Women’s health: a life course approach
Held on 18 October 2021
Conference report
Introduction

On 18 October 2021, the Royal Society and the Academy of Medical Sciences held an online event exploring the life course approach to women’s health.

Keynote talks covered experiences of the healthcare system and the importance of a wholistic approach to women’s health. Key interventions that occur at different stages across the life course were covered, including menstrual and sexual health, pelvic floor dysfunction and recovery, integration of digital health for women, and novel treatments for menopausal symptoms. A final panel discussion discussed inequalities in women’s health and research.

The conference brought together experts from industry, academia, the NHS and the wider scientific community.

This meeting, supported by AstraZeneca, forms part of the Royal Society’s Transforming our Future series and the Academy of Medical Sciences’ FORUM programme. The meeting organisers were Professor Philippa Saunders FMedSci FRSE, University of Edinburgh; Dr Pauline Williams CBE FMedSci, GlaxoSmithKline and Professor Dame Valerie Beral DBE FMedSci FRS, Nuffield Department of Population Health.

The Transforming our future meetings are unique, high-level events that address scientific and technical challenges of the next decade and bring together leading experts from the wider scientific community, industry, government and charities. The meetings are organised with the support of the Royal Society Science, Industry and Translation Committee.

The Academy’s FORUM programme brings together industry, academia and the NHS, as well as the charity, regulatory and wider healthcare sectors. It provides an independent platform to bring together leaders from across the life sciences sector to discuss scientific opportunities, technology trends, translational challenges and strategic choices in healthcare.

This report is not a verbatim record, but a summary of the discussions that took place during the day and the key points raised. Comments and recommendations reflect the views and opinions of the speakers and not necessarily those of the Royal Society or the Academy of Medical Sciences.
Executive summary

In March 2021, the UK Government launched a call for evidence seeking views to a Women’s health strategy in the UK. The rationale was that women are often failed by the healthcare system, that women spend a greater proportion of their lives in ill health than men, and that there are growing geographic disparities for women in terms of access to services, experiences, and outcomes.

Social and economic status are strong determinants of health, yet globally women have an unequal offering compared to men. Women’s health has historically not been considered a primary policy target by life sciences research and the healthcare system, yet new interventions and technologies are being developed to support a holistic life arc approach that would empower women and improve their health. However, new solutions must be evidenced-based and be inclusive. Key themes from the meeting include:

Equality in research and treatment
- Research into new therapies and health solutions must be inclusive and consider gendered data1. Over 70% of recent biomedical experiments did not report sex as a variable of interest.
- Although more women are being recruited into phase 3 trials, the meaningful analysis of outcome by sex remains absent or incomplete.
- Despite advances in understanding, treatment of pre-eclampsia is still based on science from 1950. Only one medicine designed to treat pregnancy-related symptoms has been licensed in four decades.
- Funders from the UK should note that sex, gender, or diversity analysis can and should be embedded across all areas.

Funding for women’s health
- A lack of funding in Women’s health research means that scientists are disincentivized from working in the area.
- Policy environment changes means that there is a shift from government, funders and regulators to support women’s health. This needs to be accompanied by prioritising women’s health in funding to allow opportunities to be seized.
- Increased funding support into women’s health research is important and there are many global examples of countries doing this.
- A UK based women’s health fund could work similarly to the Diabetes Transformation Fund.
- Period-related problems do not have similar advocacy groups as other clinical conditions, and periods are still a taboo topic, which hampers change and funding.

Effective evidence-based approaches
- Experts believe only 15% of new digital health tools aimed at women meet quality thresholds. Evidence is crucial to ensure women are given the best health solutions.
- The traditional approach to training doctors focuses on disease intervention rather than prevention. There is a need to consider the life environment and to focus on the things that matter to every girl or woman.
- Middle government bureaucracy has prevented many simple and practical solutions for women’s health being implemented. One such solution would be to develop women’s health hubs, which deal with all elements of service providers in one visit.

