

LONDON'S GLOBAL UNIVERSITY

# Our Vision

# Better lives for women and babies across the world

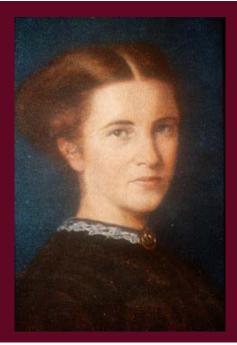
# Our Mission

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 qualify as 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.



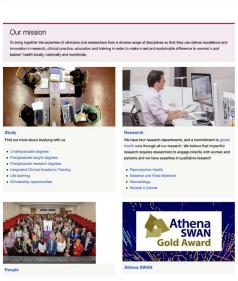
# Contents



Facebook: www.facebook.com/ucl.ega.ifwh Twitter: @UCL\_IfWH

Youtube: www.youtube.com/user/UCLlfWH









# Director's Report



# I am delighted to welcome you to our first EGA Institute for Women's Health report since the emergence of COVID-19

Professor Anna David, Director

During the recent "COVID" years, threats to women's health have come from all directions, including gender violence, lack of choice in planning their families, and isolation. The pandemic has only highlighted further the need for a coherent strategy to women's health. The Institute's unique Life-Course Approach, looking holistically and strategically at the full range of health issues that women face in every stage of their lives, has driven much-needed progress: from shaping national and international sexual health policy to developing the first successful intervention for asphyxia in newborn babies, a leading cause of newborn deaths worldwide.

This biennial report is a celebration of our continued research and teaching in the 'extraordinary' and difficult COVID years. When lockdown happened in March 2020, I was struck by the speed and determination with which the hospitals and university came together. Specialist university laboratory equipment was moved to facilities north of London to ramp up analysis of COVID swab tests. Research staff relocated to clinical care of patients in maternity and on the medical wards at UCLH. Educators rapidly pivoted, seemingly overnight to online teaching and we all began to appreciate ways to make teaching more interactive with Slido and other technology. Steadfast colleagues rapidly developed new clinical guidelines, and then changed them again the next week when more evidence emerged about the SARS-CoV-2 virus. Access to our laboratories was swiftly reinstated using an efficient online booking system. It was a year not only of breathtaking change, but also appreciation. I found myself enjoying the small things in life; the full moon behind silhouetted trees on my walk around our local park in the evenings, and finding our coffee shop had reopened on our local high street after the first lockdown was lifted. I found myself marvelling at the advantages of remote working: debating across continents with colleagues in women's health via virtual conferencing, and the convenience and opportunity to provide patient care remotely via EPIC, our electronic patient healthcare records at UCLH.

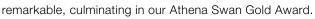
In 2021 and 2022 despite the ongoing pandemic and renewed concerns about Omicron, we have still been able to provide excellence in research, education and clinical care towards our mission of better lives for women and babies across the world. Staff have continued to generate novel research findings with impact, for example in screening for ovarian cancer, fetal imaging, neonatal gene transfer and hypoxia. The Institute Education team in close collaboration with UCLH has successfully launched a new two-year MSc in Obstetric Ultrasound which combines rigorous daily hands on training in fetal ultrasound at the hospital with the best theoretical courses on prenatal diagnosis, fetal development, pregnancy and perinatal care. New clinical services in complex pelvic mesh and pelvic congestion have been set up and are thriving despite the pandemic. Teams at the Institute with UCLH colleagues publicized widely how COVID has impacted on reproductive health services and early pregnancy, and considered how to address inequalities in women's healthcare outcomes. As we come out of the pandemic we are appreciating that staff and students need time to readjust to the post-pandemic changes, to reconnect with others face to face and find ways to mitigate the stress and anxiety of the last few years. Our most recent Institute meeting in December 2022 was a roaring success with nearly 150 in person delegates, a rigorous debate on whether menopause is a hormone deficiency state, and our keynote lecture from the Women's Health Ambassador Professor Dame Lesley Regan. I hope you enjoy reading our report!

# Athena SWAN at IfWH



### 2020

Professor Simon Waddington, Department of Maternal & Fetal Medicine, was appointed the new Lead of the EGA IfWH Equality, Diversity and Inclusion (EDIT) team. Simon took over from Suzy Buckley and Judith Stephenson who stepped down from co-leading the EDIT Team. Suzy had led it since 2017 and Judith since 2015. Their dedication and support in this role since this time has been



Dr Suzy Buckley, Vice Dean (Equality, Diversity and Inclusion) for the Faculty of Population Health Sciences, was nominated for 'the Provost's Award for Embedding Equality, Diversity and Inclusion'.

'Suzy was nominated for this award for her leadership, commitment and delivery within the EDI arena. In the IfWH she has ensured that the principles of EDI have

been absolutely embedded, whilst at Faculty level she has led by example but also empathetically and constructively engaged across all Institutes to ensure that EDI issues are considered in all areas of activity'.



### **April 2021**

The EGA Institute for Women's Health was reawarded the Athena Swan Gold for a further 5 years in 2021, making UCL one of only two universities in the UK to have achieved three Golds



since the inception of the awards in 2006. The Athena SWAN panel was unanimous in its decision and praised the IfWH for its sustained efforts and achievements. The panel highlighted the introduction of job sharing, including the Director's role, which led to an increase in women involved in senior leadership roles, both within the IfWH and elsewhere.

The panel also highlighted:

- An increase in women at senior level linked to uptake of leadership courses
- Flexible working practices as evidenced in take-up and survey responses
- Culture change due to beacon activity
- Improvement in appraisal take up

This wonderful achievement reflects IfWH's long journey towards greater Equality, Diversity & Inclusion, with success following each of our three Athena SWAN applications: Silver in 2013, Gold in 2017 and Gold in 2021. Among the many staff and students whose contributions made this possible, we wish to remember Professor John Timms, who sadly died earlier in 2021, who played a key role from start to finish, including being Co-Chair for the IfWH's first Gold award.

Although COVID was an incredibility difficult time for all staff and students, it did provide opportunity to appraise working practises and increase working flexibility. In some cases this had a positive impact on work life balance.

The ethos of the EDI team is to;

- Promote & support Earlier Career researchers within the institute
- To ensure and promote inclusion of all ethnic minorities within the institute
- To recognise and provide support for disability both visible and non-visible
- To financially support visa applications of student and staff members
- To support and encourage the mentoring system within the Institute
- To liaise with Well-being champions within the institute to maximise the well-being of student and staff members

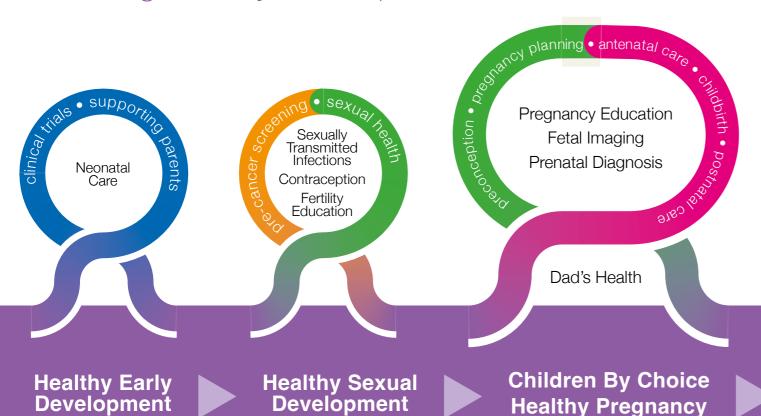
The current EDI team consists of the following members, Simon N Waddington, Rajvinder Karda, Marcia Jacks, Pascale Guillot, Vasanti Jadva, Jenny Rattray, Anna Keegan, Joanne Ng, Ashley Boyle, Christina Ahlfors, Bola Grace, Ian Waller, Alexey Zaikin, Tania Castillo Hernandez.

The team meet every month to address issues of race, disability, equality, inclusion and providing support to student and staff members with their retrospective careers.

For more information go to the Athena SWAN EGA IfWH webpage www.ucl.ac.uk/womens-health/equality/athena-swar

# The Life Course and the Institute for Women's Health

Promoting Healthy Development



Disorders of sexual

development

restriction

Pregnancy

Complications

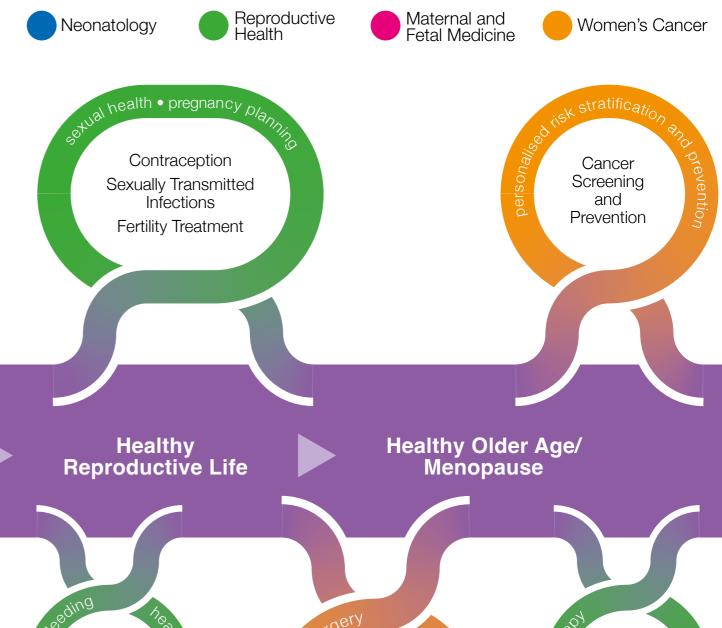
Fetal Therapy

Fetal Medicine

Maternal Medicine

10ss • preterm birth

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.



Early

Detection

and Cancer

Treatment

preservation

Menopause

Urogynaecology

Restoring Health

Newborn Brain Injury

Lung and Cardiovascular

Health

Genetic Therapies

16/ fuerapies

UCL EGA Institute for Women's Health

2020-2022 EGA IfWH Report • 4

5 • 2020-2022 EGA IfWH Report

UCL EGA Institute for Women's Health

Polycystic

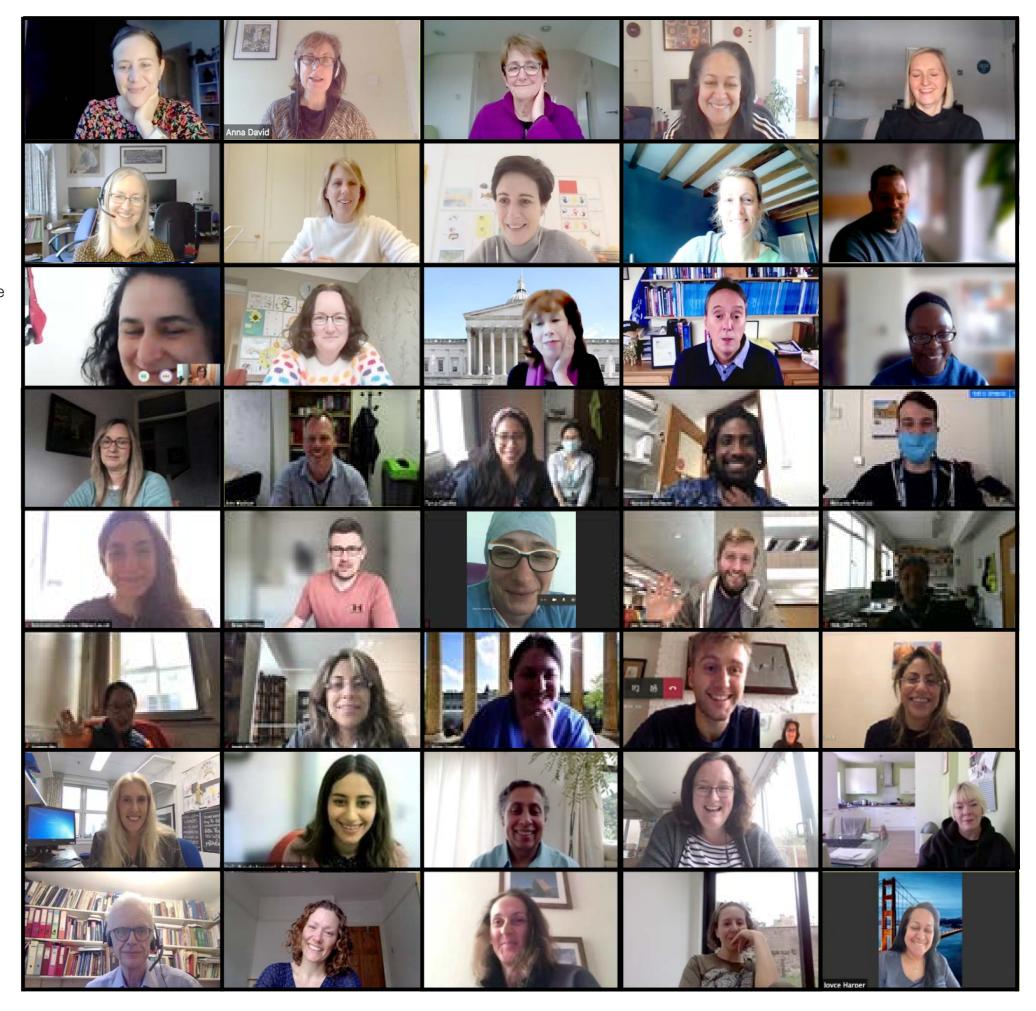
Ovaries

Endometriosis

**Fibroids** 

# People

On the 31st December 2021 there were 72 staff employed by the UCL EGA Institute for Women's Health. In addition we had more than 150 honorary staff members, many who work at University College London Hospitals NHS Foundation Trust. During 2021/22 we had 92 academic visitors to the Institute, hosted 150 postgraduate taught students and 81 postgraduate research students.



UCL EGA Institute for Women's Health

2020-2022 EGA IfWH Report • 6 7 • 2020-2022 EGA IfWH Report UCL EGA Institute for Women's Health

# Institute for Women's Health Organisational Structure

Institute Manager IfWH Deputy Director Howard Clark Methodological Support Alexey Zaikin **Professional Services Staff Academic Research Departments UCLH Women's Health Division** Maternal and Reproductive Health **Fetal Medicine** Neonatology **Women's Cancer** Sioban SenGupta Pascale Guillot **Howard Clark** Education **Prenatal Therapy Women's Health Division Clinical Director Preclinical Neonatal** Director of Education Anna David Neuroprotection **(Taught)** Suzy Buckley Mariya Hristova Nikki Robertson Pre eclampsia **Translational Ovarian** iBSc Lead Melissa Whitten Neonatal Pain **Divisional Manager** Nicola Winn Physiology and **Gene Transfer** Judith Meek **Pathophysiology Technology** Simon Waddington Paul Hardiman IfWH Graduate Tutor (Research) Neonatal Reproductive Science Placenta Imaging Rosalind Aughwane Integrated Clinical and Society and Biomarkers Reproductive Medicine Unit Academic Training (iCAT)
Dimitrios Siassakos Nikki Robertson Suzy Buckley Stem Cell & Exosome Therapy **Neonatal Seizures** Janet Rennie Breast **Global Women's Health** Reproduction Massi Cariatti Preimplantation Genetics Sioban SenGupta omarkers secondmen Helen O'Neill Jenny Hall Sara Hillman Eric Jauniaux Neonatal Neuromonitoring & Neuroimaging Subhabrata Mitra Perinatal Brain Repair Mariya Hristova **Gynaecology** Arvind Vashisht **Early Placentation** Targeted Lung Immunotherapy group Howard Clark & Jens Madsen **Preterm Labour** Ashley Boyle Female Pelvic Medicine and Reconstructive Surgery Sohier Elneil Perinatal Care and Neonatology Leigh Dyet **Operative Birth Neonatal Nursing** . Dimitrios Siassakos Katie Gallagher **Gene Therapy** for Childhood Gynaecological Development and Function **Obstetrics Neurological Disorders** George Attilakos Joanne Ng **Thrombosis** and Haemostasis Rezan Kadir **Gynae Oncology** Nicola Macdonald NHS England National laternity Safety Lead **Donald Peebles** Fetal Medicine **Midwifery Lead** David Connor

IfWH Director Anna David

UCL EGA Institute for Women's Health

2020-2022 EGA IfWH Report • 8

9 • 2020-2022 EGA IfWH Report

UCL EGA Institute for Women's Health

# Education

The EGA-Institute for Women's Health has a strong programme of teaching at both undergraduate and postgraduate level and is a recognized centre for postgraduate academic and clinical training. Our student numbers continue to grow with 31 UG, 92 PGT and 50 PGR students in 2021/2022. The new challenges introduced by the COVID-19 pandemic during the 2020/2021 and 2021/2022 academic years have required flexibility and compromise by both staff and students. The Senior Education Team and all teaching staff within the institue have seen their workloads increase significantly as they have endeavoured to provide a blended learning experience for students and as well as increased pastoral support during these difficult times. The team have made sure that all students have had frequent contact with their personal tutors and programme directors through weekly meetings. The implementation of blended learning has also proved beneficial in some ways as it has allowed us to provide some remote teaching and learning which has been welcomed by the majority of students. The Senior Education team has continued to meet weekly to support its new programme directors and to ensure any challenges were discussed and expertise was shared.

# Undergraduate Education

Obstetrics and Gynaecology are part of the core curriculum for all UCL 5th year medical students, and development and delivery of the teaching programme is a key part of the IfWH's work. Clinical and academic staff lead in the organisation, administration and delivery of the programme on behalf of the Medical School, with students participating in clinical activities across the three core teaching sites at Bloomsbury, Archway and Royal Free campuses. Students are taught by a wide range of clinicians and academics to make sure they have a comprehensive understanding of key issues in Women's Health from a clinical, ethical and person-centred perspective. Students are encouraged to get involved with IfWH activities, and regularly stay involved once they have moved into later clinical or postgraduate studies.

During the first lockdown of the pandemic, students across the country were sent home from campus. The IfWH worked to develop online teaching resources at great pace, in order that students could continue to gain valuable knowledge skills. We were delighted to welcome students back onto campus in September 2021 and a focus was made on bedside teaching, acquisition of core clinical skills and supporting students to gain important clinical abilities at a time when the clinical service was still undergoing massive change



Joyce Harper Director of Education 2020/21



Suzy Buckley Co-Director of Education 2021/22



Mariya Hristova Co-Director of Education 2021/22



Sioban SenGupta Departmental Graduate Tutor (Research)



Melissa Whitten Undergraduate Education Lead

as we went towards the second and third lockdowns. Students were an integral part of our clinical teams in maternity and gynaecology during a challenging time for the health service.

During 2020-21 and 21-22, we were pleased to host our final year UCL MBBS students for their medical electives, which could not be taken abroad due to travel restrictions. We did however have to pause on accepting visiting clinical students from other institutions, to ensure that our internal student learning objectives could be met during a time when inpatient visiting was extremely restricted. We are delighted that as we moved towards the summer of 2022, we were able to start hosting visiting elective placements again, and we expect to be able to expand our work experience opportunities as we move to the post-pandemic phase.

In September 2016, we commenced a new Integrated BSc in Women's Health for UCL 3rd year medical students, with external students admitted for the BSc from 2019-20 onwards. This has been a significant part of education programme development for the Institute. We have now had over 100 students complete the iBSc since its inception and are looking forward to welcome 30 more students in the Autumn of 2023. Students from the iBSc have completed a huge amount of research as part of their research module and have contributed amazingly to the body of work emanating from the Institute!

# Postgraduate Education

# Taught Programmes

One of the main challenges of the pandemic was the provision of remote teaching and learning. The closure of UCL campus and UCLH, and the restriction of access to clinical and research labs imposed an obstacle for provision of clinical observation days. Taking on board the restrictions, the clinical staff took observation days to a new level, providing live footage from the Fetal Medicine Unit which allowed students "access" to areas, which would have been restricted under normal circumstances. After significant work by the teaching administration team, the observations days have been re-instated and have been very popular with the students.

The advantages of online platforms allowed students to participate in Q&A sessions with world experts in

different fields of women's health, thus enriching their knowledge and understanding.

Two of the taught MSc programmes, Prenatal Genetics and Fetal Medicine, and Reproductive Sciences and Women's Health, were taken over by new programme directors, Pascale V Guillot and Vasanti Javda, respectively.



The limited access to research labs during the academic year had a large impact on the provision of MSc projects and the completion of the final dissertations by the students. Many of the students on our taught MSc programmes prefer lab-based projects and the pandemic restrictions disappointed their expectations and challenged the inventive thinking of the scientific supervisors. However, a significant number of those projects were transformed into systematic reviews, many of which have since been published.

The MRes in Reproductive Sciences and Women's Health has a high credit weight on the final dissertation. As access to research labs during the academic year



2020/2021 was restricted, the MRes programme did not run, but was re-instated for 2021/2022 under the new programme director, Jens Madsen.

In 2021/2022 our new taught MSc programme in Obstetric Ultrasound and Fetal Medicine started, which is run by the programme director Raffaele Napolitano in partnership with UCLH. This programme runs in parallel with a practical professional training programme in obstetric ultrasound. It provides medical and science based students with comprehensive academic knowledge, understanding and practical skills in the field of obstetric ultrasound and fetal medicine, specifically in the areas of ultrasound technical skills, fetal



development, prenatal diagnosis and fetal medicine.

The restricted access to the UCL campus required all our exams in 2020/2021 to be taken online. For 2021/2022 only one multiple choice questionnaire was taken as an online exam, and all other assessments were transformed into open book tests thus accommodating the challenges imposed by online examining.

The graduation ceremonies in 2020/2021 took place online with many of our staff and students participating. In 2022, there was a chance for these students to attend a face-to-face graduation ceremony in the Excel Centre.





