundera

A monochorionic (MC) pregnancy is a multiple pregnancy, usually a twin pregnancy, in which babies share a single placenta. MC twins have a significantly higher perinatal mortality and morbidity compared to dichorionic (DC) twins because of the vascular anastomoses on the surface of the single placenta, which allow communication of the two feto-placental circulations. The inter-twin communications are normally balanced, but an imbalance in the net flow of blood from one twin (the donor) to the other twin (the recipient) can result in a condition known as Twin-Twin Transfusion Syndrome (TTTS), which complicates approximately 15% of MC pregnancies. Severe TTTS can lead to perinatal loss in 90% of cases. However, it can be treated with fetoscopic laser coagulation of the anastomotic vessels on the placenta. Following treatment, at least one fetus can survive in about 85% of cases and both fetuses can survive in up to 60% of cases.

Another complication of monochorionic pregnancies is Twin Anaemia Polycythaemia sequence (TAPS). This is characterized by large differences in fetal haemoglobin without any growth or amniotic fluid discordance. TAPS occurs in about 2% of uncomplicated monochorionic pregnancies and up to 13% of monochorionic twins post laser ablation.

The Fetal Medicine Unit monitors more than 150 MC pregnancies annually and treats with fetoscopic laser about 30-35. It accepts national and international referrals. We also offer selective reduction with Radiofrequency Ablation (RFA) for complicated monochorionic pregnancies and dichorionic triplet pregnancies. Our data for the latter suggests that this procedure can be successful with co-twin survival in at least 90% of cases.

The multiple pregnancy team contribute data to the TAMBA TTTS registry and was the best recruiting team nationally for the STOPPIT-2 study of a treatment to prevent preterm birth in twins.



www.youtube.com/watch?v=XhKJiaZyke0

The UCLH Preterm Birth Clinical service

AL David, R Napolitano, N Greenwold, A Tetteh, D Casagrandi, D Warner, E Greig, L Kindinger, A Banerjee

Since 2008 the UCLH Preterm Birth clinical service has cared for women with a higher chance of delivering preterm, before 37 weeks of gestation. The multidisciplinary service provides holistic antenatal care at the same time as transvaginal ultrasound scanning, infection testing and counselling. As one of the largest specialist prematurity clinics in the UK, over the last 10 years we have managed the care of nearly 4000 pregnant women through the clinic, a few coming back to have their second and third babies! During that time we have tested out and implemented predictive tools and preventive therapies. With St Thomas's Hospital we optimised cervicovaginal fetal fibronectin concentration to predict preterm birth. Our team specialises in the care of women with cervical weakness who have transabdominal cervical cerclage. We also have a unique experience of managing women who conceive after experiencing childhood cancer and have had total body irradiation and stem cell transplantation as children.

This past year our team members have lead contributions to Element 5 "Reducing preterm birth" in the recently published NHS England Saving Babies Lives Version 2 Care Bundle. This supports the Department of Health aim, to reduce preterm births from 8% to 6%, by focussing on implementing and spreading best practice nationally.

Cervical Immunity and Preterm labour

D Peebles, N Suff, A David, P Hunter, N Klein, M Bajaj Elliott, A Boyle

Many cases of premature labour occur because bacteria, originating from the vagina, colonise the inside of the uterus, initiating an inflammatory response and triggering labour. Samples collected in the specialised Preterm Birth Clinic at UCLH show that women who go on to deliver prematurely have impaired cellular immunity at the level of the cervix; further studies are being performed to determine whether this can be used as a test to determine risk of preterm birth early in pregnancy. With funding from Wellbeing of Women and more recently Action Medical Research, the group has also been investigating whether over-expression of a naturally occurring antimicrobial peptide, human B defensin 3, using a viral vector to transfect cells in the cervical canal, can prevent bacterial ascent to the uterus via the cervix. Initial studies suggest that this might be a novel preventative therapy for women at risk of preterm delivery.

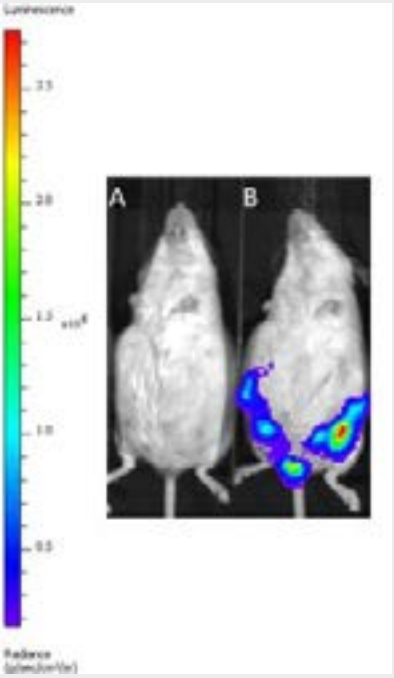
Cervical gene delivery of antimicrobial peptides for the prevention of infection-related preterm birth and the subsequent neonatal brain injury

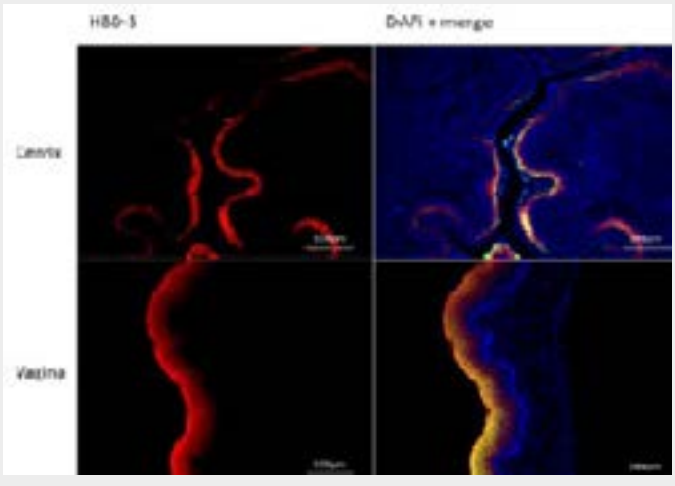
A Boyle, N Suff, A Rahim, J Ng, R Karda, S Waddington, D Peebles, S Buckley

Intrauterine infection accounts for at least 40% of cases of spontaneous preterm birth. Preterm birth is a major cause of perinatal mortality worldwide, with significant neurological morbidity in those that survive.

Our preliminary studies showed that a vector based delivery system for the natural antimicrobial peptide human beta defensin (HBD3) can prevent bacteria accessing the uterus by enhancing cervical antimicrobial activity. Using a mouse model of ascending vaginal infection with bioluminescent Escherichia coli we are investigating whether it is also possible to prevent adverse neonatal outcomes using this gene therapy approach. This project has had ongoing funding which will enable us to bring this work closer to clinical translation in the future.

Pathogenic E. coli K1 ascends into the pregnant uterine cavity, leading to preterm delivery. Bioluminescent images taken 24h following treatment with A) PBS and B) E. Coli K1.





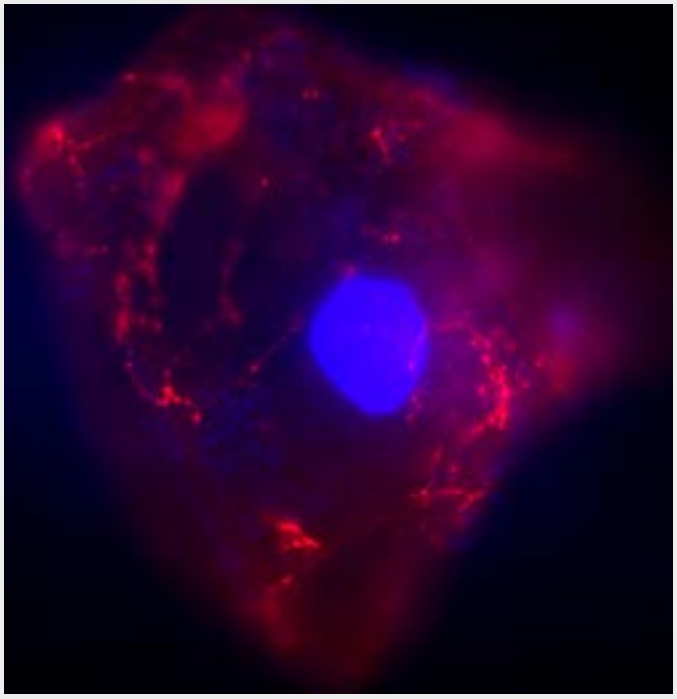
Urinary pathology in pregnancy

J Currie, C James, D Peebles, A David, J Rohn, J Malone-Lee

Urinary tract infection (UTI) has been associated with birth and pyelonephritis. However, the standard culture test for UTI is based on discredited assumptions. For example: urine is not sterile; epithelial cells and mixed bacterial growth do not always represent contamination. Alternative diagnostic methods have been developed in patients with chronic UTI, in whom standard culture tests are not useful.

We investigated these methods in pregnant women. We used four settings: pregnant women with abdominal pain, women at increased risk of preterm birth, women with urinary catheters, and pregnant women with chronic UTI. The alternative methods included objective symptoms inventory, fresh unspun microscopy, urinary ATP, an enhanced culture method using urinary sediment, urinary cytokines, and epifluorescent microscopy of urinary epithelial cells.

Neither standard tests nor alternative tests were able to discriminate subjects from controls in any settings. We found a large range in symptoms and pathology, suggesting the spectrum of urinary pathology in pregnancy remains poorly understood.



A uroplakin-3 positive stained epithelial cell from a urine sample with associated bacteria (epithelial clue cell)

Jane Currie has now been funded by a Chadburn Lectureship to investigate UTI in pregnancy and its diagnosis and treatment.

Home Blood Pressure Monitoring App

D Peebles

This project is centred around providing expectant mothers with a blood pressure monitor and an app which allows patients to input BP results on a daily basis. On average 8-10% of patients require hypertension monitoring throughout pregnancy. The app links with a clinical portal in the trust that displays patient readings in real time. If the reading is 'unsafe' a warning message is displayed with details for patient to visit the local maternity unit as soon as possible. If the reading is safe, the patient is reassured and encouraged to continue home monitoring. Patients will either buy or be offered the BP monitor on loan. The following outcomes are envisaged: reduction in visits, reduction in average clinic appointment from 114 minutes to 66 minutes (by 53%), reduction in patient anxiety and more frequent monitoring, empowers patients to take control of their health, average NHS savings per patient is £1,580

Training in Obstetric Ultrasound and Fetal Medicine

P Pandya, R Napolitano, D Casagrandi with other Fetal Medicine subspeciality trained consultants D Peebles, R Wimalasundera, G Attilakos, A David, M Whitten

The team established this innovative two year UCLH Training Fellowship in Obstetric Ultrasound and Fetal Medicine which has recruited 16 fellows providing training and clinical service in obstetric ultrasound. Trainees acquire skills in obstetric ultrasound from 11 weeks to full term and go to work in the Fetal Medicine Unit participating in the management of complex pregnancies.

Separately UCLH received RCOG recognition for a second academic subspecialty training post in Maternal Fetal Medicine providing training for four trainees; two full-time clinical and two 50% clinical 50% research. UCLH are the only centre in the UK with four SST trainees in MFM, the programme is led by Pranav Pandya.

Our vision for the next 15 years is to be the best department of Fetal Medicine in the UK and one of the best in the world. Providing the highest standard of care to women and their family.