“There has never been a more pressing need, or better time to grasp the opportunity to reframe and rethink the delivery of patient-centred health care that will address the needs of all women, and those who identify as female, throughout the life course regardless of their location or health status.”
Philippa Saunders, University of Edinburgh

1. This report uses the ONS definitions of ‘sex’ and ‘gender’. What is the difference between sex and gender? The Office for National Statistics https://www.ons.gov.uk/economy/environmentalaccounts/articles/whatisthedifferencebetweensexandgender/2019-02-21 (accessed 29 March 2022)
A wholistic life course approach to women’s health

Professor Neena Modi, Imperial College London spoke about factors adversely affecting health across the life course, inequity for women in the healthcare system, and the policies needed to improve positive health trajectories.

Human health is a cardinal determinant of productivity, innovation, resilience and a country’s wealth and wellbeing. However, failure to recognise these relationships, coupled with gender-inequity, has meant the contribution of women’s health to population health and wellbeing has not been a primary policy focus.

A life course approach and determinants of human health

Life course health starts with genetic endowment and is then influenced by multiple external factors pre-birth, in early life, and through to end of life care. Scientists increasingly understand the biological mechanisms, such as epigenetic programming, that lead from adverse early exposures and experiences to compromised health and health trajectories.

The principal determinants of health lie outside healthcare and are the conditions in which we are conceived, grow-up, and age. For example, diabetes and cardiovascular disease are the principal chronic, non-communicable diseases that ravage societies around the world, and risk factors for these diseases start at birth. Most recent estimates suggest that healthcare only contributes ~11% to overall health.

In the UK, healthcare is biased against women, with only one medicine designed for use in pregnancy having been licensed in four decades. Additionally, 98% of all medicines have insufficient or no safety data to guide dosing during pregnancy and lactation. Women are also 50% more likely to have a heart attack misdiagnosed and less likely to be prescribed medications to prevent a second attack.

COVID-19 has shown that women have been more adversely indirectly impacted through reallocation of resources and priorities, increases in unpaid care work, increase in gender-based violence, and an increase in food, employment, and financial insecurity. Even personal protective equipment is designed primarily for men.

“A focus on women’s’ health as a policy priority would bring immense benefit to economic prosperity, and help redress the cumulative adverse effects of longstanding gender inequity.”

Neena Modi, Imperial College London

An unequal healthcare system in the UK and globally

Inequity starts early. Maternal physical and mental health are prime determinants of infant and hence population health. Yet, in many countries, over 50% of pregnant women are overweight, 40% are anaemic, 10% experience peripartum or postpartum depression, and 20% have no access to a health professional during childbirth. The social preference for boys results in unequal treatment of young girls, including poorer nutrition, less expenditure on healthcare, and lower immunisation rates.

References:
2. IHME, Global Burden of Disease (2018)
4. Chakladar and Ascott, BMJ 2021
What should be done?
Research must be smarter. Large databases, such as the UK National Neonatal Research Database and eNewborn, allow the disaggregation of data, which helps to measure and evaluate outcomes by sex and other sub-groups. Collaboration would help the development of these datasets that have large enough power to detect sex-based effects. Research should include fair representation of men and women, a standard that funders, sponsors, and regulators could require.

At an economic scale, current policies penalise practices that improve health such as breast-feeding and parenting, through financial and career progression penalties. There is wider responsibility to ensure economic systems measure and assign value to activities that initiate healthy life course trajectories and promote health, and with science, are rooted in social justice.
An evidence-based approach: fair representation and early intervention

Baroness Nicola Blackwood, spoke as a patient and the Chair of Genomics England, about the need for more disaggregated data to help women make evidence-based decisions about their health.

Nicola was thirty-three when she was diagnosed with a genetic condition that had caused her significant physical and mental health issues since childhood. Despite the diagnosis, it was a struggle to become medically stabilized. Not only is the disease poorly researched, but the medication had not been tested in pregnancy and so there was a lack of data on what pregnancy and childcare would mean for her or her child’s health. This led to Nicola deciding that she could not have biological children of her own.

The gender health gap
Statistics show that too many women are affected by late or misdiagnoses, are more likely to have a burden of care reducing time to seek treatment, and more likely to face workplace discrimination when they suffer from ill health. When women seek to make informed decisions to maintain health, data is heavily focused on men.

Dementia is the leading cause of death among British women, yet a UCL study from 2016 found that women with dementia have fewer visits to the GP, receive less health monitoring and take more potentially harmful medication than men with dementia. Women reporting pain symptoms are often prescribed sedatives instead of pain medication, implying their symptoms are ascribed to anxiety by health providers; and while three quarters of women take medication during pregnancy, 73% of drugs have no safety information for pregnant women.