# Research Programmes

The IfWH had approximately 40-60 PGR students (MD(Res) and MPhil /PhD) registered between 2020-2022 across the four research departments. In spite of the pandemic, most students managed to continue progressing their projects. The online world of 'Teams' and 'Zoom' ensured continuity of supervisory meetings, lab meetings and vivas. In August 2020 a rota system was put into place to allow students access to buildings and equipment whilst maintaining social distancing. In October 2021, PGR students and post docs set up the IfWH Early Career Researchers group. The organising committee (Tania Castillo, Konstantina Tetorou, Nandaki Keshavan, Ashley Boyle, Riccardo Privolizzi, Juan Antinao and Brian Dromey) arranged online talks, training sessions and workshops. Their efforts ensured that students who work in different buildings and who were kept apart by the pandemic could still come together for academic pursuits and social activities.

# Coming up

Teaching at UCL for 2022/23 will again look very different. Shaped by the regulatory environment and the broader context in which UCL operates, in person, on campus teaching will be the default for all programmes. For the 2023/24 academic year, we plan to rename the MSc Prenatal Genetics and Fetal Medicine programme so that it becomes the MSc Reproductive Genetics and Fetal Medicine. This decision was taken after consultation with current staff, current students on all our programmes and prospective students on this degree. We believe the new name better reflects the content of the masters and will also hopefully increase its visibility on search profiles thus increasing the number of applications.

# UCLH Division of Women's Health



Stuart Lavery
Clinical Director



Arvind Vashisht Clinical Lead Gynaecology



Nicola Winn
Divisional
Manager



David Connor

Director of

Midwifery –

previous



Lyndsey Smith Director of Midwifery – current



George Attilakos Clinical Lead Obstetrics



Massi Cariati
Breast Lead –
previous



Dibendu Betal Breast Lead – current



Georgina Bull Matron for Gynaecology & Breast



Ann Griffin
Matron for
Governance,
Safety & Patient
Experience



Anna White
Matron:
Outpatients,
Antenatal
Services, Fetal
Medicine Unit,
Birth Centre,
Community



Ana Esquerdo Consultant Midwife



Salome Ngugi Matron for Maternity Inpatients



Constance Mvududu Deputy Matron for Labour ward and COB



Colleen
WedderburnTate
Consultant
Midwife



Lianne
Phipps
Lead Midwife for
Education



Arezou Rezvani Consultant Midwife

Our Division of Women's Health represents the very best of NHS care: committed professionals delivering high quality care not only to our local population, but with levels of expertise attracting patients from around the nation, and around the world. One of our strengths is our close links to the Institute of Women's Health at UCL. Many of our consultants hold joint posts, allowing translation of the very latest cutting edge academic research from the laboratory directly to the bedside. It was a privilege to be part of the team operating under the pressures and strains of the pandemic. It is remarkable that the most difficult times and challenging circumstances can often bring out the very best in people, in particular in the health service. It also emphasised that our greatest resource and asset is our people. To survive and prosper in the competitive atmosphere of London teaching hospitals, we need to leverage the relationship between our clinical care and expertise and the academic research and teaching output of the university. The award of Biomedical Research Centre (4) exemplifies this.

- UCLH Women's Health activities in 2020-2021 were heavily shaped by the Covid-19 pandemic.
- We kept Maternity and Neonatal services at UCLH fully open throughout, although there were limited time periods when it was necessary to pause home births due to the pressures experienced by the London Ambulance Service. We maintained the ability for women to have a birth partner with them in labour throughout the pandemic, as well as partner attendance at key scan appointments. But at various times we had to significantly limit visitors including partners in other parts of the maternity pathway in order to keep our UCLH patients and staff safe. In Neonatology we supported parents to spend as much time as possible with their babies. We worked very closely with colleagues in Virology and in Infection Prevention and Control throughout. We were able to make the most of the 'MyCare App', part of our EPIC™ electronic patient records at UCLH, to keep our women updated in real time of changes to visiting policy as well as advice relating to COVID19 infections and pregnancy as the situation evolved during the pandemic. Through weekly meetings with our Maternity Voices Partnership (MVPs) we were able to ensure that we considered the perspectives

- of our service users as we made decisions relating to changes to the service.
- Our staff demonstrated tremendous flexibility in order to keep services running. Many doctors, midwives and nursing staff volunteered to cover shifts in the UCLH Intensive Care Unit, providing direct patient care, being part of proning teams to turn ventilated patients over, and providing family liaison. For several weeks during the height of the pandemic our Maternity service was supported by colleagues from the Dental division (nurses and doctors in training) whilst many of our junior doctors from Obstetrics and Gynaecology were redeployed to work in Critical Care and the Acute Medical Units.
- We were able to continue to see and treat cancer patients throughout the pandemic and are grateful to our teams for their flexibility in achieving this as it involved moving both Breast and Gynaecology Surgery to new sites both across the UCLH estate and into the independent sector for extended periods. During 2020-21 our surgical patients receiving treatment at UCLH were co-located in a combined surgical ward in order to enable wards to be created where COVID19 positive patients could be cared for together in cohorts. We have since been able to move back into a dedicated Women's Health ward and our teams are working exceptionally hard to support delivering care to patients who have been kept waiting for a long time.
- We utilised facilities to support remote provision of care and support across the service, by using advances in remote technology to be able to deliver outpatient clinic appointments remotely where appropriate. Maternity staff who needed to shield at the height of the pandemic developed an innovative remote midwifery team. We also enhanced our maternity YouTube<sup>TM</sup> channel, providing online information for women and developed Zoom antenatal classes. The Neonatal Unit pioneered use of AngelEyes technology to be able to allow parents who were not able to be on the unit the ability to see their babies.
- We were fortunate, as many NHS services, to receive additional support for staff during the difficult times of the pandemic; UCLH Charity were exceptionally supportive, providing food and refreshments for staff on-site, and in nearby locations such as the Wellcome Trust which was set up as a support hub where staff could take time out when we had severely limited capacity in the rest areas adjacent to our clinical services.

Although COVID19 was never far from our thoughts we were able to develop some of our services:

- We were successful in becoming the designated centre for Maternal Medicine for North Central London (NCL), providing a service to all our partners across NCL. Our Maternal Medicine team expanded, taking on additional specialist midwifery and medical colleagues.
- We also opened up The London Complex Mesh Centre
  as one of nine national centres for the treatment of
  women with complications following pelvic mesh
  insertion for urinary incontinence and vaginal prolapse in
  a multi-disciplinary setting. The service is housed within
  Women's Health but including colleagues from Surgical
  specialities, Psychology, Imaging and Pain management
  in order to provide a holistic service for patients.
- Our maternity service responded to the Ockenden report received in December 2020 – largely meeting the IEAs (Immediate and Essential Actions) identified but with some areas highlighted for improvement. We were able to access external funding to support improvements including extensions to Obstetric ward rounds and consultant-led care, enhancing fetal monitoring support and provision of Multi Disciplinary Team training. We were also able to continue to provide small group in person Obstetric emergency training for our teams throughout the pandemic.
- Prof. Donald Peebles stepped down as Divisional Clinical Director after 6 years in post, moving onto an NHS England National role in Maternity Safety. We welcomed Stuart Lavery as our new Divisional Clinical Director. Stuart joined the leadership team following 18 years as a Consultant in Gynaecology, Reproductive Medicine and Surgery at Hammersmith Hospital. We also welcomed David Connor as our Head of Midwifery in April 2020, taking over from Natilla Henry who was promoted to be Deputy Chief Nurse at UCLH. We further strengthened our clinical teams with the appointments of a number of substantive consultants including loannis Kotsopoulos and Dhivya Chandrasekaran (both Gynae Oncology), Kunal Babla and Audrienne Sammut (Neonatology), Dan Stott (Obstetrics) and Hazel Learner (Paediatric and Adolescent Gynaecology).
- In the UCLH Celebrating Excellence Awards for 2021 our Women's Health Safety Team won Team of the Year for 'Safety' and midwife Josephine Oamen was awarded Nurse Midwife of the Year. Josephine spearheaded a staff wellbeing initiative for her colleagues in the EGA wing organising treatments such as massage for staff on site so that they could take a little time out of their incredibly difficult job to recharge.

# Social media and communications

From the start of the pandemic, the need for dissemination of information to staff was immense; new guidelines were being developed at pace both nationally, across the Trust and within the Women's Health Division, adapting existing clinical care and service pathways as well as developing guidance on how to care for patients with COVID19. Infection prevention and control policies relating to safe working, distancing, and screening and testing protocols for both patients and staff members expanded and adapted rapidly. Social media was used innovatively from the start of the pandemic to help disseminate guidance and updates to staff across the division. A regular divisional COVID19 e-newsletter was developed to update teams about changes; this was supported by the development by members of our specialist Infectious Diseases team (specialist midwife Camille Mallet and Obstetrician Melissa Whitten) of specific COVID19 information WhatsApp groups to be able to disseminate often rapidly-changing guidance to teams at speed, and for team members to be able to share queries about process when uncertain.

# National guideline development

Several of our senior clinicians were involved in the development of key national guidance on strategic provision of care throughout the pandemic for women and babies, including the development and ongoing revision of the RCOG/RCM COVID19 Guidelines for pregnant women including Consultant Obstetricians Patrick O'Brien (Vice President for Membership, RCOG) and Donald Peebles amongst others.

# Teaching and training for junior doctors, midwives and nurses

The Women's Health Division was able to maintain provision of teaching and training for our MDT teams throughout the pandemic. Emergency skills training continued to be delivered in person, utilising small group adapted skills training approaches. The use of online technology such as Zoom and MS Teams allowed us to continue to deliver dedicated topic-based interactive teaching to our junior doctors in O&G and to our wider MDT groups, enabling staff to continue to learn throughout the peak of the pandemic.

# Research Department of Reproductive Health



Sioban SenGupta Head of Research Department; Preimplantation Genetics



Judith Stephenson Head of Sexual and Reproductive Health



Hardiman
Head of
Translational
ovarian
physiology and
pathophysiology

Paul



Joyce
Harper
Head of
Reproductive
Science and
Society



Eric Jauniaux Head of Early Placentation Disorders



Soheir Elneil Head of Female Pelvic Medicine and Reconstructive Surgery

The COVID-19 pandemic defined 2020 and 2021 and our clinical and research teams worked together to assess its impact on pregnancy outcome and clinical services such as IVF treatments and access to contraception. The Contraception Choices website developed by Judith Stephenson's group has proved to be a useful source of information for women. Now the group are exploring its use as an educational tool in schools. The group has established a measure for unplanned pregnancy and are developing methods to determine women's preferences for future pregnancies so that they can receive appropriate contraception advice. They are also examining pre-conception health care. Joyce Harper has established a new international group within ESHRE on Fertility Education. New research relating to families has been started through the work of Vasanti Jadva. Work by an international group including Eric Jauniaux and Davor Jurkovic has led to ground-breaking discoveries on the pathophysiology of accreta placentation. In the Reproductive Medicine Unit, clinical trials on endometriosis, adenomyosis, premature ovarian insufficiency and menopause are ongoing.

# Pregnancy during COVID-19

Clinicians at UCLH led by Neerujah Balachandren, Dimitrios Mavrelos and Ephia Yasmin partnered with UCL academics Jennifer Hall, Geraldine Barrett, Anna David and



Judith Stephenson to launch a survey investigation on the outcome of pregnancies conceived during the first and second waves of the COVID pandemic. The study was funded by the EGA Hospital Charity.

A cohort study of nearly 10 000 pregnant women recruited from across the UK in May-December 2020 examined the effect of COVID-19 on access to contraception, pregnancy planning and pregnancy outcomes. Women were more than 10 times more likely to say it was hard to access contraception during the first national lockdown and were twice as likely to describe their pregnancy as unplanned if they conceived during lockdown. These findings were published in Oct 2021 with extensive media coverage.

A second analysis, using the same patient cohort, found that miscarriage before 13 weeks was 1.7 times more likely in women with self-reported SARS-CoV-2

infection in the first trimester. Due to the small number of confirmed first trimester COVID-19 infections the study was underpowered and the observed difference was not statistically significant, however it highlights the need to focus on preventative measures, including vaccination, for pregnant women.

# IVF Treatments and COVID-19

# Gurtin Z., Yasmin E., Khanjani S., Dennehy C., da Silva P., Harper J.

Following the closure of fertility clinics in the UK due to Covid-19, researchers from the IfWH and Reproductive Medicine Unit at UCLH collaborated on a rapidresponse, multi-disciplinary research project exploring the experiences of fertility patients whose treatment had been delayed or disrupted. The online questionnaire received 501 responses and provided important insights into patients' concerns, anxieties, and desires from clinics during a time of extreme uncertainty. This topical research was presented at ESHRE 2021, and also featured in The Guardian, BBC Radio 4's Women's Hour, UCL's Coronavirus Podcast, The Fertility Podcast, and a special webinar hosted by the Progress Educational Trust. The first paper from the research has been published (2022) in Reproductive BioMedicine and Society Online, and further publications are in progress.





# Supporting choice of contraception

### Stephenson J, Bailey J. and others.

Contraception Choices (www.contraceptionchoices.org) is an interactive website designed to help women choose the type of contraception that best suits them. We codeveloped and trialled the website with young women and funding from NIHR. With over 30,000 visits per month, the website is very popular with women for its design, trustworthy information, and guidance in choosing a method tailored to individual preferences.

"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 is also valued by contraceptive providers and promoted by the NHS.

# Contraception after successful IVF: what do women need?

Thwaites A, Hall J, Barrett G, Stephenson J.



Women's reactions to post-natal contraception after IVF live birth.

This study showed that the post-natal contraceptive needs of women following an IVF livebirth are real but currently ignored. It presents the first meta-analysis of the 'risk' of spontaneous pregnancy following an IVF livebirth which affects at least 1 in 5 women. It also explores in-depth women's perceptions of their risk of pregnancy following an IVF live birth. Dr. Annette Thwaites, Academic Clinical Fellow in Community Sexual & Reproductive Health, was awarded her MD(Res) on the basis of this research.

# E-health for family planning in Botswana: acceptability and feasibility

C Bawn, J Stephenson, J Bailey, C Morroni



**Botswana Sexual and Reproductive Health Initiative** 

This study used in-depth qualitative interviews with women, healthcare providers, key policy stakeholders in family planning and eHealth specialists in Botswana to explore the factors influencing women's choice, uptake, and use of contraception, as well as the potential and feasibility of designing an eHealth intervention for family planning, such as a website or mobile phone application.

Interviews revealed many cultural, social, and practical barriers to women's use of contraception, with partner control over decision making, and patriarchal cultural attitudes towards sex and gender the most prominent and influential. Additionally, a lack of trained personnel and inconsistent clinical resources are problematic for provision of contraceptive methods. Participants expressed a need, and desire, for more detailed, balanced, upto-date family planning information - for women, their partners, and the providers who counsel them. An eHealth intervention that adheres to the realities of technology and infrastructure limitations in Botswana, and is client-led in terms of content, design, and implementation, could be highly effective in addressing these gaps. Research was conducted through strong collaboration with the Botswana Sexual and Reproductive Initiative, and their partners www.bsrhi.org. Dr. Caitlin Bawn was awarded her PhD on the basis of this research.

Teacher's attitudes to teaching Relationships and Sex Education, and the potential contribution of the Contraception Choices website."

## C Horan, J Stephenson and others

"Frankly, it's clear and I liked it for that reason. I think the emphasis on decision making and agency, it feels like this is something where they have options. ... It's an aspect of education where... they feel quite quickly trapped by the conversation. So, this is a way of opening the conversation..." Teacher C discussing the Contraception Choices website

This ongoing study is exploring the utility of the Contraception Choices website for teachers delivering mandatory Relationships & Sex Education in schools. It is led by Dr. Corrina Horan, Academic Clinical Fellow in Community Sexual & Reproductive Health.

# Measuring pregnancy intention:

### Barrett, Hall, Stephenson

The P3 Study: Assessing women's feelings and preferences regarding a future pregnancy.

Funded by an NIHR Advanced Fellowship,
Dr. Jennifer Hall has evaluated a new
scale for measuring preferences towards
a future pregnancy (the Desire to
Avoid Pregnancy scale) and calculated
predictive estimates of the incidence of
pregnancy over 12 months. Interviews
with women and health care professionals
are revealing the best way to ask women about their
preferences in clinical settings and provide contraceptive or
preconception advice accordingly.

# The London Measure of Pregnancy (LMUP)

The LMUP is a simple set of questions that measures the plannedness of a pregnancy (from 0 to 12). The LMUP was developed by Dr. Geraldine Barrett in 2004 and has been recently updated for newer family forms. It has been used in research across six continents, with validated translation into 19 languages. Dr Barrett and Dr Hall advise people around the world on the use of the LMUP. Further research, led by Dr. Hall, paves the way for the LMUP to be routinely recorded in maternity services, leading to the first national surveillance system for unplanned pregnancy in England.

# Health before pregnancy (preconception health)

J Stephenson, J Hall, G Barrett, B Grace, D Schoenaker.

Following a Lancet series of papers on Preconception Health led by Professor Judith Stephenson, we formed the UK Preconception Partnership, a coalition



of organisations and

individuals with an interest and expertise in different aspects of preconception health, to translate evidence into policy and practice and normalise the notion of preparing for a health pregnancy.

The period before pregnancy is seldom acknowledged by individuals or health services, despite 9 out of 10 women of reproductive age having modifiable risk factors for a future pregnancy. To develop a way of monitoring preconception health nationally, we have identified core metrics from routine data sources, analysed the national Maternity Services Dataset (MSDS 2018-19) and prepared the first annual report card on the state of preconception health in England. This work is led by Dr. Danielle Schoenaker. A scoping review of community-based models of Preconception Care, led by Dr. Jennifer Hall with Government funding, has also been completed. Both are awaiting publication.



Following her PhD thesis (2018) on Fertility Awareness, which revealed large gaps in knowledge of fertility among health care professionals as well as the general population, and the need to better engage men, Dr. Bola Grace has created a simple taxonomy of reproductive intention – *Avoiders*, *Betweeners*, *Completers*, *Desirers*, *Expectants and Flexers*.

Following her PhD thesis (2018) on Fertility Awareness, which revealed large gaps in knowledge of fertility among health care professionals as well as the general population, and the need to better engage men, Dr. Bola Grace has created a simple taxonomy of reproductive intention – Avoiders, Betweeners, Completers, Desirers, Expectants and Flexers.

Research into how men experience problems with fertility, and how to support them, supervised by Professors Ann Blandford, Judith Stephenson and Jill Shawe, has been completed by PhD candidate Dilisha Patel.

# The consent process

A series of studies on women's experiences of the consent process in ante-natal and intra-partum care. In parallel another series of studies concerns healthcare professionals' knowledge and experience of the consent process and in particular their response to recent changes in the law.

In collaboration with Birthrights and in parallel to the human rights inquiry on Racial Injustice in Maternity Care we have conducted an initial study examining the experiences of consent in minorotosed women.

# Northern Network for Medical Humanities: Reproduction, narratives of consent and invisible women

UCL (Dr Jaqueline Nicholls) is co-leading this collaborative project with Dr Samantha Halliday (Durham CELLS) and Birthrights which addresses the issue of choice in the context of reproduction, focusing upon narratives of consent as they pertain to women and birthing people who all too often are rendered invisible by the law, by the healthcare professionals treating them, or by society

# New Family Arrangements

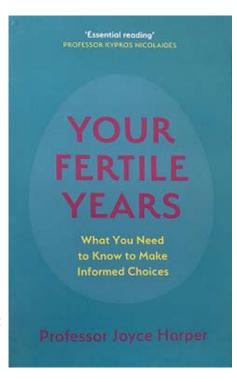
Vasanti Jadva is continuing her Wellcome funded projects with colleagues at the Centre for Family Research, University of Cambridge. The project is investigating new family arrangements involving non-cohabiting coparents, transgender parents, elective single fathers, and identifiable egg donors. Dr Jadva is also involved in a 20-year longitudinal study following families formed through surrogacy, egg donation and sperm donation. Families were first seen when the target child was aged 1 year and subsequently at ages 2, 3, 7, 10, 14 and most recently, 21 years. It remains the only longitudinal study of surrogacy families in the world. Data for all the projects have now been collected and the research team are currently writing up findings for publication.

# Fertility Education & Treatments

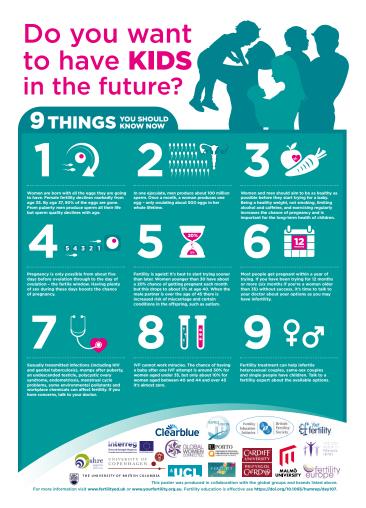
Joyce Harper has worked on many different areas relating to fertility treatment and education. She was



one of the first to bring the discussion of IVF add-ons to the forefront and has published many papers on this topic. She was part of the HFEA advisory committee who set up the add-ons traffic light system. She is one of the authors of the ESHRE good practice recommendations for add-ons. For fertility education, Joyce is co-founder of the UK Fertility **Education Initiative** and founder of the International Fertility Education Initiative). Her latest book on fertility education, Your Fertile Years, What



you need to know to make informed choices, has been published by JOHN MURRAY PRESS, SHELDON PRESS in 2021. She is founder of Reproductive Health at Work, helping companies ensure that the reproductive health needs of their staff are catered for.



# Ovarian Freezing

### **Professor Paul Hardiman**



The Ovarian Cryopreservation service at the Royal Free Hospital has been storing tissue for 42 months. The first patients have now been given approval by their oncologists for their tissue to be transplanted. Paul Hardiman and two laparoscopic surgeons visited Aarhus Hospital, Denmark in May to observe three transplant procedures. A validation study is now underway to confirm the reproductive potential of representative cryopreserved tissue. The results will be submitted to the Human Tissue Authority before the first transplant is performed. We hope to be reporting a pregnancy within the next year and are planning a major expansion of the service as funding from NHS England is expected in 2023.