UCLH Perinatal History Clinic

M Whitten, D Siassakos, S Hillman, N Gist

The UCLH Perinatal History Clinic was set up in 2008 as a multidisciplinary antenatal service with initially 2 NHS PAs of healthcare professional time (1 consultant, 1 midwife). The aim of the clinic was to provide an integrated package of antenatal care for women with a history of obstetric complications related to perinatal loss and placental pathology. The referral criteria for the clinic include history of second trimester intrauterine death or stillbirth after 24 weeks; early neonatal loss; previous severe early onset pre-eclampsia and fetal growth restriction. The clinic sees around 130 women each year, around half of whom have a history of perinatal loss and around a quarter each due to previous pre-eclampsia or fetal growth restriction respectively. A personalised plan of care is established dependent on the clinical background, with serial ultrasound assessments and early delivery planning being key. An emphasis is placed upon continuity of care to enable appropriate support of women both in terms of their ongoing assessment but also in relation to shared decision-making regarding delivery recommendations. In 2018 the clinic expanded with a second consultant in recognition of the clinical need. The clinic was also featured in TrueVision's award winning 2018 film Child of Mine which highlighted stillbirth in the developed world as a hidden bereavement that is rarely talked about, often leaving parents isolated and alone.

Ultimately a positive film about life after loss, Child of Mine followed parents through their journey of stillbirth to brings this tragic topic into the open.

Maternal immune factors that lead to chronic histiocytic intervillositis (CHI)

E Cornish, W Heywood, H Williams, M Noursadeghi, D Williams, M Whitten

Dr Emily Cornish, is an academic clinical fellow (ACF), supported by a Wellbeing of Women Entry Level scholarship and a grant from the EGA Charity. In collaboration with Professor Maddy Noursadeghi, UCL Division of Infection and Immunity, Dr Wendy Heywood, UCL Biological Mass Spectrometry Centre, Dr Hywel Williams, Centre for Genetics and Genomics, University of Cardiff, we aim to discover maternal immune factors that lead to chronic histiocytic intervillositis (CHI). This rare, 1:10,000 pregnancies, but devastating syndrome of pregnancy causes recurrent stillbirth and miscarriages. A recent patient engagement day at UCL drew together more than 20 women with CHI to discuss their experiences and link with our research. An international group of experts subsequently gathered at UCL to plan strategies for the prevention of CHI and allied placental disorders.

UCL Stillbirth & Serious incident Prevention and Research Centre (SPaRC)

D Siassakos, A David, S Hillman, G Attilakos, M Whitten, N Cooper, E Cornish

The SPaRC centre will integrate stillbirth care, investigation and prevention research conducted at UCL and other partners. We are currently building an exciting portfolio of cross-linked studies to investigate and eventually prevent adverse perinatal outcome associated with fetal macrosomia in singleton and twin pregnancies.

CASSAVA Preterm Mode of Birth Feasibility Trial

D Siassakos, J Norman, S Stock, S Whyte, J Brewin, N Hallowell, D Odd, J Lawton, J Norrie, H Tebbutt, M Patel, J Broad

The perinatal care group at UCL led the development of a national consensus project on preterm birth: CASSAVA.

With funding from the National Institute for Health Research, we completed a 'Delphi' process (3 rounds of surveys and a consensus building workshop) with national experts, stakeholders, support charities, and patients with experience of preterm birth. We are now working together with the Universities of Edinburgh and Bristol to interview women at risk of preterm birth, or with experience of preterm birth, and the clinicians who look after them, to understand how to best involve them in future research.

We are specifically investigating which groups of pregnant women having a preterm birth would benefit from participation in a randomised clinical trial of vaginal versus caesarean birth. The ultimate aim is to improve outcomes for the several thousands of babies born prematurely every year in the UK and their mothers and families.

CASSAVA
Optimal mode of delivery in preterm labour

Late Fetal Growth Restriction clinical service

R Napolitano, R Peasley

Since joining UCLH in 2018 as a Consultant in Obstetrics and Fetal Medicine, Raf Napolitano has set up the clinical service for women with pregnancies affected by fetal growth restriction in the last third of pregnancy. These projects have created new standards of growth for healthy babies and infants and management of babies with growth problems. The clinic provides care for women whose baby is small and optimises their management to maximise outcomes.

Raf is a member of the INTERGROWTH-21st Project, the TRUFFLE group, the RCOG Intrapartum Clinical Study Group and ISUOG Clinical Standards Committee. He always had a special interest in education leading national training courses in obstetric ultrasound in Sri Lanka and in Kenya.

Dad's Health Study: Paternal obesity-associated DNA methylation: an investigation into its reproducibility, reversibility and association with fetal growth restriction

D Williams, S Hillman, M Holland, F Asenius, S Marzi, R Lowe, A Elwin, V Rakyan, P Magnus

The Dad's Health Study, led by Dr David Williams, is a 3-year MRC funded collaboration with QMUL and the MoBA cohort, Norway, which aims to discover paternal factors that influence fetal growth. Aims are to identify (i) robust epigenetic marks associated with obesity in 1000 obese men (ii) if obesity-related epigenetic marks in blood and sperm are reversed following weight-loss surgery and (iii) whether there is a link between paternal obesity and offspring birth-weight. Dr Fredrika Asenius, funded by the Rosetrees Trust, is completing her PhD on this project.

Pre-eclampsia

T Kubba, S Davidson, D Williams

Dr Tamara Kubba is a clinical PhD student investigating the relative contribution of maternal endothelial function and maternal circulating factors to pre-eclampsia. In collaboration with Dr Sean Davidson, The Hatter Cardiovascular Institute, we are investigating whether ischaemic preconditioning, improves endothelial function in women at-risk of pre-eclampsia and women with pre-eclampsia and how this beneficial effect is transmitted from one part of the body to another.

An Investigation into the aetiology of Acute Fatty Liver of Pregnancy

M Kaler, S Hillman, DJ Williams, P Hennis, H Williams

Acute fatty liver of pregnancy (AFLP) is a rare, but devastating gestational syndrome. Women present in the third trimester with the clinical and biochemical characteristics of a defect in energy metabolism. A minority of AFLP cases are associated with a defect in mitochondrial fatty acid oxidation (LCHAD deficiency). The main aim of our study was to discover whether women who have had AFLP, but who do not have LCHAD deficiency, have an alternative subclinical defect in fat metabolism.

A phenotype study of 33 women who had AFLP was initially performed. Only 19 of these women had urinalysis at the time of presentation and despite prolonged starvation, none of them had ketonuria. This observation supported our hypothesis that AFLP is associated with a defect in fatty acid oxidation (FAO).

Having confirmed that fasting during the third trimester of healthy pregnancy leads to accelerated ketosis, we tested the hypothesis that non-pregnant women who had AFLP have a sub-clinical defect in fat metabolism. Following a 24-hour fast and fat-burning exercise, women who had AFLP (n=13) generated ketones at a similar rate to 23 women who had not had AFLP.

Our study suggests AFLP is a pregnancy-specific defect in maternal FAO, which has no latent impact on maternal FAO. The study of women with AFLP during pregnancy is necessary to identify altered concentrations of pregnancy-specific factors that inhibit maternal FAO.

Comprehensive Anaemia Programme and Personalised therapies (CAPPT)

Investigators from UCL; Dr Sara Hillman (PI), Dr Naomi Saville, Dr Joanna Morrison, Dr Jolene Skordis-Worrall and Dr Andrew Copas; from the London School Hygeine and Tropical Medcine, Dr Helen Harris Fry; From the All India Institute Medical Sciences, New Delhi, Dr Vatsla Dadhwal, Dr Vandana Jain, Dr Shashi Kant, Dr Aparna Sharma and Dr Gurdeep Kaur and from HERD NGO Kathmandu, Nepal, Dr Sushil Baral.

This study is investigating whether a tailored home visiting intervention and participatory women's groups will improve haemoglobin levels in pregnant women. It will be recruiting in India and Nepal, funded by the MRC/Newton Fund and the Department of Biotechnology, Indian Government.

T-cells in Pregnancy (TRIP) study

Investigators from UCL; Dr Sara Hillman (PI), Dr Beth Laverick MD student and Dr Lizzy Rosser, Postdoc.

Colllaborators UCL Professor Lucy Wedderburn, Dr Chiara Bacchelli and UCL Genomics; University California San Francisco Dr Joanna Halkias and Dr Trevor Burt.

Funded initially through an Academy for Medical Sciences award and now a Mason award this project is investigating the role of Tcells in pregnancy conditions specifically pre-eclampsia. Work done collaboratively with Dr Halkias at UCSF has just been accepted for publication in the Journal of Clinical Investigation.

My main collaborator at University California, San Francisco Joanna Halkias (to my right) and lab members at The Keystone Conference Washington DC 2018 'Investigating the Maternal-Fetal Interface'.

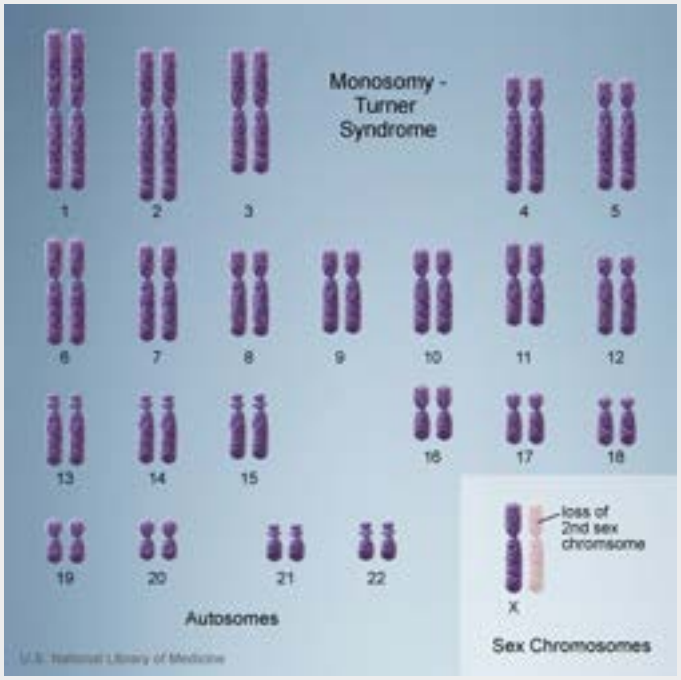
Healthy Reproductive Life

The Institute believes that all women around the world have the right to enjoy healthy sexual relationships and to choose whether and when to have children. Our research focuses on optimising contraception use to plan pregnancy, prevent sexually transmitted infections and to develop innovations in fertility.

UCLH Adult Turner Syndrome Clinic

GS Conway, MC Davies

The Adult Turner Syndrome Clinic at UCLH has grown to be a world renowned resource of clinical excellence over the past 20 years. The clinic is probably the largest in the world with over 850 women attending clinic over its lifetime and approximately 500 women under surveillance currently. This service has been a model for multidisciplinary care for women with Turner Syndrome spawning over 20 smaller clinics in the UK and attracting international visitors extending the model abroad. Research from this cohort has resulted in 43 publications to date. The team have taken part in producing international guidelines at every meeting of organising committees including Naples in 2000, National Institute for Health 2006 and Cincinnati in 2016.



Members of Turner Syndrome Support Society

Minimal access surgery at UCL Institute for Women's Health and UCLH Women's Health Division

A Cutner, E Saridogan, T Mould, A Olaitan, M Widschwenter, A Vashisht, D Jurkovic, N Aslam, J Naftalin, E Yasmin, D Mavrelos, K Doufekas, A Kupelian

The minimal access gynaecological surgery team started at UCLH in the late 1990's with the appointment of Mr Alfred Cutner and expanded rapidly during the foundation of UCL IfWH to form one of the leading centres internationally. The core team initially developed laparoscopic and hysteroscopic surgery in general benign gynaecology, urogynaecology, reproductive surgery and paediatric and adolescent gynaecology (PAG) and subsequently in gynaecological oncology. The team not only introduced many minimal access procedures for the first time into UK practice such as laparoscopic ovarian transposition, laparoscopic vaginoplasty and laparoscopic hysteropexy but also developed entirely innovative approaches such as laparoscopic temporary ovarian suspension. For some of the services they developed such as pregnancy-associated glycoprotein (PAG) and laparoscopic transabdominal cervical cerclage (TAC, Figure) UCLH has become a regional or national referral centre. A TAC is needed when women have a high risk of preterm birth, often due to a short or weak cervix. Usually to place a TAC the women needs a laparotomy but the minimally invasive laparoscopic approach means that recovery is faster. To date over 60 laparoscopic TACs have been placed at UCH with 75% delivery at term.