Genomics England
A strong foundation of unbiased data is needed to give women early and accurate diagnosis, and clear clinical options. At Genomics England (GE) data sets are diversified to remove bias through structure, ethics, and analytics, ensuring equality of access to the services.

GE’s 100,000 genomes project is the largest national sequencing project in a healthcare setting globally. Already, many strands of research have led to diagnoses and clinical care for thousands of patients. One in four undiagnosed rare disease participants are now being diagnosed and 50% of cancer participants are shown to have cancer-causing mutations in their genome. GE’s growing collection of breast cancer genome sequences link to radiology and pathology images generated during the patient’s care, giving new insights.

These multi-modal approaches are a world first and have led to success with COVID sequencing studies in partnership with REACT. GE’s ambition is to embed whole genome sequencing in routine healthcare and ensure equitable access to early accurate diagnosis.

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Vision for the future

The bigger clinical picture still excludes women with low representation in clinical trials (phase 1 ~ 22%), and as of 2016, 70% of biomedical experiments did not report sex as a variable of interest. Although, recent regulatory changes mean more women are being recruited into phase 3 trials, the meaningful analyses of outcomes by sex remain absent or incomplete.

The vision of the clinical research strategy will be important for improving the diversity and pace of research whilst maintaining quality. The newly formed UK clinical research recovery resilience and growth programme will be responsible for the implementation of the new strategy. Given our knowledge about the sex differences with drugs and medical care, the continued exclusion of 50% of the population for clinical research for cost or hormonal reasons is bad science and unethical. All ethics committees should insist on proper representation of women in research.

Experience of endometriosis

Candice McKenzie, Endo Warriors West Lothian, spoke about her lived experience of endometriosis and what it is to live with a chronic condition.

What is endometriosis?
Endometriosis is a condition with no cure. Endometrial tissue, similar to the lining of the uterus, starts to grow in other places, such as the ovaries and fallopian tubes. Some of the early symptoms include severe and debilitating cramps, pelvic pain, long periods, and bowel and urinary disorders. In rare cases, the tissue grows extra-pelvically, occurring away from the gynaecological organs such as lungs, kidneys, bladder. Extra-pelvic endometriosis can be extremely challenging and delays diagnosis.

A patient journey
Candice was diagnosed with extra-pelvic endometriosis when she was 21, a full 11 years after she first noticed bowel issues. After her periods started, her lifestyle deteriorated. Despite the delay, she was still relatively young for an endometriosis diagnosis as ~ 60% of patients are misdiagnosed initially.

After diagnosis in 1999, there was limited access to information on the condition through the library and online. Candice was told that she had lost her ovary on the left-hand side, and the right-hand side was impaired, so fertility was already a problem. She underwent two surgeries within three months to try to conserve her fertility and was started on a drug which put her into a chemical form of menopause. Management of the disease required multiple surgeries, averaging one every two years. Candice did manage to get pregnant at the age of 27, however there were multiple complications, and associated pain. At the age of 36, Candice underwent a hysterectomy and oophorectomy and was placed on a hormone replacement therapy (HRT), which caused severe problems for her health. Two weeks after her surgery, she had a painful protrusion from her pelvis that took two years to be diagnosed as endometriosis. Because of her surgery, she has no reproductive organs which meant that her gynecologist discharged her as a chronic pain patient. This meant that she was unable to receive the subsequent operations that she needed.

Ten years later, she is still taking multiple medications including one which prevents estrogen production and causes bone and hair thinning, amongst other side effects. As Candice entered menopause, lack of awareness as to how HRT affects endometriosis patients meant that she was prescribed oestrogen add back. Her body’s reaction to HRT caused her to suffer severe health problems, which were misdiagnosed, and only improved when she stopped treatment.

Endometriosis is considered a pelvic condition, yet it has affected Candice’s whole body and caused social isolation through her life because of stigma associated with the condition and illness preventing social engagement.

The work of Endo Warriors
Endo Warriors provide support, action and awareness to the endometriosis community. Their private members hub, which has over 600 members currently, have access to monthly support meetings and one-to-ones where required.