# Preimplantation Genetics

### Joy Delhanty

After 65 continuous years at UCL from being an undergraduate student to an Emeritus Professor, Joy Delhanty passed away on the 1st of October 2021. In her long and distinguished career, she had supervised 25 PhD students, been awarded 27 research grants, and

she had published over 190 peer reviewed research papers. Her final work on the extent of chromosome anomalies in oocytes due to gonadal or germinal mosaicism was published in January 2022.



# Gene Expression in Oocytes and Embryos

Harita Ghevaria, Arwa Almutlaq, Xavier Vinals Gonzales, Xuhui Sun, Rabi Odia, Seema Dhanjal, Roy Naja, Paul Serhal, Sioban SenGupta

We have investigated the correlation between the transcriptome profile of human oocytes / blastocysts and aneuploidy to identify potential mRNA and miRNAs biomarkers for oocyte / embryo quality.

# Accreta Placentation

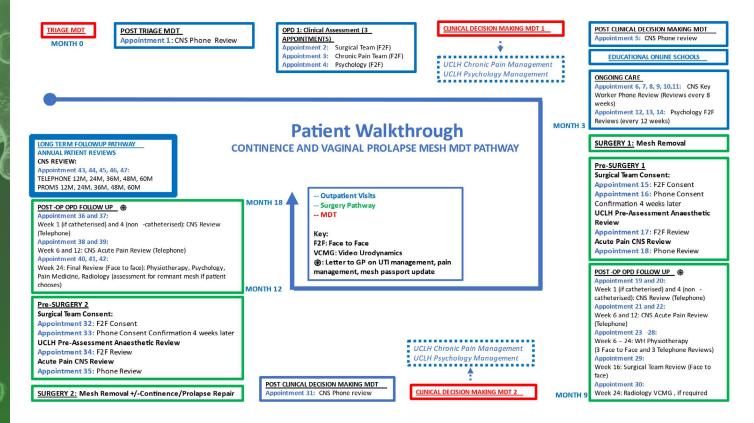
Prof Eric Jauniaux and Prof Davor Jurkovic in collaboration with Prof Ahmed Hussein: (Cairo University Hospitals, University of Cairo Cairo, Egypt); Prof Ron Maymon: Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; Dr Jonathan L. Hecht: Beth Israel Deaconess Medical Center, Harvard University, Boston, MA, USA; Dr Karin Fox.

We are investigating the pathophysiology of accreta placentation and have published breakthrough data on how the implantation of the gestational sac and its primitive placenta inside a previous caesarean section scar (caesarean scar pregnancy) impact the surrounding circulation as early as 6 weeks of gestation and how during the development and growth of the definitive placenta in a uterine scar the rapid increase of the

intraplacental circulation is associated with excessive fibrinoids deposition at the level of the utero-placental interface leading to the abnormal attachment of the placenta to the uterine wall at birth.

# London Complex Mesh Centre at UCLH

The management of continence and prolapse mesh complications in the United Kingdom came to the fore in the last decade. Throughout this time, changes in the approaches by the regulatory authorities had a direct effect on the use of mesh in women. Furthermore, with the outcomes of the Cumberlege First Do No Harm Report, in 2020, addressing the issues raised by women harmed by mesh, specialised services were set up. The Women's Health Directorate at UCLH has a long-standing history in helping women with mesh complications dating back to 2005, and thus put in a successful bid to NHS England to run a centre where women could have individualised and holistic care after suffering such complications. It is one of nine national centres of excellence. Their experience in a multi-disciplinary approach to managing such patients, and their development of surgical techniques used both nationally and internationally, was portent in their being selected to run the London and South-East service for NHS England. The LCMC opened its doors on 1st July 2021.



In the last 14 months the centre has received over 220 new referrals, operated on over 140 patients, provided pain and clinical psychology support to over 300 new and legacy patients. The clinical outcomes continue to be collected. All of this would not have been possible without the critical success of the multi-disciplinary team and the defined pathway. The latter was developed with the active participation of the UCLH Patient Focus Group – they form an integral part of the LCMC service evaluation.

The multi-disciplinary team consists of surgeons (urogynaecology, urology and colo-rectal), radiologists, pain medicine specialists, clinical psychologists, physiotherapists, and specialist nurses. A quorate meeting is held every Monday morning for 4 hours. In the last 14 months, over fifty meetings have been held.

With such complex surgery, clinical governance within the LCMC is key to its development and consistent with the Trust's principles of a systematic approach to maintaining and improving patient care, it supports a culture of encouraging incident reporting, identifying where improvements can be made, and addressing issues at the earliest opportunity.

In May 2022, the LCMC had a review by NHS England. The outcomes were favourable. Indeed, UCLH remains the hospital of choice that patients with mesh complications choose to attend.

As part of the LCMC's wider role, it will participate in the November 2022 UCLH meeting on complex pelvic surgery. A month later, in December 2022, the LCMC will host members of all the nine national complex mesh centres, and those from the devolved nations, for a meeting to discuss outcomes and challenges in the 18 months since opening. It promises to be an interesting and highly engaging opportunity to evaluate services, discuss challenges, and to learn from each other.

# Reproductive Medicine Unit at UCLH

**Ertan Saridogan** is a co-applicant of 2 large NIHR trials. Recurrence of endometriosis: A randomized controlled trial of clinical and cost-effectiveness of gonadotropin releasing hormone analogues with add back hormone therapy versus repeat laparoscopic surgery (REGAL) trial and Laparoscopic versus abdominal hysterectomy (LAVA) trial

Ertan Saridogan was part of a Guideline Development Group within The European Society of Human Reproduction and Embryology (ESHRE) who informed and published a new set of clinical guidelines for the diagnosis, treatment and management of Endometriosis. This new 3rd, entirely updated version of the guidelines also expands on important issues such as the clinical evidence on Endometriosis in adolescents and postmenopausal women. It outlines the diagnostic process, challenges laparoscopy and histology as the overall gold standard diagnostic tests, and it evaluates surgical, medical and non-pharmacological treatments.

**Melanie Davies** received multi-million pound grants for two trials:

# POISE (Premature Ovarian Insufficiency Study of Effectiveness of hormonal therapy)

POISE

This £2+ million NIHR grant started in April 2020 and was awarded to Professor

Melanie Davies to run a randomised trial of Hormone Replacement Therapy versus the Combined Oral Contraception Pill for women under 40 years of age with premature ovarian insufficiency. Young women may need treatment for at least 20 years so the outcomes of bone density, blood pressure and cardiovascular risk are to be monitored, as well as symptom control and wellbeing. The trial is being run in conjuction with the Nottingham Clinical Trials Unit.

www.nctu.ac.uk/studies/current-studies/poise.aspx www.isrctn.com/ISRCTNISRCTN91141124

# BLUSH (OxyButynin for non-hormonal treatment of hot fLUSHes) to research management of premature ovarian insufficiency and symptoms of menopause.

Most menopausal women experience vasomotor symptoms (VMS), including hot flushes and night sweats, lasting several years. VMS are more frequent and intense in women taking breast cancer treatment, which can reduce compliance. All alternatives are less effective than HRT and have side effects. The study is investigating if oxybutynin is more effective and better value for money than venlafaxine at controlling VMS in two groups of women: those who prefer not to use menopausal Hormone Replacement Treatment (HRT), and those with contraindications to HRT. The trial is being run in conjuction with the Nottingham Clinical Trials Unit.

www.nctu.ac.uk/studies/current-studies/blush.aspx

# Adenoymosis Reseach

# Sania Latif, Bassel H Al Wattar, Shaheer Saeed, Yipeng Hu,Neerujah Balachandren, Tomasz Lukaszewski, Ephia Yasmin, Ertan Saridogan Dimitrios Mavrelos

Adenomyosis can adversely affect chances of pregnancy in couples undergoing assisted conception. To date there is no consensus on the optimal protocol for management of subfertile women with adenomyosis.

# MODA (Modified Downregulation for Women wiith Adenomyosis of the Uterus Prior to Frozen-thawed Embryo Transfer).

At the Reproductive Medicine Unit we are leading the MODA trial – a pragmatic, multi-site, randomised controlled trial of two parallel arms comparing prolonged downregulation with GnRH analogue for 6 weeks to standard downregulation with GnRH analogue for 1 week prior to frozen-thawed embryo transfer. We are recruiting participants from fertility centres across London over the next 3 years. The MODA trial aims to determine whether modified downregulation prior to frozen-thawed embryo transfer improves the chance of clinical pregnancy in women with moderate and severe adenomyosis..

## https://clinicaltrials.gov/ct2/show/NCT03946722

Altered uterine peristalsis has been proposed as a mechanism to explain the reduction in chances of conception in women with adenomyosis. Uterine peristalsis can be visualised by transvaginal sonography and plays an important role in sperm transport and embryo implantation. In collaboration with UCL and WEISS we are developing an objective tool to quantify uterine peristalsis on transvaginal sonography using an algorithm based on optical flow for wave motion quantification in women with adenomyosis.



BMJ Open

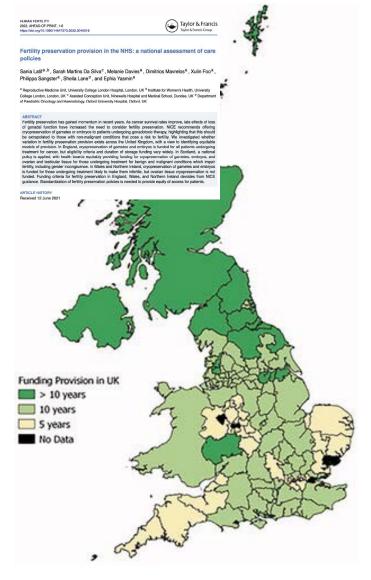
Effectiveness of modified downregulation for women with moderate and severe a denomysosis of the uterus prior to frozen thawed embryo transfer (MODA) study protocol: a pragmatic randomised-controlled trial

Sana Lataf ® " Bassed H A Wittar. Need-gain Basic-horden." Tomas Lukasevella. "Barn Sariotogar," Epin Yazerin, "Paul Berhal." Dimition Moreous and the second of th

# Investigating disparities in fertility preservation funding

# Sania Latif, Sarah Martins Da Silva, Melanie Davies, Dimitrios Mavrelos, Xulin Foo, Philippa Sangster, Sheila Lane, Ephia Yasmin

Dr. Sania Latif won the best oral presentation award at the British Fertility Society Annual meeting in 2021. Her work aiming to highlight disparity in funding for fertility preservation showed that there is considerable variation in the criteria and duration of funding in England, Wales, and Northern Ireland, deviating from NICE guidance. Notably, funding for those undergoing treatment for gender incongruence and ovarian tissue cryopreservation is inconsistent and needs to be addressed. This national audit serves as a tool for all stakeholders including clinicians and care providers to appeal to their local commissioners for uniformity of policy, equal access to care for patients and implementation of standardized fertility preservation provision in the UK.

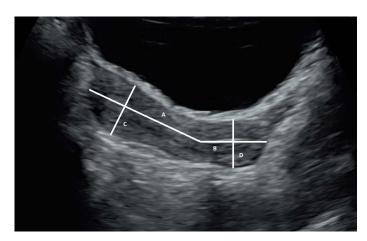


# Induction of puberty

### **Elizabeth Burt**

Elizabeth Burt's research in induction of puberty has shown the importance of regular monitoring and individualised oestrogen dose titration to achieve optimal uterine and breast development. In a retrospective study it was seen that, despite seemingly adequate oestrogen dosing, the majority of women who had undergone induced puberty had smaller uterine dimensions, measured by ultrasound, compared to those with spontaneous puberty. This may have potential implications for future fertility. A prospective study examining induction of puberty with exogenous oestrogen demonstrated considerable variability in final uterine and breast volumes after 8 months of standardised treatment. The uterine transverse measurement was most closely associated with oestradiol levels and may be used as a surrogate marker of oestrogen sensitivity to guide early individualised dose adjustment. Whilst Tanner breast staging is the current gold standard for breast assessment, a novel technique of breast volume assessment, using 3D imaging, has been developed demonstrating excellent reproducibility and validity. This would provide a quantitative assessment to compliment Tanner breast staging in the context of induced breast development.

A longitudinal transabdominal ultrasound image of the uterus showing landmark points for measurement.



Figures demonstrating 3D breast imaging in a male participant, completed as part of the technique development. Warping was used to mimic a change in breast volume and a difference in surfaces technique was used to measure differential volume.

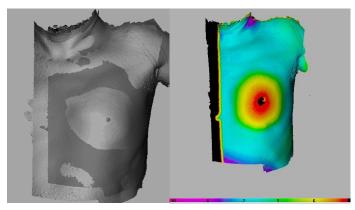


Figure A (left) – A static image of male participant (dark grey) superimposed with the 10mm warped image (light grey).

Figure B (right) – The differences of surfaces represented as a colour overlay with the blue area demonstrating minimal volume change through to the black area demonstrating the maximum area of volume change.

# Evidence synthesis in fertility and Reproductive Medicine

# Bassel Al Wattar, Ephia Yasmin, Anna David, Dimitri Mavrelos

The Reproductive Medicine Unit at University College London Hospitals offers world-class health services for couples seeking to get pregnant with a strong focus on producing impactful research that directly addresses the reproductive health needs of women and their families.

The unit is focused on hosting talented young researchers undertaking iBSc and MSc projects. Two of our students recently concluded a large meta-analysis that identified best practices around the time of embryo transfer to optimise the chances of women undergoing In-vitro fertilisation to get pregnant. This work has been published in the highest impact factor journal for women's health (Human Reproduction Update) and has been featured in several international news outlets.

The Reproductive Medicine Unit is focused on collaborating with top researchers in the UK to produce best quality research in this field. A collaboration with UCL and Warwick University saw the publication of another systematic review which illustrated the risks associated with assisted reproduction and how antenatal, intrapartum, and postnatal care could be tailored to help women with IVF pregnancies reduce these risk and achieve safer pregnancy and childbirth. Based on this work, our team has been commissioned by the British Fertility Society to produce a national

evidence-based guideline to inform patients and health professionals on how to best mitigate the risks associated with assisted reproduction.

# Management of polycystic ovarian syndrome

# Bassel Al Wattar, Vikram Talaulikar, Melanie Davies, Gerry Conway, Ephia Yasmin

Polycystic ovary syndrome is the commonest endocrine condition affecting women of reproductive age. The syndrome manifest in varied symptoms including menstrual disorders, hirsutism, acne, subfertility, endometrial hyperplasia, and insulin resistance.

The Reproductive Medicine Unit at University College London is driving a multidisciplinary research programme focused on evaluating novel treatments for women with PCOS.

Our team recently published a key systematic review that highlighted the variation across PCOS guidelines and the remaining knowledge gap. We also assessed the quality of available randomised trials that evaluated promising lifestyle interventions for women with PCOS and currently running a pilot study to evaluate the role of fasting and low glycaemic intake diet to restore ovulation in this cohort. We are also collaborating with international researchers in this field to optimise the quality of research and reporting of studies on PCOS.

We are focused on building a strong collaboration with the community to produce better quality research in the future. This year we are hosting the first patient day in collaboration with the PCOS Verity charity with the aim to empower women's voices, understand the challenges and health needs of women with PCOS and set a joint research agenda for the future. Future work aims to explore promising interventions to optimise the assisted conception treatments offered to women with PCOS and also new medications to help reduce their insulin resistance and restore natural fertility.

# Important Publications

Burt E, Davies MC, Yasmin E, Cameron-Pimblett A, Mavrelos D, Talaulikar V, et al. Reduced uterine volume after induction of puberty in women with hypogonadism. Clin Endocrinol (Oxf). 2019;91(6):798-804.

B Grace, J Shawe, S Johnson, J Stephenson, You did not turn up... I did not realise I was invited...: understanding male attitudes towards engagement in fertility and reproductive health discussions, Human Reproduction Open, Volume 2019, Issue 3, 2019, hoz014, https://doi.org/10.1093/hropen/hoz014

Jauniaux E, Hussein AM, Zosmer N, Elbarmelgy RM, Elbarmelgy RA, Shaikh H, Burton GJ. A new methodologic approach for clinico-pathologic correlations in invasive placenta previa accreta. Am J Obstet Gynecol. 2020 Apr;222(4):379.e1-379.e11.

Jauniaux E, Zosmer N, Subramanian D, Shaikh H, Burton GJ. Ultrasound-histopathologic features of the utero-placental interface in placenta accreta spectrum. Placenta. 2020 Aug;97:58-64. doi: 10.1016/j.placenta.2020.05.011.

Barrett G, Nolan EM, Gürtin ZB, Stephenson J, Hall JA. 2020 London Measure of Unplanned Pregnancy and newer family forms: an update Journal of Epidemiology and Community Health

Das S, Hall J, Barrett G, Osrin D, Kapadia S, Jayaraman A. 2021 Evaluation of the Hindi version of the London Measure of Unplanned Pregnancy among pregnant and postnatal women in urban India BMC Pregnancy and Childbirth 21:602

Stephenson J, Schoenaker DA, Hinton W, Poston L, Barker M, Alwan NA, Godfrey K, Hanson M, de Lusignan S. A wake-up call for preconception health: a clinical review. British Journal of General Practice. 2021 May 1;71(706):233-6. https://pubmed.ncbi.nlm.nih.gov/33926884/

Balachandren N, Barrett G, Stephenson JM, Yasmin E, Mavrelos D, Davies M, David A, Hall JA

BMJ SEXUAL & REPRODUCTIVE HEALTH 48(1):60-65 (6 pages) 16 Oct 2021 Impact of the SARS-CoV-2 pandemic on access to contraception and pregnancy intentions: a national prospective cohort study of the UK population

Jauniaux E, Hecht JL, Elbarmelgy RA, Elbarmelgy RM, Thabet MM, Hussein AM Searching for placenta percreta: a prospective cohort and systematic review of case reports. Am J Obstet Gynecol. 2021 Dec 29:S0002-9378(21)02694-6.

Jauniaux E, Mavrelos D, De Braud LV, Dooley W, Knez J, Jurkovic D. Impact of location on placentation in live tubal and caesarean scar ectopic pregnancies.

Placenta. 2021 May;108:109-113. doi: 10.1016/j. placenta. 2021.03.019.

Joanna Melville, Aisling Stringer, Naomi Black, Siobhan Quenby, Stephen D. Keay, Anna L. David, Ephia Yasmin, Bassel H. Al Wattar, The impact of assisted reproductive technology treatments on maternal and offspring outcomes in singleton pregnancies: a review of systematic reviews,F&S Reviews,Volume 2, Issue 4, 2021,Pages 287-301

Al Wattar BH, Fisher M, Bevington L, Talaulikar V, Davies M, Conway G, Yasmin E. Clinical Practice Guidelines on the Diagnosis and Management of Polycystic Ovary Syndrome: A Systematic Review and Quality Assessment Study. J Clin Endocrinol Metab. 2021 Jul 13;106(8):2436-2446. doi: 10.1210/clinem/dgab232.

Al Wattar BH, Fisher M, Bevington L, Talaulikar V, Davies M, Conway G, Yasmin E. Clinical Practice Guidelines on the Diagnosis and Management of Polycystic Ovary Syndrome: A Systematic Review and Quality Assessment Study. J Clin Endocrinol Metab. 2021 Jul 13;106(8):2436-2446. doi: 10.1210/clinem/dgab232.

Al Wattar BH, Bueno A, Martin MG, Ibáñez NC, Harasani K, Garad R, Franks S, Balen A, Bhide P, Piltonen T, Romualdi D. Harmonizing research outcomes for polycystic ovary syndrome (HARP), a marathon not a sprint: current challenges and future research need. Human Reproduction. 2021 Mar;36(3):523-8.

Joanna Melville, Aisling Stringer, Naomi Black, Siobhan Quenby, Stephen D. Keay, Anna L. David, Ephia Yasmin, Bassel H. Al Wattar, The impact of assisted reproductive technology treatments on maternal and offspring outcomes in singleton pregnancies: a review of systematic reviews,F&S Reviews,Volume 2, Issue 4,2021,Pages 287-301,

Balachandren N, Davies MC, Hall JA, Stephenson JM, David AL, Barrett G, O'Neill HC, Ploubidis GB, Yasmin E, Mavrelos D. SARS-CoV-2 infection in the first trimester and the risk of early miscarriage: a UK population-based prospective cohort study of 3041 pregnancies conceived during the pandemic. Hum Reprod. 2022 Apr 7:deac062. doi: 10.1093/humrep/deac062.

Gürtin, Z. B., Jasmin, E., Da Silva, P., Dennehy, C., Harper, J., & Kanjani, S. (2022). Fertility treatment delays during COVID-19: Profiles, feelings and concerns of impacted patients. Reproductive biomedicine & society online, 14, 251–264. https://doi.org/10.1016/j.rbms.2021.12.004

Thwaites, A., Hall, J., Barrett, G., and Stephenson J. Contraception after in vitro fertilisation (IVF): a qualitative study of the views of women who have had spontaneous pregnancies after successful IVF. Reprod Health 19, 40 (2022). https://doi.org/10.1186/s12978-022-01349-2)

Manual Muleva BR, Borges ALV, Hall JA, Barrett G. 2022 Evaluation of the Portuguese version of the London Measure of Unplanned Pregnancy in Mozambique: a psychometric measurement study

African Journal of Reproductive Health

B Grace, J Shawe, S Johnson, N O Usman, J Stephenson, The ABC of reproductive intentions: a mixed-methods study exploring the spectrum of attitudes towards family building, Human Reproduction, 2022;, deac036, https://doi.org/10.1093/humrep/deac036

Latif S, Martins Da Silva S, Davies M, Mavrelos D, Foo X, Sangster P, Lane S, Yasmin E. Fertility preservation provision in the NHS: a national assessment of care policies. Hum Fertil (Camb). 2022 Apr 10:1-6. doi: 10.1080/14647273.2022.2045519. Epub ahead of print. PMID: 35400285.

Tyler B, Walford H, Tamblyn J, Keay SD, Mavrelos D, Yasmin E, Al Wattar BH. Interventions to optimize embryo transfer in women undergoing assisted conception: a comprehensive systematic review and meta-analyses. Hum Reprod Update. 2022 Mar 24:dmac009. doi: 10.1093/humupd/dmac009.

