

NUFFIELD DEPARTMENT OF  
WOMEN'S &  
REPRODUCTIVE HEALTH  
Medical Sciences Division



# AIMday in Women's Health

TUESDAY 22ND MARCH 2022

ST ANNE'S COLLEGE, OXFORD



# Welcome

“ Our AIMday was a huge milestone event in championing women's and reproductive health research. External companies each submitted a question that would benefit from academic input and insight which formed a 1-hour workshop hosted by the company. Here follows a collection of blogs by our early career researchers and students from the University of Oxford, who shared their thoughts from the fruitful discussions on the day. We hope it encourages continued engagement between academics and industry.



**Professor Krina Zondervan**  
Head of Department, Professor of Reproductive &  
Genomic Epidemiology, Co-Director, Oxford  
Endometriosis CaRe centre

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## Blogger Bio

I am really interested in better understanding the biology, target candidates and potential therapeutic avenues in Uterine Fibroid related Heavy Menstrual Bleeding, PCOS and Endometriosis. Also to discuss the ways that digital and clinical health, and omics powerful applications can translate into improved women's health diagnostics, facilitated ART and IVF routes, as well as safe, complementary FemTech innovative options.

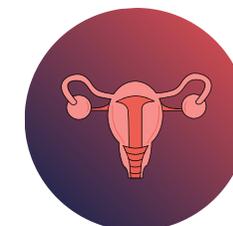


**BEATRIZ MARTINEZ BURGO**  
**PHD**, Research Fellow at EndoCare  
Group, Senior Scientist in Immunology &  
Microbiology

# WHAT IS THE FUTURE OF MOLECULAR TARGET DISCOVERY IN ART AND, GENERALLY SPEAKING IN REPRODUCTIVE MEDICINE AND MATERNAL HEALTH?

**Reproductive Medicine advances**, in an era of accelerated discovery in the field, do bring new challenges, to maximize clinical care, live birth rate, and Maternal Health through better understanding of basic biological processes, and through safe, effective interventions.

**Key advances** range from fertility breakthroughs allowing egg freezing for clinical use, and reliable embryo selection for In Vitro Fertilisation (IVF); to options of uterus transplantation, currently in trial in the UK, and approved in other countries as Sweden (2012) or Spain (2020), for very particular pregnancy needs; or to extensive developments in intrauterine devices (IUD) with different hormonal dose options which now facilitate further amelioration of symptoms, crucial to minimise the requirement for hysterectomy, such as it may occur for uterine fibroid-related heavy menstrual bleeding (HMB). There have also been important innovation steps in the field of pre-eclampsia with more accurate testing, which has been approved for use via the NHS according to recent NICE guidelines, thanks to work also developed within the Nuffield Department of Women's and Reproductive Health (NDWRH). Potential further options for treatment are also in development. In addition, advances aim to support cancer patients, and particularly pursuing fertility preservation. Certainly, this should translate into further progress for the scientific community and society.



**Future of  
Reproductive  
Medicine**

Company: **Ferring**  
Chair: **Dr Bec Dragovic**





In this fantastic session packed with questions, 'back-to-normal' face-to-face discussions developed around recommendations, ongoing research, and thought-provoking proposals, to explore next. **Declan Jones**, and colleagues from **Ferring Pharmaceuticals** joined, and together with our chair **Rebecca Dragovic**, walked us to discuss this and related topics at **AIMday 2022 in Women's Health** celebrated, in a great spring day, at **St Anne's College at Oxford University**.

One of the key challenges discussed is the need for standardisation and harmonisation of clinical samples in the field through robust tracking, and biobanking, in both academia, medical practice and for healthcare. For instance, recent guidelines from the **European Society of Human Reproduction and Embryology (ESHRE)** in fertility preservation are instrumental in this line. Furthermore, ESHRE updates in endometriosis also encourage it. The guidance also applies to highly researched fields such as **Assisted Reproductive Technologies (ART)** for instance in **IVF**, technique which celebrates the 44th anniversary of the first baby born this year. Furthermore, discussions spanned from recommendations on technological improvement in target identification and validation pipelines in Women's, Men's, and Reproductive Health, and how it may accelerate the current pace of target candidate developments for clinical trials. Besides, recommendations pointed at the need of better patient stratification, as well as microbiome insights translating to diagnostic solutions and for therapy.

Certainly, a fascinating topic during the brainstorming pointed at the relevance of genomics, big data, and target discovery, with some amazing work carried out at the University, in collaboration with the NHS, together with other companies to ease sample stratification, data management and subsequent onsite research for healthcare. In addition, **Kevin Coward** also pointed at the recent **Public Health England (PHE)** studies to improve measurement of population reproductive health, with a new indicator set developed combining efforts from the Delphi consensus process.



Women's, and Reproductive Health conditions with high unmet needs. Adapted from Ferring Pharmaceuticals. Clinical sample standardisation and harmonisation remain still a key challenge in the field.

Furthermore, a key take home point is the need for improved dataset phenotyping and curation during clinical sample characterisation. The latter will enormously facilitate subsequent stratification duties, for target discovery and validation in in vitro and in vivo assays, at both a preclinical and clinical level. This applies to gynaecological conditions such as endometriosis, PCOS, or uterine fibroids, as well as to ART, preterm labour, and pre-eclampsia.

The microbiome is a key area of interest of Ferring, and there was consensus on the need to establish collaborations and research programmes that investigate this area. The study on the endometrial microbiome, a hot topic in reproductive health, is in its infancy, for instance in relation to endometriosis. Here, preliminary data suggests that the endometrial microbiota is potentially more diverse in patients with endometriosis. Experts in this session emphasized the relevance of better understanding the fetal-maternal interaction in terms of microbiome, including oral and gut microbiome, but also placental, cervix, as well as vaginal microbiome. Critically, larger datasets and reproducible outcomes will help to decipher the role of microbiota in the causality or effect of diseases affecting women, such as pre-eclampsia, preterm development, or endometriosis; also, in other associated diseases affecting women and men, such as infertility; and in comorbidities such as diabetes.

In addition, the potential of microbiota transplantation was also addressed in the session. Initial work emphasises that comprehensive population selection, research and patient stratification remain vital. Further studies in this arena sure promise further advancements.



## Blogger Bio

“ My research interest is in endometriosis-associated pain, specifically better characterising extra-pelvic pain. Whilst I spend most of my time running analyses on my computer, I am passionate about science communication and using different tools to communicate research about women's reproductive health.



**DANIELLE PERRO**  
DPhil Student in Department of  
Women's Reproductive Health  
University of Oxford

# WHAT MUST WE BE SURE WE DON'T DO? DISCUSSING THE DEVELOPMENT OF AN APP FOR RECURRENT PREGNANCY LOSS WITH CAMBRIDGE DIGITAL HEALTH

Company: Cambridge Digital Health  
Chair: Prof Ingrid Granne

## THE FUTURE OF FEMTECH

Once I knew of this year's AIMDay, I couldn't await the opportunity for researchers and FemTech to convene. I was fortunate to have covered conversations from the [Cambridge Digital Health](#) session, chaired by [Professor Ingrid Granne](#), and led by [Dr Oriane Chausiaux](#) and [Dr Gina Oliver](#). The session began by understanding digital health apps for women. Digital technologies and phone apps have become quite popular as a means to track and support our health. In fact by many, it is used as a supplement to existing health care. Perhaps unsurprisingly, **62% of health app users are women**. This large proportion, however, strikes in stark comparison to the disparity in funding and data on women's health. To explore an unmet need in Femtech, Oriane introduced key questions that needed to be answered in order to design an application to support those dealing with [recurrent pregnancy losses \(RPL\)](#).



# DO APPS PROVIDE REASSURANCE TO ITS USERS?

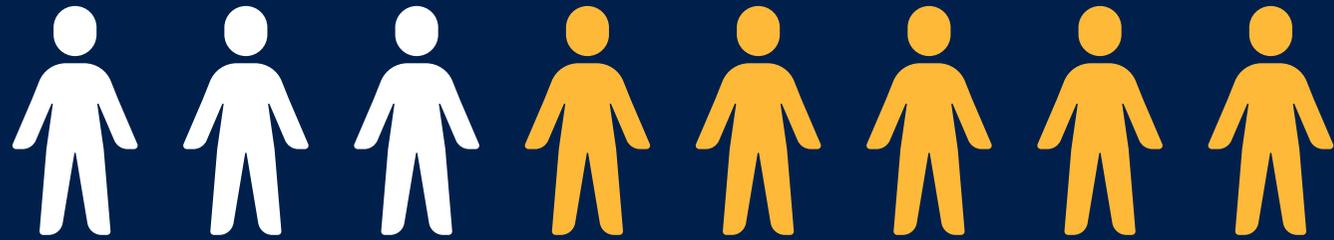
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Perhaps one of the most important issues raised during our discussions were the potential ethical concerns and considerations of an application providing information and support during a vulnerable time in both a woman and their partners' life. While RPL is devastating, it is not uncommon. One in four pregnancies will end in loss, and as many as 2% of women will experience RPL.