As well as campaigning to raise research funds for and awareness of endometriosis nationally, Endo Warriors advise and collaborate with the Scottish Government. They are members of the Scottish women’s health collaboration forum for endometriosis and were appointed to the first council to support menstrual wellbeing in education in Scotland.

“If you know 10 women then you should know endometriosis.”

Candice McKenzie, Endo Warriors West Lothian
Successful health interventions across the Life course: The menstrual health and wellbeing of young women

Professor Hilary Critchley, University of Edinburgh, spoke about the need to remove the taboo around periods, the effects of heavy menstrual bleeding, and new classifications to enable better communication.

Menstrual health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity, in relation to the menstrual cycle\(^8\). Sommer et al estimate that a quarter of the world’s population of women and adolescent girls of reproductive age, around 500 million, do not have everything they need to manage their menstruation\(^9\).

There is a growing movement to ensure that all adolescent girls and women have access to safe, hygienic menstrual management and assured menstrual health. Typical challenges include menstrual stigma, insufficient education, and limited access to menstrual materials, toilets with water, disposal mechanisms or privacy.

**Breaking the taboo around menstrual health**

Right now, 800 million women and girls are having their period. It is a fundamental biological function and necessary for the continuation of humanity. Yet period research remains a tough area for finding funding. As period-related problems are not a single disease entity, they do not have similar advocacy groups or organisations as other clinical conditions, and periods are still a taboo topic, which hampers change.

To break the taboo, methods of communication need to be changed. The menstrual disorders committee at the International Federation of Gynecology and Obstetrics (FIGO) have devised two systems, one for terminology and one for classification, to help clinical study interpretation, dialogue between physicians and patients, and with the public.

Nomenclature is important for understanding, and the recommended classifications go under the acronyms PALM (Polyp, Adenomyosis, Leiomyoma, Malignancy & hyperplasia) for structural causes and COEIN (Coagulopathy, Ovulatory dysfunction, Endometrial, iatrogenic, Not otherwise classified) for non-structural causes\(^10\).

**Menstrual flow and anaemia**

The normal volume of blood loss from menstruation is around 35ml, however, heavy menstrual flow can lead to far greater loss of menstrual blood every month, not so uncommonly, as much as equivalent to a pint of blood. If menstrual blood loss exceeds iron intake, then iron deficiency and anaemia can occur. Approximately 30% of reproductive age women are anaemic worldwide, and a much higher number may be iron deficient, which has an impact on quality of life, with fatigue and other symptoms.

The WHO is aiming for a 50% reduction in the population of women with anaemia by 2025 but menstruation remains under recognised as an underlying cause.

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FIGURE 1

The PALM-COEIN classification for abnormal uterine bleeding in the reproductive years
Illustrating the structural (PALM) and nonstructural causes (COEIN) and as described in Munro et al.\textsuperscript{11}

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**Life course approach to women’s health care**

There is an opportunity to consider gynaecological health, particularly between pregnancies, and improve iron stores and reduce risk of anaemia before someone becomes pregnant, whether they are young or in a later reproductive age. It is known now that there are intergenerational risks for anaemia and the infant.

We need to talk about periods. Women are now having more periods over their lifetime (estimated as 400 now vs 40 in recent history). The impact of heavy menstrual bleeding is known, and period-related problems are indicators of underlying issues such as fibroids (also known as, leiomyoma), adenomyosis and endometriosis. There is a need for age-appropriate management options, which change across the life course.

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The sexual health and wellbeing of women: The national survey of sexual attitudes and lifestyles

Professor Pam Sonnenberg, UCL, explained the National Surveys of Sexual Attitudes and Lifestyles and described the sexual lifestyles of women over the life-course, as well as interventions to improve sexual and reproductive health.

The National Surveys of Sexual Attitudes and Lifestyles (NATSAL) are among the largest bio-behavioural surveys of sexual behaviour in the world. The random probability sample design means that the results are broadly representative of the British general population. Sexual lifestyles are increasingly recognised as a legitimate focus of public health policy, practice, and research.

NATSAL surveys have covered over 45,000 people and include respondents born through much of the 20th century. NATSAL-1 (1990-1991) was held in response to the HIV pandemic, NATSAL-2 (1999-2001) measured sexually transmitted infections (STIs) directly looking at Chlamydia and HPV, and NATSAL-3 (2010-2012) took a life course approach, increasing upper age limits to 74 and expanded biological sampling.

