## Summary

- Women's health is an important policy issue with relevance across society and implications for individual and population health and wellbeing, the economy and equality. While the Academy welcomes the Government's ambitious plans to develop an evidence-based Women's Health Strategy, we also recognise the huge scope of this topic, particularly given that the historical neglect of women's perspectives has led to a data gap and systems that are not built to meet the needs of women. Our Fellows emphasised that for this Strategy to be effective, sustainable and inclusive, the Government must commit to addressing women's health in its entirety, using a comprehensive system-level approach.
- Systems, including the healthcare system, that meet women's health needs must be built on a foundation of scientific evidence that is representative of women's biology, experiences, and perspectives. The exclusion of female animals and women from preclinical and clinical research, respectively, and the failure to disaggregate data by sex and gender ${ }^{1}$ weakens this foundation, undermining the safety of women in the health system, preventing them from benefitting from research, and representing a huge opportunity cost for the UK R\&D sector and economy. Therefore, it is essential that the needs of women are routinely considered, by collecting accurate and relevant clinical data and considering sex/gender as an experimental variable by default at all stages of research and policy making.
- Women are at an increased risk of experiencing multiple long-term conditions and will therefore benefit from an integrated system that treats patients holistically rather than from the perspective of a single service or disease. To achieve the NHS Long Term Plan's vision of an integrated health service that prioritises prevention as well as treatment, key intervention points should be used to provide personalised risk prediction, so that preventive measures can be targeted in relation to risk. ${ }^{2}$ The Academy strongly believes that embedding multidisciplinary and collaborative research within the health system is crucial to achieving these aims, as well as benefitting patients and researchers. ${ }^{3}$
- While we use the terms 'women' and 'girls' throughout this response, the Academy is aware that we live in a gender diverse society. Despite a significant lack of evidence about the care and experiences of transgender, non-binary and intersex individuals within the UK healthcare system, the limited evidence available suggests that these groups face discrimination within the health system and worse health outcomes. ${ }^{4}$ We believe that a Women's Health Strategy should be inclusive of all those who identify as women, as well as those assigned female at birth who do not identify as women, while also acknowledging the specific needs of these populations.
- We give multiple examples where the intersection of gender with ethnicity, language, level of education and other characteristics impacts a woman's ability to access healthcare and lead a healthy

[^0]health and social care. https://acmedsci.ac.uk/filedownload/17381964; Academy of Medical Sciences (2021). Transforming health through innovation: Integrating the NHS and academia.
https://acmedsci.ac.uk/file-download/23932583
${ }^{4}$ Scottish Trans Alliance (2016). Non-binary people's experiences of using UK gender identity clinics; Monro S , et al. (2017). Intersex, variations of sex characteristics and DSD: the need for change; Hobster K. \& McLuskey J (2020). Transgender patients' experiences of healthcare. British journal of nursing 29(22), 1348-1353.

## life. We believe it is necessary for the Strategy to consider the effects of intersectionality across all six themes outlined in the consultation.

- Furthermore, the Academy recognises that increasing health inequalities in the UK cannot be attributed solely to the health system, instead also reflecting inequities across the social determinants of health, many of which intersect with gender. Therefore, the Women's Health Strategy should consider the impact of all government policy and legislation on women's health and be designed alongside other government strategies to reduce inequalities across the UK, such as the 'levelling up' agenda.


## Introduction

The Academy of Medical Sciences promotes advances in medical science and supports efforts to translate these advances into healthcare benefits for society. In April 2021, the Department of Health and Social Care (DHSC) opened a call for evidence to inform the priorities, content and actions of England's first Women's Health Strategy. Our response is based on our previous policy work across a broad range of topics with relevance to women's health, as well as written and spoken evidence from members of our elected Fellowship (Annex 1), which includes some of the UK's foremost experts in clinical and academic medical research. The consultation asked for evidence on six core themes. ${ }^{5}$ Our response includes sections on Themes 1-5 with signposted evidence relevant to Theme 6 throughout. ${ }^{6}$ Due to space limitations, we are unable to cover the topics of gender-based and domestic violence, sexual abuse, and female genital mutilation. However, these are also important issues with significant impacts on women's health and wellbeing. ${ }^{7}$