2

Jack Pearson from Natural Cycles (NC) shared invaluable insight; NC is the first FDA approved birth control app to prevent, plan and monitor pregnancy. Many NC users have had RPL, and the app has found success in supporting these women by providing a virtual community. He described this support in likeness to that you'd get from friends and family, as many may not have yet told their support networks of the pregnancy loss. With this in mind, I agree that to provide reassurance to app users during such a difficult time, there needs to be an element of personalised medicine, tailored to the unique needs of that user.



**What is the most  
important thing an app  
can do?**



## DISCUSSION

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When Oriane posed this question to the group, Dr Jehan Karim countered with the contrary; what is the most important thing that an app should not do? If a woman experiences RPL, we (the designers and scientific intel behind the apps) should be doing our due diligence to ensure that if women are downloading such apps, they will not endure additional stress and worry as a result.

# HOW DO YOU GET WOMEN INTERESTED IN THE APP?



While these were no simple conversations, and we could have easily spent the entire day discussing, the group arrived at a few conclusions. First of all; know your market. The group acknowledged that scaling an app to many countries may be impractical, as certain markets would not be as willing to engage with such apps. It was also noted that many successful FemTech applications come with an associated device (i.e. a thermometer, as is seen in NC). For anyone interested in designing an app to support women during their pregnancy should consider adding an additional tool that gives users a more personalised experience.

All in all, the day was a massive success, and this session in particular was eye-opening. While apps generally seem harmless, and downloading one is as easy as scanning your thumb or face, I hadn't previously appreciated the great responsibility that comes with designing an application to support people during a difficult time. While there is an evident need for such support, we must be cautious in the information provided, how it is provided and when.

I hope that after the AIMDay, these types of insightful and challenging conversations between industry and academia continue. Even after only an hour, it's clear how these collaborations can only improve the work that we are all trying to accomplish in improving the lives of women.





## **Blogger Bio**

“ Katrien Bens is a MSc student in Clinical Embryology at the University of Oxford. This programme introduces her to all aspects of women's and reproductive health with emphasis on assisted reproductive technologies. Before, she graduated in Biomedical Sciences at the KU Leuven in Belgium where her master thesis was focussed on reproductive genomics.



**KATRIEN BENS**

MSc in Clinical Embryology student,  
Nuffield Department of Women's &  
Reproductive Health Oxford

01

## Advanced screening of the vaginal microbiome, promising for women's health care

At the start of this session, the founder of Daye, Valentina Milanova, introduced the tampon as a diagnostic device, contrary to the traditional smear test. Studies have demonstrated a higher efficacy and safety when using advanced tampons. Moreover, the widespread and convenient use of tampons are a great advantage. Bearing this in mind, Valentina explained that Daye is exploring the potential of the tampon to screen the vaginal microbiome for infections or its prognostic value for women's health outcomes.

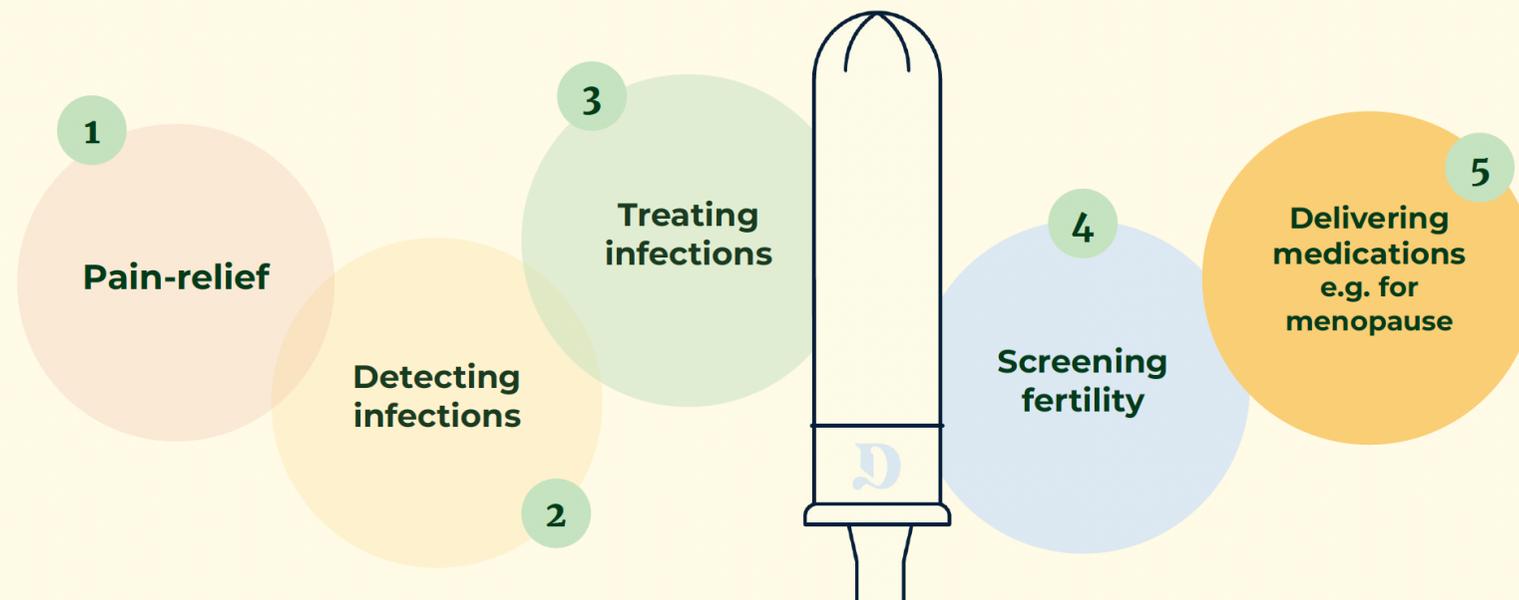


Company: **Daye**  
Chair: **Prof Christian Becker**

## 02

# Workshop Introduction

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Serving women from **puberty through menopause** and beyond,  
to remove pain, shame and time wasted.



## Blogger Bio

Nechama Wieder is a 2nd year DPhil student at the Wellcome Centre for Human Genetics, University of Oxford. Her current research focusses on the role of non-coding regions of the genome in rare disease using large-scale multi-omics data. She is passionate about utilising technology and big data to end diagnostic odysseys and advance personalised medicine.



**NECHAMA WIEDER**  
DPhil student at the Wellcome Centre  
for Human Genomics, Oxford

# Introduction

As someone interested in using technology to improve patients' lives, I was particularly drawn to this session. In a world where we collect so much data, I love the concept of utilising this data to benefit people and improve health.

**93%**  
with typical use

Company: **Natural Cycles**  
Chair: **Prof Antonia Georgieva**

**Dr Jack Pearson** kicked off the session with a run through of how Natural Cycles works. Natural Cycles is a non-hormonal contraception with high protection rates (93% with typical use and 98% with perfect use). The user takes their temperature first thing when they wake up in the morning and records it on a specifically designed app. The app, based on a sophisticated algorithm, then tells the user whether they are not fertile or should use protection. Due to the regular logging of temperature and other symptoms like bleeding, the app can give tailored insight to the user about their unique cycle.

**98%**  
with perfect use

**Natural Cycles** have a large tranche of women (~2 million) recording biometrics regularly and it's being owned, accessible and beneficial to the user. Natural Cycles has used this data to research into women's health such as Covid-19 vaccine effects on menstrual cycle, coming off hormonal birth control and effect on libido to name a few.

The focal point of the AIMday discussion was what other areas of women's health can Natural Cycles investigate using their existing methods? There was a lively and interesting discussion, from which I will highlight the key points of:

## How to make the temperature taking process easier for users was discussed at length

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Wearables seem like a good option but there are several drawbacks such as many of the existing options do not record temperature accurately enough or are too expensive. It is a matter of time before the right wearable for this will be identified and marketed, but once a suitable wearable is in place, collecting a wider range of biometrics will be even easier.

## Possibility of using such a method to collect biometrics and do research into breastfeeding.

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Professor Manu Vatish raised the idea of how this technology could be useful in recording women in pregnancy with conditions such as placental abruption where you are constantly taking temperature in hospital. Discussion about whether the technology can be incorporated into a hospital setting and how this could be very valuable.