Demographic and behavioural changes in sexual lifestyle
Data shows that over the life course, frequency of sex reduces, however a sizeable proportion of survey respondents (20% – 40%) report recent sex well into the 60s and 70s. The median age of first sexual intercourse for women has reduced over time from 20 to 16, however, the median age of first child has increased from 24 to 28. Effectively, the period between first sex and first child is larger and so there are longer periods of contraception, greater partner change and this generally represents a higher risk period.

NATSAL have developed a concept of sexual competence, which incorporates consent, autonomy of decision, contraception used, and whether they felt ready. In the last survey, nearly 30% of younger women reported having sex before the age of 16 with less than 40% sexual competence.

Data indicates that if educated about sex in school, respondents were less likely to have sex before the age of 15, and less likely to undergo a number of adverse sexual health outcomes eg STI diagnosis, unsafe sex, and lack of sexual competence.

Since 1994, trends in conception have seen a steady decrease in women under 18. Several interventions have combined, including the introduction of intrauterine contraception, the successful introduction of the teenage pregnancy strategy, sexual health strategy and working with education. A critical factor is funding, and data shows that the greatest impact has been in the most deprived areas where there has been the most funding.

Interventions towards reducing cervical cancer risk, include the human papillomavirus (HPV) vaccine programme, started in 2008 with adolescent girls aged 12-13 years and catch-up at 18, and cervical cancer screening. After vaccination, data from NATSAL-3 in 2012, shows a 50% reduction in the prevalence of HPV-16/18 in the age group that was targeted. Additionally, over 70% of women aged 26-49 report having had a screen in the last 3 years, but 12% report never having had a screen, 75% of whom are at high risk.

Impact of COVID on sexual lifestyle
NATSAL COVID looked at how sexual reproductive health has been affected by the Coronavirus pandemic, conducted in July 2020 and March 2021, including 6,500 people aged 15-59 in both waves. The surveys show a reduction in sexual occurrences, but the impacts have been different across the life course, with younger people (18-24) seeing the greatest reduction. The reporting of Chlamydia testing has also decreased, possible due to the change in emphasis of the national screening programming moving away from reducing prevalence to reducing consequences of infection. The main part of NATSAL-4 will happen in summer 2022.
Pelvic floor dysfunction after childbirth: can we predict and prevent it?

Professor Suzanne Hagen, Glasgow Caledonian University, spoke about her work towards a longitudinal study that looks at pelvic floor dysfunction after childbirth and what could be done to prevent it.

Pelvic floor dysfunction (PFD) is a common problem after childbirth. The prevalence of postnatal PFD (symptoms of which can include urinary incontinence, faecal incontinence, pelvic organ prolapse) varies in the literature according to definition, method of data collection and follow-up duration. Few studies have followed a large cohort to monitor the prevalence over time.

The ProLong study, recruited over 8,000 women who gave birth in 1993 and 1994, in three centres: Aberdeen, Birmingham, in the UK and Dunedin in New Zealand. The cohorts were followed up at 6 and 12 years in all three centres. A 26-year follow up in the UK centres has recently been completed and the results have the potential to enable development of a prediction model to aid intervention.

The effect of delivery mode history
The study investigated the impact of mode of delivery of the baby during birth, exploring five categories; spontaneous vaginal delivery only, caesarean section delivery only, 1 or more deliveries involving forceps, 1 or more vacuum extractions without forceps, a mix of spontaneous vaginal or caesarian section deliveries only.

After 26 years, symptoms were still common with 60% of respondents reporting urinary incontinence, 21% reporting faecal incontinence, and 17% reporting symptoms associated with prolapse within a four week period. Results on delivery mode indicated that the highest prevalence after 26 years, across all three key symptoms, came from vacuum or forcep delivery groups. The lowest prevalence of symptoms came from the Caesarian section group.

Can we intervene?
Data can be used to identify risk factors such as the delivery mode history and other modifiable risk factors eg Body Mass Index (BMI). Once identified, selective use of caesarian section, and interventions known to be effective such as weight management, and pelvic floor training can be employed.

To develop a validated statistical risk prediction model, collaborations were set up with teams in Sweden, New Zealand and the US. The model will be used to predict individual risk of PFD at 12- and 20-years post-delivery using two prospective cohort studies. Data from 8,000 women has since been gathered and translated into a freely available risk calculator (UR-Choice) that can be used to counsel a women before and after pregnancy and consider care pathways to mitigate against the risk.