## 1. Women's voices

## Evidence of women's voices not being listened to

1.1. The Independent Medical Devices and Medicines Safety Review exposed systematic problems with respect to how the English healthcare system listens and responds to women's concerns about their health and care. ${ }^{8}$ As outlined below, these issues extend beyond the reporting of adverse effects of medical interventions.
1.2. At the level of the individual, there is a plethora of evidence of women not being listened to, not being asked the right questions at the right time, having their pain or symptoms normalised, or being dismissed entirely by healthcare professionals (HCPs). We were informed of examples relating to menstrual disorders (including abnormal uterine bleeding and menstrual pain), ${ }^{9}$ pregnancy, ${ }^{10}$ miscarriage, ${ }^{11}$ and chronic pain. ${ }^{12}$
1.3. HCPs exhibit the same levels of implicit bias as the general population with regards to characteristics such as gender and race, likely influencing diagnosis and treatment decisions and levels of care (1.9). ${ }^{13}$ As an example, women from ethnic minority groups are more likely to report not always

[^1]O'Flynn N \& Britten N (2000). Menorrhagia in general practice--disease or illness. Soc Sci Med 50(5), 65161; APPG on Women's Health (2017). Informed
Choice? Giving women control of their healthcare.
${ }^{10}$ National Perinatal Epidemiology Unit (2014). Safely
delivered: a national survey of women's experience of maternity care.
${ }^{11}$ The Lancet (2021). Miscarriage: worldwide reform of care is needed. Lancet 397(10285), P1597.
${ }^{12}$ Unruh AM (1996). Gender variations in clinical pain experience. Pain 65(2-3), 123-167; National Institutes of Health. How Sex/Gender Influence Health \& Disease $(A-Z)$.
${ }^{13}$ FitzGerald C \& Hurst S (2017). Implicit bias in healthcare professionals: a systematic review. BMC medical ethics 18(1), 19.
being involved in decisions about their care or not having confidence and trust in HCPs before, during and after pregnancy. ${ }^{14}$
1.4. As well as ensuring women's voices are listened to, it is vitally important that the healthcare system actively creates opportunities for women's voices to be heard. For example, in a 2016 survey, although 84\% of women felt comfortable talking to an HCP about their mental health during and after pregnancy, only $31 \%$ were asked about their mental health by a GP and only $4 \%$ by an obstetrician. ${ }^{15}$
1.5. In 2000, it was said of menstruation and menstrual disorders: 'There can be no other disease or condition that affects so many people on such a regular basis with consequences, at both the individual and societal levels, which is not prioritised in some way by health professionals or policy makers'. ${ }^{16}$ We were informed that little has changed since; indeed, there have been no new nonhormonal medical interventions for heavy menstrual bleeding in the last 30 years. ${ }^{17}$ Dismissal at the institutional level can also be seen in miscarriage care, with a lack of progress in care and medical research being attributed to a 'pervasive acceptance' of miscarriage. ${ }^{18}$

## The impact of taboos and stigma

1.6. Stigma surrounding gynaecological health influences women's care seeking behaviours and ability to communicate symptoms, which has consequences for their future reproductive and sexual health. A survey of 7,367 women revealed that over $30 \%$ experienced severe reproductive health problems in the last 12 months, yet less than half sought help. ${ }^{19}$ Menstruation, ${ }^{20}$ sexual health, ${ }^{21}$ the transition to menopause, ${ }^{22}$ incontinence ${ }^{23}$ and perinatal mental illness ${ }^{24}$ all have significant impacts on women's physical, sexual, mental and social wellbeing and yet are still seen as a taboo subjects, discouraging women from seeking advice and treatment.
1.7. Gynaecological and mental health stigma is impacted by the intersecting effects of gender, race, disability, sexuality, and other protected characteristics. For example, although Black women are the group most likely to experience a mental health disorder, a white person is more than twice as likely to be receiving mental health treatment than a Black person. ${ }^{25}$ Reasons for this include stigma, racism, and fear or mistrust of services. ${ }^{26}$ At a recent Academy workshop about mental health, ${ }^{27}$ one expert with lived experience stated that these fears are well-founded, given evidence that Black people are four times as likely to be detained under the Mental Health Act than white people. ${ }^{28}$