Burt E, Yasmin E, Davies MC, Creighton S, Brain C, Ruff C, et al. Variability of response to early puberty induction demonstrated by transverse uterine diameter measurement and a novel method of 3D breast imaging. Clin Endocrinol (Oxf). 2022.

Burt E, Ruff C, Yasmin E, Davies M, Cameron-Pimblett A, Butler G, et al. Challenges in developing a quantitative method of measuring breast development using 3D imaging: An example of a novel method for use in induced breast development with exogenous oestrogen. Clin Endocrinol (Oxf). 2022.

Al Wattar BH, Hussain NM, Khan KS. Lifestyle interventions in women with polycystic ovary syndrome: A scoping systematic review of randomised evidence. Medicina de Familia. SEMERGEN. 2022 Feb 10.

Tyler B, Walford H, Tamblyn J, Keay SD, Mavrelos D, Yasmin E, Al Wattar BH. Interventions to optimize embryo transfer in women undergoing assisted conception: a comprehensive systematic review and meta-analyses. Hum Reprod Update. 2022 Mar 24:dmac009. doi: 10.1093/humupd/dmac009.

# Highlights

**Eric Jauniaux** lectured at the Placenta Accreta Scientific virtual Forum at the 41st Annual Pregnancy Meeting of the Society for Maternal Fetal Medicine (SMFM) in January 2021

**Joyce Harper's** new book "Your Fertile Years' was published and launched in June 2021

**Sania Latif** won the best oral presentation award at the British Fertility Society Annual meeting in 2021. Her work aiming to highlight disparity in funding for fertility preservation has now been published.

**Jonathan Lewin** was awarded the Iwan Lewis Jones Prize for 'A comparison of outcome of ICSI with epididymal and testicular sperm – a decade of nationwide data at the British Fertility Society Annual Meeting in 2021

**Zeynep Gurtin** became a UCL Arena Fellow and will become an Arena Mentor for the IfWH.

Bola Grace, Honorary Research Fellow with IfWH Sexual & Reproductive Health Team, won 'Women of the Future' Award in 2021. The awards recognise successful women in Britain and this year's special award for 'Mentor of the Year' was given to Dr Grace, in recognition of her years of work with young people, students, colleagues and peers. The judging panel highlighted Dr Bola Grace's commitment to developing students in academia, colleagues in the healthcare industry, and young people in her work with non-profit organisations; as evinced by the numerous references and testimonials from mentees and colleagues.

**Dr Vasanti Jadva,** Lecturer in Reproductive Science at IfWH/UCL, was invited to speak at the Canadian Fertiity & Andrology Society 67th Annual Meeting, Vancouver, Canada, October 2021. This was a hybrid meeting and Vasanti attended virtually. The title of her presentation was 'The UK Longitudinal Study of ART Famlies'

**Davor Jurkoic** was awarded the prestigious Ian Donald Gold Medal whilst attending The International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) virtual meeting in October 2020.

# **External Appointments**

Eric Jauniaux was appointed as:

- National lead clinical advisor for NHS England Women and Children's Programme of Care service for the development of Specialised Maternity Care for Patients Diagnosed with for the placenta accreta spectrum, June 2020.
- Member of Public Health England's (now UK health security agency) Advisory Committee on the medical effects of air pollutants on the effects of maternal exposure to ambient air pollution on adverse births outcome, December 2019.
- Chair of the special interest group on anomalies of the placenta and umbilical cord of the European Association of Perinatal Medicine (EAPM), June 2020.

**Zeynep Gurtin** was elected as a Fellow of the RSA (Royal Society of Arts, Manufacturers and Commerce) in 2021 "in recognition of [her] contributions to women's health and reproduction research in the UK, as well as [her] commitment to public education and communication on these very important issues, taking a multi-disciplinary approach to gender and health". She was also recently appointed as a member of the HFEA. She became a Fellow of the Higher Education Academy in 2021.

# **Promotions**

Ertan Saridogan - Professor of Gynaecological Surgery

**Davor Jurkovic** – Professor in Obstetrics & Gynaecology

**Suzy Buckley** – Associate Professor

Melanie Davies - Professor of Reproductive Medicine

**Jenny Hall** – Appointed as Associate Professor at the EGA IfWH

# Research Department of Maternal & Fetal Medicine



Pascale V
Guillot
Head of
Research
Department
& Stem Cell
and Exosome
Therapy



Anna David
Prenatal Therapy



Sara Hillman Pre-eclampsia



Simon Waddington Gene Transfer Technology



Rosalind Aughwane Placenta Imaging



Owen Vaughan Fetal and Placental Physiology



Helen O'Neil Reproduction biomarkers secondment



Mariya Hristova Perinatal Brain Repair



Ashley Boyle Preterm Labour



Dimitrios Siassakos Perinatal Care and Operative Birth



Joanne Ng
Gene Therapy
for Childhood
Neurological
Disorders



Karda
Gene Therapy
and Editing
for Childhood
Genetic
Epilepsies

Rajvinder



David Williams Obstetrics Medicine



Rezan Kadir Thrombosis and Haemostasis



Donald
Peebles
NHS England
National Safety
Maternity Lead



Adalina Sacco Fetal Medicine

The Maternal and Fetal Medicine Department comprises 14 groups that include clinicians and researchers, with the overarching aim to improve the outcomes for pregnant women and their babies throughout improved diagnostics and treatment. Remaining on the edge of translational discovery, the Department innovates in the fields of gene therapy, stem cell therapy and exosome therapy, developing in vitro platforms such as tissue organoids and three-dimensional dynamic cultures to bridge the gap between experimental models and clinical trials. Four main areas or research are currently developed: regenerative medicine, placental biology, preterm birth and perinatal care. The department has undergone rapid expansion with new groups on perinatal care and operative birth, fetal imaging, pre-eclampsia, fetal physiology and gene therapy for childhood neurological and epileptic disorders.

# National Safety Maternity Lead, NHS England

### **Donald Peebles**

Professor Peebles was appointed as a National Specialty Advisor in Obstetrics, NHS England, in 2020. Since then he has provided national leadership to a number of initiatives relating to maternal and fetal wellbeing. He is the obstetric lead for the Maternity Safety Support Programme which provides multidisciplinary support for Maternity services in England that have been rated inadequate by the CQC; currently the MSSP is involved with 25 Trusts in England. He has also been leading on the implementation of Maternal Medicine Networks, which will ensure that all women with existing or acquired medical complications during pregnancy will be cared for by MDT teams that are expert in the care of women that are pregnant. These networks will all be operational by the end of 2022. He is part of the central team designing and implementing the Saving Babies Lives Care Bundle, including the recently added element around preterm birth reduction, and leads on Element 4. Finally, he chairs a national steering group to improve the leadership and culture of maternity services in England – both of which have been highlighted as ongoing challenges in a number of national reports, including the recent Ockenden review.

# First in utero stem cell transplantation trial

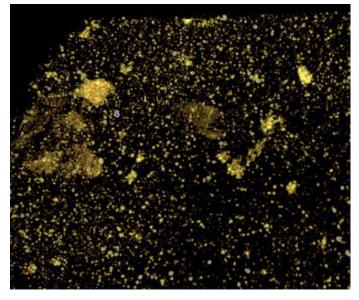
## Anna David, Rachel Sagar, Pascale Guillot

In March 2020 the European Commission's Horizon 2020-funded BOOSTB4 Phase I/II Clinical trial started to assess the safety and efficacy of prenatal and postnatal mesenchymal stem cell transplantation for the brittle bone disease osteogenesis imperfecta. The project, led by Karolinska Institute, includes ten European centres including UCL and Great Ormond Street Hospital, led by Anna David at UCL (Rachel Sagar and Pascale V Guillot are part of the UCL team). In February 2022, the pre-natal group closed but final recruiting for the postnatal group continued until the end of 2022. The trial will reveal its findings in December 2023.

Bone fragility caused by mutations in type I collagen can be counteracted using the urine of patients that have been gene edited to remove the diseasecausative mutation

# Pascale V Guillot, Ellen Petzendorfer, Michelangelo Corcelli, Anna L David

The rare skeletal dysplasia osteogenesis imperfecta (OI) starts to manifest in utero and is characterised by brittle bones that break easily. Mesenchymal stem cells (MSC) isolated from healthy fetal donors and transplanted during the neonatal period contribute to a 75-80% decrease in long bone fracture rate in mice with OI. Whilst these



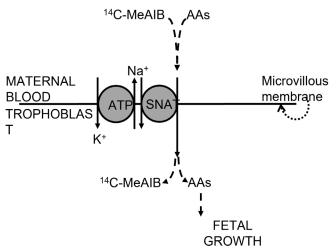
results, combined to anecdotal ones after in utero therapy in humans, paved the way for the first clinical trial (BOOSTB4), the future of cell therapy for bone health aims at avoiding the use of multiple donors. Instead, the urine of people with OI is collected to isolate epithelial cells that are subsequently reverted to pluripotency, generating induced pluripotent stem cells (iPSCs). Such rejuvenated cells are subsequently gene edited to remove the genetic defect responsible for the disease before being turned into mesenchymal stem cells that can be used for the patients themselves. Personalised medicine enables to use patients 'own cells, thereby overcoming the hurdles associated with the need of multiple donors with the problem of genetic mismatch.

# Discovery of a protein that could treat fetal growth restriction

## Owen Vaughan, Sara Hillman, Anna L David

Fetal growth restriction (FGR) is a complication of pregnancy that reduces birth weight, increases infant mortality and is associated with later-life cardiometabolic disease, but no treatments are currently available. The research, carried out in mice, found that low levels of the protein Slc38a2/SNAT2 causes FGR, raising the hope to develop a treatment for late-onset fetal growth restriction in humans.

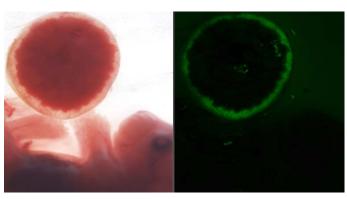




# A cure for Dopamine Transporter Deficiency Syndrome (DTDS) has been found in mice

# Jo Ng, Serena Barral, Simon Waddington, Manju Kurian

Dopamine Transporter Deficiency Syndrome – or DTDS – is an extremely rare degenerative brain disorder that is caused by the mutation of a single gene in the brain. In collaboration with colleagues Dr Barral and Professor Kurian at the Zayed Centre for Research, UCL and Great Ormond Street Institute of Child Health experiments in patient-derived neuronal models and mice showed that by delivering functional genes into the affected neurons can override the faulty genes, thereby curing them of symptoms such as involuntary and disordered movements. The researchers are now preparing for clinical trial of this gene therapy in DTDS children at Great Ormond Street Hospital.



# Family history of pre-eclampsia and cardiovascular disease increases the risk of pre-eclampsia

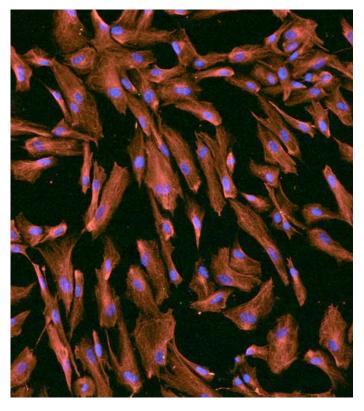
### **David Williams**

Pre-eclampsia is a multi-system syndrome of pregnancy which is classically defined as the new onset of hypertension and proteinuria in the second half of pregnancy, and which resolves after childbirth. Pre-eclampsia affects 3-5% of first-time mothers and causes critical illness in about 1:250 pregnancies. Childbirth remains the only cure, but the decision to deliver needs to balance opposing risks to mother and infant. Immediate childbirth is good for maternal health, but the infant may suffer complications of prematurity. Research found that just as daily Aspirin 150mg reduces the risk of recurrent cardiovascular events outside of pregnancy, so too Aspirin 150mg taken each evening from the first trimester until 36 weeks' gestation, reduces the risk of pre-term pre-eclampsia.

# Developing cell free therapeutics to overcome the hurdles of cell therapy

# Ellen Petzendorfer, Mehedi Hasan, Sneha Prajapati, Pascale V Guillot

The therapeutic potential of primary mesenchymal stem cells (MSCs) isolated from healthy donor tissues has been reported widely in the literature and MSCs are currently tested in clinical trials. However, the properties and therapeutic efficacy of primary MSCs depend on their tissue of origin, stage of development, the number of in vitro cell divisions and culture conditions. The need to obtain a sufficient number of MSCs requires extensive in vitro expansion, during which the cells undergo replicative senescence and progressively lose their repair potential. Instead, induced pluripotent stem cells (iPSCs) can be scaled up without senescing in 3D suspension bioreactors and subsequently differentiated into MSCs. The small extracellular vesicles released by these cells (exosomes) have been shown to present superior regenerative efficacy and represent a cell-free alternative that circumvent the disadvantages and limitations of iMSC transplantation, including the risks of ectopic engraftment and differentiation in various cell types into the brain, tumorigenicity and immune rejection. These cells are currently being tested in human models of bone, brain and lung pathologies.



# Revolutionizing operative birth

### **Dimitrios Siassakos**

Persistent malposition of the fetal head at full cervical dilatation affects 4% of women giving birth vaginally (30,000 per year in the UK) and is a strong predictor for poor maternal and neonatal outcomes such as anal sphincter injury and caesarean section. There is no consensus as to which is the safest and most effective method of expediting birth. The ROTATE study (£1.8m) will determine if manual rotation of the fetal head is superior to instrumental rotation for women and their babies with malposition in the second stage. This will enable national guidelines and training to identify and facilitate the mode of birth that promotes outcomes that are important to women and their families. ROTATE is a pragmatic, multicentre, 2-arm parallel group, open-label

randomised controlled trial with an internal pilot. A total sample of 5,200 women from approximately 40 sites will be recruited. ADD IN IMAGE 5

We are also developing a new type of glove for obstetric examination that may improve the safety of operative birth.

Sensorized glove for obstetrics, to improve the safety of operative birth.

# Fetal membranes can repair themselves after injury

## **Anna David**

The integrity of the fetal membranes that surround the baby in the womb during pregnancy is vital for normal development. But fetal membranes can become damaged as a result of infection, bleeding, or after fetal surgery and even diagnostic tests during pregnancy, such as amniocentesis. This research has investigated the reasons why holes made in the amniotic membrane never seem to heal up even ten weeks later and aims to develop ways to make this hole repair itself. Our studies found that myofibroblast cells in the fetal membranes can crawl towards the edges of the wound and into the defect site, producing cell collagen and starting to pull the edges of the

wound, contracting the tissues together and repairing the wound. Finding that the fetal membranes have this potential to heal is a huge step towards developing treatments for women with preterm prelabour rupture of the membranes (PPROM).

# Fetal and placental MRI

# Nada Mufti, Roz Aughwane, Andrew Melbourne, Anna David



There has been extensive work ongoing in fetal and placental MRI as part of the Wellcome Trust/EPSRC funded GIFT-Surg project in collaboration with engineers and medical physicists at UCL and Kings College London.

Firstly, our team of fetal medicine experts and engineers developed a multi-compartment magnetic resonance imaging (MRI) technique called DECIDE (Figure), that is sensitive to fetal blood oxygenation, so as to better examine placental characteristics in pregnancies complicated by early-onset fetal growth restriction (FGR). Using this technique, we quantified fetal and maternal blood volume and feto-placental blood oxygenation. MRI-derived feto-placental oxygen saturation was higher in normal pregnancies compared with FGR pregnancies, and the degree of abnormality correlated with disease severity defined by ultrasound Doppler findings.

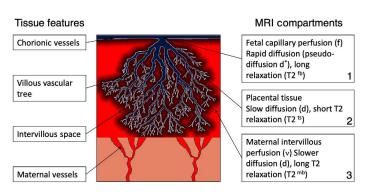
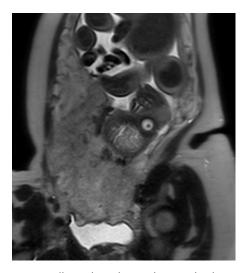


Illustration of the division of the placenta into three different MRI compartments (right hand side) and their respective MRI properties. Augwane et al. BJOG, Volume: 128, Issue: 2, Pages: 337-345, First published: 30 June 2020, DOI: (10.1111/1471-0528.16387)

The team have since worked with a group at University of Auckland, New Zealand, lead by Professor Peter Stone. Using the DECIDE technique we explored the reason why maternal supine sleep position in late pregnancy is associated with an increased risk of stillbirth. Maternal supine position in late pregnancy is known to reduce

maternal cardiac output and uterine blood flow. Using the DECIDE MRI technique, we found that compared to the left lateral position, maternal supine position in late pregnancy is associated with reduced utero-placental blood flow and oxygen transfer across the placenta. There is an average 6.2% reduction in oxygen delivery to the fetus and an average 11% reduction in fetal umbilical venous blood flow when women lay flat on their baby rather than on their side in late pregnancy. We are now studying how supine position affects fetoplacental oxygenation in women with pregnancies affected by fetal growth restriction.

There has also been work to use novel MRI algorithms to better image the placenta in patients with placenta accreta spectrum disorder (PAS, Figure). Better visualisation of the degree of



placental attachment can allow the obstetric surgical team to plan the delivery better.

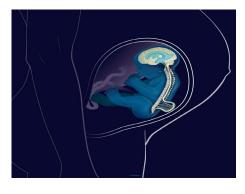
In the MRI shown, there is uterine bulging and bladder wall interruption present at the placental-myometrium-bladder interface which are pathological PAS MRI markers. A noted irregularity in the normally smooth hypointense bladder wall is seen. This is caused by the abnormal adherence of the placenta to the thinned myometrium due to loss of the decidual layer caused by previous caesarean section scars.

# Fetal Surgery for Spina Bifida

Anna David, Jan Deprest, Adalina Sacco, Emma Bredaki, Ruwan Wimalasundera, George Attilakos, Donald Peebles, Pranav Pandya with Dominic Thompson, Paolo De Coppi and Zubair Tahir from Great Ormond Street Hospital (GOSH), London.

In 2019, the NHS England Highly Specialised services commissioned us to provide the first NHS fetal surgery for spina bifida service nationally. The service commenced in November 2019 as a single service across two sites – London UCLH/GOSH and University Hospital (UZ) Leuven,

Belgium. The service serves the populations of England, Northern Ireland, Scotland and Wales.
Service outcomes are reviewed on a six-monthly rolling basis by



NHS England commissioners and we meet regularly with SHINE and SBH Scotland, the national Spina Bifida charities.

The initial 2-year outcomes by end of 2021 show that in total, 41 fetal surgeries took place across both Fetal Surgery Centres, out of 88 referrals. The remaining patients either had a history of preterm delivery so were not eligible; declined the offer of assessment or opted to terminate their pregnancy prior to assessment. Primary skin closure of the spina bifida defect was achieved in the majority of fetuses. There were no intra-operative complications or intra-uterine deaths within 28 days of the procedure. Most fetuses showed an improvement in hindbrain herniation by 32 weeks of gestation as assessed by MRI. The median gestational age at delivery was 35 weeks and 5 days, neonatal and maternal outcomes are good.

The service has remained fully accessible and operational to both referring Fetal Medicine Units (FMUs) and patients during COVID-19 pandemic. All outcomes were in line with the findings reported in the 'MOMS' trial. In addition, the service all Quality Metric measures were met.

Patients have reported a very good overall experience of the service and high satisfaction rates.

# The Intercovid Multinational Cohort Study

### **Raf Napolitano**

Effects of prenatal exposure to maternal COVID-19 and perinatal care on neonatal outcome: results from the INTERCOVID Multinational Cohort Study. Effects of prenatal exposure to maternal COVID-19 and perinatal care on neonataloutcome: results from the INTERCOVID Multinational Cohort Study.



American journal of obstetrics and gynecology, 227(3)

Between March 2020 and March 2021, Women's Health Research Team at UCLH, along with 42 collaborators in 18 countries worked together to rapidly collect evidence on the impact of COVID-19 on fetal and neonatal outcomes.

The study examined the role of COVID-19 on mode of delivery, pregnancy complications and neonatal outcomes. These findings have influenced clinical practice and vaccine policy worldwide. In this large-scale cohort study, unexposed women were concomitantly enrolled immediately after an infected woman was identified at any stage of pregnancy and delivery. Women and their babies were followed up until hospital discharge. A total number of 586 neonates born to women with COVID-19 diagnosis, and 1535 neonates born to women without COVID-19 diagnosis were enrolled into the study. The study concluded that women with a confirmed COVID-19 diagnosis had a higher rate of caesarean delivery compared to those without COVID-19 (52.8% vs 38.5, p<.001). Higher cases of the pregnancy related complications, such as hypertensive disorders and fetal distress was identified amongst the women with COVID-19 compared to women without the disease (p<.001). Furthermore, COVID-19 greatly influenced perinatal and neonatal outcomes, with increased rates of preterm birth (p<.001) and low birth weight, head circumference and length at birth (p<.001). There was also a significant correlation between the risk of the neonate testing positive and the length of in-utero exposure. Caesarean delivery was also a risk factor for the neonate testing positive. INTERCOVID reopened in March 2022 to evaluate the effects of COVID-19 variants and vaccination in pregnancy. UCLH research team, led by Mr Raffaele Napolitano, consultant in maternal fetal medicine and obstructs, rapidly recruited 150 women in a short space of time. We look forward to discovering the findings at the end of 2022.

# Highlights

### **Dimitrios Siassakos**

- developed a Training programme in Obstetric Emergencies on Labour Ward, Labour Ward and Puerperium (Fetal-Maternal Medicine Postgraduate Training Programme), University of Thessaloniki, Greece, in December 2022
- gave a virtual talk on Shoulder dystocia. World Perinatal Congress, World Association of Perinatal Medicine, November 2021

### Rajvinder Karda

started a new series of talks, Public & Patient
 Engagement series, British Society of Cell and Gene
 Therapy and Simon Waddington provided the first talk of the series on Gene therapy.