The multidisciplinary team approach model for endometriosis care developed for the management of advanced endometriosis has formed the basis for the National Endometriosis Centres which are now accredited by the British Society for Gynecologic Endoscopy. This model has now been adopted in the NICE Guidelines.
The minimal access team have also led or contributed to the development of many national and international guidelines in their field such as European guideline for the management of women with endometriosis and NICE guidelines for endometriosis and has an international reputation as a centre of excellence.

Image of a transabdominal cervical cerclage placed by laparoscpy to prevent preterm birth

Ovarian Tissue Freezing

P Hardiman, B Fuller, M Lowdell, N Getreu

In 2012, we set up a research programme in ovarian tissue freezing/transplantation (OTC) with the aim of improving pregnancy rates. In the first phase of the research, we optimised the protocol for thawing to reduce tissue damage. In the second phase assessed novel strategies to reduce post transplantation ischaemia (the major cause of follicle loss). In 2016, we commenced validation studies which were required by the HTA before we could open a clinical OTC fertility preservation service. An NHS contract was obtained and the first patient was treated in February 2019. The clinical Ovarian Tissue Cryopreservation service is the first in London and only the third in the UK. We aim to expand the clinical OTC service to become one of the leading centres in Europe whilst continuing research in to the efficiency of the procedure.

Reproductive effects of cancer

MC Davies, VS Talaulikar, E Yasmin, D Mavrelos, G Morris, N Balachandren, A David, E Williamson, E Robson

We have led the way in developing a service for patients with cancer to provide reproductive, gynaecological and obstetric care. We see acute referrals for young men and women with a new cancer diagnosis, to whom we can offer fertility preservation prior to treatment with chemotherapy or pelvic radiation. After successful treatment for cancer, young people may suffer numerous “late effects” and we provide a multidisciplinary long-term follow-up service in the Macmillan centre and dedicated weekly clinics in EGA. This is nationally recognised as the largest “late effects” service. Ephia Yasmin led the development of guidelines on female fertility preservation (British Fertility Society, published 2018), Melanie Davies set up a national network for fertility preservation and chairs the special interest group of the BFS, both publish and lecture frequently on these topics.

Transplantation and Polycystic Ovary Syndrome

P Hardiman, B Fuller, M Lowdell, N Getreu

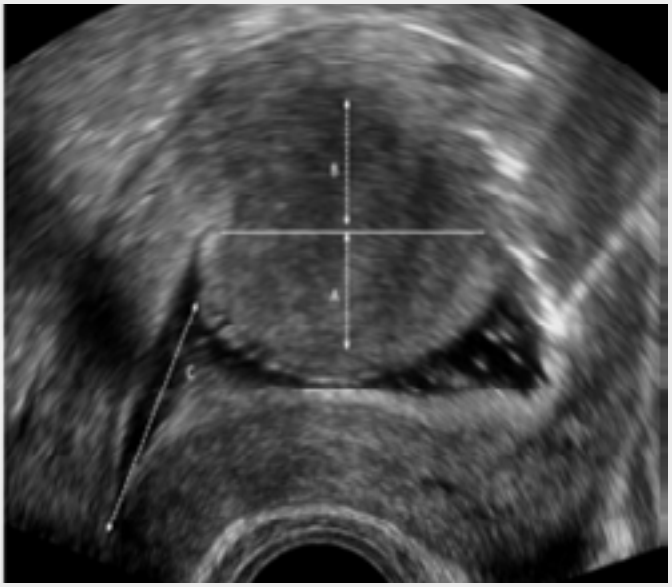
Our research in polycystic ovary syndrome (PCOS) is focused on the growth and development of babies born (60,000 each year in the UK) to mothers with this syndrome. We run a prospective longitudinal cohort study of babies born to mothers with PCOS and those without PCOS and will explore follow up through infancy including neurophysiological assessment. We collaborate with the Autism Research Unit in Cambridge, Steroid Biochemistry team in Berne University and Zhejiang University, China.

Classification and treatment of fibroids prior to surgery

D Mavrelos, J Ben Nagi, J Naftalin and D Jurkovic

Uterine fibroids are common benign tumours of the uterus that cause significant morbidity by making periods heavier and reducing women’s fertility.

Working with the benign gynaecology team at King’s College Hospital and University College London Hospital we contributed to define the optimum diagnosis and management of submucous fibroids. We published on the preoperative assessment of uterine fibroids to allow better planning of surgery and completed the only randomised trial on use of GnRh analogues before transcervical resection. This showed there is no benefit in the use of these medicines thereby saving women being exposed to 3 months of unnecessary treatment.



Preoperative assessment of submucous fibroids

In vitro fertilisation (IVF) at University College London Hospital

D Mavrelos, E Saridogan, E Yasmin, M Davies

The first steps toward establishing an NHS funded IVF service at University College London Hospital were taken in 2009 with 10 ovarian stimulation cycles funded by Haringay Clinical Commissioning Group. Two years later, under the leadership of Mr Ertan Saridogan, Camden, Islington and later North West London Clinical Commissioning Groups recognised the Reproductive Medicine Unit at UCLH as an NHS IVF provider and in 2011 we completed the initial 50 cycles. Starting out, the service was led by Mr Rehan Salim with support from one clinical nurse specialist. In 2013 Miss Ephia Yasmin took on the leadership role and expanded the service in collaboration with Miss Lisa Webber. Under their guidance, the service grew with the appointment of 3 more clinical nurse specialists, 3 clinical fellows and in 2016 Mr Dimitrios Mavrelos as a full time Reproductive Medicine consultant. By 2018 we were delivering over 800 cycles of IVF or ICSI and frozen thawed embryo transfers. At the same time, alongside a pre-existing national male fertility preservation service, the fertility preservation for women has seen remarkable growth led by Miss Melanie Davies. Oocyte cryopreservation and ovarian tissue freezing is now routine for women with breast cancer, haematological malignancies and other fertility threatening conditions, offering hope to patients at a difficult time.

The Reproductive Medicine Unit at UCLH works with the Centre for Reproductive and Genetic health (CRGH) to deliver excellent patient experience and some of the highest pregnancy rates of all NHS IVF units. In the next ten years we will look to consolidate this position, expand our offering to other local CCGs and enhance the unit's research portfolio.

Fertility Education Initiative.

J Harper

Professor Joyce Harper has been working in the fertility field for over 30 years. In 2016 she co-founded the Fertility Education Initiative which is a special interest group of the British Fertility Society and a collaboration of key partners including the Royal College of Obstetrics and Gynaecology. The initiative has been working to ensure that fertility education is taught in schools and was delighted that the Relationship and Sex Education guidance produced in February 2019 by the Department of Education finally included the need for fertility education. The Initiative has created a web site to provide information (www.fertilityed.uk) and is making a suite of animations, with the first two already produced (YouTube – Fertility Ed). Joyce has led on two papers from the Initiative, one involving the use of theatrical and visual art to engage young people on this topic. Joyce is leading a survey of year 10-13 school children from around the UK to determine their knowledge and attitude to fertility education and the initiative is working on a school package for teachers to deliver fertility education. Joyce is very active on TV, radio and social media to deliver fertility education to a wider audience. She is writing a book on fertility awareness for women in their 20s and 30s.

Healthy Menopause and Older Age

The Institute focuses on supporting gynaecologic health in later years including reducing the burden of menopausal symptoms, prolapse and urine problems. We research women specific cancers to screen and prevent their development. We create clinical interventions and extend disease knowledge so that fewer women receive a cancer diagnosis and treatment and quality of life are improved for those who do.

EC H2020 FORECEE (Female cancer prediction using cervical omics to individualise screening and prevention)

M Widschwendter and the FORECEE Consortium

The EC H2020 FORECEE programme (https://forecee.eu) is a clinical research programme funded by the European Commission and The Eve Appeal (https://eveappeal.org.uk) focusing on individual risk predictors for the 4 cancers that are hormone-associated and specific to women (breast, ovarian, endometrial and cervical cancers). These represent more than 45% of all cancers in women and amongst them are cancers with a 5-year survival rate of less than 40%. Professor Martin Widschwendter is the UCL Principal Investigator and Coordinator of FORECEE programme which comprises of 12 partners. The programme seeks to introduce an augmented screening process using cells collected in the cervical smear test to predict the development of the 4 women-only cancers by tracking each individual woman's risk factors and how her own body responds to them. This innovative research, which seeks to translate the outputs into recommendations for new clinical pathways for screening and prevention of the 4 key female cancers for implementation nationally and internationally, is now in its final year. Patient recruitment has been very successful and sample analysis is well underway. A number of Consortium face-to-face meetings and workshops have been held since the inception of the project in a number of partner countries such as Austria, Czech Republic, Germany, Italy, Norway, Sweden and the UK.

Mainstreamed Genetic Testing in Ovarian Cancer

A Lanceley, B Rahman, L Side, R Kristeleit

Up to 17% of ovarian cancer cases can be attributed to BRCA1/2 mutations which are inherited and known as germline mutations. An additional 5-7% of ovarian cancer patients will have a non-inherited 'somatic' mutation only identifiable by genetic testing of tumour tissue. As novel targeted therapies, such as PARP-inhibitors, are effective for patients with germline or somatic BRCA mutations, tumour testing is becoming increasingly important. This is a case study of BRCA tumour testing for ovarian cancer patients examining implementation, patient experience and clinical outcomes of testing. Fifty five patients have consented and proceeded with BRCA tumour testing.

A number of patients have required follow-up germline testing due to test factors, e.g. inconclusive or failed tumour testing, or clinical factors e.g. relevant family history and/or ethnicity. The average testing turnaround time is 55 working days. The main motivation for testing was the potential of prevention and medical care aspects; overall decisional conflict was low. Qualitative interviews are currently underway to explore patients' experiences of testing.

Discovery of Biomarkers for the Early Detection of Cancer

O Blyuss, J Cuenco, T Samuriwo, A Gentry-Maharaj, U Menon, A Zaikin, S Pereira, JF Timms

The early detection of cancer is critical to reducing mortality and identification and development of blood-borne biomarkers may hold the key. Work since 2016 has seen the development of our biomarker panels for early detection and/or differential diagnosis of ovarian, breast, colorectal and pancreatic-biliary cancers. Biomarker models are being validated in independent sample sets. Research has focused on the application of proteomic technologies to pre-diagnosis samples sourced from the UKCTOCS biobank and application of novel methods to combine biomarkers longitudinally or using network approaches where all measurements are considered. These models outperform current single marker models for early detection of ovarian and pancreatic cancers.

Gynaecological Cancer Research Centre

U Menon, A Gentry Maharaj

Professor Usha Menon and her Gynaecological Cancer Research Centre team were part of the Department of Women's Cancer, Institute for Women's Health, University College London from inception in 2004 to 2018 and in charge of the Familial Gynaecological Cancer Clinic at University College Hospital, London. The team has recently relocated to the MRC Clinical Trials Unit (CTU) at UCL.

Our group has worked since the mid-eighties, initially at Bart's and The London Medical School and since 2004 at UCL on improving outcomes in gynaecological cancers, particularly ovarian cancer through screening, early detection and risk prediction.

We undertook the first randomised controlled trial of ovarian cancer screening ever in the mid-eighties and developed a novel longitudinal ovarian cancer-screening algorithm in the nineties. Finally, we undertook one of the largest individual randomised controlled trials to date, the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) to address comprehensively whether there should be an ovarian cancer screening programme similar to cervical and breast screening. In 2016, we showed for the first time that screening using a multimodal strategy can detect invasive ovarian cancer earlier compared to no-screening.

In parallel, we stopped ad-hoc screening of women at increased risk of ovarian cancer in the NHS and undertook across 42 NHS Trusts the UK Familial Ovarian Cancer Screening Study (UKFOCSS). In 2017, we showed that in high-risk women, multimodal screening resulted in diagnosis at less advanced stage compared to no-screening.