## There was also interest in using this technology to gather information in the post-partum period.

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Menopause was another condition that many people agreed this could be useful for, even just as a logbook so they can share it with their health professionals.

Endometriosis patients could also benefit from gathering information and being able to share with their clinician. In addition, research across many endometriosis patients' data could be done to possibly detect common triggers or patterns between patients.

**The final interesting idea was if there could be a way to link the software to genetic data of the user such as from 23andMe.**

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**The session was enlightening and personally left me with some ideas to consider. I would like to thank the organisers and Dr Jack Pearson for such a wonderful discussion and event, and I look forward to developments from Natural Cycles.**

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## Blogger Bio

“ I am a Clinical Embryology Masters student at the University of Oxford. My interests lie within the fields of assisted reproductive technologies, preimplantation genetic testing and improving fertility treatment in endometriosis, LGBTQ+ and cancer patients. I aim to work in embryology and reproductive medicine and make a meaningful difference in the field. ”



**SABRIYA ABDUL KADER**  
MSc in Clinical Embryology student,  
Oxford

# NON-INVASIVE DIAGNOSTIC TESTING FOR ENDOMETRIOSIS

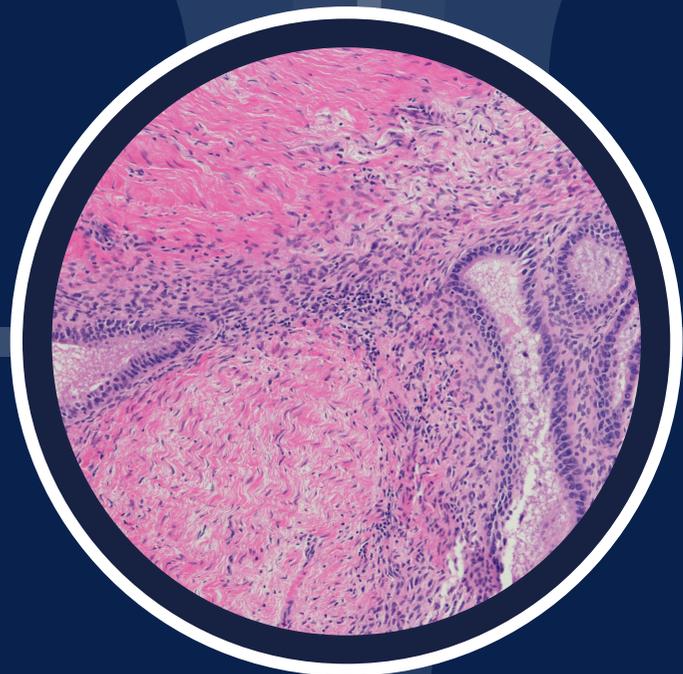
Company: Endodiag

Chair: Professor Christian Becker

01

## Workshop Introduction

During this AIMday workshop, researchers, clinicians, and industry partners gathered in Oxford to exchange ideas and expertise to further the field of women's health. The workshop was framed around the question of where a non-invasive diagnostic test for endometriosis could fit in the medical journey of patients suffering from pain and/or infertility. This topic resonated with me on a personal level, as I am currently being treated for endometriosis but was never officially diagnosed due to the invasiveness of the diagnostic procedure. The discussion was led by Cécile Real, the CEO and co-founder of Endodiag, along with Dr Christian Becker of the Nuffield Department of Women's & Reproductive Health (NDWRH) at the University of Oxford.



## 02 Endodiag and Endometriosis

The session kicked off with a presentation by Cécile Real, in which she introduced her company Endodiag. Endodiag is an inspiring company dedicated to making a difference in the lives of women suffering from endometriosis. Endometriosis affects approximately 10% of all reproductive age women, translating to roughly 190 million women worldwide. There is a major delay between disease onset and diagnosis - leading to misdiagnosis, associated unsuitable treatments, unchecked disease progression and damage to reproductive organs. This delay can be attributed to the lack of a non-invasive diagnostic test, as endometriosis is currently only diagnosed via laparoscopic surgery under general anaesthesia. Thus, Endodiag specialises in the development of novel, non-invasive endometriosis diagnostic tests to contribute to a better diagnosis, personalised patient management and more efficient treatment options.



# 03 The Discussion – Clinical and Scientific Aspects



Cécile suggested we break down the discussion into clinical and scientific aspects.

Several clinical aspects were highlighted during the discussion. For example, when considering where a non-invasive test can fit in the overall patient journey, it was revealed that there was a large variation in patient management between countries and practices. Thus, we found that a gold standard of patient management needed to be established and maintained amongst clinical practices to move forward.

Additionally, this novel diagnostic tool needs to be cost-effective within the NHS, and it was queried whether the test should be offered to anyone who requests it or if they need to show symptoms first.



The scientific side of the discussion looked toward the biological biomarkers used to diagnose the disease. Endodiag has built an international regulatory compliant biobank called EndoBiobank®, which contains over 1000 biological samples from endometriosis patients and controls from various parts of the world. Through these many biological samples – such as fixed biopsies, plasma and peritoneal fluid, endometrium, can biomarkers of endometriosis be detected. One scientist noted that as there is large heterogeneity of the disease, each disease stage may have different biomarkers. Thus, disease stage should be considered during testing to improve diagnostic accuracy.

It was important to highlight the challenges that remain. For example, the mechanisms underlying the disease need to be further explored. Additionally, there is still no gold standard in patient management, and this needs to be evaluated. However, there has been rapid growth this past decade, and so the future of endometriosis diagnosis and management looks promising. Not only is there is a greater awareness of endometriosis, but rapid technological advancements bring forth innovative new tools. These include radiology improvements, clinical algorithms using artificial intelligence, and readily available mobile apps to screen or track disease progression. I am personally very excited for what the future holds and look forward to the continued improvement in healthcare for women with endometriosis.



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## **Blogger Bio**

“ I am passionate about exploring different treatments for women’s health issues, specifically in pain management. I believe there is an urgency in our world to start prioritising listening to women’s pain and treating them the best way we can. I am particularly excited about exploring novel therapeutic treatments to treat women’s health problems with materials we can find in our environment.

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**EMILIE PATERSON**  
MSc in Clinical Embryology student,  
Oxford

# —Gynica

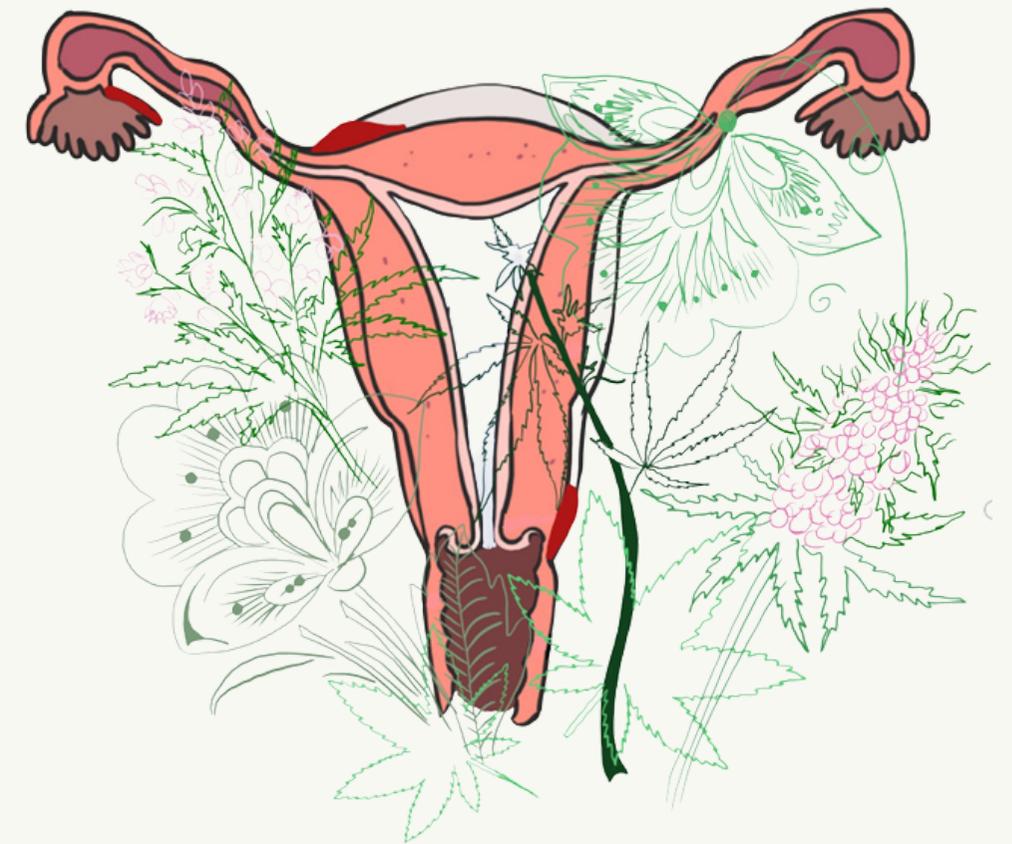
Company: Gynica  
Chair: Professor Katy Vincent

**Cannabis based pharmacology for the female body.**

## INTRODUCTION



“The workshop opened my eyes to the many ways that natural products such as cannabis can be used to treat women’s health conditions and side effects. I am a current student at the University of Oxford MSc Clinical Embryology with a keen interest in novel natural treatments for women’s health and emerging femtech. AIMDay was an amazing experience to explore new ideas for women’s health medicine and those currently in the works.”