Future plans
Professor Hagan and colleagues are developing a protocol for a randomised controlled trial of the UR-Choice intervention. The project is timed well as there are widespread concerns around women’s pelvic health eg the Cumberlege report highlighted that women are not being listened to. NHS England plan to develop pelvic health services for postnatal women as well as adopting recent NICE Guidelines (December 2021), which are making research recommendations about production tools for pelvic floor dysfunction.

Digital technology to empower women about their health

Jenny Thomas, DigitalHealth.London, spoke about FemTech and its potential to help those who identify as women, to understand their bodies and empower them to manage their own health.

Women plus digital health
Femtech is short for female technology and it’s used to describe services, products, and software, which are created with a specific focus on women’s health. The term itself is controversial with calls for a change to “Women plus digital health” as a more inclusive term. Ida Tin who initially coined “FemTech” wanted to create an umbrella phrase which would aid venture capital investment into the sector.

In 2019, the Femtech industry was valued at £19 billion; by 2027 it is expected to reach £60 billion. A recent report released by Rock Health categorised the various market sectors for Femtech including pregnancy, postpartum, and parenthood; primary and preventative care; fertility; sexual and reproductive care; chronic disease; hormone related conditions, and behavioural health. Femtech is already here and making services more convenient.

How can digital technology be used to empower women?
Technology can be used to empower women in straightforward ways. Online platforms are increasing the reach of healthcare service providers and aid accessibility by gaining feedback from women more rapidly in a more diverse way, which has a critical function in designing effective services for all women. Irth (Birth, with the B dropped for bias) is an app with the goal of ending racism in maternity care by allowing mothers to discreetly report their experiences.

New services are being implemented to deliver direct to women, reducing the pressure on GPs eg HANX, an online contraceptive pill delivery service and Healthy.io which enables women to take a urine test at home, take it straight to the pharmacy for diagnosis by Artificial Intelligence (AI) and therefore get a much more rapid diagnosis/treatment of urinary infections. Another example is Peppy Health which provides expert support and resources for people, especially women, during critical life transitions. One of their services, Peppy Menopause provides women with access to virtual consultations and instant messaging with experts to help them navigate this difficult life transition.

“The NHS is one of the biggest employers of women in the world. With one in eight women leaving the workforce due to the menopause, it makes huge sense to invest in tools to retain experienced NHS staff...”

Jenny Thomas, DigitalHealth.London

13 As ‘Femtech’ is still the most widely recognised term, we have continued to use it throughout this section.
Key challenges
New technologies empowering women’s health face challenges around data privacy, evidence generation and adoption. ORCHA review and certify digital health technology and believe only 15% of new digital health tools aimed at women meet quality thresholds. Evidence is crucial to ensure women are given the best health solutions.

Widespread adoption of evidence backed digital tools would support an under-pressure health system. However, for the UK to benefit from the technology, the workforce requires upskilling, empowerment, and support. At NHS leadership level, work is being done to upgrade IT systems and the quality of data being shared. Although important as a foundation, there is little reimagining of pathways and considerations about improvements for women.

There is growing evidence that shows that health tech can reduce inequalities and access to healthcare advice. The taboo of women’s health is being reduced and sickness absence rates are being reduced. However, founders need access to the tools required to evaluate their solutions. A women’s health Fund would help to accelerate innovations in this space and could mirror the impact seen from the Diabetes Transformation Fund.

“Since launching the DigitalHealth.London Accelerator programme five years ago, I’ve seen the tide slowly begin to turn and we are starting to see new digital technologies emerge to support women.”

Jenny Thomas, DigitalHealth.London
Developing a non-hormonal therapy for menopause symptoms

Dr Mary Kerr, CEO of NeRRe Therapeutics, spoke about the unmet need and exploration of the potential role of a non-hormonal treatment for symptoms of menopause.

Menopause affects all women, with 20 – 40% of menopausal and perimenopausal women experiencing symptoms that affect their daily functioning to an extent that requires them to see a physician. These symptoms are chronic, affecting women for up to ten years, and can be debilitating. Recent news reporting indicates that up to 13 million women in the UK are currently going through the menopause or perimenopause.