The Familial Gynaecological Cancer Clinic that Prof Menon established at UCH in 2004 has set the standards for gynaecological cancer risk management of high-risk women. In the last five years, the MDT has expanded to cover the whole genetics referral base of North, Central and West London (GOSH, Marsden, Frimley Park) and expanded to include the Gynaecological Oncology Centre at Bart's.

A key focus in the last five years has been in converting the large bioresource developed during the course of UKCTOCS (UKCTOCS Longitudinal Women's Cohort, UKLWC) into a sustainable research platform for the study of chronic diseases with robust governance and access policies. We have continued to contribute data and samples from our large UK Ovarian Cancer Population Study (UKOPS) to international consortia and contribute to other international efforts (co-lead for the International Cancer Benchmarking Partnership Module 4).

Since 2013, this has resulted in 165 original publications in, for example, The Lancet, The Lancet Oncology, Journal of Clinical Oncology, 6 invited reviews and 5 chapters in the leading gynaecological oncology textbooks. Eight PhD students have also completed their degree.

Dr Gentry-Maharaj has led the team in making a significant contribution to the UCL education mission through delivery of the iBSc and MSc Women's Cancer modules.

The stage shift with screening, found in both UKCTOCS and UKFOCSS, are the first ever to show definitive evidence of the impact of screening, and follow extensive research and many trials over the past 4 decades. Both trials form the basis of all current ovarian cancer screening guidelines. Meanwhile, the UKFOCSS results have resulted in the instigation of the Cancer Vanguard pilot project (ALDO) which aims to explore multimodal screening of BRCA mutation carriers in the NHS.

Our work has resulted in a greater understanding of the superiority of longitudinal biomarkers algorithms for cancer screening. As part of the Ovarian Cancer Association Consortium (OCAC), we have helped to establish reliable and reproducible risk estimates for ovarian cancer genetic and epidemiological risk factors as well as prognostic biomarkers.

Results of further follow-up of UKCTOCS will establish whether the trend to mortality reduction is true, and inform whether health care systems should implement ovarian cancer screening.

The ALDO screening study for high-risk women, would pave the way for the introduction of ovarian cancer screening to high-risk women in the NHS.

Further use of samples/data from the trial biobanks would lead to novel biomarkers for risk prediction and early detection of a host of cancers/diseases, insights into the natural history of disease and further the cause of precision medicine through drug target discovery and validation.

Patient Care Research

A Lanceley, B Rahman, K O'Donoghue, D Koutoukidis, K Hann, N Balogun.

The Patient Care Research Group was set up in 2008 and has established a reputation for work that seeks to understand the experiences and perspectives of women as a prelude to designing interventions aimed at improving the quality of women's lives. The integration of psychosocial perspectives and methodologies with clinical science is intrinsic to our approach as is our commitment to the engagement and promotion of capacity building across healthcare professions. Major achievements include the completion of a randomised-controlled trial of individualised versus conventional medical follow up of women after primary treatment for ovarian cancer. The results showed that the individualised approach not only improved quality of life and delayed symptomatic relapse it was also cost-effective. This provides an important input to the UK Cancer Survival Initiative. Whether a diet and lifestyle programme can improve the quality of life of endometrial cancer survivors has been a compelling question for women and their clinicians so the results of a pilot trial using adapted 'Shape–up' materials indicating the potential effectiveness of the intervention are very encouraging. A rich body of internationally recognised work has built up, for example, around our exploration of women's attitudes to a programme of risk assessment and stratified management for ovarian cancer, and our conversation analytic work and leadership of the UK clinical roll out of a 'Managing Cancer and Living Meaningfully' (CALM) therapy. In the future we plan to refine and prospectively evaluate our cancer patient and survivor interventions for uptake in the NHS. Going forward, we will consider the application of our tri-fold research approach to other women's health and wellbeing contexts.

Targeting Breast Cancer Metabolism for Novel Management Strategies

N Patani, J Franks, R Stein, G Szabadkai, M Yuneva

Mr Neill Patani, Consultant Oncoplastic Breast Surgeon at UCLH, Honorary Senior Lecturer at the UCL Cancer Institute and Postdoctoral Clinical Research Fellow in the Oncogenes and Tumour Metabolism Laboratory at the Francis Crick Institute, is exploring how breast cancer metabolism can be targeted for novel management strategies. The way tumour cells generate energy and use nutrients can differ significantly from healthy tissue. The breast unit at UCLH, led by Miss Joanna Franks, is part of a multi-centre trial, Enabling the Study of Metabolism in Breast Cancer Through Collection of Fresh-Tissue Biopsies (ENSEMBLE), led by Dr Mariia Yuneva at the Francis Crick Institute.

Working collaboratively with radiologists, oncologists and scientists, this project employs cutting edge laboratory techniques, including imaging mass spectrometry and patient-derived experimental models. This approach will provide unique insights into the cellular processes underpinning cancer development and spread. These metabolic differences may allow earlier diagnosis, better monitoring of response and more effective management with novel anti-cancer treatments.

Relations with Objects

A Lanceley, K O'Donoghue, B Butler, M Rowlands

Therapies that are feasible, acceptable and cost effective are needed to help relieve the often profound emotional and psychosocial distress experienced by individuals receiving cancer treatment. Previous work identified the potential benefit of using heritage (museum objects) and personal objects (objects that represent our history and identity) as resources for enhanced recovery and wellbeing in women with cancer. We will open a new Horizon 2020 funded Critical Heritage Studies and the Future of Europe (CHEurope) project. This observational study will recruit patients along their cancer treatment trajectory and involve them in interviews, focus groups and creative activities to inform the future design of an object-based therapy intervention.

The Eve Appeal

The Eve Appeal is the only UK national charity raising awareness and funding research into risk prediction, prevention and early diagnosis into women specific cancers.

The charity was set up to save women's lives by funding ground-breaking research focused on developing effective methods of screening for ovarian cancer. It has moved on to focus on funding world-class research programmes in risk prediction, earlier detection and prevention for all women-only cancers. The Eve Appeal has provided £9 million over the past 15 years to UCL's Department of Women's Cancers. They have also pioneered public engagement around the research and what it can deliver for health outcomes and services, campaigning and raising awareness which is so important alongside driving research investment. This is reflected by the fact that The Eve Appeal won the Provost's Award for Public Engagement 2018.

The Eve Appeal has grown and developed in parallel with the Department of Women's Cancer, EGA Institute for Women's Health, UCL under the leadership of Prof Martin Widschwendter with a shared vision: A future where fewer women develop and more women survive womb, ovarian, cervical and breast cancer. From the outset, the charity has sought to invest its donations in the most innovative 'discovery' research programmes where more conventional funding is harder to come by. This 'seed funding' is used to leverage other funds later on down the line when evidence starts to come through. A good example of this was the charity investing £250,000 in a BRCA Research Clinic at UCLH in 2017. The Eve Appeal was the sole charity to support this clinic and with the results emerging from it, the Principal Investigator Professor Martin Widschwendter went on to win a prestigious ERC Advance Award which brought in a further 2.5 million euros to prevention research.

Sir John Pattinson's conclusion at the most recent quinquennial review was: "The review panel was convinced of the key role that funding from The Eve Appeal has played, and continues to play, in supporting the ambitious research programme. The charity can take credit for the elements it has funded in whole or in part and the manner in which its support has enabled the UCL Department of Women's Cancer to be innovative and leverage further external funding. There is no doubt that this research is contributing to international understanding of gynaecological cancers and their management. It will have significant impacts. The Trustees of The Eve Appeal can be very satisfied with the return on the charity's investments in the last 5 years."

NHS ovarian cancer surveillance programme for BRCA1/2 mutation-carriers

A Rosenthal, M Widschwendter, U Menon, L Fraser

We have introduced the UK's first pilot NHS ovarian cancer surveillance programme for BRCA1/2 mutation-carriers. Previously, our team has shown that use of serial tumour-marker measurements in women at high risk for ovarian cancer can down-stage tumours. This results in the women needing less aggressive surgery and puts them into a better-prognosis group. We hope that the ovarian cancer surveillance programme will be adopted as NHS best practice for women not yet ready to undergo risk-reducing surgery to remove their ovaries and fallopian tubes. If successful, this will provide the impetus for ovarian cancer surveillance in high-risk women worldwide.

Women have donated their DNA samples in our clinical research study and, in utilising these samples, we provided a key validation set used in two seminal papers confirming the pathogenicity of candidate moderate-penetrance ovarian cancer risk genes (RAD51C, RAD51D and BRIP1). This resulted in their inclusion in an ovarian cancer gene panel now in routine use at NHS clinical genetics centres. Patients with these mutations are now being identified worldwide and referred for potentially life-saving risk-reducing surgery.

Our Familial Gynaecological Cancer Clinic is known internationally and was rated 'outstanding' in the last UCLH CQC visit. We recently performed the first reported risk-reducing surgery at the time of Caesarean Section, and were featured on Channel 4 News.

Looking forward, we hope that ovarian cancer surveillance will be established as standard care worldwide and to develop tests which can identify more accurately which women in the general population are at high ovarian cancer risk, and at what age their cancer will develop, allowing most to safely defer risk-reducing surgery until after the menopause.

Premature Ovarian Insufficiency

MC Davies, Z Nash

Over the last 5 years, Melanie Davies has been a clinician member of the NICE guideline group on Menopause (published 2015) and co-chaired European guidelines on Premature Ovarian Insufficiency (published 2016). Both these identified a lack of information on oestrogen replacement therapy for young women. We have a large service for premature ovarian insufficiency at UCLH, and are aware that the commonest prescription in the community is the Pill, but most specialists favour Hormone Replacement Therapy as it is more physiological. No adequate trials exist comparing these treatments. As the Chair of the Clinical Research Group on Post-Reproductive Health, Melanie put forward a proposal to NIHR which led to a commissioned call. Currently she is leading a collaborative group of clinicians from 10 centres across the UK and have support from the largest patient organisation in this area, Daisy Network.

The Urogynaecology and Pelvic Floor Unit

A Vashisht and UCLH team

This unit has established itself as a UK leader in the field of minimal access pelvic floor surgery. We have published studies on innovative uterine conserving surgery and bladder dysfunction after surgery for advanced endometriosis. Our team has ongoing studies on anatomical, bowel and bladder function following laparoscopic pelvic floor surgery and projects on surgery involving mesh, vaginal pessaries and vaginal vault surgery.

Our Unit receives around 1,000 new referrals per year and will be further growing following further consultant appointments. We have recently been awarded national unit accreditation by the British Society of Urogynaecology achieving the highest ever awarded score in the Society's history, a reflection of the governance, excellence and multidisciplinary working patterns of the team.

Athena SWAN Gold Award for the Institute

The Athena Scientific Women's Academic Network (Athena SWAN) Charter was originally set up to recognise commitment to advancing women's careers in science, technology, engineering, maths and medicine (STEMM) in higher education. This scheme was recently expanded to other academic fields and to include work undertaken to address gender equality more broadly, and not just barriers to progression that affect women.

It is vitally important that women are adequately represented in what has traditionally been, and is still, a male-dominated area. Science cannot reach its full potential unless it can benefit from the talents of the whole population, and until women and men can benefit equally from the opportunities it affords.

Our Journey to Gold

Following our first successful application to Athena SWAN for a Silver award in 2013, we successfully applied for Gold in 2016. The IfWH is now one of only 10 departments in the UK to hold a Gold award.

What does a Gold award signify? These awards recognise beacons of achievement in gender equality and champion and promotion of good practice to the wider community. In particular, IfWH was commended for embedding equality in everyday practise and demonstrating many examples of sustained impact and innovative beacon activities, with strong leadership in equality and diversity.

IfWH has also expanded its remit in this area with its newly formed Equality, Diversity and Inclusion team (EDIT). This committee meets monthly and now also addresses issues of race, sexuality, disability and other protected characteristics.

The ethos of IfWH is to:

- Promote science to all regardless of gender, race, disability or sexuality.
- Provide tailored support for the development needs of every staff member – with a focus on key career transition points
- Provide a supportive, flexible and family-friendly workplace
- Always be open and transparent in our recruitment, promotion and working practices

Did you know?