# WHAT IS THE ENDO-CANNABINOID SYSTEM?

The endo-cannabinoid system (ECS) is a biological system. The ECS exists and is active in your body even if you don't use cannabis. It plays a big role in keeping your internal processes stable. The ECS is made up of CB<sub>1</sub> and CB<sub>2</sub> receptors.



## CB<sub>1</sub>

### CB<sub>1</sub> RECEPTORS TARGET:

- Motor activity
- Thinking
- Motor coordination
- Appetite
- Short term memory
- Pain perception
- Immune cells

## CB<sub>2</sub>

### CB<sub>2</sub> RECEPTORS ARE MUCH BROADER THAN CB<sub>1</sub> AND INFLUENCE MOST OF THE BODY

- Gut
- Kidneys
- Pancreas
- Adipose tissue
- Skeletal muscle
- Bone
- Eye
- Tumours
- Reproductive system
- Cardiovascular system
- Immune system
- Respiratory tract
- Skin
- CNS
- Liver

-Gynica is a Cannabis based pharmaceutical product company aiming to target women's health pain using the natural endocannabinoid receptors in the body. Utilising cannabis for pain management is one of the oldest forms of self-medicated pain management and has been used for thousands of years in different areas including Israel, China, and Persia. These products could become revolutionary in treating pelvic pain during menstruation or specifically conditions such as endometriosis causing chronic pain in such a large population of women. Gynica creates formulations using one or several of the 144 total cannabinoids identified in cannabis plants so far, as well as other active ingredients such as terpenes, flavanoids etc.

**'The Endocannabinoid receptor system is a biological system composed of cannabinoid neurotransmitters found all over the body involved in several physiological processes, most notably pain' (Kilaru 2020).**

Dysfunction in the endocannabinoid system (ECS) is associated with many diseases. The cannabinoids used in treatment work with the endocannabinoid receptors and provide relief for painful symptoms. Studies have suggested that a dysfunction in the endocannabinoid system is present in endometriosis patients and that aspects of endometriosis-associated pain may be targeted using cannabis-based pharmaceuticals such as the ones developed by Gynica (Sinclair 2021).



## What is Endometriosis?

Endometriosis is a common, chronic inflammatory condition in women characterised by the presence of endometrial tissue found outside the uterus. Prevalence rates of the disease have been estimated at 11% of reproductive-aged women, impacting an estimated 176 million women worldwide.

In addition, endometriosis can also affect post-menopausal women, ranging from between 2–5% of cases.

Endometriosis is associated with a variety of symptoms including chronic pelvic pain, fatigue, dysmenorrhoea (period pain), dyspareunia (painful sex), dyschezia (painful bowel movements) and dysuria (pain related to urination). In addition, comorbid anxiety and/or depression is frequently reported along with irritable bowel syndrome (IBS)-like gastrointestinal symptoms leading to a severely decreased quality of life (Parasar 2017).

## How cannabis can be effective for pelvic pain

One of the areas of the body with the highest amount of endocannabinoid receptors, the pelvis can be treated effectively using cannabinoids for local and/or systemic pain relief. A randomised clinical trial is on the way by Gynica, showing promise in the treatment of endometriosis pain, comorbid symptoms, and other areas of female pelvic pain. Gynica created these products with all sorts of pain in mind, and the results reported from users have spoken volumes to its effectiveness. A study conducted reported that cannabis appears to be effective across all symptoms, with a noted propensity for inhaled delivery due to the potential increased speed of onset of effects (Sinclair 2021). Gynica's products avoid the use of inhaling the cannabis directly and use the suppository method of delivery, providing effective, local relief in a short amount of time.

## Safety and clinical validation

The importance of quality-assured and standardised (i.e., cannabinoid potency and ratios) cannabis products to obtain reproducible clinical results, and to mitigate possible adverse effects is an important clinical consideration for Gynica's products, currently within the company's intentions. Some of the other effects cannabinoids may have include increased sexual arousal, an anxiolytic effect, and muscle relaxation. Cannabis based products are never recommended for pregnant women.

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## **Blogger Bio**

“ I am passionate about providing healthcare to women in rural areas globally. I would love to be able to use technology and mobile apps to provide easier access to women’s health centres in a platform accessible to all regardless of background. ”



**YASMIN AZIZBAYLI**

**MSc student in Clinical Embryology, Oxford**

**Could a mobile application with psychosocial care features change the overall outcome for female IVF patients in terms of:**  
a) Psychosocial wellbeing; b) Patient experience; c) IVF success rates?



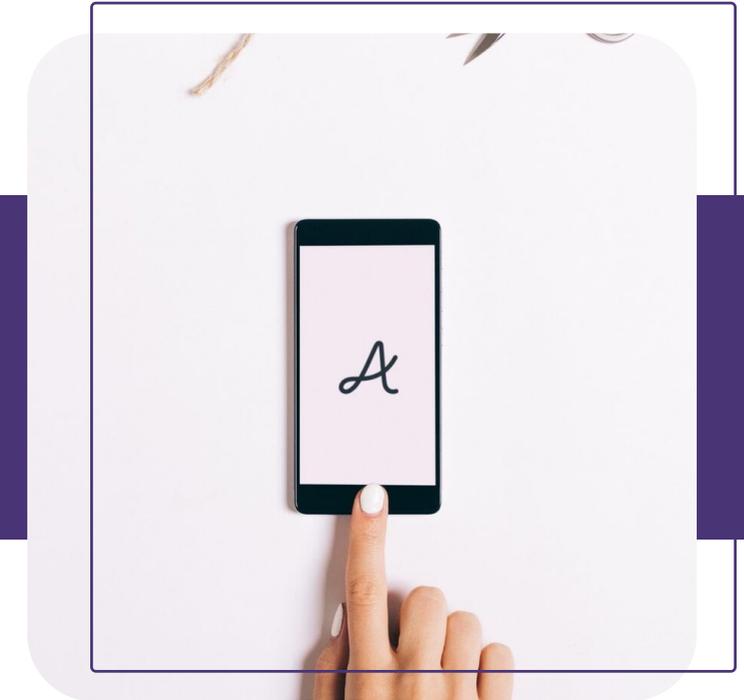
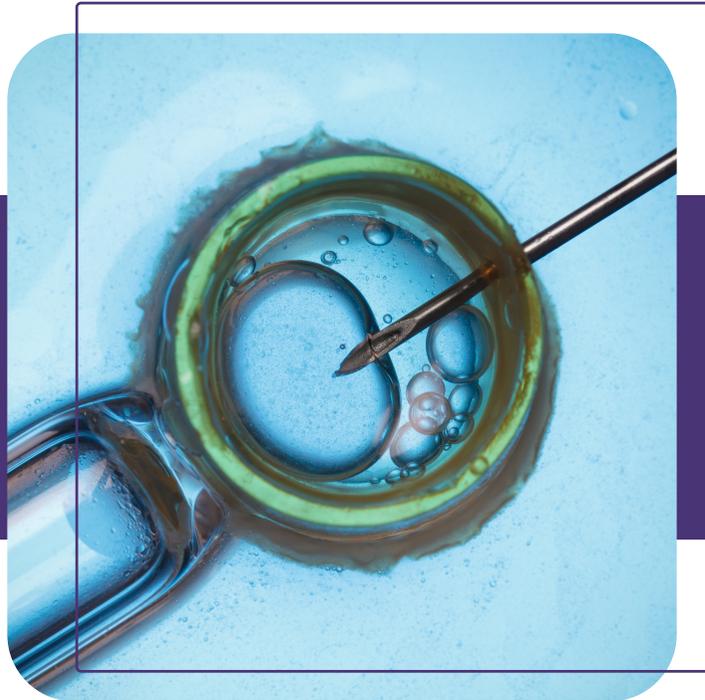
Did you know?

Patients have rated the stress of undergoing IVF treatment as more stressful than death of family member or divorcing a partner.