### Helen O'Neill

- invited to give a lecture on Genome Editing in Human Embryos at the Latin American Society for Reproductive Medicine.
- awarded Top Twenty Women in Data and Technology.
   Women in Data UK works to connect women across
  the profession, providing mentoring and showcashing
  for real-world female role models. This was part of a
  billboard campaign promoting STEM jobs to schoolgirls
- featured in The Times in 2021 in relation to 'Hertility Health', of which Helen is co-founder. The business was established in 2019 and provides at-home hormone health and fertility testing and is conducting research into reproductive health.

### **Pascale Guillot**

- invited to present her work on bone repair and personalized medicine for bone fragility (osteogenesis imperfecta) in Stanmore in the Orthopaedic Engineering department.
- accepted on the UKCGE (UK Council for Graduate Education) Supervisor Recognition Programme
- published quarterly open access scientific publications about cell and exosome therapy on the Open Access Government website, which has over 240,000 users including Government Ministers, and Heads of Research Council and Funding Agencies.

### **Simon Waddington**

 attended and presented at the 33rd International Epilepsy Congress in Bangkok, organised jointly by The International League Against Epilepsy and The International Bureau for Epilepsy.

### **Ashley Boyle**

- presented "Cervical Gene Delivery of the Antimicrobial Peptide Human Defensin 3 (HBD3) Reduces Perinatal Neuroinflammation in a Mouse Model of Ascending Infection-Associated Preterm Birth" at both the 68th Annual Society for Reproductive Investigation (SRI) Meeting and the 47th Fetal and Neonatal Physiological Society (FNPS) Meeting
- spoke about how ascending bacterial infection through the vagina leads to neuroinflammation at the Preterm 2020 Virtual Conference, November 2020.

### Ellen Petzendorfer

 Ellen Petzendorfer presented her work on human iPSderived MSC and exosomes at the International Society for Stem Cell Research (ISSCR) conference in San Francisco in June 2022 (Guillot lab)

### **Anna David**

- attended the Innovations in Fetal Therapy expert event at the Leiden University Medical Centre Global Conference in April 2021. She presented on 'Fetal stem cell treatment for osteogenesis imperfecta'
- chaired the Fetal Therapy session at the virtual International Society of Prenatal Diagnosis (ISPD) conference in June 2021. She ran a joint IFetis Session for the ISPD, which formed in 2014 to promote basic and translational research in fetal therapies. This was the first joint iFetis session with ISPD. Anna talked about the new terminology that her team have developed to define and grade material and fetal adverse events for pregnancy trials and ran the Q&A session.
- gave an invited plenary lecture on Precision Medicine in Utero, at the Precision Medicine and Functional Genomics conference 2021, Sidra Medicine, Qatar.

### **Emily Cornish**

 awarded an MRC Clinical Research Training Fellowship for her research on 'Investigation of the maternal immune phenotype in women with recurrent pregnancy loss due to chronic histiocytic intervillositis' in 2021

# Federation of European Neuroscience Societies meeting 2020

 Konstantina Tetorou and Mariya Hristova presented their work on the neuroprotective effect of curcumin in neonatal hypoxic-ischaemic brain injury and adult neuronal regeneration.

# Preterm 2020 Virtual Conference, November 2020

 Amrita Banerjee spoke about caesarean section scars and the risk of preterm birth and was awarded the Oral Presentation 1st Prize.

### **RCOG Annual Academic Meeting 2021**

- Lindsay Kindinger, Subspecialty Trainee, Maternal & Fetal Medicine, presented an oral poster on 'A comparison of obstetric outcomes among antenatal women with gestational diabetes, reactive hypoglycaemia and normal glucose tolerance results.
- Jane Currie, Subspecialty Trainee in Maternal & Fetal Medicine presented an oral poster on 'pregnancy in patients with chronic urinary tract infection – experiences from a specialist clinic'.
- Nada Mufti presented two posters on 'cortical spectral matching and shape and volume analysis of the fetal brain pre and post fetal surgery for spina bifidia' and on 'the use of super resolution reconstruction (SRR) for surgical planning in fetal neck masses and congenital high airway obstruction syndrome (CHAOS): A Retrospective Case Series'.
- Rebecca Spencer presented a poster on 'Development of standard maternal and fetal adverse event definitions and criteria'.

# Society for Reproductive Investigation conference, Denver Colorado (March 2022)

 Owen Vaughan, Anna David, Sara Hillman, Kasia Maksym and Ashley Boyle attended and presented orals and posters.

# European Society for Gene and Cell Therapy annual congress 2021.

 Riccardo Privolizzi (PhD student) gave a talk on "In vivo evaluation of novel synthetic promoters for CNS gene therapy" included some work from his PhD.

# FDA-CERSI (Centers of Excellence in Regulatory Science and Innovation) workshops

- Anna David and Simon Waddington took part in two workshops in October 2021. Simon presented on Fetal gene therapy at the workshop on Fetal Pharmacology & Therapeutics.
- Anna presented on the new Maternal Fetal Adverse
   Event Terminology (MFAET) to grade and define
   maternal and fetal safety at that workshop and the 2nd
   FDA-CERSI workshop on Prenatal Somatic Cell Gene
   Therapy Workshop the following week.

# **External Appointments**

**Rajvinder Karda** became a member of the Advisory Board of the new Scientific Committee of the Dravet Syndrome Foundation in Spain.

# COVID-19 Research Highlights

The SAPPHIRE study on seroconversion of maternity staff led by Sam Bampoe and Dimitrios Siassakos was published in the Journal of Anaesthesia in 2020. The paper showed that a significant proportion (about 1 in 6) of maternity care professionals at the time had been exposed to SARS-CoV2. Importantly, 60% of professionals positive for COVID-19 antibodies never qualified for isolation and continued to work and commute, either because they were asymptomatic (1 in 3) or because their symptoms were not included in guidance for isolation at the time they experienced them. The study was kindly funded by UCLH charity and was a collaboration between the obstetric and obstetric anaesthesia academic departments.

**Top Abstract Award at the International Society** for Prenatal Diagnosis meeting, June 2021. Joe Davidson presented on 'The susceptibility of fetal tissues to SARS-CoV2 infection". The study led by UCL researchers from Great Ormond Street Institute of Child Health, the Institute for Women's Health, Great Ormond Street Hospital for Children and the NIHR Great Ormond Street Biomedical Research Centre found that an unborn baby could become infected with Covid-19 if their gut is exposed to the SARS-CoV-2 virus. Although the study did not look specifically at mothers with Covid-19 and whether their infection was transmitted to an unborn baby, it found that certain fetal organs, such as the intestine, are more susceptible to infection than others. https://www. ucl.ac.uk/news/2021/nov/unborn-babies-could-contractcovid-19-finds-study-it-would-be-uncommon

Running a Spina Bifida Fetal Surgery Service across two countries. This was featured in an International Society for Prenatal Diagnosis Global Update in 2021.

When the COVID-19 pandemic arrived in Europe in Spring 2020, the four-month-old NHS England highly specialised commissioned fetal surgery service for open spina bifida was fledgling. The joined-up clinical service based across two academic health science centres, at University College London Hospital in Central London, and Universitaire Ziekenhuizen (UZ) Leuven in Belgium,

was working well. Patients were travelling to each site for final imaging assessment and surgery, based on the geography of their referring unit: Northern Ireland, Scotland, North Wales and North of England patients to Leuven, and Midlands, South Wales and South of England to UCLH. The virus did not feature much in our weekly calls with NHS England specialised commissioners in February 2020. By March 2020, however, it was clear that a mitigation plan was needed to ensure the sustainability of this first NHS fetal surgery service, putting patient safety above all else. We drew up three Scenarios to cover all potential outcomes. Postnatal repair of spina bifida is always an option for patients who choose to continue their pregnancy affected by fetal spina bifida. In the end we managed to continue offering treatment despite the pandemic.

Dr Kasia Maksym, Research Fellow has recently forged a new collaboration with Warsaw Medical University and has been successful in a grant application under NAWA (Narodowa Agencja Wymiany Akademickiej -National Agency of Academical Exchange) urgency scheme. They obtained funds to work on Development of a tool for pharmacovigilance on breastfeeding and analysis of the impact of post-vaccination effects on lactation in women after receiving the COVID-19 vaccine in the perinatal period.

An interdisciplinary panel of experts representing lactation support services and research institutions worked together to share experience in monitoring lactation safety to develop widely accepted new definitions of lactation-related side effects as a result of the project. In addition, a COVID-19 vaccine surveillance study is being conducted in 100 breastfeeding women in Poland, and clinical data on the duration and effectiveness of breastfeeding after vaccination collected from the resulting registry of vaccinated lactating women. Based on its data the proposal of terminology on Adverse Events in the context of lactation will be assessed and validated. The main long-lasting result of the project will be the update and unification in medical terminology in the Adverse Event of experimental therapies in terms of initiation and maintenance of lactation and breast feeding. The leader of the project in Warsaw is Professor Alexandra Wesolowska who is the Head of Laboratory of Human Milk and Lactation Research at Regional Human Milk Bank in Holy Family Hospital Department of Medical Biology at Medical University of Warsaw.

# Important publications

- Sacco A, Van der Veeken L, Bagshaw E, Ferguson C, Van Mieghem T, David AL, Deprest J. Maternal complications following open and fetoscopic fetal surgery: A systematic review and meta-analysis. Prenat Diagn. 2019 Jan 31. doi: 10.1002/pd.5421.
- Vlahova F, Hawkins KE, Ranzoni AM, Hau K.-.L., Sagar R., De Coppi, P., David A.L., Adjaye, J, Guillot PV (2019). Human mid-trimester amniotic fluid (stem) cells lack expression of the pluripotency marker OC-T4A. Scientific Reports, 9 (1), 8126.
- Takov K, He Z, Johnston HE, Timms J, Guillot, PV, Yellon DM, Davidson SM (2020). Small extracellular vesicles secreted from human amniotic fluid mesenchymal stromal cells possess cardioprotective and promigratory potential. *Basic Research in Cardiology*, 115 (3), 26. doi: 10.1007/s00395-020-0785-3
- Bampoe S, Lucas DN, Neall G, Sceales P, Aggarwal R, Caulfield K, Siassakos D, Odor PM. A cross-sectional study of immune seroconversion to SARS-CoV-2 in frontline maternity health professionals. Anaesthesia. 2020 75(12): 1614-1619
- Couper S, Clark A, Thompson JMD, Flouri D, Aughwane R, David AL, Melbourne A, Mirjalili A, Stone PR. The effects of maternal position, in late gestation pregnancy, on placental blood flow and oxygenation: An MRI study. *J Physiol.* 2020 Dec 28. doi: 10.1113/JP280569. Editor's Choice article.
- Vaughan OR, Maksym K, Silva E, Barentsen K, Anthony RV, Brown TL, Hillman SL, Spencer R, David AL, Rosario FJ, Powell TL, Jansson T. (2021) Placenta-specific Slc38a2/SNAT2 knockdown causes fetal growth restriction in mice. *Clin Sci* (Lond). 17;135(17):2049-2066.
- Dolma P, Angchuk PT, Jain V, Dadhwal V, Kular D, Williams DJ, Montgomery HE,. Hillman SL. High-altitude population neonatal and maternal phenotypes associated with birthweight protection. (2021) Pediatr Res. 2021 Jun 8
- 8. Van der Nelson H, O'Brien S, Burnard S, Mayer M, Alvarez M, Knowlden J, Winter C, Dailami N, Marques E, Burden C, Siassakos D, Draycott T. (2021) Intramuscular oxytocin versus Syntometrine® versus carbetocin for prevention of primary postpartum haemorrhage after vaginal birth: a randomised double-blinded clinical trial of effectiveness, side effects and quality of life. BJOG. 128(7):1236-1246.

- Martinello KA, Meehan C, Avdic-Belltheus A, Lingam I, Mutshiya T, Yang Q, Akin MA, Price D, Sokolska M, Bainbridge A, Hristova M, Tachtsidis I, Tann CJ, Peebles D, Hagberg H, Wolfs TGAM, Klein N, Kramer BW, Fleiss B, Gressens P, Golay X, Robertson NJ. (2021) Hypothermia is not therapeutic in a neonatal piglet model of inflammation-sensitized hypoxia-ischemia. Pediatr Res. 28:1-12.
- Costa E, Okesola BO, Thrasivoulou C, Becker DL,
   Deprest JA, David AL, Chowdhury TT. Cx43 mediates changes in myofibroblast contraction and collagen release in human amniotic membrane defects after trauma. Sci Rep. 2021;11:16975. doi: 10.1038/s41598-021-94767-4.
- 11. Aughwane R, Mufti N, Flouri D, Maksym K, Spencer R, Sokolska M, Kendall G, Atkinson D, Bainbridge A, Deprest J, Vercauteren, Ourselin S, David AL, Melbourne A. MRI measurement of placental perfusion and oxygen saturation in early onset fetal growth restriction. BJOG 2021;128:337
- 12. Crombag N, Sacco, A, Stocks B, De Vloo P, Van Der Merwe J, Gallagher K, David AL, Marlow N, Deprest J. 'We did everything we could'- A qualitative study exploring the acceptability of maternal-fetal surgery for spina bifida to parents. Prenatal Diagnosis 2021;41:910-921. doi: 10.1002/pd.5996.

#### **Promotions**

Dimitrios Siassakos – Professor of Obstetrics
 David Williams – Professor of Obstetric Medicine
 Rajvinder Karda – Lecturer in Gene Transfer
 Mariya Hristova – Principal Research Fellow

#### Awards:

- Lilly Erinoso EGA Charity PhD Scholarship (Pls Jens Madsen and Pascale V Guillot)
- £9,819: Pascale V Guillot, Ariel Finkielsztein, Jens Madsen. <u>Funder:</u> Wellcome Trust - Translational Partnership Award Production of cancer safe iPSCderived lung progenitor cells for lung regeneration
- £7,627: Rajvinder Karda and Bernie Owusu-Yaw.
   <u>Funder:</u> Wellcome Trust Translational Partnership Award AAV Gene therapy of EEF1A2 to treat cardiac diseases in a Eef1a2 null model

#### Grants:

- £652,616: Owen Vaughan. Funder: MRC New Investigator Research Grant The mechanistic and therapeutic role of circulating microRNA-142 in pregnancies complicated by maternal obesity with fetal cardiac dysfunction.
- £19,727.88: Owen Vaughan. <u>Funder</u>: Royal Society Research Grant Physiological role and therapeutic potential of the apelin system in placental function and fetal growth.
- £213,906: New Capital Equipment grant: VisualSonicsVevo 3100 High Frequency Ultrasound system for imaging of disease and therapy in live animal models.
- £29,961 Rosalind Aughwane: <u>Funder</u>: Wellbeing
  of Women Sir Victor & Lady Blank Postdoctoral
  Research Fellowship Mar 2022- Feb 2025 Investigating
  MRI markers of placental function derived from a multiparametric computational model of placental perfusion
  in early onset Fetal Growth Restriction.
- £27,261. Rosalind Aughwane: <u>Funder</u>: Academic
  of Medical Sciences Starter Grants for Clinical
  Lecturers. Investigating MRI markers of placental
  function derived from a multiparametric computational
  model of placental perfusion in normal pregnancies.
- £1.105M: Sara Hillman and Anna David (PI Marko Ni-kolic). Funder: Chan Zuckerberg. Initiative Paediatric Networks for the Human Cell Atlas on Organ maturation in preparation for birth: will be studying single cell analysis of fetal tissues in late pregnancy to support the Chan Zuckerberg Initiative Human Cell Atlas
- £499,926: Sara Hillman and Anna David (collab. with Imperial College and Sanger Institute, Cambridge).
   <u>Funder</u>: Borne Charity BUMP: the Borne Uterine Mapping Project: study single cell analysis of uterine tissues associated with preterm birth
- £250,000 : Simon Waddington. <u>Funder</u>: Capital
   Equipment Fund PCR machine: School of Pharmacy
- £12,230: Rosalind Aughwane. Funder: EGA charity
  research grant Investigating MRI markers of placental
  function derived from a multiparametric computational
  model of placental perfusion in early onset Fetal Growth
  Restriction
- £12,230: Owen Vaughan. <u>Funder:</u> EGA charity research grant Determining the prognostic and

- therapeutic potential of the apelin system in Fetal Growth Restriction
- **£2M** Dimitrios Siassakos. <u>Funder</u>: **NIHR.** ROTATE Rotation of the fetal head at full cervical dilatation.
- £751,752 Pascale V Guillot. <u>Funder MRC</u>. Extracellular vesicles produced by hiPSC-derived mesenchymal stem cells (iEV) for the neuroprotection of the brain following neonatal encephalopathy
- £8,795,355: Dimitrios Siassakos, Anna David. <u>Funder</u>
   Wellcome/EPSRC. WEISS Centre Extension Grant 2022-2024
- £893,000: Sara Hillman. Funder: MRC Mapping the maternal-fetal interface at a single-cell resolution to interrogate the aetiology of severe pre-eclampsia and identify potential disease
- £197,931: Ashley Boyle, Simon Waddington, Donald Peebles. Funder: Wellbeing of Women Project
   Grant. Immunomodulatory therapy for vaginal bacterial infection and preterm birth

# Research Department of Neonatology



Howard Clark Head of Research Department Neonatology

Nikki

**Katie** 



Jens Madsen
Targeted Lung
Immunotherapy
group



Neil Marlow
Neonatal Clinical
Trials & Neonatal
Neurocognitive
Outcomes



Robertson
Preclinical
Neonatal
Neuroprotection
& Global
Neonatal Health



Neonatal Seizures & Neonatal Neuroimaging and Neuroimaging

Subha Mitra



Judith Meek
Development
of Neonatal
Sensory
Processing



**Gallagher**Clinical Lecturer in Neonatology

A concentration of scientists and clinicians embedded in the Research Department of Neonatology within the EGA Institute for Women's Health at UCL focuses on innovation in diagnosis and therapy to improve outcomes of babies with common perinatal and neonatal problems. There are particular strengths in acute care of the preterm newborn infant in neonatal respiratory and intensive care and in neonatal neuroscience including developing novel therapy for lung disease and birth asphyxia combined with advanced neuromonitoring via optical and magnetic resonance techniques for biomarker discovery and validation. The Department is a major centre for clinical innovation in neonatology whose investigators have international reputations for pioneering new diagnosis and therapy for brain and lung injury in babies.

## Bronchiolitis Endotracheal Surfactant Study (BESS)

#### Jens Madsen, Tania Castillo Hernandez, Howard Clark

BESS is a national multi-centre randomised controlled trial to determine the efficacy and safety of endotracheal surfactant in reducing total duration of mechanical ventilation by 18 hours or more versus air placebo in the treatment of critically ill infants with bronchiolitis. The trial is led by Calum Semple, Consultant in Paediatric Respiratory Medicine, Alder Hey Children's NHS Foundation Trust and Professor of Child Health and Outbreak Medicine, University of Liverpool.

At UCL, we are performing a mechanistic sub-study by evaluating if surfactant proteins can be used as a biomarker for bronchiolitis by quantifying the level of surfactant protein D (SP-D) and the presence and degradation patterns of



all surfactant proteins in bronchioalveolar lavages (BAL) from the participants at admission and at 24 hours. We are currently analysing the 151 samples collected so far and another two seasons are planned to recruit a total of 284 samples. These data will be co-analysed with lipidomic data from the BAL samples and clinical data once the recruitment has ended.

See: www.bess-trial.org.uk

#### Webcams in Neonatal Care

#### Gallagher K, Chant K, Meeks J, Marlow N

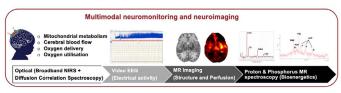
Webcams allow parents to see their baby in real time, through an app, when they are unable to be present on the neonatal unit. Parents can share the link with wider family members so they can see the baby, too. In this study we are exploring parents experiences of using these webcams and any support they may require. We are also exploring the thoughts of neonatal healthcare professionals and the impact of webcams use upon nursing workload.

# Fetal resuscitation during fetal surgery

# Gallagher K, Crombag N, Prashar K, Deprest J, Ourselin S, Marlow N, David A

Advances in fetal surgery have reduced the risk of outcome severity in infants antenatally diagnosed with spina bifida. Surgical risks however may result in the need for fetal resuscitation or emergent delivery to increase maternal and fetal chances of survival. As surgery is usually undertaken in women between 19 and 25+6 weeks of pregnancy, the infant delivered may be eligible for neonatal resuscitation. This study explored global policy to support practice for potential fetal resuscitation, emergent delivery, and subsequent neonatal resuscitation during fetal surgery in all fetal surgical centres where this operation is performed.





# Investigating the real-time and long-term impact of seizures on neonatal brain

## Mitra S, Tachtsidis I, Robertson NJ, Boylan G, Marlow N, Bainbridge A

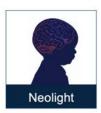
Seizures are a common manifestation of brain injury in newborn infants. We are using a new optical platform (combined broadband near-infrared spectroscopy (BNIRS) and diffusion correlation spectroscopy (DCS)) for a comprehensive real-time assessment of cerebral metabolism, haemodynamics and oxygenation at the cot side. A multimodal assessment of optical data together with physiological signals, video-electroencephalography (EEG), advanced MR neuroimaging and MR spectroscopy, will shine new lights on seizure-induced changes inside developing brain. Both preclinical and clinical INSPIRE studies are ongoing.



## Developing an optical biomarker for early stratification of injury and predicting outcome following neonatal encephalopathy

# Mitra S, Tachtsidis I, Robertson NJ, Harvey-Jones K, Lange F

There is still an unmet demand for a biomarker for early stratification of injury and prognostication of outcome following neonatal encephalopathy. Neolight study is focussed on the development of an optical biomarker of brain tissue health using a multimodal platform of





broadband near infrared spectroscopy (BNIRS), diffuse correlation spectroscopy (DCS) and physiological signals using advanced signal processing techniques. Preclinical study has completed data collection and early findings have been presented in jENS meeting. Clinical study is currently ongoing.

## Monitoring brain temperature during neonatal seizures and neonatal encephalopathy

Mitra S, Tachtsidis I, Verma V, Lange F



Perinatal brain injuries, particularly neonatal encephalopathy, and seizures, have a significant impact on the metabolic and haemodynamic state of the developing brain, and thereby likely induce changes in brain temperature. Using the property



of linear temperature-dependent changes in water absorption spectra in the near infrared range, the team is currently developing an optical technique to monitor brain tissue temperature in real time and understand the pathophysiological changes better in newborn infants with brain injury in BRENS study.