- In 2010, we had twice as many men as women at senior grades; we now have equal numbers at this level, including professors.
- We are highly regarded for our culture of family-friendly and flexible working practises, including job sharing at senior levels.
- We offer comprehensive careers advice to all our staff and students to assist them in their personal development; from multiple careers sessions for MSc students to individually tailored career surgeries for academic staff.
- The IfWH has signed up to the Race Equality Charter Mark and the Zero tolerance to Sexual Harassment initiative.
- Each year we survey our staff for their views on their working lives within the Institute; their responses have led to change including improvement of appraisal protocols and a wider range of social events.
- Our staff consistently report that they have sufficient support and flexibility in their jobs and feel a strong sense of belonging to the IfWH and to UCL.

For more information go to the IfWH Equality pages: www.ucl.ac.uk/womens-health/equality-diversity-and-inclusion


Athena
SWAN
Gold Award

Celebrating International Women's Day and 100 years of women's suffrage

In 2015, IfWH launched an annual series of events to celebrate International Women's Day. Each year we have included drama, comedy, film screenings, debate and cutting-edge science. Together, these create lively programmes of public events and are attended by over 1000 visitors each year.

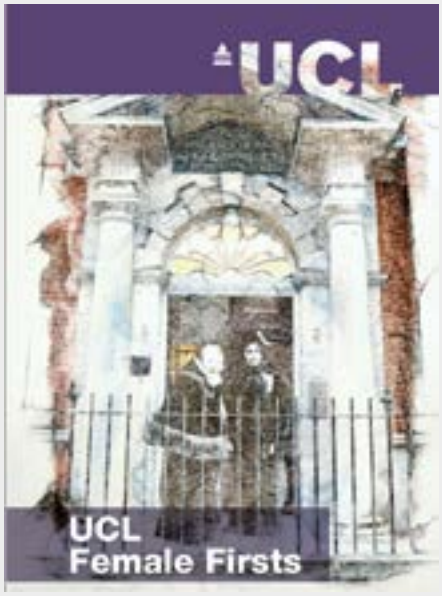
We also invited Laura Bates, well-known founder of the 'Everyday Sexism Project' and two comediennes to host an event for International Women's Day in 2016 which we called 'What's Funny about Everyday Sexism?"

An IWD event with particular impact was the documentary plan SEVEN which tells the true-life stories of seven female activists from around the world. For the performance that we staged, we had UCL's most senior men, including the Provost, read their powerful and often harrowing stories. The immediate impact on the Readers during rehearsal and the performance itself was palpable. Audience feedback was hugely positive:

"The fact that I heard only women and their stories, not the men reading them is testament to both the writing and the engagement of the readers."

"To see our most senior males at UCL identify as women who've suffered real hardship was quite unique and powerful."

The centenary of women's suffrage (2018) was a very special year. To celebrate 100 years of votes for women in 2018, we commissioned an artist-in-residence to create new artworks portraying 12 UCL Female Firsts. These women, nominated by Faculties across UCL, were selected by a panel of staff, students and alumni for their exceptional achievements and being a catalyst for gender equality. The exhibition unfolded throughout and celebrates the impact and legacy of these 12 exceptional women from 1865 to today.



The twelve women selected for inclusion in UCL Female Firsts were:

Rachel Whiteread
Internationally renowned contemporary artist, UCL Slade School alumna and the first female winner of the Turner Prize.

Dame Kathleen Lonsdale
Crystallography specialist and the first woman to be elected a fellow of the Royal Society and UCL's first female Professor.

Dame Clare Marx
A UCL alumna and the first female President of the Royal College of Surgeons.

Uta Frith
The celebrated cognitive neuroscientist who was the first woman at UCL to receive both a Fellow of the Royal Society and a Fellow of the British Academy, as well as being the first UCL psychologist to receive a DBE.

Mavis Batey
A UCL alumna and Bletchley Park code-breaker whose Enigma breakthrough was crucial to the success of D-Day.

Dame Bernice Lake
A UCL alumna and the first woman from the Eastern Caribbean to be appointed Queen's Counsel.

Clare Hollingworth
A UCL alumna who was the first correspondent to report the outbreak of WWII.

Ebony-Jewel Rainford Brent
A UCL Chemistry graduate and the first black woman to play for the England Women's Cricket team.

Dame Mary Douglas
One of the most influential social anthropologists of the 20th century, credited with establishing anthropology as a discipline at UCL.

Gertrude Leverkus
The first woman to enrol on the undergraduate Architecture programme at UCL. In 1919 Gertrude was the only woman to take her finals alongside 500 men.

Elizabeth Garrett Anderson
Elizabeth became the first female doctor to qualify in Britain. The hospital she founded, the Elizabeth Garrett Anderson Hospital, is now a wing at University College London Hospital.

Ann Oakley
The distinguished British sociologist and feminist who set up the Social Science Research Unit at the UCL Institute of Education.

People

On the 7th May 2019 there were 74 staff employed by the UCL EGA Institute for Women's Health. In addition we had 129 honorary staff members, many of whom work at University College London Hospitals NHS Foundation Trust. During 2018-19 we had 19 academic visitors to the Institute, hosted 320 medical students, 51 postgraduate taught students and 38 postgraduate research students.

'15 Year Celebration' Conference, June 2019

Education

15 Years of Education

The Institute for Women's Health runs a suite of successful undergraduate and postgraduate taught and research programmes. Our undergraduate teaching is based around the UCL medical school course, with the recent development of a highly successful iBSc course starting in 2016. The original MSc, Prenatal Genetics and Fetal Medicine, was established by Joyce Harper, Joy Delhanty and Charles Rodeck in 1996 and in 2016 we celebrated 20 years of the MSc (see below). To reflect the demand and changes in the field, a second MSc, Reproductive Science and Women's Health, was established in 2009. Recently we established an MRes in Reproductive Science and Women's Health in 2017 and a third MSc programme in Women's Health in 2018.

The Institute hosts postgraduate degree students from all four research departments. Over the last 15 years 102 MD and PhD degrees have been awarded and a further 13 degrees are in progress. Students present at the Annual Academic Meeting which last year was attended by over 200 delegates.

Our Integrated Clinical Academic Training programme was set up and led by Professor Usha Menon until 2018 who has now handed this to Dr Dimitrios Siassakos. The Institute hosts Academic Foundation Year and Academic Clinical Fellows every year, many of whom go on to be awarded Research Training Fellowships from Sparks, Action Medical Research, Wellbeing of Women, NIHR and Wellcome Trust to name a few. Our Clinical Lecturers are taking their own research programmes forward to become independent clinical academics. Clinical Lecturer alumni of the Institute are now Professors at St George's University Hospital (Prof Asma Khalil), University of Queensland (Prof Hayden Homer), University of Sydney (Prof Jon Hyett) and our own Institute Director.

We pride ourselves in our education experience before, during and after our students leave UCL. We run an annual summer school and a number of staff regularly give school talks. We have a fantastic relationship with our alumni who return for careers days and our annual alumni party. Part of the joy of teaching is seeing our alumni become leaders in the field of Women's Health and through them we are setting up internships in partnership.

Graduation and Alumnus party celebrations

Undergraduate Education

M Whitten, E Yasmin, A Kyei-Mensah, A Lokugamage, J Hockey, J Halsey, T Bourne, C Saunders, E Frewin, J Rattray, W Pereira

Our undergraduate programmes are led by Dr Melissa Whitten, Consultant in Obstetrics and Maternal Fetal Medicine at UCLH who won the patient-nominated Living the Values UCLH Celebrating Excellence Awards in 2017 and a UCL Excellence in Medical Education Award in 2014.

Women's Health and Men's Health MBBS Module

The Institute has a major role in developing and delivering teaching to UCL undergraduate medical students in all areas related to Women's Health. We organise and contribute to a major course module in Women's Health and Men's Health for approximately 340 undergraduate students each academic year within Year 5 of the MBBS programme. The module comprises Obstetrics and Gynaecology, Breast, Genito-urinary/HIV and Urology learning with a multidisciplinary approach where subject areas overlap. The focus is on the acquisition of knowledge and skills needed to be able to practice competently and safely as a junior doctor in alignment with the GMC Outcomes for Graduates framework. Teaching takes place both at central sites (UCLH, Whittington and Royal Free Hospitals) and at District General Hospitals. Student feedback about teaching is extremely positive. Our teaching staff have consistently been nominated by students for the UCL MBBS Top Teacher awards which are held annually. In 2019/20 our curriculum is integrating proposals from the GMC 2020 Outcomes for Graduates framework.

iBSc Women's Health

M Whitten, A Gentry-Maharaj, A Lanceley, S Hillman, H O'Neill, J Nicholls, G Kendall, R Eaton, D Blessing

In 2016, the Institute commenced a one year intercalated BSc in Women's Health for UCL medical students. Designed in response to a demand from the undergraduate medical community for a programme specifically in women's health, it offers a unique insight into the life-course of women's health from pregnancy to menopause and provides clinical and academic opportunities across the breadth of the Institute.

The programme is distinct from, but complementary to, the core UCL clinical curricula for Obstetrics and Gynaecology. The course has received excellent feedback from students and has expanded numbers from 8 to 25 students per year. Students from the course have gone on to present their work at national and international conferences. Following on from our successful first two years we are now opening the course to external applicants from other UK medical schools.

Postgraduate Education

J Harper, S Sengupta, E Jauniaux, S Buckley, H O'Neill, A Poulter, W Pereira

In 2016 we celebrated 20 years of the MSc programmes at the Institute for Women's Health. In 2018/2019 we had 61 Masters students over our four programmes from 22 countries including USA, Canada, Cyprus, India, Indonesia, Iceland, Ireland, Kazakhstan, Libya, Mexico, Moldova, Nigeria and Taiwan. Our students appreciate being taught by the world leaders in the field and the unique observation days in a number of clinical settings. We excel in blended learning, outstanding feedback, and an excellent student experience

www.youtube.com/watch?v=fMfh-1DYEB0

MSc Prenatal Genetics and Fetal Medicine

The Masters in Prenatal Genetics and Fetal Medicine attracts clinical and non-clinical students from all over the world. The course has evolved to introduce a range of activities developing skills in research, diagnostics, counselling and analysis of patient cases. There is a sense of 'joining a family' as our students meet with Alumni of the course during careers sessions and our annual IfWH alumni event which has led to mentoring and job opportunities.

MSc and MRes Reproductive Science and Women's Health

Beginning with just nine students in 2009, this MSc has had ten successful years, and well over 200 students who come from a more diverse set of backgrounds, including medical, scientific, industrial biomedicine and midwifery. This provides a culturally and professionally diverse studentship which remains close in friendship and academic support.

The MRes set up in 2017 enables students to have more choice in the taught modules and a longer time to undertake a more extensive research project.

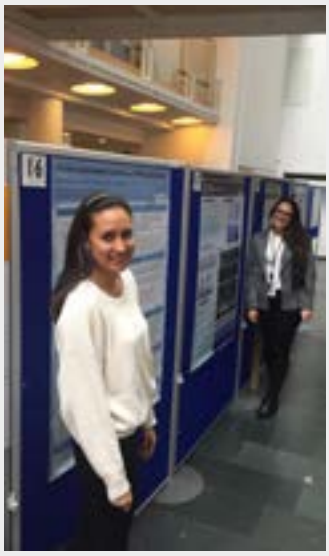
MSc Women's Health

Our newly established MSc in Women's Health uniquely covers many different aspects of women's health; physical, mental, social, cultural, legal and ethical. Students study four IfWH core modules on central themes in women's health and choose four optional modules from IfWH or across UCL to shape their learning and reflect their individual career aspirations. These include topics such as sexual health, reproductive health, pregnancy and childbirth, mental health, health psychology and health economics.