“Personally, it was very exciting to hear about a new cool tool created that cares for patients and prioritises mental wellbeing, alongside optimising physical health, for the IVF journey.” – **Yasmin**

Company: **Aura Fertility**  
Chair: **Prof Ingrid Granne**

Fertility treatment can be lonely, traumatic and dehumanising - with 90% of patients reporting symptoms of stress, anxiety or depression. Despite the fertility regulator requiring counselling to be offered by fertility clinics, a 2018 HFEA report showed that 20% of fertility patients report not receiving any information about how to access counselling.

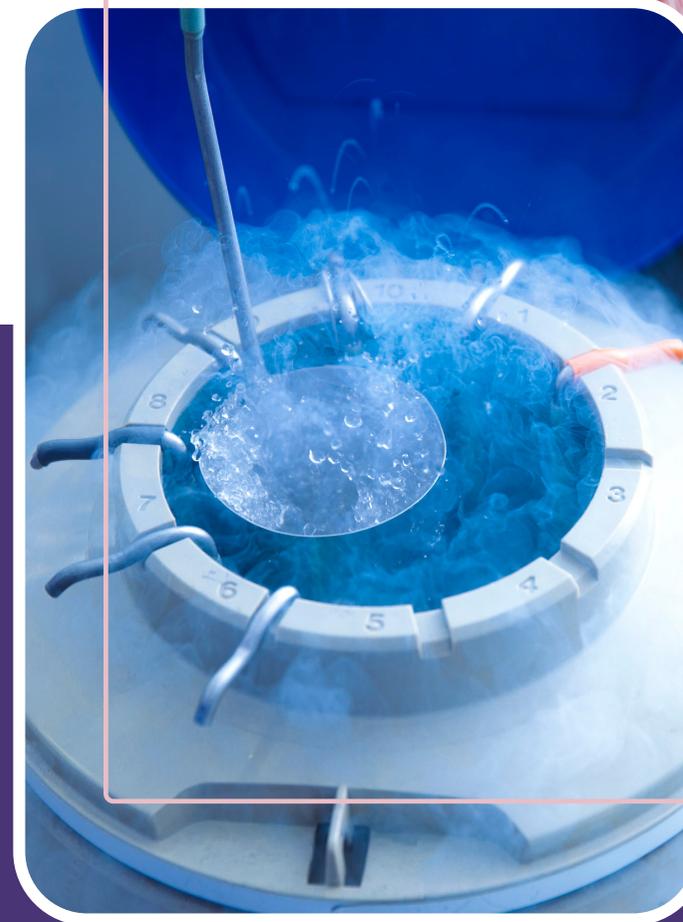


The NHS is overwhelmed by patients seeking therapists and there is a backup of patients with waiting times that often exceed the duration of the treatment. After 15 cycles of fertility treatment, Aura co-founders Abi and Karen understand the stress that accompanies infertility all too well. Aura Fertility provides a solution, aiming to transform the IVF experience with comprehensive patient care.

Aura is an evidence-based platform that offers pioneering whole-person care for every IVF cycle, including therapeutic support. Aura fertility offers 24/7 wrap-around care to navigate the IVF journey that integrates with the clinic experience.

The app was a vision of CEO Abi Hannah, who understands first hand that good fertility health is more than just a procedure. Aura aims to improve outcomes across patient experience, psychosocial health and IVF success rates.

The experience for fertility patients undergoing treatment is individual and unique. Each patient experiences the stress differently depending on their personal life and background. Dealing with the medical staff and with the side effects of treatment has its own stresses, including: hot flushes, injections, and difficult decisions about the future, to name a few. IVF treatment and its effect on quality of life can have a varying impact on the mental health of patients. It may affect all parts of their life including relational, social, physical, emotional, financial and religious areas. The time spent in treatment is stressful and the commitment leads to disruption in family, work, and social activities. The waiting periods for the treatments can be long and costs are high.



The first treatment cycle is notoriously stressful for patients with possibly the highest levels of confusion, bewilderment, and anxiety. The process is an unfamiliar experience especially for those unused to medical treatments. Many patients may feel afraid and anxious about their own actions affecting the treatment outcomes. While many patients do adjust well emotionally with help from mental health care professionals offered at clinics, the effect of the treatment may have more long term consequences such as changes in relationships pre and post treatment, depression, and post-traumatic stress.

As an evidence-based support platform, Aura offers expert knowledge and guidance that's dedicated to nurturing all aspects of a patient's fertility wellbeing and emotional health. Patients can make informed decisions based on personalised content, evidence based tools and expert guidance to improve their experience and optimise outcomes.



Shockingly, only 4% of healthcare R&D spend goes towards women's health, and only 2.3% of venture capital funding goes to female founders. But already Aura have already been able to raise £600k in their pre-seed round, to fund key hires and tech development. The future looks promising, and the app designed by Aura fertility support and expert guidance that can transform the IVF experience.



Aura is available via leading fertility clinics across the UK, and has plans for global expansion in 2023 and beyond. Any clinics wishing to lead the charge with comprehensive whole-patient care can find out more at [www.aura-fertility.com](http://www.aura-fertility.com) or be in touch with [ailsa@aura-fertility.com](mailto:ailsa@aura-fertility.com).



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## **Blogger Bio**

I am passionate about equity in global health outcomes and look forward to exploring the complex landscape of reproductive health over the year.



**CORINA STANILOIU**

MSc student in Clinical Embryology, Oxford

# ON THE BALL

## OCON Healthcare strives to deliver advancements in intrauterine ball technology to developing countries and globally

At Oxford University's AIMDay in Women's Health 2022, OCON Healthcare made waves during their discussion of their novel intrauterine ball (IUB) technology and addressed its potential application to address abnormal uterine bleeding in the developing world. The Israeli-based, fem-powered research and development company, whose goal is to "revolutionize women's health and improve quality of life" impressed me with their unique way of helping those not only seeking contraception, but also those needing more diverse and accessible treatments for abnormal uterine bleeding as well as prevalent conditions such as endometriosis and fibroids. The talk, held by Ms. Daniela Schardinger, the VP of Marketing and Medical Affairs for OCON, and moderated by Oxford's Dr Anita Makins, elucidated on the diverse range of products developed by OCON, and centring around their unique ball technology, in which devices are ball-shaped to better integrate into the uterine environment and prevent injury such as perforation with a three-dimensional spherical design. These 3D devices can also be easily inserted by non-physician medical staff with no capital equipment costs.

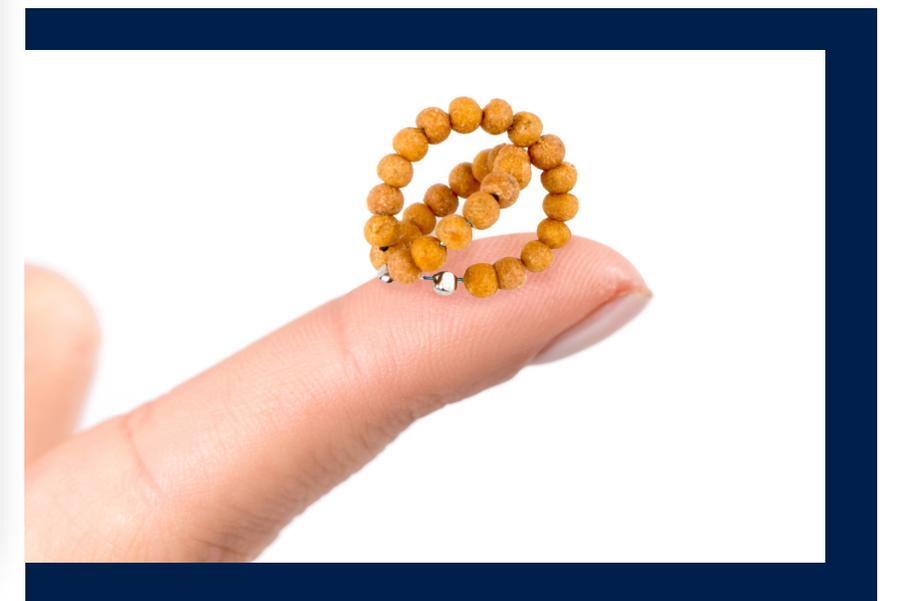
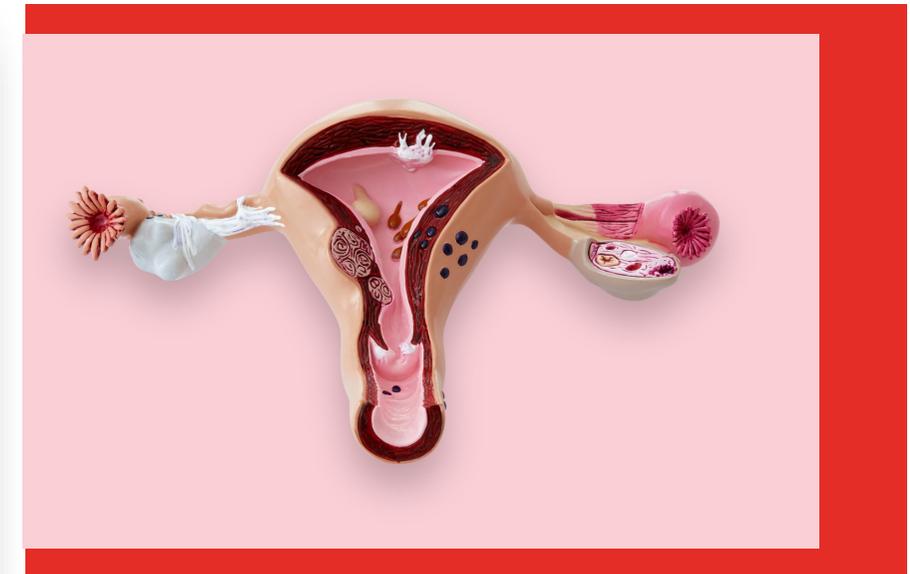
I was shocked to learn that approximately 1 in 4 people with vaginas who are of reproductive age live with abnormal uterine bleeding, and I was unsurprised by the variety of indirect economic impacts this has on life. It was noted that this condition is a common cause of visits to gynaecologists and impacts sex life and mental health. On a more clinical note, abnormal uterine bleeding can result in anaemia and iron deficiency due to the excessive loss of blood. This was concerning to hear, as even without abnormal bleeds, 1 in 3 people who menstruate are anaemic, and in the developing world, this condition affects more than 1 in 2 people.