[^2][^3]
## Male as default

1.8. Failure to disaggregate data by sex or gender in all types of research and subsequent design based on the 'standard male' has led to a default male bias in many aspects of women's lives, including the workplace and public spaces, medical research (Theme 5) and healthcare, with wide ranging impacts on women's health. ${ }^{29}$ A timely example is the supply of ill-fitting personal protective equipment (PPE) designed for men that often fails to protect women and poses additional safety hazards (relevance to Theme 6). ${ }^{30}$
1.9. The default male bias has negative consequences for women with diseases that affect both sexes. A clear example of this is in the diagnosis, treatment, and aftercare of cardiovascular disease (CVD). A woman is $50 \%$ more likely to receive the wrong initial diagnosis for a heart attack. ${ }^{31}$ However, even with improved diagnostic methods, women are half as likely to receive treatments as men, partly due to the misperception that CVD is a man's disease and unconscious bias in healthcare delivery. ${ }^{32}$ Research has found that between 2002 and 2013, 8,243 women in England and Wales lost their lives because they did not receive the same standard of care as men. ${ }^{33}$

## 2. Information and education on women's health

## Healthcare professionals' awareness and education

2.1. Areas where a lack of understanding and awareness among HCPs was identified as barrier to correct diagnosis and good care include menstrual health (including fibroids), ${ }^{34}$ endometriosis, ${ }^{35}$ the menopause and perimenopause, and multimorbidities during pregnancy. This has a direct impact on women's health outcomes and productivity and increases healthcare costs. Proposed solutions include standardisation of data collection, incorporation of patient-reported outcome measures, and supporting the implementation of existing NICE guidelines. It is important that HCPs at all career levels (including in decision-making roles) are kept up to date with the relevant NICE guidelines and latest diagnostic and treatment strategies by continued training and embedding research into the NHS (3.8, 5.27).

## Empowerment of women and education of all

2.2. Education is an important means to reduce stigma and empower women to make informed evidence-based decisions about their health.
2.3. In a YouGov survey, one in four women reported not understanding their menstrual cycle. ${ }^{36}$ A lack of awareness about 'normal' menstruation translates to a normalisation of abnormal symptoms of disorders such as heavy bleeding, endometriosis and fibroids, delaying diagnosis. ${ }^{37}$
2.4. Apps that improve menstrual health literacy were noted as important shared decision-making tools for healthy women, patients and HCPs. ${ }^{38}$ While using more technology may be convenient for some patients, it should be noted - especially as COVID-19 restrictions have increased the prevalence of virtual methods of consultation (relevance to Theme 6) - that some may be disadvantaged if

[^4][^5]they are less able to engage with the necessary technology or articulate symptoms, ${ }^{39}$ leading to health issues being diagnosed later or not at all.
2.5. The Menstrual Health Coalition, the Royal College of Obstetricians and Gynaecologists (RCOG) and others have identified education (preferably prior to or around when a girl first experiences menstruation) as an important intervention point for educating girls and boys about women's health and sexual wellbeing and reducing stigma. ${ }^{40}$ The inclusion of men and boys in women's sexual, menstrual and gynaecological health education was highlighted as essential to help reduce stigma. Education should not only aim to improve understanding of the biology of specific women's health issues, but also cover general and sexual wellbeing. ${ }^{41}$ Although the introduction of compulsory Relationship and Sex Education in the school curriculum was welcomed, it was noted that there should be mechanisms in place to track its impact on health and wellbeing to identify successes and shortcomings. Furthermore, the lack of investment in school nurses was identified by some of our Fellows as a lost opportunity for education and early identification of those with reproductive and menstrual health problems.
2.6. Pregnancy and the post-partum period were identified as other significantly underutilised but highly important intervention points for education, with targeted parenting support and education likely to benefit the health of both child and mother

## Barriers to information access

2.7. Language and low health literacy were repeatedly identified as the most significant barriers to communication of information and care provision, particularly affecting those not fluent in English, those with learning, speech or hearing impediments, those with heavily stigmatised health issues, and older people. It was also noted that reduced ability to eloquently describe symptoms can affect timeliness of care.
2.8. Several useful interventions were identified, including introducing structured prompting as best practice. The attendance of a support person, be it a family member or interpreter, can be useful in some circumstances, but can also introduce problems such as issues around patient confidentiality and challenges accurately translating complex medical information. Powerful alternatives include translation aids and apps (e.g. the Pocketalk real-time language translation devices being trialled by Lancashire and South Cumbria NHS Foundation Trust), ${ }^{42}$ and visual aids such as flip charts with standard questions in multiple languages.