Risk factors for leading therapeutics

Hormone replacement therapy (HRT) is currently the leading therapy for menopausal symptoms and is effective in treating vasomotor symptoms – hot flushes and night sweats. However, in 2002 a report by the Women’s Health Initiative showed links between HRT and increased risk of breast cancer and cardiovascular conditions. This led to an immediate and dramatic reduction in the use of HRT and increased interest in non-hormonal interventions.

Most menopausal women will experience hot flushes and night sweats. Other common symptoms include sleep deprivation, vaginal dryness, weight gain, depression, and anxiety. In another report, the Women’s Health Initiative found that any association with vasomotor symptoms gave an 18% increase in the risk of diabetes, and a 48% increase in risk for the 20% of women experiencing severe symptoms of the menopause. The underlying causes of this association are not well-understood.

Developing non-hormonal treatments

Neurokinins, which are peptide transmitters, are increasingly recognised as important modulators of sex hormone biology. The KNDy neuronal complex in the hypothalamus expresses kisspeptin, neurokinin B (NK-B), and dynorphin. Kisspeptin affects the gonadotropin-releasing hormone (GNRH) pathway, which controls sex hormone release in women (and men). KNDy neurons also project into an area of the brain associated with thermoregulation, a pathway which is disrupted in post-menopausal women, in whom the KNDy neuronal complex has been found to be enlarged.

This is accompanied by increased NK-B gene expression in the hypothalamus.

KaNDy Therapeutics began exploring the potential of Neurokinin receptor antagonists in treating women’s health conditions, focusing on the menopause, and found scientific evidence indicating a potential role of NK-B and the NK-3 receptor in vasomotor symptoms, including research showing that an infusion of NK-B induced hot flushes in women.

Neurokinin 1 receptor antagonists and symptoms of the menopause

Clinical trial data supports the role of Neurokinin 1 (NK-1) in many of the symptoms experienced by menopausal women, including hot flushes, sleep difficulty, mood, and bladder control. A study showing the efficacy of NK-1 receptor antagonists in treating insomnia found that the compound did not cause the residual cognitive impairments associated with some other insomnia treatments.

Many aspects of women’s health, including menstruation, pregnancy, conditions such as endometriosis and polycystic ovary syndrome, and the menopause are associated with mood alterations, though the nature of the association between mood and sex hormone biology is not well-understood. According to a proof-of-concept study, NK-1 receptor antagonists improve mood. Importantly, the improvement was found to be fast-acting, and did not lead to the weight gain that can be associated with other antidepressants.

Two non-hormonal compounds resulting from work initially carried out by KaNDy therapeutics, before acquisition by Bayer Pharmaceuticals, are now in stage three clinical development.
Diversity and inclusion, empowerment of women in women’s health, and the importance of an evidence-based approach

Dr Pauline Williams, GSK, chaired the session with panellists: Dr Metin Gülmezoglu, Concept Foundation; Professor Dame Lesley Regan, International Federation of Gynecology and Obstetrics; Dr Christine Ekechi, Imperial College Healthcare NHS Trust; Dr Lilian Hunt, EDIS.

Diversity, inclusion and the impact of inequality

- A national strategic plan for women’s health is needed. Women are 51% of the population and 47% of the workforce yet they have been disproportionately disadvantaged over decades.
- A recent HFEA (Human Fertilisation and Embryology Authority) report found that Black and Asian women were more likely to have poorer outcomes when seeking fertility treatments.
- The Lancet found that Black women are more likely to suffer recurrent miscarriage.
- Health inequalities exist alongside wealth inequalities. Receiving secondary education also predicts better health. In a global context, the education of women is central to women’s empowerment.
- The traditional approach to training doctors focuses on disease intervention rather than prevention, which is only a third of the problem. To make an impact, there is a need to consider the lifestyle and to focus on the things that matter most to girls and women.
- Topics that can be considered ‘embarrassing’ or ‘taboo’ around sex, fertility, abortion etc cause health inequality and must be discussed.
- All ethnicities and all races must be involved in the discussion from the beginning, and not just from a medical perspective. The social determinants of health are the main driving force of health.