Company: **OCON Healthcare**  
Chair: **Anita Makins**



OCON led the talk by first introducing their platform technology which has been validated through the company's inaugural product, the copper IUD "Ballerine", which has over 120,000 worldwide users. This product was so well-tolerated that OCON expanded their ball technology to develop the IUB "SEAD" (Spherical Endometrial Ablation Device), which can be used for abnormal uterine bleeding and heavy menstrual bleeding by performing a non-invasive endometrial ablation - the removal of the endometrial lining of the uterus, in 20 minutes using a compound called silver nitrate. This compound is compacted in beads along the IUB frame that melt and coat the uterine lining. This is a simple in-office procedure. OCON also claimed that they are expanding their offerings by developing a slow-release drug delivery IUB to utilize for contraception, fibroids and endometriosis indications with a local target (the first being levonorgestrel-based), intending to prevent the potential systemic side-effects associated with various contraceptives and treatments taken orally to women's issues.

The main goal of OCON's workshop was how to create impact in the developing world. I felt that a variety of important issues were brought up by the attending academics and students, the biggest of which was affordability, access and education. In many countries, women are sent to have hysterectomies or undergo current deliberating global endometrial ablation therapies as a common treatment for abnormal uterine bleeding, which are not only costly but can cause further complications, like any surgical intervention. For women seeking care in developing countries, modern options are often not available due to high cost, therefore a low price strategy would need to be adapted in order to make these treatments more affordable. One attendee brought up another valuable discussion point using their own experience of patient healthcare views in Central Asia, noting that there is a common perception that treatments from the "West" should not be accessible, creating patient resistance to using devices such as an IUD. Additionally, they mentioned that access to care varies in different locations and is not uniform between patients. Although OCON currently has operations in Africa, and more recently in Latin America and soon in China, their take-up data is primarily from the European market, and they note the importance of acquiring adoption data in the areas in which they have entered for further expansion. OCON's SEAD treatment, currently in Phase IIb studies, looks to be a promising more cost-effective solution especially for women in LMIC countries suffering from menstrual disorders with a lack of accessible solutions, with the product's ease of use in-any-office-setting eliminating the need for hospitalization or anesthesia. This technology also takes away the need for expensive capital equipment lowering the burden of costs associated with these treatments. The company's earlier research in Eastern Europe has demonstrated the urgent need for more modern, less invasive solutions especially in low resource settings, where women are often pushed towards hysterectomies - the removal of the uterus - due to lack of affordable alternatives. This was demonstrated by the high demand and quick recruitment of its Phase II(a) study for the novel, non-invasive SEAD treatment.





Attendees urged OCON to consider the future effects on people who utilize such products but are not done with their family planning, or have a risk of developing cancer. The long term needs are to be further investigated; Daniela admits.

Why this research is so important was what stayed with me the most. Women's health funding is difficult to score, but this research affects over half of the world's population! OCON is hoping that things can change with more conversations like those at Oxford University's AIMDay, not only for those utilizing products like the IUD and IUB in HICs but also in LICs too, to provide equal health outcomes for all – a sentiment which I, as a reproductive health student, share wholeheartedly.

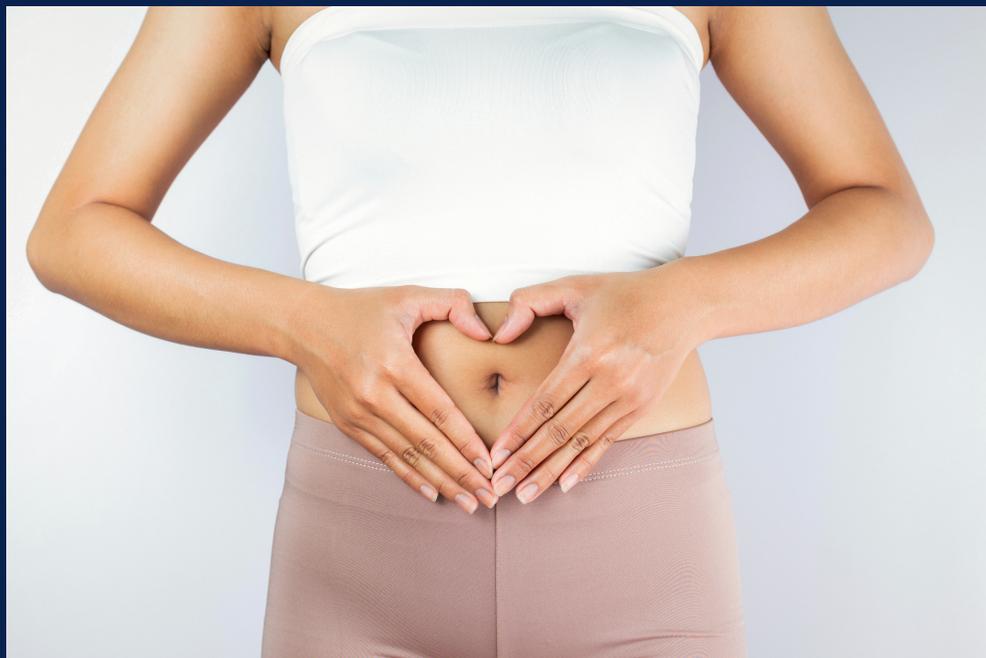
# ONE PILL WONDER

**- MirZyme's journey to developing one innovative test and pill to detect and target pre-eclampsia**

Every minute that you spend reading, a mother or child will die from pre-eclampsia or its resulting effects. At MirZyme Therapeutics' Oxford AIMDay 2022 workshop session, [Prof. Asif Ahmed](#), the company's chairman and CEO described their revolutionary product – [a single test and pill for determining pre-eclampsia risk and treating it before it occurs](#), and shared MirZyme's willingness to collaborate with the University in both research materials and knowledge exchange with the aim of "making pre-eclampsia history", ideally within this decade.



[Pre-eclampsia is a condition affects 1 in 12 pregnancies](#), and can lead to [many complications, including high blood pressure and kidney damage](#), as well as fetal growth restriction and pre-mature birth. In the workshop, I learned that innovatively, MirZyme investigated the reason why the 11 out of 12 pregnancies did not result in pre-eclampsia. They demonstrated that the factors responsible for pre-eclampsia where (i) [high levels of sFlt-1](#), a protein that regulates blood vessel growth and (ii) a defect in heme oxygenase-1, a protective enzyme that negatively regulated sFlt-1 ([link to review](#) -). This was associated with pre-eclampsia development in a major portion of the population. MirZyme's response to preventing sFlt-1 elevation in patients at risk for pre-eclampsia, monikered the "supercharged aspirin" by workshop attendees, is MZe786, a hydrogen sulfide-releasing aspirin ([link to peer-reviewed paper](#)).