## 3. Women's health across the life course

## Shortcomings in service delivery across the life course and opportunities for action, research and innovation

3.1. Lack of awareness and normalisation of specific women's health conditions and sex-specific differences across a range of disorders, compounded by pervasive stigma surrounding women's health, has impacted the ability of the healthcare service to respond to women's needs (Theme $\mathbf{1}$ and 2). We have highlighted examples in relation to menstruation (1.2, 1.5, 1.6, 2.3), endometriosis (2.1, 2.3), fibroids (2.1, 2.3), mental health (1.4, 1.6, 1.7), cardiovascular disease (1.9), pregnancy (1.2, 1.3, 1.4, 2.1), the (peri)menopause (1.6, 2.1), chronic pain (1.2), incontinence (1.6) and miscarriage (1.2, 1.5). Here we describe additional opportunities for the health service to better meet women's needs across the life course.

[^6][^7]3.2. One problem identified across a range of women's health issues was the frequent focus on, and treatment of, symptoms rather than causes; for example, the typical practice of using oral contraceptives to treat the symptoms of heavy menstrual bleeding and endometriosis, instead of developing a plan that meets the needs of the individual.
3.3. Public Health England (PHE) estimates that publicly provided contraception delivers a return on investment of $£ 9$ over 10 years for every $£ 1$ spent. ${ }^{43}$ However, we heard that the devolution of sexual health services to local authorities has resulted in a postcode lottery in service quality and increased numbers of unplanned pregnancies. A cost-effective innovation in contraception delivery is to provide women with contraception counselling during pregnancy and timely post-partum contraception, demonstrated in south-east Edinburgh and north-west London. ${ }^{44}$ Post-partum contraception before discharge after birth is recommended by leading medical organisations to reduce contact of new mothers with health services during the COVID-19 pandemic (relevance to Theme 6). ${ }^{45}$
3.4. One concern repeatedly emphasised to us was the observed decline in the quality of antenatal and post-natal care services over recent years, pre-dating but exacerbated by the COVID-19 pandemic (relevance to Theme 6). Of note, insufficient numbers of midwives, reduced in-person visits and reduced support with feeding have been associated with the increasing prevalence of perinatal mental health issues and infant readmissions. ${ }^{46}$ Health conditions such as peritoneal infection, neonatal jaundice and post-natal depression are likely diagnosed at a later stage in virtual compared to in-person examinations, particularly for women less able to clearly articulate symptoms. Later diagnosis is associated with worse health outcomes and increased care costs. Solutions include reinvestment and the implementation of already well-evidenced innovations in post-natal service delivery, such as midwifery-led post-natal care. ${ }^{47}$
3.5. Although the Academy welcomes the commitments to improve perinatal mental health services in the NHS Long Term Plan, ${ }^{48}$ it is essential that such changes are made based on strong evidence. We were informed that there is little existing UK-based research into the prevalence, severity and duration of perinatal mental health issues. Evaluation of plans to improve perinatal mental health services should be a priority to provide evidence for their effectiveness. Risk factors for perinatal mental health issues, however, are well researched, and there is now a need to translate that evidence into clinical practice. ${ }^{49}$ The Academy's 2017 FORUM report on Personalised Psychiatry noted that the NHS is increasingly enabling HCPs to track risk factors for diseases during pregnancy, and that markers for post-natal mental health issues should be incorporated into these measurements. ${ }^{50}$
3.6. Healthy life expectancy (HLE) has declined for women over the last 10 years. ${ }^{51}$ As discussed at a 2020 Academy conference on Healthy Ageing, ${ }^{52}$ in order for the Government to achieve its target of increasing HLE by at least five years by 2035, there is a need for an interdisciplinary life