MD(Res) and PhD Postgraduate Research programme

Our students study a wide range of research projects from basic science to population health within all four research departments. Interaction as a cohort occurs through a peer mentoring scheme, shared offices and meeting areas. Our students regularly participate in Faculty, and UCL poster events as well as the Three Minute Thesis competition. In addition to training courses provided by UCL, our students participate in teaching opportunities within the IfWH, including tutorials, additional lectures and co-supervise projects for iBSc and Masters students or outreach activities with school students.

Dr Angela Poulter was our Institute Graduate Administrator who in 2017 was nominated by the UCL Student's Union for Outstanding Support for Teaching. Jenny Rattray was nominated by UCL Medical Students for the Top Administrator Award in 2017.



The IfWH programme to improve women's and newborn health worldwide

We collaborate with many national and international agencies and professional organisations, specific governments and academic institutions in both resource rich and resource poor countries of the world. The introduction of the new United Nations Sustainable Development Goals has renewed focus in this area. Goal 3 covers universal access to health care with its specific WHO driven sub targets relating to maternal and child health.

The global health programme at IfWH was led by Professor Gwyneth Lewis until 2016. She designed better methods to review maternal and perinatal deaths and 'near-miss' severe obstetric morbidity in low and middle income countries to improve maternity care. Clinical academic IfWH staff have taken forward global health research in many countries around the world.

Pregnancy Intention

J Hall, G Barnett

Dr Jennifer Hall studied the relationships between the degree of pregnancy intention and key neonatal and maternal outcomes in the Mchinji district of Malawi in Africa.

With Wellcome Trust funding she tested a new measure of how planned a woman's pregnancy is, known as the London Measure of Unplanned Pregnancy (LMUP). This worked well in Malawi and she discovered that women in Malawi have very similar plans about pregnancy to women in the UK. In addition women with unplanned pregnancies were less likely to access care during and after their pregnancy, and were at higher risk of experiencing postnatal depression and stillbirth. Early identification of women who are experiencing an unplanned pregnancy and referral to appropriate support may reduce poor pregnancy outcomes. Jennifer's current NIHR funded research is now studying NHS implementation of the LMUP in the UCLH maternity service. Jennifer and her colleague Geraldine Barrett advise researchers internationally on the translation, evaluation and use of the LMUP. Current/recent collaborations include countries in every populated continent, including Uganda, Kenya, Sierra Leone, India, Nepal, Sri Lanka, Saudi Arabia, Italy, France, USA, Mexico, Brazil, and Australia.

LMUP TEAM, MAIMWANA PROJECT, MCHINJI, MALAWI 2013-2014

Global Neonatal Health

N Robertson, K Martinello, J Meek in collaboration with Dr C Enweronu-Laryea (Ghana) C Tann and LSHTM (Uganda)

Improving outcomes in neonatal encephalopathy (NE) in sub Saharan Africa.

The incidence in sub Sharan Africa is around 10 times that of the UK. Therapeutic hypothermia and high level intensive care such as that in UK (figure on left) is not available in Ghana and babies in Ghana are cared for with limited resources (figure on right). We have a current close collaboration with the University of Ghana with projects looking at the temperature control of babies with NE and seizures related to outcomes. We are keen to translate practical and effective therapies into clinical trials over the next few years.

Population studies of survival and later health following premature birth in Qatar (Q-Prem)

N Marlow, N Robertson, M Samara, H Al Rifal, G Abdoh

Q-Prem is a population study of over 700 babies born in Qatar, Middle East in 2016-17, including all very preterm births and sample from higher gestations. This cohort are now starting their 2 year assessments. This study aims to set a benchmark for studies in the middle east where rapid development has led to highly technical care but no information on outcomes as yet.

Preventing neurodisability

Dr Cally Tann works between UCLH as a Consultant Neonatologist and the London School of Hygiene and Tropical Medicine (LSHTM). She is currently a co-principal investigator of the OMWaNA Trial based in Uganda, Africa which is a multi-site randomised control trial funded through the Joint Global Health Trials Programme. The trial aims to find out whether early initiation of kangaroo mother care for unstable small neonates improves their outcome. She is also running a pilot randomised controlled trial, funded by Saving Brains, Grand Challenges Canada, on improving early detection and intervention for young infants at high-risk of developmental delay and disability in Uganda.

Fetal echocardiography workshops at AIIMS Hospital Delhi and Sonam Norboo Memorail (SNM) Hospital Leh

S Hillman, P Prandya, R Yates, M Carr, J Wolfenden

With assistance from the UCL Global Challenge fund Dr Sara Hillman NIHR Lecturer (EGA IfWH), Mr Pranav Pandya (Fetal Medicine Unit Lead), Dr Robert Yates and Dr Michelle Carr and Ms Joanne Wolfenden (GOSH Paediatric Cardiology Department) visited two hospitals in India in September 2019, to lecture and demonstrate prenatal fetal echocardiography skills. Doctors in Leh had asked specifically for a clinical workshop in this area, having identified that congenital cardiac disease is more prevalent at high altitude and better antenatal detection would improve care for pregnant women and their babies. We have a long standing relationship with both hospitals, having worked with them in a research capacity for the last 6 years, however, these successful recent clinical workshops were the first of what we hope, will become part of a regular program of clinician exchanges between UCH and AIIMS and Sonam Norboo Memorial Hospital.

Sonam Norboo Memorial hospital, Leh.

Global Maternal and Fetal Health

High Altitude Pregnancy Study "HAPS"

Dr Sara Hillman, a Clinical Lecturer and Sub-Specialty Trainee in Maternal and Fetal Medicine, is working on maternal and fetal health projects in India, Nepal and Pakistan.

Funded by the Wellcome Trust SEED award she is working with a team from UCL (H Montgomery, D Williams), Sonam Norboo Memorial Hospital Leh (P Dolma, PT Angchuk) and All India Institute of Medical Science (V Jain, V Dadhwal) and Institute for Integrative Biology and Genomics, New Delhi (M Mukerji, B Prasher) to investigate the effects of high altitude on pregnancy outcomes and birth weight. The team are investigating that there may be a genetic signature of adaptation evident in babies that are well grown despite the effects of high altitude. Over 300 families at a high altitude location – Leh, India and 100 at low altitude from Delhi, have been recruited and studied.

Dr Padma Dolam, Consultant Obstetrician from Leh, Ladakh, and Dr Sara Hilman presenting at Society for Reproductive Investigation 2019, Paris.

The Hypoxia and Pregnancy Study Teams in AIIMS Delhi 2018

Leh Palace.

She is also collaborating with the Institute of Genomics and Integrative Biology in New Delhi, India and with pregnant women and their partners. This is investigating Ayurvedic principles (holistic, ancient Indian system of medicine) using Prakriti typing of parents as a way of identifying pregnancies at risk of fetal growth restirciton. The meeting of new technologies with established clinical diagnoses and Ayurvedic medicine is an excellent example of juxtaposing ideas providing a means of equality in access to research innovation which retains cultural sensitivity whilst acknowledging differences between communities.

Dr Hillman is also Chief investigator for a tri-country MRC/ Newton funded cluster randomised trial in India and Nepal on reducing iron deficiency anaemia. This project brings together the IfWH with teams from the UCL Institute of Global Health and the London School of Hygiene and Tropical Medicine, making it a truly collaborative experience. The trial is recruiting over 2800 women to either routine antenatal care or a home counselling and personalised advice intervention to improve uptake of iron supplementation. The primary outcome is anaemia levels in pregnancy.

Non-invasive detection of anaemia using a Smartphone application (App-naemia)

S Hillman, J Meek, T Leung (UCL Engineering) in collaboration with C Enweronu-Laryea (Ghana) and R Ali (Pakistan)

This project aims to capitalise on the power of smartphone imaging technology to improve the diagnostics of maternal anaemia. The current gold standard diagnosis involves a blood test, which is an invasive procedure requiring clinical expertise, specialist equipment and consumables. For effective screening in low resourced settings, we propose a non-invasive, low-cost smartphone-based approach to detect maternal anaemia based on promising results established in our pilot studies. We aim to develop a smartphone app that will provide diagnostic information on anaemia, which can be used on women during pregnancy and on both new mothers and their babies shortly after birth.

Medical Aid Films

E Jauniaux, N Greenwold

The charity Medical Aid Films (MAF) was set up in 2006 by Eric Jauniaux and Natalie Greenwold at UCL. A need for community health education was born out of the experience of midwife Fiona Laird, working in a refugee camp in Darfur, Sudan in 2006. She witnessed babies dying needlessly from tetanus due to their cord being cut with a dirty knife. She sought a way to share simple but life-saving information with health workers and mothers in the community.

MAF brings together world-class health and medical expertise with creative film makers from around the world, developing innovative media to transform health and wellbeing in low income countries. Working in partnership with leading global NGOs, academic institutions, private sector and grassroots organisations, we have created high quality, accessible, resource-appropriate films to strengthen training and education for audiences globally. Medical Aid Films are used globally, with over 5 million views online each year.

It now provides multi-media programs for education and training in many developing countries (www.medicalaidfilms.org). It received the BAFTA's Gift of the Academy Award in 2017.

Global Bereavement Care

D Siassakos, B Kampman, S Hillman, International Stillbirth Alliance Clinical Care Group

UCL lead a global collaboration (RESPECT) established after the Lancet stillbirth series 2016 to develop a set of core and aspirational global bereavement care principles. We are working with London School of Hygiene and Tropical Medicine (LSHTM) to expand the programme of work to West and Central Africa.

Global Reproductive Health

Dr Sohier El-Neil is Consultant Urogynaecologist and Uro-neurologist at University College Hospital and the National Hospital for Neurology and Neurosurgery. For many years she has provided international leadership in the fistula community, authoring the International Federation of Gynaecology and Obstetrics (FIGO)'s first Global Competency-Based Training Manual. The manual is revolutionizing the fistula treatment landscape by standardizing fistula surgeon training and ensuring a high quality of patient care.

Global Women's Cancer

Dr Adeola Olaitan serves as Consultant Gynaecology Oncologist at UCLH and is also actively engaged in Nigeria supporting uptake of cervical screening programmes, and public health awareness and education about prevention and identification of gynaecological cancers. The Royal College of Obstetricians and Gynaecologists (RCOG) has recently awarded her the Sims Black Travelling Professorship. This fund enables practising obstetricians and gynaecologists, who are RCOG Fellows or Members, to visit countries overseas, to further the aims of the College. Adeola will be visiting Ghana in August 2019.

EGA Centre for Ethics in Women's Health

Each of the areas of research in the four Institute departments hold significant ethical challenges. We work for example at the limits of viability, designing new therapies for women with complex pregnancies and for their babies. Institute staff over many years have contributed to the formulation of ethics regulations and guidelines at the European level with ESHRE, the European Society of Human Reproduction and Embryology.

In January 2016, the IfWH EGA Centre for Ethics was established to link together the work on ethical challenges within women's health research with initial funding from NIHR. An initial focus has been on education and training including the development of a training module in female genital mutilation (FGM) by Professor Sarah Creighton and her team. This was adopted by Health Education England and is now part of national mandatory healthcare training. A new ethics curriculum for the Institute's MSc and iBSc programmes has been created.

Free online learning: Making Babies in the 21st Century

D Reisel, H O'Neill, S Sengupta, J Harper

In June 2016, the Centre of Ethics launched a six-part online educational programme freely available to both clinicians and the public called Making Babies in the 21st Century (www.futurelearn.com/admin/courses/making-babies). Funded by a UCL educational grant the course consists of interviews with scientists, clinicians, and academics as well as patients and 'experts by experience', to give learners an insight into the impact of the new technologies in reproductive medicine. Topics include egg freezing, gamete donation, international surrogacy, embryo testing and genome editing. The course has had eight successful public runs, attracting over 12,000 learners from over sixty countries.

Anthony Silverstone Fellowship Programme

Mr Anthony Silverstone was a much-loved UCLH clinician, who retired after almost 30 years' service in 2017. Renowned for his capacity to establish trust with patients and staff in the busy clinical setting, the fellowship honours his vision of treating every patient by addressing their unique needs. The Fellowship encourages excellence in innovative research on the patient-provider relationship. Funded by the EGA Hospital Charity, the first recipient was Hilary Hewitt, the lead screening midwife at UCLH, whose project is described below. Further information about the fellowship programme is available here (http://silverstonefellowship.org).