The company's main goal from the AIMDay workshop was to determine how collaboration with the University of Oxford can help accelerate their product clinical development. In addition, the founder Prof Asif Ahmed was keen to support life sciences students to gain exposure to biotech startup environment to develop a mindset of an entrepreneurial scientist. Their main needs centered around clinical trial expertise, access to laboratories as well as building closer relationships with clinicians who have first-hand experience with pre-eclamptic pregnancies to understand patient need and ideal product requirement.

Upon learning what MirZyme's product is, I recalled what I had been taught as an MSc student about the prevention of pre-eclampsia, and the role of aspirin in the early stages of pregnancy for prevention purposes - knowledge echoed by multiple clinicians and academics in attendance. If aspirin is currently recommended, why fix what isn't broken? This question was addressed, with the representatives noting that while aspirin and statins have been used, they are not very effective, have gastrointestinal side effects and do not prevent pre-eclampsia in vast majority of cases. Furthermore, targeting the direct culprit of pre-eclampsia, which is the company's revolutionary approach is going to be safer, less costly in the long run and far more efficacious and minimise side effects.

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But with every great product comes a greater number of questions to be answered to promote its success. In the discussion period, attendees brought up a variety of important collaborative points and questions to the company. A major question that I too wondered about was focused on how to know that the medication is administered to the right patient – more specifically, how can the risk of pre-eclampsia be effectively determined before the condition becomes a dangerous reality? MirZyme stated that their one test aims to address this, by stratifying the population at risk through testing for the presence of elevated sFlt-1 and other biomarkers they have patented. They have done a prospective clinical trial and determined with 97% accuracy who will go on to develop pre-eclampsia. They are uniquely placed to offer world's first companion diagnostic with their first in class therapeutics.



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The workshop ended with an engaging discussion on the concerns about fetal transfer and potential effects on other roles of the sFlt-1 protein. Dr. Rezai, the company's COO pointed out that despite their new medicine MZe786 had only been tested in animal models of pre-eclampsia, it was a "supercharged aspirin" and being considered as therapy after 20 weeks of gestation. In contrast, Aspirin is recommended from 14-16 weeks of gestation and it too could cross the placenta. An attendee stressed the need to study placental transfer in humans, as placentation slightly varies between murine and human. The company noted it and Prof Manu Vatish offered to undertake such a study using his ex-vivo human placenta model. Prof Asif stated, "Discovery is a step into the unknown to build beyond the known".

A clinician and global health expert noted there are places in the world where pre-eclampsia phenotypes are very particular. In this instance, how do you choose an effective and inclusive clinical trial study population? Another added a question about the potential presence of genetic variants influencing pre-eclampsia predisposition, and the need to consider this in research and drug development. But beyond this, there is also the need to consider that other inequalities affect pregnancy outcomes aside from genetics, such as race and socio-economic factors, which may impact study results. The company is aware of these variables and is working with the regulators to mitigate these issues.

Overall, the research and development at MirZyme is ground-breaking (link to key paper and the aim of their products are incredibly important and highly relevant to preventing pregnancy complications worldwide. As evidenced by the many discussion points of attendees of the workshop, I learned that there is great benefit in collaboration between academics and clinicians to build a unified vision for a product that is inclusive of industry, science, and its practice with patients.





## **Blogger Bio**

I enjoy exploring the application of physics to healthcare through concepts such as nuclear medicine, radiation and particles. The vast number of factors that affect treatment from the internal environment to ethnicity, intrigues me to understand how we can explore different avenues to personalising treatment for women.



**JANNAT KHAN**

MSc Student in Radiation Biology, Oxford

# How to overcome the challenges of gathering women's health data in diverse ethnic groups?



Women are twice as likely to experience UTIs and be diagnosed with anxiety and depression. These health disparities are chronic, especially across ethnic minorities. Dr Mehta, Founder and CEO of Altus Lifescience, aims to empower women to make their own correct health decision. This happens via community engagement (patients, leaders, and doctors) to encourage conversation and find common ground. Using this information, Altus Lifescience innovates health products for breast health, fertility, and maternal health care. However, a key barrier involves missing data from women of diverse ethnic groups due to women's health still being considered a taboo topic causing difficulty in sharing information. This can occur due to data security and privacy concerns, and unawareness of symptoms.

Company: **Altus LifeScience**  
Chair: **Dr Jane Hirst**

Collating diverse data ensures all ethnic groups are appropriately represented, improving the quality and availability of the data. This is important for the women who directly experience health disparities. South Asian women are more likely to be diagnosed with heart disease due to a lack of referrals, African women are four times more likely to die of childbirth, due to stress and Middle Eastern women have higher breast cancer incidence. Although socio-economic factors are often the reasons provided for these differences, other factors such as being listened to by healthcare professionals and the lack of referrals need further investigation. Collating relevant data allows risks to be identified therefore affecting the distribution to make it more accurate. Moreover, it allows the relative risk to be found, affecting treatment decisions. This opens the door to personalised medicine to ensure women are receiving appropriate treatment rather than one size fits all.



A key point within the discussion tackled the inaccessibility of collecting data. Patient data is collected at hospitals where patients must travel to and are already ill at arrival. Researchers who travel to villages receive the opportunity to collect data from healthy participants, whilst reducing travel complications. Projects such as Our Future Health tackle this, however, their replication is limited in developing countries. Overcoming accessibility challenges involves delving deeper, where patients are inaccurately represented through data, and algorithms become biased due to incorrect data input. Through widening and accessing a diverse population sample these algorithms can be improved but this is not always possible due to the community feeling like their data is being 'stolen' for research and they are left without help. As a result, accessible collaborations between communities and companies are difficult to maintain and create. Making this relationship a partnership by giving value overcomes this hurdle.

One form of this includes creating trusting collaborations between academia and companies and separating funding and sponsorship. By creating a 50/50 partnership, it may be possible to build models which are shipped and tested, but the results are sent over to the company, rather than the data, increasing community trust in companies. Excluding industry, where costs are drastically increased, and research becomes limited opens the opportunity to employ staff in countries of research however, guidelines are required to ensure high-quality research. These partnerships must be built on trust to prevent the concept of companies 'using' academia for their gain. Alternatives such as safari research were suggested, where offices in specific locations can be prioritised to recognise investments and ensure equitable data sharing.

Above all, after collecting and analysing the data, it is imperative to translate this data appropriately to communities to ensure value. Ensuring data is used according to rigorous guidelines is also necessary to make sure devices and products can be used by the communities in different developing countries. However, the low-price benefit is not enough, and changes must be long term and credible. The opportunity to engage in this discussion and be among voices that are advocating for women of diverse ethnic backgrounds was incredibly rewarding.



The image features a central text box overlaid on a background of microscopic images of embryos. The background is split into two triangular sections by a diagonal line. The left section shows a pipette tip positioned near several embryos. The right section shows a close-up of two embryos. The entire scene is set against a blue background with a grid of white dots in the top-left and bottom-right corners, and faint, stylized outlines of a brain and a hand holding a pipette in the center.