[^8][^9]course approach encompassing a range of biomedical, technological, public health and policy interventions, which takes into account the sex differences in biological ageing. ${ }^{53}$
3.7. There is evidence that women are at an increased risk of experiencing Multiple Long-Term Conditions (MLTC). ${ }^{54}$ MLTC represents a significant burden on the health system, as its presence is associated with an increased rate of GP consultations, prescriptions and hospitalisations. ${ }^{55}$ We were informed that the health system is currently not fit to respond to the needs of women with MLTC, as it is based upon fragmented 'single-disease' services. Taking a more holistic approach (3.8), improving the awareness and evidence-base of the effect of multimorbidities on women, particularly in pregnancy, and training HCPs to manage the cumulative effects of multiple conditions is required.

## A multidisciplinary and integrated life course approach to achieve holistic care

3.8. By separately treating the different health challenges that women may face throughout the life course, the current system overlooks the linkage and dependencies between health needs. As outlined in our response to the Health and Social Care Select Committee inquiry into the DHSC's White Paper on health and social care, the Academy welcomes proposals to align the healthcare, public health and social care systems. ${ }^{56}$ However, a holistic and integrated approach must be based on a framework of interdisciplinary and collaborative research. In addition to improving relationships and data linkage between different health and social care services, and embedding research within the NHS (5.27), the Academy strongly believes that the inclusion of research in the Health and Social Care Bill and the integrated care systems framework is key to deliver the Government's ambition of creating an integrated and innovative healthcare system, and one that can respond to women's needs.
3.9. The Edinburgh Excellence in Pelvic Pain and Endometriosis Care and Treatment (EXPPECT) centre is a pioneering example of integrating research and clinical care, aiming to provide high-quality, evidence-based and patient-centred treatment offered by a specialised team of clinicians and researchers across a range of disciplines. ${ }^{57}$ The challenges and opportunities posed by collaborative research and recommendations for the facilitation of interdisciplinary working are outlined in the Academy report on 'team science'. ${ }^{58}$

## Utilising intervention points

3.10. Certain symptoms and health issues can represent risk factors for health problems later in the life course. For example, although miscarriage is often treated as an independent event, it is in fact associated with a higher risk of CVD, venous thromboembolisms, mental health illnesses and complications in subsequent pregnancies. ${ }^{59}$ Therefore, every time a woman accesses healthcare should be seen as an opportunity to pick up hidden health concerns and risk factors, put a plan in place to mitigate the risk of developing further conditions, and enable precision prevention. ${ }^{60}$ Common intervention points, such as accessing sexual health services and ante- or post-natal care, were identified as particularly useful opportunities to apply these practices.

[^10][^11]3.11. A service innovation that uses precision prevention is the implementation of high-risk human papillomavirus (hrHPV) testing as the primary approach in cervical screening. ${ }^{61}$ As with many health issues, sexually transmitted infections exhibit a heterogeneous prevalence across the population. Women from more deprived areas are at greater risk of hrHPV, yet less likely to attend screening. ${ }^{62}$ Therefore, while utilising intervention points is important, healthcare services that utilise the life course approach must always also consider how to connect with women from 'hard to reach' groups.

## Looking beyond the healthcare system

3.12. Gender equality is recognised as one of the most important determinants of health of both women and men. ${ }^{63}$ Addressing systematic gender inequalities beyond health and healthcare will therefore have a profound positive impact on the health of all in society. The reverse is also true, with evidence that health policies that fail to address the needs of men or women exacerbate gender inequalities more widely. ${ }^{64}$
3.13. The Marmot Review 10 Years On highlighted that increasing health inequalities in the UK cannot be attributed solely to changes in the health and social care system, but instead reflects increasing inequities in power, money and resources - the social determinants of health - all of which are associated with a person's gender and other demographic characteristics. ${ }^{65}$
3.14. Recent analysis shows that between the most and least affluent areas in England, the difference in life expectancy and HLE for women is 7.7 and 20 years, respectively. ${ }^{66}$ The Government's goal of extending HLE by five years by 2035 can only be achieved if action is taken to reduce the marked socioeconomic inequalities that exist in women's health across the UK, ${ }^{67}$ and therefore it is important that the Women's Health Strategy is designed with the Government's levelling up agenda in mind.
3.15. We believe that the Women's Health Strategy should look beyond the role of the NHS and social care system and should consider how implementation of all government legislation affects intersections between gender and the social determinants of health throughout the life course. To this end, design, monitoring and evaluation of policy should be based on robust sex- and gender-disaggregated data and evidence, to avoid default male bias (1.8).