Educare: How Montgomery is reconfiguring consent in the UK

H Hewitt, P Pandya, N Harrison, D Reisel

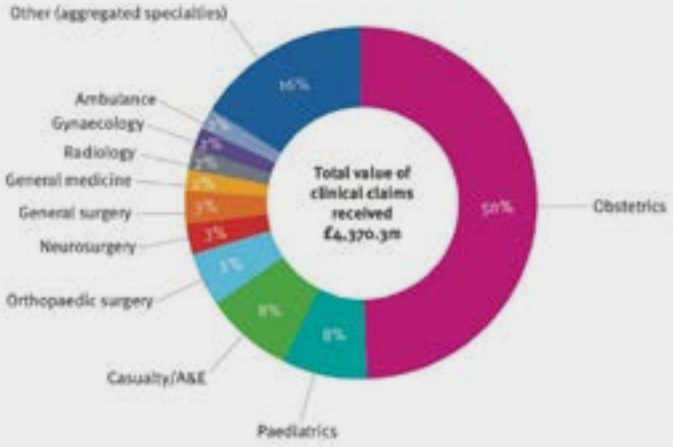
Consent is an important area in clinical ethics, and nowhere more topical than in Women's Health. In a 2015 ruling involving a case of birth complicated by shoulder dystocia resulting in a child sadly born with severe cerebral palsy (Montgomery v Lanarkshire Health Board 2015), the UK Supreme Court changed the law from focusing on the needs of the service to being centred around the service-user. The implications of this legal change have yet to be fully implemented, but already we are seeing consent being treated differently by clinicians working in Maternity care.

Funded by the EGA Hospital Charity, a new educational tool (http://educare.org.uk) is now being trialled in the Fetal Medicine Unit at UCLH. The tool provides tailored information for women who are being offered prenatal tests such as non-invasive prenatal testing or amniocentesis. Rich media with graphics and videos allows women to see how the procedure they are consenting to is performed.

Resolve: Conflict resolution training for midwives and doctors

M McCabe, D Reisel, M Whitten, P O'Brien, D Peebles

In a high-pressured service like Maternity, there are often tensions, even conflicts that occur between healthcare professionals and patients. Unless resolved, such conflicts can be traumatic and end up as costly legal cases. According to NHS Litigation Authority, the cost of legal claims in Obstetrics is equivalent to all other medical and surgical specialities combined. There is also important learning that may be lost the moment the Legal Department steps in; learning that would help prevent the next case of suboptimal outcomes.



After several staff surveys and focus groups involving both midwives and doctors, the Resolve Course was launched in 2018, with support from Health Education England's Maternity Safety Programme. Over 20 midwives and doctors participated in the initial training, and many have already implemented the principles of Restorative Practice, including the UCLH Birth Reflection Clinic, ensuring that learning is brought back into the service. Information about the Resolve Course and restorative practice can be found at http://resolvecourse.org.

"The course should be delivered to every staff member, especially Women's Health."

Senior Midwife

Institute for Women's Health Organisational Structure

IfWH Director
Anna David

Institute Manager
Marcia Jacks
Professional Services Staff

Methodological Support
Alexey Zaikin

UCLH Women's Health Division

Women's Health Division Clinical Director
Donald Peebles

Divisional Manager
Nicola Winn

Breast
Massi Cariatti

Gynaecology
Arvind Vashisht

Neonatology
Giles Kendall

Obstetrics
Ruwan Wimalasundera

Gynae Oncology
Nicola McDonald

Midwifery Lead
Natilla Henry

Education
Joyce Harper

Postgraduate Studies
Eric Jauniaux
Sioban SenGupta

Graduate Research Advisor
Suzy Buckley

Undergraduate Studies
Melissa Whitten

Integrated Clinical Academic Training (iCAT)
Dimitrios Siassakos

Global Women's Health
Jenny Hall
Sara Hillman
Judith Stevenson
Eric Jauniaux

Academic Research Departments

Reproductive Health
Joyce Harper

- **Gynaecological Development and Function** — Sarah Creighton
- **Sexual and Reproductive Health** — Judith Stephenson
- **Translational Ovarian Physiology and Pathophysiology** — Paul Hardiman
- **Reproductive Science Group** — Joyce Harper
- **Preimplantation Genetics** — Sioban SenGupta
- **Early Placentation Disorders** — Eric Jauniaux

Maternal and Fetal Medicine
Simon Waddington

- **Perinatal Brain** — Mariya Hristova
- **Maternal Medicine** — David Williams
- **Gene Transfer Technology** — Simon Waddington
- **Prenatal Cell and Gene Therapy** — Anna David
- **Centre for Prenatal Therapy** — Anna David, Donald Peebles
- **Preterm Labour** — Donald Peebles
- **Cellular Reprogramming and Perinatal Therapy** — Pascale Guillot
- **Midwifery &Nursing** — Yana Richens
- **Perinatal Care and Operative Birth** — Dimitrios Siassakos
- **Thrombosis and Haemostats** — Rezan Kadir

Neonatology
Nikki Robertson

- **Preclinical Neonatal Neuroprotection** — Nikki Robertson
- **Neonatal Pain** — Judith Meek
- **Neonatal Neuroimaging and Biomarkers** — Nikki Robertson
- **Neonatal Seizures** — Janet Rennie
- **Neonatal Clinical Trials** — Neil Marlow
- **Neurodevelopmental and Neurocognitive Outcomes** — Neil Marlow
- **Neonatal Neuromonitoring & Neuroimaging** — Subhabrata Mitra

Women's Cancer
Martin Widschwendter

- **Translational Research Centre** — Martin Widschwendter
- **Cancer Proteomics Group** — John Timms
- **Patient Care Research Group** — Anne Lanceley

The UCLH Division of Women's Health

Donald Peebles
Clinical Director

Arvind Vashisht
Clinical Lead – Gynaecology

Nicola Winn
Divisional Manager

Natilla Henry
Head of Midwifery

Ruwan Wimalasundera
Clinical Lead – Obstetrics

Massi Cariati
Breast Lead

There is no doubt that 15 years after the launch of the Institute for Women's Health as a joint venture between UCL and UCLH we clearly see the benefits. The wealth of innovation and research being carried out in the hospital by clinical staff is clear from the number of fascinating projects detailed in this report. I am struck by a number of things: first, the breadth of this work, extending as it does across all stages of a woman's life, from managing a very premature baby to the challenges of cancer and the menopause in later life. Second, the range of different approaches used from surgical innovation, biomedical engineering, psychological assessment, new methods of diagnosis and therapy, clinical trials – they are all in there. And finally the high quality of this work, feeding into national recommendations, funded by major national and international grant giving bodies and delivering novel methods to improve clinical outcomes in Women's Health. This has all been aided by the close links that exist between university and hospital.

We have been extremely fortunate to be based for the last 10 years in a wonderful clinical facility – the Elizabeth Garrett Anderson wing, appropriately named after a pioneer of women in medicine linked to this hospital, and the Tower (theatres and in patient wards). This has supported a massive expansion in the scale of our clinical services in Maternity, Neonatology, Gynaecology and Breast surgery over this time – to the extent that we are now again short of space! However, such challenges lead to new ways of working that can provide more efficient, patient centred services, sometimes out of hospital and closer to home. The implementation of EPIC, an electronic health record system, in April 2019 poses many ongoing challenges which are being addressed in the anticipation that this will make a real difference to clinical pathways, research, safety, as well as important areas such as admin processes. A testament to the quality of our services is that the Care Quality Commission have rated us as Good twice in 3 years with some areas such as our One Stop Gynaecology Clinic and Fetal Medicine Service considered outstanding.

Finally, something that hasn't changed significantly, despite clear and well described challenges, are the people who provide these services and look after women and their babies in our hospital. They have worked extremely hard, with pride and commitment, in a constant and unchanging manner over all this time. Much of what is done is not glamorous and doesn't benefit from the spotlight of obvious reward or fame – it doesn't feature elsewhere in this report. Yet, it is the backbone that enables us to provide a safe and compassionate service day in and day out. I would like to take this opportunity to say a huge thank you to all of them.

Donald Peebles
Clinical Director

Liz Davies
Matron for Gynaecology & Breast

Rebecca Shelley
Matron for Neonates

Maureen McCabe
Matron for Patient Experience & Safety

Ana Esquerdo
Matron for Maternity Inpatients

Anna White
Matron for Maternity Outpatients

Cait Kielty-Adey
General Manager for Maternity & Neonates

Katrina Hughes
General Manager for Gynaecology & Breast

Jan Bradley
Deputy Head of Midwifery

The NIHR and the Biomedical Research Centre

The National Institute for Health Research (NIHR) supports our research in a variety of ways. The NIHR UCLH Biomedical Research Centre funds experimental medicine research at UCLH and UCL with the aim of turning innovations in basic science into treatments and therapies that have a direct effect on patients. Institute for Women's Health research features in many of the themes, funding staff in Inflammation, Immunity and Immunotherapeutics (David, Peebles, Siassakos), Healthcare Engineering and Imaging (Siassakos), Cardiovascular Diseases (Williams), Cancer (Widschwendter, Rosenthal) and Neurological Diseases (Robertson, Marlow). The NIHR funds our future clinical academics supporting Academic Foundation year posts, Academic Clinical Fellow posts (Reisel), and Clinical Lecturers (Hillman, Kindinger).

The North Thames Clinical Research Network (CRN) funds a team of Research Nurses and Midwives (1 research manager funded by the UCLH Joint Research Office, 6 midwives, 1 nurse and a data manager) who recruit to a large number of studies on the UK national research portfolio. The team are to be congratulated on their outstanding results: an 86% increase in women's health research participation between 2015 to the end of 2017, up from 912 to 1698 women recruited, and an increase in actively recruiting NIHR portfolio studies from 11 studies in 2015 to 24 by the end of 2018.

Research Department of Reproductive Health

Sarah Creighton
Gynaecological Development & Function

Judith Stephenson
Sexual & Reproductive Health

Paul Hardiman
Translational Ovarian Physiology & Pathophysiology

Siobhan Sengupta
Preimplantation Genetics

Eric Jauniaux
Early Placentation Disorders

Joyce Harper
Reproductive Science & Head of Department

The Department brings together six teams working on the clinical, scientific, global and ethical issues related to gynaecological function and development, sexual and reproductive health, the ovary, reproductive science, preimplantation genetics and diagnosis and early placental disorders. We deliver high class translational research across the breadth of reproductive health including close collaboration with clinical departments at UCLH.

Reproductive Science Group

A multi-disciplinary team of basic scientists, social scientists and lawyers working on various aspects of reproductive technologies including considering the social, ethical and legal aspects of assisted reproduction, from puberty to the menopause.

Gynaecological Development and Function

The group comprises several teams researching into different benign gynaecological conditions. These include disorders of sex development, paediatric and adolescent gynaecology and urogynaecology including lower urinary tract dysfunction and pelvic organ prolapse.

Sexual & Reproductive Health Research Group

Focussing research on the many aspects of sexual and reproductive health care from use of contraception and the prevention of sexually transmitted infections to pregnancy planning and healthcare before and after pregnancy.

Translational Ovarian Physiology and Pathophysiology

Conducting clinical and laboratory-based research programmes in reproductive medicine with a major interest in polycystic ovary syndrome, the commonest cause of anovulatory infertility and a major risk factor for type 2 diabetes.

Preimplantation Genetics

Researching the underlying genetic causes for infertility with the aim of helping couples undergoing assisted reproduction select embryos that are likely to lead to birth of a healthy child.

Early Placentation Disorders

The main objective of our research is to better understand the pathophysiology of placental-related diseases of pregnancy with the aim of improving their diagnosis, management and outcome.

Centre for Human Reproduction

Bringing together the expertise of clinicians at UCLH working in reproductive medicine and other conditions such as endometriosis, menopause and menstrual health.