Data gaps in women’s health

- There is a significant lack of data around race and ethnicity in areas such as fertility, maternal mortality and postmenopausal health.
- Collecting data based on ethnicity, such as diet amongst geographical groups, will provide more information than data based on race, which is a social construct. Recent immigrants, as a culture, are often healthier than their second or third generation descendants.
- Black and Asian Minority groups are overrepresented in the lower socio-economic groups, which is a major marker for poorer outcomes. It is important to understand why this is the case.
- Basic science of pregnancy and the understanding of early pregnancy and complications should be improved. For example, in the treatment of pre-eclampsia, magnesium sulphate has been used since the 1950s. Based on the scientific advances in the last 70 years across other fields, we would expect there to have also been more innovation in the treatment of pre-eclampsia.

“Often, we talk about Black, Asian, or ethnic minority women only as receivers of innovation, rather them being the drivers and innovators of new technology.”

Dr Christine Ekechi, Imperial College Healthcare NHS Trust

14. The panel discussion focused on ethnic diversity
Diversity in research

- Diversity and inclusion must be considered across the entire cycle from funding and prioritization of where unmet needs are, design of research, evaluation, and the sharing of results. Collaboration across funders and organizations is critical to ensure success.

- The UK is far behind its peers. Many organisations across the globe have put into practice policies that require sex or gender analysis within research at the proposal stage. The Canadian Institute for Health Research has been supporting diversity in research for over a decade.

- The UK is starting to make progress and discussing the use of both male and female mouse models, which is widely considered to be good research.

- Large shifts to support historically under supported areas are needed and funders have a responsibility to help researchers fill the gap. Greater funding support into women’s health research is important and there are many global examples of countries doing this. A report by EDIS is documenting this approach. Funders from the UK should note that sex, gender, or diversity analysis can and should be embedded across all areas.

- Cross disciplinary teams including social scientists, engineers and others should be encouraged to bring in new innovations.

“Why are pregnant women at risk of pre-eclampsia or pre-term labour? There are still no dedicated, effective and safe medicines, despite huge progress in our understanding in the last thirty years.”

A Metin Gülmezoglu, Concept Foundation

“It’s vital that the research we commission, design, and fund includes consideration of sex and gender wherever relevant and this is both promoted and supported by inclusive education and policies.”

Dr Lilian Hunt, EDIS, Wellcome Trust

17. https://osf.io/3agxf/
Barriers to implementation

- Developing solutions and new medicines for pregnancy specific conditions can only be done with the participation of pregnant women.

- Any medicine with a chance of being delivered to pregnant women must go through clinical trials with women. Currently, the responsibility of the choice is passed onto the care provider and the patient.

- Collaborations between global regulatory bodies have potential to change and reduce barriers.

- Women’s health and the life arc much be approached from two aspects – prevention through social determinants and new treatments. Currently, there is an issue with the development of new treatments for pregnancy.

- The term “Femtech” has isolated what is actually “inclusive health care technology” and may have led to reduced funding in an essential area.

- The UK has a high 45% unplanned pregnancy rate, which signifies lack of necessary sexual education.

- Abortion figures have risen in recent years amongst women in their thirties and forties who are unable to access long term reversible contraception.

- COVID-19 has assisted in simple key recommendations being implemented such as the contraceptive pill becoming available over the counter. Comparably, a fraction of the years of research went into Viagra before it became available in this way.

- It is unlikely that any single institution can deal with big challenges such as pregnancy complications and new medicines. They require population-wide studies. Similarly international collaborations in other diseases have been very successful.

- Government bureaucracy has prevented many simple and practical solutions for women’s health being implemented. One such solution would be to develop women’s health hubs, which deal with all elements of service providers in one visit.

- The problem with a lack of funding in women’s health research means that engineers and scientists are disincentivized from working in this area.

- The UK is on the cusp of a change in funding policy. The lack of activity in women’s health research means there is a lot of low hanging fruit to be harvested.

“The UK is far behind its peers. There are many organisations across Europe and North America that have put policies within their funding bodies that requires sex or gender analysis within research at the proposal stage.”

Dr Lilian Hunt, EDIS, Wellcome Trust

“When you get it right for women, everyone benefits. When you do it right, it is much, much cheaper, because it is always more cost-effective to prevent problems from developing.”

Professor Dame Lesley Regan, International Federation of Gynecology and Obstetrics

Women’s health: a life course approach – Conference report 18
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