# Developing a robust clinical MR biomarker of outcome following neonatal encephalopathy and neonatal seizures

#### Mitra S, Robertson NJ, Bainbridge A, Kendall G, Sokolska M, Srinivasan L, Pegoretti Baruteau K

We have shown that the cerebral deep grey matter (DGM) lactate/N acetyl aspartate (Lac/NAA) peak area ratio on proton magnetic resonance spectroscopy (MRS) is a robust predictor of neurodevelopmental outcome following neonatal encephalopathy. This has now been incorporated in the new BAPM guideline as 'the most accurate predictor of outcome in babies who have undergone therapeutic hypothermia'. We have now further demonstrated that individual metabolite disturbances following NE and seizures relate to outcome and can be assessed without increased scanning time and. This new methodology



gives specific insights to mitochondrial injury, deranged phospholipid metabolism and increased anaerobic state (presented in PAS meeting and ISMRM meeting 2022).

# Improving parental experience following perinatal brain injury

#### Mitra S, Gallagher K, Chant K, Grey K

The team was awarded a Patient and Public Involvement (PPI) Bursary from NIHR UCLH BRC, which helped to develop a parental advisory group (PAG). Discussions with PAG identified the need for an online platform with a clear visual guidance of the infant's and parental journey in the first few days after birth and later beyond the boundary of the neonatal intensive care unit. The team was further successful with an Innovation Fund award from the Elizabeth Garrett Anderson Charity to develop this digital platform and is currently working with related agencies

and charities. This is expected to be published online at the end of summer 2022.



# Reducing the burden of disability from birth asphyxia in Imic





## PAINT Study (2020-2024)

R Pang, NJ Robertson

## Piglet Asphyxia-Inflammation Model for Neuroprotective Therapies

The burden of neonatal encephalopathy (NE) is high in LMIC, with over 1 million babies affected every year globally. There are concerns about the safety and efficacy of therapeutic hypothermia in LMIC, so single therapies are urgently needed. The Bill and Melinda Gate Foundation are supporting Prof Robertson's Neonatal Neuroprotection Lab at UCL to perform a series of preclinical studies including metabolomic and proteinomic studies with the aim to move to early phase clinical trials in LMIC in 2024. Our lab is testing repurposed therapies such as Azithromycin, Melatonin and Caffeine as well as Omega-3 diglycerides.

# Stem cell therapy for neonatal encephalopathy



Medical Research Council



## INSTINCT Study (2021-2024)

## Intranasal stem Cells to Improve Outcomes with and without Cooling Therapy

#### X Golay, M Lowdell, NJ Robertson

Stem cell therapy has huge potential to reduce neonatal brain injury in neonatal encephalopathy, targeting inflammation, regeneration and repair. Using human umbilical cord mesenchymal stem cells (huMSC) we showed safety and benefit of intranasal stem cells given as single therapy, with improvements in brain energy status, EEG recovery and reduction in cell death in brain white matter (Robertson NJ, Cytotherapy 2021). We received funding from the MRC to run a large preclinical study at the Roslin Institute, LARIF facility https://www.

ed.ac.uk/roslin/facilities-resources/larif to study the benefit of huMSC in males and females, with and without therapeutic hypothermia. If positive results are seen, the aim is to move this therapy to early phase clinical trials.

# Reducing the burden of disability in units offering therapeutic hypothermia



Medical Research Council

EMPATHY Study (2017-2019)

## Epo and Melatonin for Perinatal Asphyxia with Therapeutic Hypothermia

#### R Pang, X Golay, NJ Robertson

Although therapeutic hypothermia reduces adverse outcomes, there are still significant cognitive and language problems in treated children with neonatal encephalopathy at school age. This preclinical study looked at adjunct therapies (melatonin and Epo) as double and triple therapy with cooling. Melatonin and Epo each improved outcomes above cooling, but triple therapy was no better than double therapy with melatonin having most overall benefit (Pang et al., Brain Comm 2021). These results concur with the clinical trial of Epo with cooling showing no benefit of Epo.

## CAMELLIA Study (2020-2023)

## Cooling and Melatonin in LPSsensitized Birth Asphyxia



#### R Pang, K Martinello, X Golay, NJ Robertson

Melatonin is a endogenous hormone that in pharmacological doses has potent anti-oxidant, anti-

inflammatory and anti-apoptotic effects. Using the preclinical inflammation-augmented HI model relevant to LMIC, we are assessing the potential benefit of high levels of intravenous melatonin on brain protection using aEEG, brain biochemistry and cell death markers. If positive we plan to move this to early phase RCT in LMIC in collaboration with Bill and Melinda Gates Foundation.

# Understanding sex differences in response to therapeutic hypothermia





## **CHIP Study**

# Cooling for Hypoxia Ischaemia in the Piglet

#### R Pang, NJ Robertson

Recent studies suggest male vulnerability to brain injury and dimorphic pathways of cell death according to sex. This study aims to assess the neuroprotective response to therapeutic hypothermia in the pre-clinical model according to sex.

### PAIN STUDIES

# Skin-to-skin care can reduce neonatal pain-related brain activity

# Jones L, Laudiano-Dray MP, Whitehead K, Meek J, Fitzgerald M, Fabrizi L, Pillai Riddell R

The benefits of skin-to-skin care have been used in NICU's across the world to support development in premature neonates. Using electroencephalography (EEG), we have shown that skin-to-skin care can reduce neonatal brain activity following a painful procedure, which may ameliorate the negative impact of these procedures upon development. We are now measuring anxiety levels and attachment styles of mothers, as well as recording their heart rate and behaviour during the procedure.

Characterising the underlying mechanisms of skin-to-skin care may result in procedures for maximising the impact upon neonatal pain experience.

# Using artificial intelligence to assess pain in babies

## Rupawala M, Bucsea O, Laudiano-Dray MP, Jones L, Pillai Riddell R, Fitzgerald M, Meek J, Fabrizi L

The neonatal pain research group at UCLH commenced data collection for an international and multidisciplinary collaboration funded by the Canadian tri-research councils. This work combines the expertise of Clinicians, Neuroscientists, Psychologists, and Mathematicians from UCLH and UCL in London, and Mount Sinai Hospital and York University in Canada. Our aim is to train an Al algorithm to detect when a baby is in pain using mutlimodal recordings following a clinically-required painful procedure. As part of this work we are exploring the social, ethical and legal implications of using Al tools in a clinical setting and plan to interview parents and clinicians in both countries regarding their views.

# The development of pain-related brain networks

#### Rupawala M, Bucsea O, Laudiano-Dray MP, Pillai Riddell R, Fitzgerald M, Meek J, Jones L, Fabrizi L,

Understanding how premature neonates process pain is important for both their health and development. The neonatal pain research group at UCLH has collected extensive data following a clinically-required blood test and have developed an advanced technique to analyse their pain-related brain activity. Using this approach, we are exploring how this activity is continually changing over the final trimester of gestation, and unlike term babies, premature neonates may be unable to adapt to multiple procedures. Combining this technique with behavioural analysis from Clinical Psychologists at York University in Canada, we are investigating if clinically-significant behavioural pain scores are associated with a switch in how the brain processes a painful procedure.

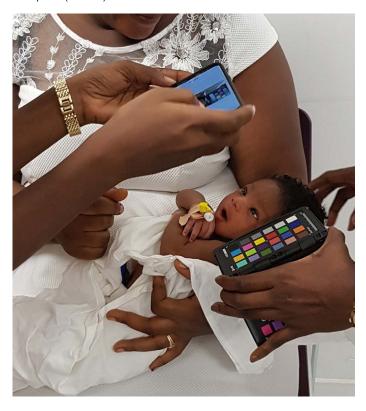
### Jaundice app

#### Leung T, Enweronu-Laryea C, Meek J

Include: DOI 10.1542/2021-053600

https://www.bbc.co.uk/sounds/play/w3ct3754

A project led by Dr Terence Leung (Associate Professor in Biomedical Optics, Department of medical Physics and Bioengineering, UCL) and Professor Chrsistabel Enweronu-Laryea (Professor of Paedaitrics and Child Health, University of Ghana) and Dr Judith Meek (Consultant Neonatologist UCLH) has developed a smartphone app that identifies severe jaundice in newborn babies by scanning their eyes. The results of a clinical trial in over 300 newborn babies in Ghana, followed a pilot study on 37 newborns at University College London Hospital (UCLH) in 2020.



For the large-scale study, published in Paediatrics, the team tested 336 babies with the app, which analyses images taken on a smartphone camera to quantify the yellowness of the sclera. The result for each baby was compared to the serum bilirubin level and the measurement using a transcutaneous bilirubinometer.

The study compared the effectiveness of the neoSCB app with conventional screening methods. Of the 336 babies tested by the app, 79 were severely jaundiced newborns, and the app correctly identified 74 of them. This is in line with the accuracy of the most common conventional

screening method, a transcutaneous bilirubinometer. When the app was optimised the sensitivity and specificity matched that of the transcutaneous bilirubinometer. Doctors and midwives found that it was easy to use.

Newborns in low- and middle-income countries are typically at a greater risk of severe jaundice, or neonatal hyperbilirubinemia, because of the lack of resources required for screening. A commercial transcutaneous bilirubinometer typically costs around £4,000 per device, and blood tests require a large amount of capacity. Additional factors such as a higher prevalence of home births and early postnatal discharge can contribute to fewer newborns going through screening. Babies in sub-Saharan Africa are also at a greater risk because of a high prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency.



The study was supported by the Saving Lives at Birth consortium and the EPSRC UCL Centre for Doctoral Training in Intelligent Integrated Imaging in Healthcare.

### Highlights

**Subhabrata Mitra** was awarded a 4-year Wellcome Trust Fellowship to investigate the impact of seizures on the developing brain. Subha has started his Fellowship in August 2020.

**Subhabrata Mitra** was awarded the UK Neonatal Society Young Investigator Award in 2020 and presented his award lecture in the annual summer meeting in 2021.

**Neil Marlow** was involved in a feature in 'Nature' – Survival of the Littlest by Amber Dance, about long term survival after extreme preterm birth

**2020:** The development of a purpose-built piglet MRI compatible incubator in collaboration with LMT Medical Systems for neuroprotection studies (UCL and Edinburgh)

**2021:** Opening of a second neonatal neuroprotection laboratory based at the Roslin Institute, University of Edinburgh to establish a recovery piglet model (INSTINCT study)

**2022:** Collaboration with University of Dublin (Prof Eleanor Molloy), University of Cork (Prof Deirdre Murray, Prof Geraldine Boyan), University of Edinburgh and Monash University (Prof Suzie Miller) to develop a neonatal neuroprotection trial

## Covid Highlights

Preterm babies below 32 weeks are deficient in the lining fluid of the lungs (also known as surfactant), which reduces surface tension in the lung and enables breathing. Surfactant replacement treatment with animal derived preparations from bovine or porcine origins has helped millions of preterm babies since the late 1980s. Adult patients with severe COVID-19 in the intensive care unit display some of the same symptoms as preterm babies and part of the symptoms profile was indicative of acute respiratory distress syndrome. Professor Howard Clark and Dr Jens Madsen were involved in setting up two open label, phase II randomised clinical trials with re-purposed surfactant therapy for intubated adult COVID-19 patients in intensive care units 1): A Clinical Trial of Nebulized Surfactant for the Treatment of Moderate to Severe COVID-19 (COVSurf) and 2) Poractant Alfa - Curosurf and SARS-COV-19 ARDS (Covid-19)

COVSurf is a two-centre trial (University College London Hospital (UCLH) and Southampton General Hospital)

(SGH) with Prof Mike Grocott (University of Southampton) as PI and Prof Howard Clark as UCLH PI. The study is funded by the Belinda and Bill Gates Foundation. 20 patients were recruited, three doses of nebulised Bovactant (Alveofact) were administrated within 24 hours of enrolment into the study and primary outcomes were improvement in oxygenation and pulmonary ventilation. An exploratory arm of the study investigated multiple parameters to try and deduce the mechanisms behind the symptoms experienced by the patients and exploring if any of these could be used as biomarkers in the future to predict which patients would respond well to treatment and who would require more or other treatments. Levels of surfactant proteins and degradation levels of these in tracheal aspirates (TA) and plasma samples were quantified at UCL (Prof Howard, Clark, Dr Jens Madsen, Dr Tania Castillo-Hernandez), Surface tension were measure in TA samples (Dr Jorge Bernardino de la Serna, Imperial College London), lipidomic analysis of TA samples (Prof Anthony Postle, University of Southampton) and levels of reactive species and antioxidants (Prof Martin Feelisch, University of Southampton) and the cellular immune response (Prof Tracey Hussel), University of Manchester) were quantified in plasma samples. The obtain results are currently being correlated with clinical data.

The following papers from the study has been published:

- Method paper
- Lipid paper

#### Poractant Alfa - Curosurf and SARS-COV-19 ARDS

(Covid-19 is part of an international trial and in the UK was a three-centre trial (UCLH, SGH and the Royal Brompton and Harefield Hospitals with Prof Howard Clark as Pl. The study is funded by Chiesi Farmaceutica. 10 patients were recruited in the UK, three doses of Curosurf (Poractant) were administrated within 48 hours of enrolment into the study and primary outcomes were number of days alive and ventilator-free days [Time Frame: up to 21 days]. An exploratory arm of the study investigated multiple parameters to try and deduce the mechanisms behind the symptoms experienced by the patients and exploring if any of these could be used as biomarkers in the future to predict which patients would respond well to treatment and who would require more or other treatments. Levels of surfactant proteins and degradation levels of these in tracheal aspirates (TA) and plasma samples were quantified at UCL (Prof Howard, Clark, Dr Jens Madsen and Dr Tania Castillo-Hernandez) and surface tension (Dr Jorge Bernardino de la Serna,

Imperial College London) and lipidomic were quantified in TA samples. The obtain results are currently being correlated with clinical data.

Prof Howard Clark, Dr Jens Madsen and Dr Ariel Finkielsztein is characterising the interaction of SARS-CoV-2 virus with surfactant protein D (SP-D) to evaluate if a recombinant fragment of human SP-D (rfhSP-D) that the Targeted Lung Immunotherapy group is taking into "first in man" phase I safety study in 2022/23 (the RESPONSE trial sponsored by the MRC) would have the potential to be further developed as an anti-COVID-19 drug.

Dr Madsen has been involved, as a co-pl, in further SARS-CoV-2s studies including "Assessing the vulnerability of the fetus to SARS-CoV2 infection across development" (funded by the UKRI COVID-19 Rapid Response Rolling Call (COV0175)) with Dr Mattia Gerli (PI, IfWH) and 6 other co-Pls and "The role of ACE2R expression in protecting children from severe acute respiratory syndrome in COVID-19 disease, and severe susceptibility in adults" (funded by NIHR Health Protection Research Unit in Emerging and Zoonotic Infections (HPRU EZI)) with Paul McNamara (PI, University of Liverpool) and 14 other co-Pls.

## Important publications

Robertson NJ, Meehan C, Martinello KA, Avdic-Belltheus A, Boggini T, Mutshiya T, Lingam I, Yang Q, Sokolska M, Charalambous X, Bainbridge A, Hristova M, Kramer BW, Golay X, Weil B, Lowdell MW. Human umbilical cord mesenchymal stromal cells as an adjunct therapy with therapeutic hypothermia in a piglet model of perinatal asphyxia. Cytotherapy. 2021 Jun;23(6):521-535. doi: 10.1016/j.jcyt.2020.10.005. Epub 2020 Nov 28. PMID: 33262073; PMCID: PMC8139415.

Lingam, I., Avdic-Belltheus, A., Meehan, C., Martinello, K., Ragab, S., Peebles, D., Barkhuizen, M., Tann, C. J., Tachtsidis, I., Wolfs, T., Hagberg, H., Klein, N., Fleiss, B., Gressens, P., Golay, X., Kramer, B. W., & **Robertson, N.**J. (2020). Serial blood cytokine and chemokine mRNA and microRNA over 48 h are insult specific in a piglet model of inflammation-sensitized hypoxia-ischaemia. *Pediatr Res.*<a href="https://doi.org/10.1038/s41390-020-0986-3">https://doi.org/10.1038/s41390-020-0986-3</a>

Maria Pureza Laudiano-Dray; Rebecca R. Pillai Riddell; Laura Jones; Rajeshwari Iyer; Kimberley Whitehead; Maria Fitzgerald, Lorenzo Fabrizi **Judith Meek.** (2020) Quantification of neonatal procedural pain severity: a platform for estimating total pain burden in individual infants. ID: PAIN-D-19-00896R1.

Felix Outlaw, Miranda Nixon, Oluwatobiloba Odeyemi, Lindsay W. MacDonald, **Judith Meek,** Terence S. Leung. (2020) Smartphone screening for neonatal jaundice via ambient-subtracted sclera chromaticity. PLOS1. PONE-D-19-11682R1

Laura Jones, Maria Pureza Laudiano-Dray, Kimberley Whitehead, **Judith Meek**, Maria Fitzgerald, Lorenzo Fabrizi and Rebecca Pillai Riddell. The impact of parental contact upon cortical noxious-related activity in human neonates. September 2020. European journal of pain (London, England) 25(4).

Robertson, N. J., Lingam, I., Meehan, C., Martinello, K. A., Avdic-Belltheus, A., Stein, L., Tachrount, M., Price, D., Sokolska, M., Bainbridge, A., Hristova, M., Fleiss, B., Kramer, B. W., Gressens, P., & Golay, X. (2020). High-dose melatonin and ethanol excipient combined with therapeutic hypothermia in a newborn piglet asphyxia model. *Sci Rep, 10*(1), 3898. <a href="https://doi.org/10.1038/s41598-020-60858-x">https://doi.org/10.1038/s41598-020-60858-x</a>

Pang R, Mintoft A, Crowley R, Sellwood M, Mitra S, **Robertson NJ**. Optimizing hemodynamic care in neonatal encephalopathy. Semin Fetal Neonatal Med. 2020 Oct;25(5):101139.

Pang, R., Martinello, K. A., Meehan, C., Avdic-Belltheus, A., Lingam, I., Sokolska, M., Mutshiya, T., Bainbridge, A., Golay, X., & **Robertson, N. J**. (2020). Proton Magnetic Resonance Spectroscopy Lactate/N-Acetylaspartate Within 48 h Predicts Cell Death Following Varied Neuroprotective Interventions in a Piglet Model of Hypoxia-Ischemia With and Without Inflammation-Sensitization. Front Neurol, 11, 883. https://doi.org/10.3389/fneur.2020.00883

Pang R, Avdic-Belltheus A, Meehan C, Martinello K, Mutshiya T, Yang Q, Sokolska M, Torrealdea F, Hristova M, Bainbridge A, Golay X, Juul SE, **Robertson NJ**. Melatonin and/or erythropoietin combined with hypothermia in a piglet model of perinatal asphyxia. Brain Commun. 2020 Dec 1;3(1):fcaa211. doi: 10.1093/braincomms/fcaa211. PMID: 33604569; PMCID: PMC7876304.

Bale G, **Mitra S**, Tachtsidis I. Metabolic brain measurements in the newborn: Advances in optical technologies. Physiol Rep. 2020 Sep;8(17):e14548.

Pang R, Mintoft A, Crowley R, Sellwood M, **Mitra S**, Robertson NJ. Optimizing hemodynamic care in neonatal encephalopathy. Semin Fetal Neonatal Med. 2020 Oct;25(5):101139.

**Mitra S**, Bale G, Meek J, Tachtsidis I, Robertson NJ. Cerebral Near Infrared Spectroscopy Monitoring in Term Infants With Hypoxic Ischemic Encephalopathy-A Systematic Review. Front Neurol. 2020 May 27;11:393.

Pavel AM, Rennie JM, de Vries LS, Blennow M, Foran A, Shah DK, Pressler RM, Kapellou O, Dempsey EM, Mathieson SR, Pavlidis E, van Huffelen AC, Livingstone V, Toet MC, Weeke LC, Finder M, **Mitra S**, Murray DM, Marnane WP, Boylan GB. A machine-learning algorithm for neonatal seizure recognition: a multicentre, randomised, controlled trial. Lancet Child Adolesc Health. 2020 Oct;4(10):740-749.

Tachtsidis I, Lange F, Pinti P, Bale G, Sokolska M, Avdic-Belltheus A, Meehan C, Robertson N, Parsa S, Weigel U, Dududran T, **Mitra S** (2021). An optical biomarker of hypoxic-ischaemic injury severity in the neonatal brain. Proc. SPIE Vol. 11920 Diffuse Optical Spectroscopy and Imaging VIII, 119200I.

Koskela T, Kendall GS, Memon S, Sokolska M, Mabuza T, Huertas-Ceballos A, **Mitra S**, Robertson NJ, Meek J, Whitehead K. Prognostic value of neonatal EEG following therapeutic hypothermia in survivors of hypoxic-ischemic encephalopathy. Clin Neurophysiol. 2021 Sep;132(9):2091-2100.

Harvey-Jones K, Lange F, Tachtsidis I, Robertson NJ, **Mitra S**. Role of Optical Neuromonitoring in Neonatal Encephalopathy-Current State and Recent Advances. Front Pediatr. 2021 Apr 9;9:653676.

Kovacsova Z, Bale G, **Mitra S**, Lange F, Tachtsidis I. Absolute quantification of cerebral tissue oxygen saturation with multidistance broadband NIRS in newborn brain. Biomed Opt Express. 2021 Jan 15;12(2):907-925.

Chakkarapani AA, Aly H, Benders M, Cotten CM, El-Dib M, Gressens P, Hagberg H, Sabir H, Wintermark P, **Robertson NJ**; Newborn Brain Society Guidelines and Publications Committee. Therapies for neonatal encephalopathy: Targeting the latent, secondary and tertiary phases of evolving brain injury. Semin Fetal Neonatal Med. 2021 Oct;26(5):101256. doi: 10.1016/j.siny.2021.101256. Epub 2021 Jun 12. PMID: 34154945.