Research Department of Maternal & Fetal Medicine

Simon Waddington
Gene Therapy & Head of Department

Donald Peebles
Preterm Labour

Anna David
Prenatal Cell & Gene Therapy

David Williams
Maternal Medicine

Mariya Hristova
Perinatal Brain

Jan Deprest
Fetal Medicine

Yana Richens
Midwifery and Nursing

Pascale Guillot
Cellular Reprogramming and Perinatal Therapy

Rezan Abdul-Kadir
Thrombosis and Haemostasis

Dimitrios Siassakos
Perinatal Care & Operative Birth

Our collaboration of scientists and clinicians aims to improve outcomes for pregnant women and their babies through better diagnosis and treatment of disease. We study the pathology, prevention and treatment of preterm birth, fetal growth restriction, stillbirth and perinatally acquired brain injury, with an aim to also improve maternal outcomes.

Gene Transfer Technology Group

We use the latest developments in gene transfer technology to develop perinatal gene therapy for early onset lethal genetic diseases and to provide novel methods to understand fundamental cell signalling and disease pathways.

Maternal Medicine Group

We research the causes of pregnancy-related syndromes to design novel therapies to optimise mother and child pregnancy outcomes, which also provides new opportunities to prevent future diseases in families in later life.

Perinatal Brain Group

Understanding the molecular signals triggered in the developing brain by damaging oxygen deprivation or infection is important for designing therapies to optimize neurological outcomes after preterm birth and labour complications.

Centre for Prenatal Therapy

We are developing novel interventions for parents whose unborn baby has a structural abnormality or genetic disease, for example, open fetal surgery for spina bifida in the UK and MRI algorithms to better diagnose fetal anomalies.

Prenatal Cell and Gene Therapy Group

We combine advances in stem cell transplantation, gene transfer and bioengineering to treat the fetus, and consider related areas such as ethics, biobanking fetal stem cells, and healing the amniotic membrane after fetal surgery.

Preterm Labour Group

To develop new predictive tools and therapeutic targets to prevent preterm birth, we study the complex interactions between maternal immune responses and resident bacterial populations called the microbiome.

Thrombosis and Haemostasis Group

We are exploring bleeding and clotting issues in women to improve general and reproductive health of women affected with these disorders in the UK and internationally.

Cellular Reprogramming and Perinatal Therapy

We explore reprogramming fetal cells to become pluripotent, becoming a valuable cell source for therapy such as repairing the developing brain after oxygen deprivation and treating brittle bone disease (osteogenesis imperfecta).

Midwifery and Nursing Research

Our multidisciplinary research approach is focused on improving women's experience of pregnancy and childbirth.

Perinatal Care & Operative Birth

We research perinatal care, stillbirth & bereavement care, complex pregnancy and recurrent pregnancy loss to improve outcomes for families, including close collaboration with parents and international initiatives.

Research Department of Neonatology

Nikki Robertson
Neuroprotection &
Head of Department

Neil Marlow
Outcomes Research

Janet Rennie
Neurophysiology

Judith Meek
Neonatal Pain

Cally Tann
Global Neonatal Health

Giles Kendall
Neuroimaging

Angela Huertas
Neurodevelopment

Subhabrata Mitra
Neuromonitoring

The Department of Neonatology, led by Professor Nicola Robertson, comprises a talented group of researchers from both UCL and UCLH. They are focused on providing better lives for babies through minimising harm and providing novel treatment options for newborn babies that are directed at improving long term outcomes following premature birth and brain injury. The Neonatal Service at UCLH is a busy tertiary neonatal intensive care service serving North Central London and working closely with the Hospital for Sick Children Great Ormond Street. It is the National Centre for Training in Neonatal Individualised Care (NIDCAP).

Neuroprotection research group

The target of the research is to develop new treatments to protect the newborn brain against the effects of brain injury. This group has led the development of a therapy "pipeline" evaluating interventions in the laboratory and then bringing them into the clinical setting in trials. The unique laboratory models have led the introduction first of therapeutic hypothermia and subsequently a range of adjunct therapies.

Alongside this research there are important studies in to the effects of brain blood flow and metabolism that help us understand the responses to treatments and improve the identification of babies at risk of later disability. Working with international colleagues we are also developing new ways of looking at the pattern of neonatal brainwaves (EEG) and using these techniques to develop new treatment for neonatal seizures in particular.

Outcomes research group

This group has developed research into the long term effects of being born extremely early on neurodevelopment, lung, cardiovascular and educational development. Based around two National Cohort Studies – The EPICure Studies – this group have studied outcomes to adult life and contributed to our understanding of the long term effects of being born early. In addition, this group have, and are involved in, a large number of clinical trials in obstetrics and neonatology and international collaborations. Their research has changed our approaches to looking after this vulnerable group of patients.

Neonatal Pain

Working closely with the UCL Pain Group (Professor Maria Fitzgerald) this group have carried out internationally renowned research into the responses of newborn and premature babies to painful procedures that are part of everyday clinical care in the neonatal unit that have led to better understanding of the effects of their treatment.

Global Neonatal Health

Working in a range of settings in Uganda and Ghana we have collaborations and funded studies in both countries (Robertson, Tann) evaluating the impact and treatment of babies with birth asphyxia. We are running a population study of preterm development in Qatar (Marlow) to determine the outcome for a very preterm group for the first time in this rapidly developing population.

Research Department of Women's Cancer

Martin Widschwendter
Head of Research Department, Translational Research Centre

Usha Menon
Gynaecological Cancer

Anne Lanceley
Patient Care

John Timms
Cancer Proteomics

Working For Women, Working Against Cancer

The Department of Women's Cancer, headed by Professor Martin Widschwendter, has an exceptionally talented group of academics and clinicians dedicated to the Department's mission which is to conduct multidisciplinary research into women specific cancers, to create clinical interventions and to extend disease knowledge so that fewer women receive a cancer diagnosis and treatment and quality of life are improved for those who do. In order to achieve this, we are not only a tertiary referral centre for gynaecological cancers treating between 400 and 500 women with primary gynaecological cancers but we also have developed an integrated research pathway including all women specific cancers for risk stratification, prevention, early detection and diagnosis, which incorporates clinical, epidemiological, genetic, epigenetic, proteomic, symptom and imaging data, and applies them to populations. The shared VISION 2040 of the UCL DoWC and its partner charity, The Eve Appeal, is to make women's cancers a thing of the past.

The Translational Research Centre

The Translational Research Centre has a specialist interest in increasing the understanding of the development of women specific cancer, both in women who inherit known genetic mutations, but also in the vast majority who do not. We study all four major women specific cancers: ovarian, breast, endometrial and cervical cancer, and have numerous on-going research activities centred on understanding cancer development, identification of novel tools to predict the risk and thus the prevention of cancer and development of non-invasive early detection tools. Prof Widschwendter and his team have attracted substantial funding from the EC FP7, the EC H2020, the European Research Council as well as from The Eve Appeal and other funding sources since 2011 in order to run research programmes which aim to build on recent insights and further validate these within large scale clinical trials.

The Gynaecological Cancer Research Centre

The GCRC's focus whilst based in the Department of Women's Cancer was centred on reducing mortality and morbidity of women with gynaecological malignancies through screening, early diagnosis and risk prediction. In addition, the group was committed to maximising the research benefits of the large biobanks resulting from the clinical trials and in using the clinical trial capabilities developed over the years to improve the research ecosystem in other countries (particularly India).

The Proteomics Group

The Cancer Proteomics group develop proteomic workflows which they apply to clinical specimens and cell models in research focused on the discovery of cancer biomarkers and to understand gene function and the molecular basis of cancer.

The Patient Care Research Group

The Patient Care Research Group aims to improve quality of life and reduce suffering for women at risk of or diagnosed with a women's cancer. To do this we consider what matters most to women and seek to understand their experiences in the widest social, psychosocial and cultural contexts. This knowledge is integrated with clinical science to develop interventions to improve diet, nutrition and lifestyle, relieve symtoms and promote psychological resilience and recovery.

The IfWH Professional Services Team (PSS)

Led by Marcia Jacks (Institute Manager), the professional services team (PSS) is integral to the Institute for Women's Health, delivering on its mission and objectives and has met the evolving needs of the Institute from inception to its current position. The Institute is currently supported by 21 members of staff, 12 of whom are core funded, 4 project funded support staff and 4 laboratory technicians.

The professional services team is responsible for providing a comprehensive and effective service that facilitates the work of our academic and research staff. This team is subdivided into Human Resources, Finance, Education and general Institute support.

The team has successfully organised the IfWH Annual Conference for many years, which is the highlight of the Institute's calendar and in 2018 we hosted >200 delegates.

Institute Manager Marcia Jacks received a Provost Excellence Award in 2016 for her work in advancing race equality at UCL. The administrative team includes Sarah Mayhew, Executive Assistant to the Director supported by Aqsa Hjiej-Andaloussi, and Personal Assistant Carla Logon. Human Resources is led by Christina Ahlfors. Ian Waller leads the Finance team comprising of Sarah Clegg, Finance Officer and Emma Bryan, Costing Officer.

Faculty of Population Health Sciences (FPHS)

The EGA Institute for Women's Health (IfWH) was one of four Institutes in the UCL School of Life & Medical Sciences to choose to join the fledgling UCL Faculty of Population Health Sciences in 2011.

Professor Graham Hart
Inaugural Dean,
UCL Faculty of Population Health Sciences

I was personally delighted with this decision. It meant that we could truly badge ourselves as the **Lifecourse** Faculty, with women's and babies health, paediatric and adolescent health (**Great Ormond Street Institute of Child Health**) and adult and elderly health (**Institute of Epidemiology & Health Care**; **Institute of Cardiovascular Science**) encompassed in terms of research, teaching and enterprise.

We have since created three new entities in the Faculty: the **Institute for Global Health**; the **Institute of Clinical Trials and Methodology** and the **Institute of Health Informatics**. The IfWH has been an enthusiastic supporter of and collaborator with colleagues across the Faculty, exemplifying its multidisciplinary approach to making a real and sustainable difference to women and babies' health – locally, national and worldwide.

This impressive report has set out how this has been achieved over the first 15 years. But with so much more to be done, I am confident that the EGA Institute for Women's Health has many more years ahead of it. The Director and staff will continue to deliver on the Institute's ambitious plans for research, education and enterprise in the coming decades of the 21st Century.

The Elizabeth Garrett Anderson Hospital Charity

The Elizabeth Garrett Anderson Hospital Charity is in its 40th year having been set up in 1979 to save the EGA hospital from closure. With advances in medicine small independent hospitals could no longer exist to provide all modern amenities and modalities of treatment. The ability of the charity to do more for Women's Health developed when it received a £1,000,000 legacy from Dr Joan Haram, who had been a pathologist at the hospital.

Following a merger of the EGA Hospital with University College London Hospital, the Elizabeth Garrett Anderson Wing at UCLH now provides the services for women. The role of the charity therefore has changed but remains true to the original Deed of Trust which was "the relief of sickness among women and the protection and preservations of the health of women particularly but not exclusively at the Elizabeth Garrett Anderson Hospital".

John Osborne who has been chairman of the EGA Hospital Charity for the last fourteen years is this year handing over to Dr Melanie Davies. John who was consultant obstetrician and gynaecologist until 2007 was instrumental in setting up the charity and we thank him for his great support for women's health and the hospital. The charity has extended its role to provide pump priming finance for exciting new research projects as well as specialist equipment and refurbishment of facilities for patient comfort. These recently include funding equipment to support the new spina bifida fetal surgery program, research to evaluate a vaccine in prevention of vulval cancer and funding an international lecturer for the Institute for Women's Health Annual Conference. The charity also provides the Anne Boutwood Annual Travelling Fellowship for a trainee in obstetrics and gynaecology.

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UCL EGA Institute for Women's Health

Thank you

Our achievements over the past 15 years could not have happened without the support of our partners, donors and friends.

NHS
University College London Hospitals
NHS Foundation Trust

To find out more about our plans and how you can join us to realise a better future for women and babies across the world, contact:

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