**What is the best research strategy to discover critical factors and/or conditions for successful embryo plantation?**

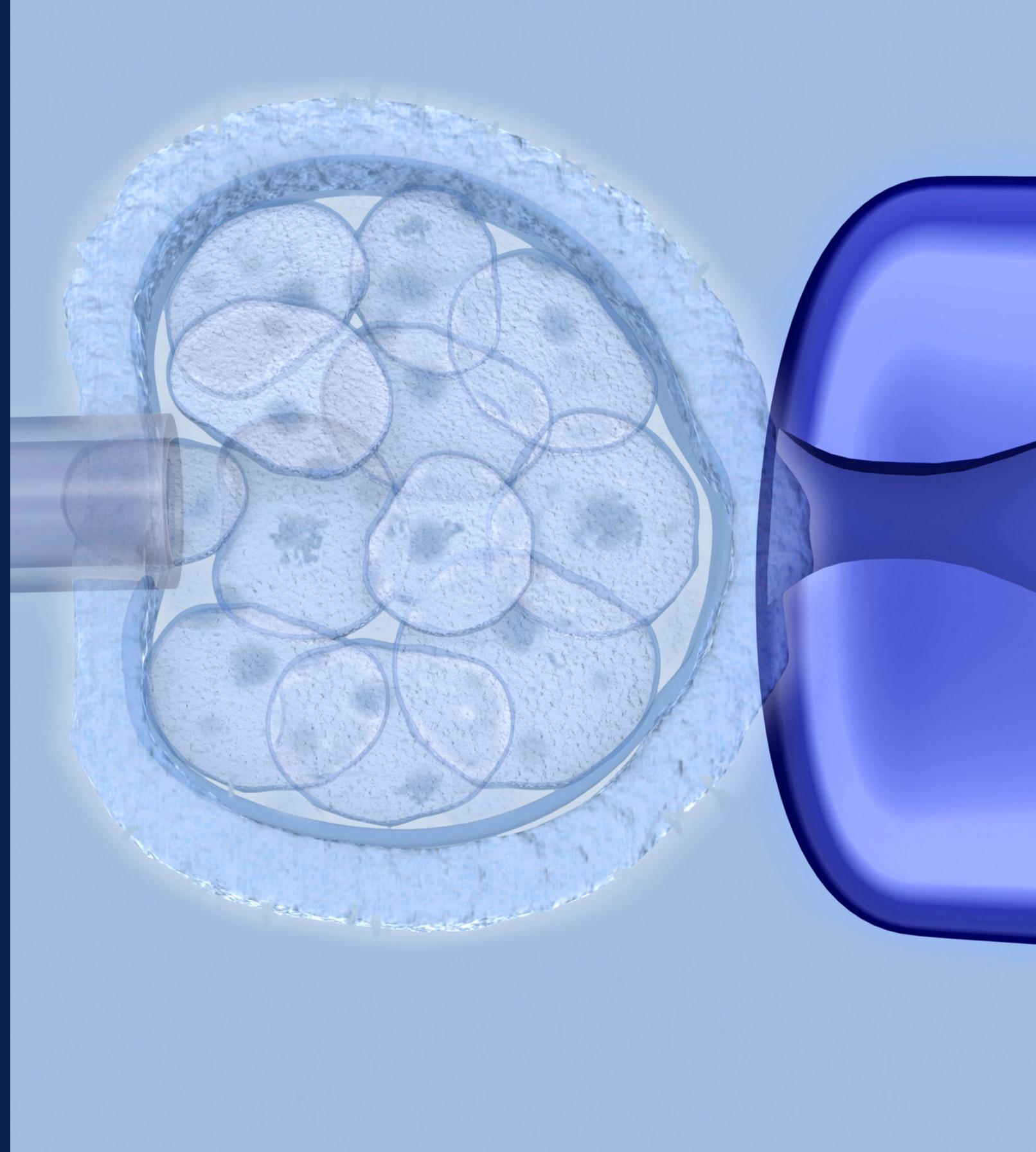
Company: **Organon**  
Chair: **Professor Suzannah Williams**



Dr van Duin, the Head of External Innovation & Emerging Science at Organon, highlighted the importance of tackling key diseases which are dominant in women. Organon focuses on disorders such as PCOS and endometriosis and is very interested in finding non-hormonal methods for both male and female contraception as well as the unmet need in male and female infertility. In addition, Organon is committed to explore solutions for peripartum complications such as pre-term labour and preeclampsia. This is an extremely difficult field to navigate as pregnant women and their babies are vulnerable and testing new drugs comes with hesitancy, however, research is urgent. Pregnant women in deprived areas are twice as likely to die than those living in less deprived areas and women of black ethnicity are four times more likely to die than women of white backgrounds. To approach this, Organon's external innovation strategy is drug modality agnostic and where possible includes solutions involving diagnostic, device and digital innovation.

As we explored the concept of fertility, I came to realise that there are key fundamental topics that are poorly understood. For instance, the mechanism of action of embryo-endometrium crosstalk is largely unknown and therefore the understanding of the embryo implantation process is still considered a 'black box'. It is presently poorly understood what determines the fate of a blastocyst on its way to implantation. Does the embryo 'talk' to the endometrium or vice versa or is it a well orchestrated biological process between the two parties? As yet the question remains unanswered as to why a good looking blastocyst (through the microscope) does not successfully implant and result in a healthy pregnancy. Much more research needs to be done to determine the critical components that together make a good embryo and a good receptive endometrium.

Initially, the key concern was addressed: even if the pathophysiology was understood, how can pre-clinical research be translated into the clinic? If there would be an implantation-medicine this would require information, the mechanism of action, the safety of the drug, the route and best time of administration and understanding of the patient characteristics and more. And if this could all be tested in a laboratory setting with animal models, what would be the strategy to go into the clinic is a paramount question.

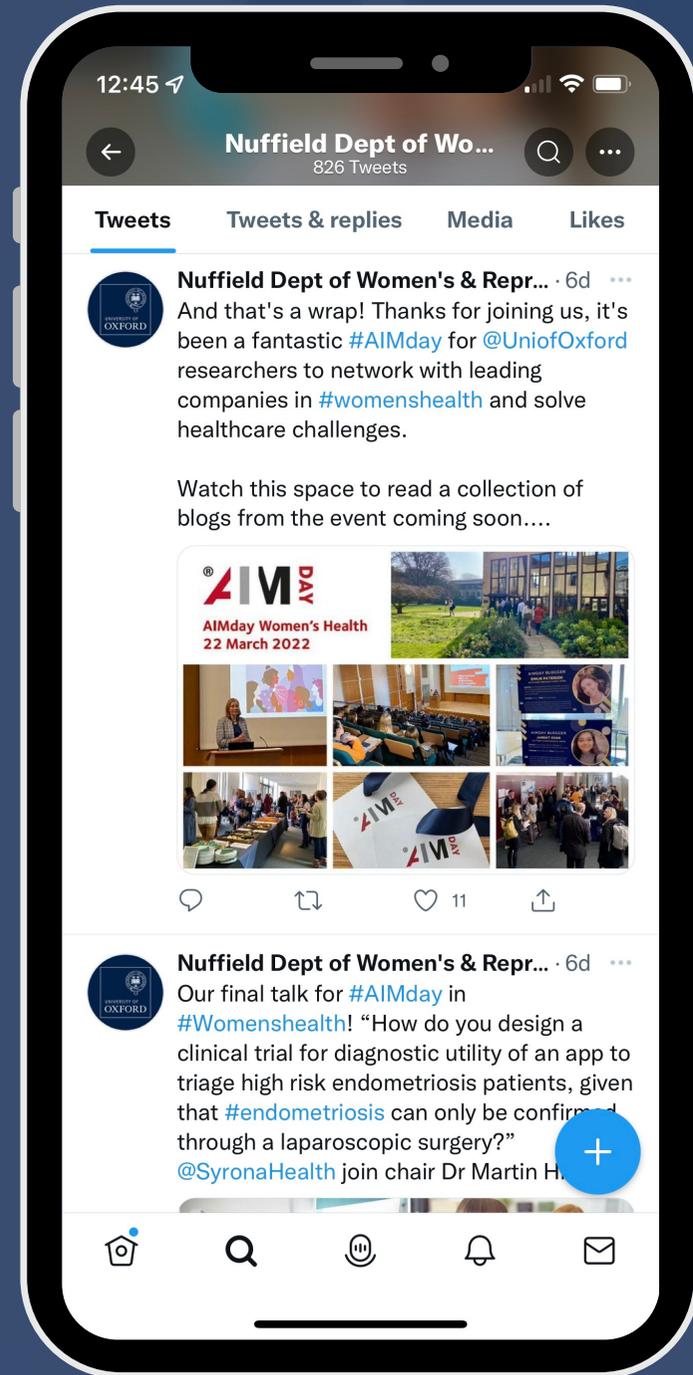




Involving immunology, and genetics to understand what makes a 'good' gene profile could support implantation. This understanding comes from identifying that research is multidisciplinary and cells communicate with each other, therefore specific targeting may not be optimal. This requires better in vitro models which are multi-cellular. Identifying key drug targets is fundamental, however, it was mentioned that testing everything, may highlight suitable targets which have not been before. Furthermore, research into uncertainties via error testing will support analysis for treatment effectiveness.

I found that the discussion navigated a research story, where we identified the need for embryo imitation, creating acceptable embryo standards and assessing the criteria for a possible drug. But it also highlighted the importance of remembering the translation to the clinic, the importance of vast patient diversity, suitable criteria for drug administration and implantation drug design which are all equally important. Standardised research, and robust data collection via images, consistent scoring, and transparent culture medium design, are needed for reproducible research.

This can be supported by novel technologies such as AI for image analysis, however, limitations such as the small resolution need to be overcome. With evolving research, these research questions have opened up the potential for further personalising fertility treatment and for improving collaborations between academia and companies. Attending this workshop heightened my awareness of how multidisciplinary these collaborations need to be and through combining research efforts, more women can be treated and saved.



# Stay connected!



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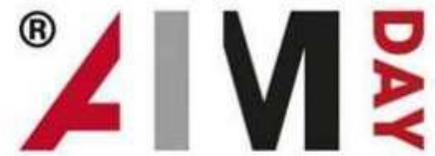
NUFFIELD DEPT OF WOMEN'S  
& REPRODUCTIVE HEALTH



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REPRODUCTIVE HEALTH,  
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# Thank you



**AIMday Women's Health  
22 March 2022**