Pang, R., Mujuni, B. M., Martinello, K. A., Webb, E. L., Nalwoga, A., Ssekyewa, J., Musoke, M., Kurinczuk, J. J., Sewegaba, M., Cowan, F. M., Cose, S., Nakakeeto, M., Elliott, A. M., Sebire, N. J., Klein, N., **Robertson, N. J.**, & Tann, C. J. (2021). Elevated serum IL-10 is associated with severity of neonatal encephalopathy and adverse

early childhood outcomes. *Pediatr Res.* <u>https://doi.org/10.1038/s41390-021-01438-1</u>

Pang R, Advic-Belltheus A, Meehan C, Fullen DJ, Golay X, **Robertson NJ**. Melatonin for Neonatal Encephalopathy: From Bench to Bedside. International Journal of Molecular Sciences. 2021;22(11).

Pang R, **Robertson NJ**. Optimizing neonatal outcomes with melatonin - Huge promise but slow progress. Eur J Paediatr Neurol. 2021 Mar;31:102-103. doi: 10.1016/j. ejpn.2021.03.001. Epub 2021 Mar 6. PMID: 33736883.

Ahmed, J., Pullattayil, S. A., **Robertson, N. J.,** & More, K. (2021). Melatonin for neuroprotection in neonatal encephalopathy: A systematic review & meta-analysis of clinical trials. *Eur J Paediatr Neurol, 31,* 38-45. <a href="https://doi.org/10.1016/j.ejpn.2021.02.003">https://doi.org/10.1016/j.ejpn.2021.02.003</a>

Anastasias Georgoulas, Laura Jones, Maria Pureza Laudiano-Dray, **Judith Meek,** Lorenzo Fabrizi, Kimberley Whitehead. (2021). Sleep 44(1); zsaa148

Nana Ayegua, Hagan Seneadza, Genevieve Insaidoo, Hilda Boye, Mary Ani-Amponsah, Terence S Leung, **Judith Meek** and Christabel Enweronu-Laryea. Neonatal jaundice in Ghanaian children: Assessing maternal knowledge, attitude, and perceptions. (2022).PLoS ONE 17(3):e0264694 DOI:10.1371/journal.pone.0264694

C Enweronu-Laryea, T Leung, Felix Outlaw, Nana Okai Brako, enevieve Insaidoo, Nana Ayegu Hagan-Seneadza, Mary Ani-Amponsah, Miranda Nixon-Hill, **Judith Meek**. Validating a sclera-based smartphone application for screening jaundiced newborns in Ghana. (2022). Pediatrics 150(1): e2021053600

Pang R, Han HJ, Meehan C, Golay X, Miller SL, **Robertson NJ**. Efficacy of melatonin in term neonatal models of perinatal hypoxia-ischaemia. Ann Clin Transl Neurol. 2022 Jun;9(6):795-809. doi: 10.1002/acn3.51559. Epub 2022 Apr 12. PMID: 35413154; PMCID: PMC9186150.

Martinello KA, Meehan C, Avdic-Belltheus A, Lingam I, Mutshiya T, Yang Q, Akin MA, Price D, Sokolska M, Bainbridge A, Hristova M, Tachtsidis I, Tann CJ, Peebles D, Hagberg H, Wolfs TGAM, Klein N, Kramer BW, Fleiss B, Gressens P, Golay X, **Robertson NJ**. Hypothermia is not therapeutic in a neonatal piglet model of inflammation-sensitized hypoxia-ischemia. Pediatr Res. 2022 May;91(6):1416-1427. doi: 10.1038/s41390-021-01584-6. Epub 2021 May 28. PMID: 34050269; PMCID: PMC8160560.

#### Awards:

Dr Reena Bhatt attended the Neonatal Society Summer Meeting in Winchester 23rd and 24th July 22 with the oral presentation "Recombinant Surfactant Protein D: a Potential Therapeutic in Infants at High Risk of Bronchopulmonary Dysplasia" and won the award for "Best Presentation by a Consultant".

**Dr Katie Gallagher** was awarded an NIHR Clinical Lectureship to develop a Core Outcome Set for Neonatal Palliative Care (the NeoPace study).

**2020: Dr Raymand Pang** – Neonatal Society Prize for Best Oral Presentation

Ms Lilly Erinoso was awarded the EGA charity scholarship for her PhD project entitled "Does female hormones influence the immunological response in airway infection and inflammation in people with asthma?". The project will create patient specific airway epithelial



cells lines from people with asthma using inducible pluripotent stem cells and evaluate how these respond in the presence of different female and male sex hormones to asthmatic triggers such as pollen and respiratory syncytial virus. Supervisors are Dr Jens Madsen (Neonatology) and Dr Pascale Guillot (Maternal & Fetal Medicine).

Dr Ariel Finkielsztein was awarded an American Thoracic Society (ATS) International Trainee Scholarship for this abstract entitled "A Recombinant Fragment of Human Surfactant Protein D (rfhSP-D) Decreases Inflammation in Ventilated Pre-term Lambs" to give an oral presentation at the annual



conference in San Francisco, USA, 13-18th May 2022. This is part of the "first in human" phase I safety "RESPONSE" trial. Academic investigators are Prof Howard Clark (PI) and Dr Jens Madsen and the project is sponsored by the MRC.





**Dr Madsen** was awarded a Travel Award from the British Society for Immunology to present the abstract entitled "Characterisation of the Structural Requirements for the Immunomodulatory Surfactant Protein D (SP-D) to Bind to Maltose Based

Ligands" at the annual conference in San Francisco, USA, 13-18th May 2022.





Medical Research Council

# British Society for Immunolog

Ms Georgina Brown was awarded a travel bursary from the John Timms Fund to attend the annual European Respiratory Society conference. Her PhD project is entitled "Characterisation of the role of innate immune proteins in inflammatory lung diseases" and supervisors are Dr Jens Madsen



(Neonatology) and Prof Howard Clark (Neonatology).

Ms Georgina Brown won the Institute for Women's Health 3 Minute Competition (3MT) 27th April 2022 for her presentation on her PhD project entitled "Characterisation of the role of innate immune proteins in inflammatory lung diseases". Supervisors are Dr Jens Madsen (Neonatology) and Prof



Howard Clark (Neonatology). She will attend the Faculty of Population Health Sciences finale on Friday 6th May 2022

and winner of that competition will proceed to the UCL Finale (date to be confirmed).



Ms Naz Shagufta won the Institute for Women's Health Early Career Researcher Changemakers Poster Session Wednesday 4th May 2022. This was organised by the Institute for Women's Health Early



Career Researcher Network, with an award from UCL ChangeMakers, which provides project funding and support to students and staff who want to work together to enhance the learning experience of students at UCL.

See: https://www.ucl.ac.uk/womens-health/ucl-ifwh-early-career-researchers-network and https://www.ucl.ac.uk/changemakers

#### Grants:

# Sir Halley Stewart Trust

Development of functional human Alveolar Type I, human Alveolar Type II cells and lung organoids from cognate iPSC. UCL Therapeutic Innovation Networks (TINs) Award. **£10,000.** Dr Ariel Finkielsztein.

Surfactant Proteins and Inflammatory Markers, targets for therapeutic intervention in infants at risk of Bronchopulmonary dysplasia. Sir Halley Stewart Trust. Reena Bhatt. £55,744. 2022-2024

Include: Neonatology image 32

Assessing the vulnerability of the fetus to SARS-CoV2 infection across development (COV0175). UKRI COVID-19 Rapid Response Rolling Call. Mattia Gerli (PI) (UCL) and 6 other co-PIs including Jens Madsen. £25,000. 2020-21

The role of ACE2R expression in protecting children from severe acute respiratory syndrome in COVID-19 disease, and severe susceptibility in adults. NIHR Health Protection Research Unit in Emerging and Zoonotic Infections (HPRU EZI). Paul McNamara (PI - University of Liverpool) and 14 other co-PIs including Jens Madsen. £38,000. 2020-21.

COVSurf: A pilot phase II escalation dose trial of nebulized surfactant as a treatment in adult Covid-19 patients in intensive care testing 12 patients in Southampton and UCLH. Melinda and Bill Gates Foundation. Mike Groccott (PI – University of Southampton) and 15 other co-Investigators incl Howard Clark (UCL PI) and Jens Madsen. £1,150,000, 2020-2022.

Multicenter, open-label, randomised trial to assess the efficacy and tolerability of poractant alfa (porcine surfactant, Curosurf®) in hospitalized patients with SARS- COV-19 acute respiratory distress syndrome (ARDS). Chiesi Farmaceutica. Howard Clark (PI) and Jens Madsen. £220,000. 2020 – 2022.

Development of recombinant surfactant protein D therapy to prevent neonatal chronic lung disease (MR/P026907/1). MRC Catalyst: Developmental Pathway Funding Scheme (DPFS). Howard Clark (PI) and Jens Madsen. £2,896,956. 2019 – 2024.

Combining the Strengths of Mid-IR and Raman Spectroscopies on Single Chip for Rapid Bedside Biomarker Diagnostics (EP/S03109X/1). EPSRC ICT Prioritisation Panel. Senthil Ganapathy (PI – University of Southampton), James Wilkinson (UoS), Howard Clark and Jens Madsen. £805,209. 2019 – 2023.

The Bronchiolitis Endotracheal Surfactant Study (BESS) study.14 multicentre blinded randomised placebocontrolled phase-2 trial of endotracheal surfactant as therapy for bronchiolitis in critically ill infants (NIHR EME number 15/21/01). NIHR. Prof Calum Semple (PI - University of Liverpool) and 5 other co-PIs including Howard Clark and Jens Madsen (UCL £360,000). £2.5M 2018-2024.

# Research Department of Women's Cancer



Anne
Lanceley
Head of
Research
Department,
Patient Care
Research.



Martin Widschwendter Translational Research



Oleg Blyuss
Cancer
Proteomics



Alexey Zaikin
Systems
Medicine



Alex Gentry-Maharaj Screening and Early Detection



Adam Rosenthal

It has been an immensely challenging period for the Women's Cancer Dept. The death of our we continue to miss John's intellectual contribution and leadership in all that we do. Even so we have had lots of successes and we are as determined as ever in our efforts 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 for those who do, treatment and in our department's history, the large UKCTOCS on ovarian cancer mortality was completed by Prof Usha Menon and her team now at MRC Clinical Trials Unit at UCL. Prof Widschwendter's FORECEE study of markers for risk prediction for all four women specific cancers also drew to a ALDO study. Several significant grant awards were made, and these projects are highlighted below.

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

Jones A, Reisel D, Knapp S, Evans I, Gunu R, Bennett J, Widschwendter M

The FORECEE clinical research programme ended in 2020. Launched in 2015 and funded by the European Commission and The Eve Appeal (https://eveappeal.org.uk/), the study aimed to harness cervical smear tests for risk prediction and/or early detection of several women specific



cancers (including breast, ovarian, and womb cancer but also aiming to improve upon the performance of current cervical screening). The programme has resulted in the development of 4 risk/early detection cancer assays that have demonstrated very promising performance in multiple validation sets. The results for the WID-BC and WID-OC indices (tests for breast and ovarian cancer risk) have been published in Nature Communications. The results for the WID-EC and WID-CIN tests. Work is ongoing to further

refine and validate the cancer indices in prospective clinical settings.

In addition to the development of the WID cancer tests, we have also examined the role of epigenetic ageing in the wider context of health and disease – a recent publication appeared in Genome Biology. We have developed tests referred to as 'epigenetic clocks' that can measure tissue specific epigenetic ageing in cervical smear samples. The 'tick rate' measure of these clocks not only appears to be associated with cancer risk but also with HRT response in post-menopause, implying the possible dual utility of these tests to predict both cancer risk and personalise optimal HRT regimens.

ERC Grant - BRCA-ERC (Understanding cancer development in BRCA 1/2 mutation carriers for improved Early detection and Risk Control) Running from 01/09/2017 – 31/05/2023

# Chindera K, Bartlett Tom, Haran S, Evans I, Jones A, Bennett J, Widschwendter M

In 2017, Prof Widschwendter was awarded an ERC grant to further understand cancer



development and risk prediction in women with BRCA1/2 mutations. The core of the programme is to understand how both cell autonomous and non-cell autonomous (systemic) factors contribute to cancer risk in BRCA mutation positive women and specifically in the tissue at risk i.e., breast tissue and Fallopian Tube. Several studies within the research programme have been successfully published including work demonstrating a microbial dysbiosis in the cervico-vaginal samples from women at higher risk of ovarian cancer, and evidence of an epigenetic field defect in the fimbriae of women with BRCA mutations. Papers currently under review demonstrate that BRCA mutation carriers have higher levels of systemic hormones than non BRCA carriers, and the development of an epigenetic index representing luminal progenitor cells

in breast tissue that changes dynamically in response to the progesterone antagonist Mifepristone when it is administered as a means of primary breast cancer prevention. Patient collections are ongoing that include sampling of both the 'tissue at risk' (e.g. in ovarian cancer setting the fimbrial Fallopian Tube) and matched cervical smears taken at the time of risk reducing surgery. These collections will allow for the identification of relationships between carcinogenic molecular transitions within tissues at risk and molecular features of surrogate tissues, and hence for the development of cancer risk tests that can be obtained solely through non-invasive means.

Serial artificial intelligence/ machine learning classifiers for personalised risk stratification and early detection of lung, bowel and pancreatic cancers in women (SAICRED)

#### Blyuss O, Zaikin A, Menon U, Rangel L, Whitwell H,

We have previously been using UKCTOCS samples in our pursuit of early detection



CANCER RESEARCH UK

biomarkers and have made significant progress in new biomarker discovery and developing novel approaches to analyse serial data. In the proposed study, we will expand on this work by collecting additional large-scale biomarker data from serial sample sets in lung, bowel and pancreatic cancer. We will then use this data to build and test biomarker models capable of improving early detection rates in these important cancers. In doing so, the research aims to provide blood tests for cancer screening or surveillance of high-risk individuals. In turn, earlier detection will allow more effective treatments that will ultimately improve survival rates.

Dynamic predictive model for baseline early detection and follow-up re-evaluation of the risk of prostate cancer progression on active surveillance (PROGRESS Prostate)

#### Blyuss O, Jaiswal A, Zaikin A

This CRUK ACED collaboration seeks to develop a personalised dynamic predictive model able to estimate the risk of prostate cancer progression throughout the whole active surveillance continuum starting from the initial



appointment. To develop the model, we will use a range of novel high-performance modelling methodologies utilising serial biomarker measurements, which we have previously developed and trialed as part of UKCTOCS trial. To train and validate the model, which would include standardof-care clinical and imaging biomarkers to maximise its translational potential, we will gain access to a data-rich active surveillance cohort tapping into clinical, academic, and translational excellence of the Cambridge team. The produced model will be further validated within ACED postpilot, with the end product being an open-source clinical decision support tool for patients and clinicians.

Identifying strategies to support gynaecological cancer patients and carers during COVID-19: learning from patient-charity interactions

Lanceley A. Saha P, Hebbar M, Sheikh J, Sundar S.



This study investigated gynaecological cancer patient and carer charity interactions

to explore the support role of charities and identify the concerns of patients' and their families in the pandemic.

UNIVERSITYOF **BIRMINGHAM**  Digital interactions on forum posts and social media were collected from four gynaecological cancer charities before and during the pandemic. Semi structured interviews were conducted with charity staff (n= 8). Thematic analysis of these data revealed three areas of major concern to patients: 1) COVID-19 imposed healthcare changes and the effect on cancer care delivery 2) Psychological impact of lockdown and changed treatments; 3) COVID, self-assessment of risk and the complexity of the risk calculus. During the pandemic patients often contacted charities as the first port of call, anxious not to further burden the health system. Cancer charities supported patients through proactive and agile use of technology, including data analytics, to identify recurring topics in forum posts. A "RESET" of cancer trajectories for COVID impacted patients is crucial and to deliver, this needs healthcare systems to work in concert with cancer charities.

## Circulating HPV DNA as a biomarker for pre-invasive and early invasive cervical cancer

#### Bryan S, Olaitan A, Blyuss O

This MD student project is a collaboration with The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research. It is funded by a joint Royal Marsden and Imperial confidence in concept grant and supported by the NIHR. Royal Marsden, the ICR BRC and the Clinical Research Facility BRC. The study will look to see if a new circulating DNA test for HPV is a reliable marker for early invasive cervical cancer.

### Highlights

The PROTECTOR trial at UCLH - one of top 10 recruiting centres nationally on this trial offering experimental 2stage surgery for prevention of ovarian cancer

Anne Lanceley with students and colleagues from the University of Birmingham won first prize in the British Gynaecological Cancer Society project awards (student section) with their COVID-19 project 'Learning from patient-charity interactions'.

The colposcopy team led by Adam Rosenthal had 2 posters presented at the British Society for Colposcopy and Cervical Pathology annual scientific meeting in April 2021. Lead authors were Dr Stacey Bryan (Circulating HPVDNA markers in CIN and early stage cervical cancer) and Dr Kevin Tjandraprawira (Conservative Management of CIN)

## **External Appointments**

**Anne Lanceley** was elected to EORTC Quality of Life Group Executive Committee with the special remit of Publications Editor

**Adam Rosenthal** was appointed as Colposcopy Advisor to Public Health England's National Cervical Screening Programme Research Advisory Committee.

### Important publications

Nene NR, Reisel D, Leimbach A, Franchi D, Jones A, Evans I, Knapp S, Ghazali T, Timms JF, Paprotka T, Bjorge L, Zikan M, Cibula D, Colombo N, Widschwendter M. Association Between the Cervicovaginal Microbiome, BRCA1 Mutation Status, and Risk of Ovarian Cancer: A Case-Control Study. **The Lancet Oncology.** (2019 Aug); 20(8):1171-1182. doi: 10.1016/S1470-2045(19)30340-7. Epub 2019 Jul 9. PMID: 31300207.

Yang X, Song H, Leslie G, Engel C, Hahnen E, Auber B, Horváth J, Kast K, Niederacher D, Turnbull C, Houlston R, Hanson H, Loveday C, Dolinsky JS, LaDuca H, Ramus SJ, Menon U, Rosenthal AN, Jacobs I, Gayther SA, Dicks E, Nevanlinna H, Aittomäki K, Pelttari LM, Ehrencrona H, Borg Å, Kvist A, Rivera B, Hansen TVO, Djursby M, Lee A, Dennis J, Bowtell DD, Traficante N, Diez O, Balmaña J, Gruber SB, Chenevix-Trench G, Investigators K, Jensen A, Kjær SK, Høgdall E, Castéra L, Garber J, Janavicius R, Osorio A, Golmard L, Vega A, Couch FJ, Robson M, Gronwald J, Domchek SM, Culver JO, de la Hoya M, Easton DF, Foulkes WD, Tischkowitz M, Meindl A, Schmutzler RK, Pharoah PDP, Antoniou AC. Ovarian and Breast Cancer Risks Associated With Pathogenic Variants in RAD51C and RAD51D. J Natl Cancer Inst. (2020 Dec 14);112(12):1242-1250. Doi 10.1093/jnci/ diaa030.PMID: 32107557

Therond C, <u>Lanceley A</u>, Gibbon S, <u>Rahman B</u>. The narrative paradox of the BRCA gene: an ethnographic study in the clinical encounters of ovarian cancer patients. **Anthropology and Medicine**, (2020) 1-16. doi: 10.1080/13648470.2019.1663784

Whitwell H, Worthington J, <u>Blyuss O</u>, <u>Gentry-Maharaj</u> A, Ryan A, <u>Gunu R</u>, Kalsi J, Menon U, Jacobs I, <u>Zaikin A</u>, <u>Timms J</u>, Improved Early detection of Ovarian Cancer Using Longitudinal Multimarker Models, **British Journal of Cancer** (2020) 122, 847-856.

Gaba F, Blyuss O, Liu X, Goyal S, Lahoti N,

Chandrasekaran D, Kurzer, M, Kalsi J, Sanderson S, Lanceley A, Ahmed M, Gentry-Maharaj A, Wallis Y, Wallace A, Waller J, Luccarini C, Yang X, Dennis J, Dunning Lee A, Antoniou AC, Legood R, Menon U, Jacobs I, Manchanda R. (2020). Population Study of Ovarian Cancer Risk Prediction for Targeted Screening and Prevention. **Cancers** (Basle) May 15; 12(5):1241. doi: 10.3390/cancers12051241.

Nené NR, Barrett J, Jones A, Evans I, Reisel D, Timms JF, Paprotka T, Leimbach A, Franchi D, Colombo N, Bjørge L, Zikan M, Cibula D, Widschwendter M. DNA methylation signatures to predict the cervicovaginal microbiome status. Clin Epigenetics. (2020 Nov 23); 12(1):180. doi: 10.1186/s13148-020-00966-7. PMID: 33228781.

Roncolato FT, O'Connell R, Joly F, <u>Lanceley A</u>, Hilpert F, Buizen L, Okamoto A, Aotani E, Salutari V, Donnellan P, Oza A, Avall-Lundquist E, Berek J, Fehm T, Ledermann J, Roemer-Becuwe C, Stockler MR, King MT, Freidlander ML. (2020). Predictors of progression free survival, overall survival and early cessation of chemotherapy in women with potentially platinum sensitive (PPS) recurrent ovarian cancer (ROC) starting third or subsequent line (> 3) chemotherapy – the GCIG Symptom Benefit Study (SBS). Gynecol Oncol, Jan; 156(1):45-53.

Cappello C, Cuming T, Bowring J, Rosenthal AN, Chindawi N, Nathan M. High-Resolution Anoscopy Surveillance After Anal Squamous Cell Carcinoma: High-Grade Squamous Intraepithelial Lesion Detection and Treatment May Influence Local Recurrence. **Dis Colon Rectum**. 2020 Oct;63(10):1363-1371. doi:10.1097/DCR.00000000000001750.PMID: 32969879.

Nazarenko T, Whitwell HJ, Blyuss O, Zaikin A, Parenclitic and Synolytic networks revisited, **Frontiers in Genetics** 12, 733783 (2021), doi: 10.3389/fgene.2021.733783.

Abrego L, Gordleeva S, Kanakov O, Krivonosov M, Zaikin A. Estimating integrated information in bidirectional neuron-astrocyte communication. **Physical Review** E 103, 022410 (2021).

Dawson H, Smrke A, Ellery PM, Wilkinson N, Rosenthal AN, McVeigh TP. Fibroadenoma in vulval ectopic breast tissue in a patient with PTEN Hamartoma Tumour Syndrome. **Fam Cancer**. 2021 Sep 15. doi: 10.1007/s10689-021-00275-9. Online ahead of print. PMID: 34524588

Demichev V, Tober-Lau P, Lemke O, <u>Nazarenko T</u>, Thibeault C, Whitwell H, <u>Zaikin A</u>, ... Schmidt, S. (2021). A time-resolved proteomic and prognostic map of COVID-19. **Cell Systems**. doi:10.1016/j.cels.2021.05.005

Greimel E, Nagele E, Lanceley A, Oberguggenberger AS, Nordin A, Kuljanic K, Arraras JI, Wei-Chu C, Jensen PT, Tomaszewski KA, Creutzberg CL, Galalae R, Toelen H, Zimmermann K, Bjelic-Radisic V, Costantini A, Almont T, Serpentini S, Paskeviciute Frøding L, Vistad I, Schmalz C; EORTC Quality of Life Group. Psychometric validation of the European Organisation for Research and Treatment of Cancer-Quality of Life Questionnaire Sexual Health (EORTC QLQ-SH22). **Eur J Cancer**. 2021 Sep;154:235-245. doi: 10.1016/j.ejca.2021.06.003. Epub 2021 Jul 20. PMID: 34298374.

Albuquerque A, Godfrey MAL, Cappello C, Pesola F, Bowring J, Cuming T, De Masi A, Rosenthal AN, Sasieni P, Nathan M. Multizonal anogenital neoplasia in women: a cohort analysis. **BMC Cancer.** 2021 Mar 6;21(1):232. doi: 10.1186/s12885-021-07949-8.PMID: 33676451

Barrett JE, Herzog C, Kim Y-N, Bartlett TE, <u>Jones A</u>, Evans I, Cibula D, Zikan M, Bjørge L, Harbeck N, Colombo N, Howell SJ, Flöter Rådestad A, Gemzell-Danielsson K, <u>Widschwendter M</u>. Susceptibility to hormone-mediated cancer is reflected by different tick rates of the epithelial and general epigenetic clock. **Genome Biol.** (2022 Feb 22); 23(1):52. doi: 10.1186/s13059-022-02603-3. PMID: 35189945.

Barrett JE, Herzog C, Jones A, Leavy OC, Evans I, Knapp S, Reisel D, Nazarenko T, Kim Y-N, Franchi D, Ryan A, Franks J, Bjørge L, Zikan M, Cibula D, Harbeck N, Colombo N, Dudbridge F, Jones L, Sundström K, Dillner J, Flöter Rådestad A, Gemzell-Danielsson K, Pashayan N, Widschwendter M. The WID-BC-index identifies women with primary poor prognostic breast cancer based on DNA methylation in cervical samples. **Nat Commun.** (2022 Feb 01); 13(1):449. doi: 10.1038/s41467-021-27918-w. PMID: 35105882.

Barrett JE, Jones A, Evans I, Reisel D, Herzog C, Chindera K, Kristiansen M, Leavy OC, Manchanda R, Bjørge L, Zikan M, Cibula D, Widschwendter M. The DNA methylome of cervical cells can predict the presence of ovarian cancer. **Nature Commun.** (2022 Feb 01); 13(1):448. doi: 10.1038/s41467-021-26615-y. PMID: 35105887.

## Coming up

New Grant from The Eve Appeal - Clinical Assessment & Work up of the WIDTM-qEC test in women at high risk for Endometrial Cancer.

#### Jones A, Evans I, Reisel D, Widschwendter M

An application to The Eve Appeal for the clinical assessment and work up of the WIDTM-qEC test in women at high risk for Endometrial Cancer has been successfully awarded and will run from April 2022 to April 2023. The aim is to evaluate the performance of the WIDTM-qEC test, developed during the H2020 FORECEE programme to accurately identify women with endometrial cancer when presenting at UCLH with abnormal vaginal bleeding (AVB). Whilst a red flag symptom of endometrial cancer, AVB often results from common benign gynaecological conditions. At UCLH, Prof Davor Jurkovic will perform state of the art transvaginal ultrasonographic assessment immediately after a cervical smear is taken as part of the WIDTM-gEC test. Both tests will be directly compared and the potential utility of the WIDTM-qEC test as a triage tool for risk stratifying women at high risk assessed.

## ACED – Alliance for Cancer Early Detection - Breast CANcer Risk Assessment Young women (BCAN-RAY).

#### Jones A, Evans I, Reisel D, Widschwendter M

We will shortly begin a collaboration with Prof Gareth Evans and Dr Sasha Howell at the University of Manchester, who are leading on a CRUK ACED research programme entitled 'BCAN RAY' which involves a case control study of women aged 30-39 years in order to augment breast cancer risk prediction and assess acceptability and preference of a systematic risk prediction approach through primary care. We will be undertaking a cervical smear sub-study, whereby we will provide self-collect smear kits for young women recently diagnosed with breast cancer and healthy volunteers and will test the performance of the WID-BC index developed for breast cancer risk prediction during the H2020 FORECEE programme. The WID-BC will be used

in combination with current state of the art breast cancer risk prediction models and a novel low dose mammogram to determine whether breast cancer risk is effective in, and acceptable to, younger women.

#### **Promotions**

Anne Lanceley – Professor of Women's Cancer CareProfessor John Timms – posthumous appointment toProfessor of Cancer Proteomics

#### Grants:

**The Eve Appeal** – PhD student project looking at Lynch Syndrome Prediction of Endometrial Cancer (LSPEC). Rosenthal, Widschwendter & Scott

**Pancreatic Cancer UK** - A multimodal longitudinal generative adversarial network to discriminate high-risk cysts for the early detection of pancreatic cancer (PAN-CYS-GAN) Blyuss & Zaikin

An evening of memories – Our dear colleague John Timms died on 7th January 2021. Friends and workmates spanning John's career met for an informal gathering on the 8th April to remember him. The evening was spent sharing stories of John and honouring his passion for quizzes by



holding a fiendishly difficult one which was aptly won by the proteomics table.



# Making women's lives better: qualitative research at the IfWH

Qualitative enquiry is a vital component of all research to ensure that the views and experiences of patients are heard, and that research translation into practice remains patient focused. At the IfWH we have a vibrant team of researchers deploying qualitative methods leading on the implementation of rigorous studies, providing an insight into how women's health and well-being is impacted at all stages of the life cycle including: pregnancy planning and antenatal care, assisted reproduction, neonatal care, the transition to parenthood, cancer care, and pre, peri and post menopause experience. During the COVID-19 pandemic qualitative researchers collaborated with colleagues both across the Institute and at UCLH to undertake research highlighting patients' experiences of Covid-19. Examples include: the exploration of IVF patients' experiences of delays and disruptions of COVID-19, the impact of COVID-19 upon pregnant women in the CAP-COVID study, and the identification of strategies to support gynaecological cancer patients and carers during COVID-19 from patient – charity interactions.



Our world leading researchers have vast experience in using a variety of qualitative methodologies to support their enquiries, from conversation and discourse analysis to thematic and framework analysis. We work in close collaboration with patient and public advisory groups to develop, undertake, analyse and disseminate research together. At the IfWH our qualitative researchers also work together to advance qualitative methodologies to better understand the evolving needs of health care service users, raising the profile of high-quality methodological innovations alongside world leading qualitative research.

Katie Gallagher, Jackie Nicholls, Zeynep Gurtin

# The EGA IfWH Professional Support Staff



At the time of writing the Institute is supported by our Professional Services (PS) Team, namely 11 administrative staff (9.1fte) and 4 technicians, a reduction of 6 staff since the last report in 2019. This reduction is mainly due to the transfer of postgraduate education staff to the Faculty and completion of research projects.

The Professional Services Team (PS) led by Marcia Jacks has continued to support the Institute's delivering on its mission and objectives by effectively supporting the work of our academic and research staff. The team has kept pace with the changes of the last two years and we rose above the challenges of the pandemic when we had to revert to working fully from home. Flexible working was something we had been practicing for several years but 100% home working, without preparation still came as a shock. We ensured plans were put into place to have regular once a week meet ups on Microsoft Teams to check on everyone's well being. Our computer representatives, Agsa Hjiej-Andaloussi and Sarah Mayhew quickly learnt the skills to enable Microsoft Teams meetings, although this was foreign to many of us prior to the pandemic. Systems change in our HR system was also a big challenge and we were a few months into this change before the pandemic hit, the difficultly with this caused frustrations for our HR team, Christina Ahlfors, HR lead, and Agsa Hjiej-Andaloussi, HR support but did not interfere with the service to staff. Our core team has remained stable over the last few years, lan Waller as Finance Manager, Sarah Clegg, Procurement Office and with only one change, Sarah Kim our new Grants Officer. The Postgraduate Education team which was considered

as part of the core team has now moved into the new Faculty structure under the Education Administrator Student Experience (EASE) project which was set up to streamline education administration across the Faculty. There will be a similar review for the MBBS administrators but in the meantime Jenny Rattray and Wendy Pereira, remains as part of the core team. Our laboratory manager, Hanaa El-Hachami and Carla Logon Bishop Personal Assistant to Professors Howard and Stephenson make up the Team. We have a group of Technicians that support the work of Professor Nicola Robertson, Christopher Meenan, Georgina Norris, Katie Tucker and Ellie Campbell.

The highlight of our annual calendar is our Annual Conference and despite the pandemic we were able to put on this event on line by Zoom in the December of 2020 calling it IfWH Extraordinary Conference, with 115 delegates joining. In December 2021 the technical issues had been ironed out and we had a fantastic 16th year conference with 140 delegates joining. We thoroughly enjoyed the in-person conference for December 2022.

Marcia Jacks, Manager of the EGA IfWH, featured in 2021 in one of the Black Lives at UCL podcasts. Black Lives at UCL was a podcast series launched in 2021 amplifying and sharing the voices of UCL's black staff and students. In each episode, three people from the UCL community, talk about their experiences of race, racialisation and systemic racism through the lens of higher education, and explore what UCL need to change in order to be better.



# EGA IfWH Events for International Women's Day 2020 & 2021





The yearly events organised in 2020 by Judith Stephenson and in 2021 by Joyce Harper, were a great success, with the 2020 events taking place in person, before lockdown, and in 2021 with some very engaging and inspiring events held online.

## Highlights

March 2020

Play: Shades of our Lives by Black Women Let Loose



Those who attended this event were privilege to watch an inspiring and powerful production from the cast of Black Women Let Loose (BWLL), a theatre company based in Bristol. Their play entitled 'Shades of our Lives', highlighted the experiences of women of African and Caribbean descents through theatre, with a combination of spoken word, dance and music. Lacara Barnes-Rowe, from UCL Equality, Diversity & Inclusion team chaired a Q&A session following the play with BWLL. This was an informal way of finding out more about the production, the actor's process and some issues from the show such as identity, belonging, racism and black women's voices. They tackled

interesting questions about how the show came about, exploring some of the themes raised and the idea of black women telling their own narratives and why this was important for them to do this.





## Lunchtime event: Call the midwife! Call the nurse! An international celebration

The midwives and nurses from the Elizabeth Garrett Anderson Unit at UCLH were delighted to be invited to contribute to the EGA IfWH International Women's Day event, Call the midwife! Call the nurse! The World Health Organisation declared 2020 the first International year of the Nurse and the Midwife, and it also marks the 200th anniversary of Florence Nightingale's birth. Presentations from Meg Wilkinson - Consultant Midwife for normality, gave an enlightening presentation on her role on keeping



birth normal and using balloon induction of labour for women as an outpatient. Kate Welford and Ann Lyons, shared different ways of managing incontinence in women, and Yana Richens shared some findings from her clinical doctorate on how women with fear of birth are recognised and supported. Each presentation demonstrated the advances in nursing and clinical roles over the last century, and how their work continues to impact the lives of women around the world.

#### March 2021

The theme of this year's International Women's Day was #ChooseToChallenge #iwd2021

# Your Fertile Years - What you need to know to make informed choices

The event was chaired by Joyce
Harper, Professor of
Reproductive Science
and author of Your
Fertile Years, who was joined by a panel of fertility experts to discuss why we need fertility education with a Q and A from the audience.
Chairing the event



was Dr Larisa Corda, Obstetrician and Gynaecologist and a passionate champion of women's rights and on the panel were Dr Mara Simopoulou, Chair of the Greek MyFertility campaign, Emma Haslett, Journalist and co-host of @bigfatnegative podcast, Mariana Martins, Assistant Professor at Porto University and a Clinical Psychologist and Alexandra Carvalho, a clinical embryologist developing strategies to raise awareness about reproductive health.

To view the full video of the event pleast go to - Your Fertile Years; what you need to know to make informed choices



#### Panel: Women open water swimming



On the evening of International Women's Day, we held a sold out event on women open water swimming. A growing number of women are turning to open water swimming to enjoy a vibrant community, getting back to nature and the health benefits. We talked to some inspiring women who told us all about it. On the panel were Professor Sasha Roseneil, University College London, Pro-Vice-Provost (Equity and Inclusion), Dean of the Faculty of Social and Historical Sciences and Professor of Interdisciplinary Social Science, Jessica Hepburn, fertility advocate, founder of Fertility Fest, channel swimmer and author of 21 Miles, Dr Heather Massey, University of Portsmouth, a channel swimmer and ice 1km swimmer and currently researching the physiology of cold water swimming and its impacts on physical and mental health, Dr Ruth Williamson, Radiologist and Deputy Chief Medical Officer at University Hospitals Dorset, a channel relay and winter swimmer with research interests in the health benefits and risk management of cold water swimming and Rachel Ashe, founder of Mental Health Swims, a community that empowers people of all body shapes, age, colour, background, gender, sexuality and ability. The event was chaired by Professor Joyce Harper, a novice open water swimmer, who had used open water swimming to keep herself sane during lockdown.

To view the full video of the event please go to - Women open water swimming



# Global Health

# Understanding outcomes for mothers and babies after Covid-19 exposure in different stages of pregnancy

Dr Sara Hillman (UCL Faculty of Population Health Sciences) used the UCL Global Engagement Funds to explore how Covid-19 infection impacts women and their babies in India and the UK.

As the Covid-19 pandemic unfolded, the risks of infection to pregnant women and their babies was unclear. Early in the pandemic, pregnant women in the UK were told to shield at home, since data wasn't available on the impact Covid-19 could have. Some of the earlier research that was done focused on women after they delivered their babies. However, there was still little information about the possible knock-on effects of women catching Covid-19 at different stages of their pregnancies.

To explore this further, UCL collaborated with one of its strategic partners, the All India Institute Of Medical Sciences (AllMS) in Delhi. The teams worked with the partner hospitals – UCLH in London and AllMS itself in Delhi – to recruit pregnant women to take part in the study throughout their pregnancies.

#### Covid-19 in all trimesters of pregnancy

"The idea of this research was to recruit women throughout pregnancy, test their antibody levels, and look at their outcomes," Sara explained. "Previously we didn't know what the specific implications were (particularly about the risk of transmission to babies in the womb) depending on which trimester of pregnancy you caught covid-19, for example."

Partnering with AIIMS was crucial to understand whether there were any global differences in this topic too. First the teams had to decide on what they wanted to measure in order to explore the issue, and how they would go about it. They agreed that part of the study would be to test women's blood during pregnancy and their placentas after delivery for SARS-COV2 placentitis. This is a rare condition in which Covid-19 affects the placenta and can cause complications, particularly later on in pregnancy.

"It proved to be difficult to get the placentas of women in Delhi and easy to get placentas in the UK," Sara said. This was because many of the women recruited for the study in Delhi were delivering their babies in the community, with some living in more rural settings. On the other hand, most women on the British side of the study delivered in UCLH, meaning the placentas could be sent easily to Great Ormond Street for testing. Despite this difference, the teams were able to collect enough data to draw scientific conclusions from the study, focusing on blood results from the Delhi populations and placentas in the UK cohort.

# Good outcomes for most women and babies

"We were able to show that outcomes are very good for most women who get Covid-19 whilst pregnant," Sara said. "If you get Covid-19, generally you remain very well, and the baby isn't significantly affected by my mum having Covid-19." The team also found that catching Covid-19 during the first trimester of pregnancy does not seem to affect how the placenta responds. "Our interest in the placenta is that if Covid-19 is in the placenta, it could be in the baby due to transmission from mum to baby through the placenta," Sara explained. "And again, we found the incidence of SARS-COV2 placentitis was very rare."

The findings have been published in the International Journal of Gynaecology and Obstetrics (IJGO), with a further paper pending with the American Journal of Obstetrics and Gynaecology (AJOG). As well as being reassuring for pregnant women, the research has also contributed to the global understanding of the impact of Covid-19 on pregnancy. "It's an underfunded area, but this research has had an impact in terms of adding to better global understanding about pregnancy and Covid-19" Sara said.

Although Sara has been working with AIIMS for a number of years, this project enabled her to make links with other medical professionals in the organisation too. "What was new about this relationship we developed was that I worked with immunologists and pathologists who I hadn't worked with before," she said. As well as undertaking this research together, "we were all really interested in deepening relationships and capacity building."

The ability for each team's obstetrics, pathology and

immunology departments to work directly with each other was particularly beneficial. "It's really helped to cement a truly collaborative and equal working relationship," Sara explained. "Developing this expertise together, and creating an ability to do molecular studies at AIIMS, at the same time as doing them at UCL has been a real find for us." The teams are planning future partnerships, and they currently have a \$5 million bid in with the Wellcome Trust to continue their work on placentation.

Links

- Seroprevalence of SARS-CoV-2 antibodies among first-trimester pregnant women during the second wave of the pandemic in India, International Journal of Gynaecology and Obstetrics
- https://www.rcog.org.uk/guidance/coronavirus-covid-19-pregnancy-and-women-s-health

## Pregnancy Intention

Dr Jennifer Hall and Dr Geraldine Barrett work with Dr Ana Borges, an Associate Professor at the University of Sao Paulo Public Health Nursing Department, Brazil on a range of projects on measurement of pregnancy intention and contraception use. Her interest is sexual and reproductive health, with a focus on understanding contraceptive use patterns among Brazilian women, in particular, the relationships between contraceptive behaviour and unintended pregnancy, since the use of both modern contraceptives and unplanned pregnancies are high in Brazil.

In 2020 we translated the Desire to Avoid Pregnancy Scale into Brazilian Portuguese, tested it through cognitive



interviews and are implemented it in a mirror of Dr Hall's P3 study in Brazil in 2021. Given the timing we took the opportunity to explore how COVID-19 affected women's intentions regarding a future pregnancy and contraception use. This work is under review for publication.

#### **RFACH Alliance**

The Reach Alliance is inspired by the United Nations' call to eliminate global poverty by 2030 as part of a set of Sustainable Development Goals intended to transform our world. The UCL team is led by Dr Sara Hillman at EGA IfWH and Dr Kate Roll, Assistant Professor in Innovation, Development and Purpose at the Institute for Innovation and Public Purpose and the Bartlett Faculty Lead for Public Policy.

The team is leading the first UK based case study on Barriers to Perinatal Mental Health Services for Refugees and Asylum-Seekers in Camden

## Tackling Massive Obstetric Haemorrhage in Tanzania through training

The Mbeya London project is delivering easy to access, robust, updated teaching on common obstetric problems. Funded by THET, this course is focused on Massive Obstetric Haemorrhage (bleeding).

The London Mbeya Project
THET – Partnerships for Blogal Health

# Fundraising

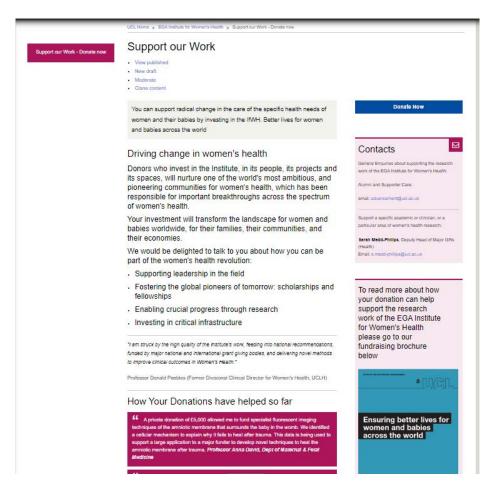
The Institute is keen to attract donors to invest in our projects, people and spaces. Our website now features a Support our work section with a Donate now link.

## Support Our Work

We have worked with the Office of the Vice-President (Advancement) to develop a fundraising brochure:

#### Case for Support

Our strapline is 'Better lives for women and babies across the world' and we are asking people to support radical change in the care of specific health needs of women and their babies by investing in the Institute for Women's Health.



# "Driving change in women's health"

Donors who invest in the Institute, in its people, its projects and its spaces, will nurture one of the world's most ambitious, and pioneering communities for women's health, which has been responsible for important breakthroughs across the spectrum of women's health."

We currently have 7 priority themes:

- The Perinatal Brain
- The Preterm Baby
- Sexual and Reproductive Health
- Maternal and Fetal Health
- Women's Cancer
- Global Women's Health
- Learning and Understanding in Women's Health

For more information, please read our Case for Support

For further information on donating please use the contacts below:

General Enquiries about supporting the research work of the EGA Institute for Women's Health: Alumni and Supporter Care:

email: advancement@ucl.ac.uk

Support a specific academic or clinician, or a particular area of women's health research: Sarah Medd-Philips, Deputy Head of Major Gifts (Health)

Email: s.medd-phillips@ucl.ac.uk















UCL EGA Institute for Women's Health

2020-2022 EGA IfWH Report • 64

65 • 2020-2022 EGA IfWH Report

UCL EGA Institute for Women's Health