## 4. Women's health in the workplace

4.1. Gender-diverse workforces benefit from improved productivity, innovation, decision-making, employee retention and satisfaction, ${ }^{68}$ and promote the consideration of women-specific issues in life sciences research (5.19). However, the burden of women's health issues and unpaid care load can affect their productivity, workforce participation and wealth.
4.2. Although UK-based research on these subjects is lacking, conditions such as heavy menstrual bleeding, fibroids, endometriosis and chronic pelvic pain, as well as symptoms of menopausal transition cause women to lose productivity, ${ }^{69}$ reduce their working hours, receive disciplinary

[^12]action, resign from leadership roles, and leave the workforce altogether. ${ }^{70}$ This problem is in part due to significant stigma surrounding these issues in the workplace. Symptoms of the menopausal transition (particularly the perimenopause) have a debilitating impact on one in four women's working lives, at a stage when they are breaking through to senior, decision-making roles in the workforce (with implications for research, 5.19). ${ }^{71}$ There is an urgent need to research and address the impact of debilitating reproductive health problems on younger women and of the menopausal transition on the ability of women to remain productive in the work place, particularly in the over half of women in low-paid or manual jobs. ${ }^{72}$ To facilitate this, we agree that menstrual disorders and menopausal symptoms should be listed as reasons for absenteeism in the ONS annual Sickness absence in the UK labour market datasets.
4.3. Globally, $75 \%$ of vital societal yet unpaid work is done by women, including caring for children, partners and elderly relatives. ${ }^{73}$ The burden of this unpaid work can negatively impact women's health, wealth, employment, productivity and retention in the workforce. While men with two children have $22 \%$ higher median weekly earnings than those without, the median weekly pay of women in the same age bracket with two children is $26 \%$ lower than women with none. ${ }^{74}$ Although the reasons for this are multifactorial, loss of employment track record and discrimination against women (especially mothers) in the labour market are key drivers of the gender pay gap. ${ }^{75}$
4.4. This unpaid work is essential in a functioning society; incorporation of such services into measures of GDP would increase it by between $15-70 \%$ depending on the country and valuation method, in addition to other macro-economic benefits. ${ }^{76}$ Despite this, unpaid care work is seen as low-status and low-skill, hugely impacting women's confidence and status, particularly in the workforce, with negative implications for women returning to work after career breaks. ${ }^{77}$ A cultural and political shift is required in how society and governments view caring responsibilities (as called for in Sustainable Development Goal 5, target 4), ${ }^{78}$ for example, by integrating unpaid work into national economic frameworks and indices of economic progress.
4.5. Other measures to improve women's health and support workforce participation include flexible working; providing mentorship and support for physical and mental health (e.g., paid returner programmes); ${ }^{79}$ raising awareness of women's health issues to remove taboo/stigma; considering women's needs when designing the workplace environment; and embedding women's health issues into workplace policies, including health and safety practices and sickness and absence management policies. ${ }^{80}$ Most importantly, there is no one-size-fits-all approach to supporting women in the workplace. Individuals with different health issues, backgrounds and roles will require tailored support.

9(6); Davies SC (2014). Annual Report of the Chief Medical Officer, The Health of the 51\%: Women. ${ }^{70}$ British Medical Association (2021). Challenging the culture on menopause for working doctors report; Critchley J, Schwarz M \& Baruah R (2021) The female medical workforce. Anaesthesia 76(S4), 14-23.
${ }^{71}$ Davies SC (2014). Annual Report of the Chief Medical Officer, The Health of the 51\%: Women.; Brewis J, et al. for the Department for Education (2017).
Menopause transition: effects on women's economic participation.
${ }^{72}$ Brewis J, et al. for the Department for Education (2017). Menopause transition: effects on women's economic participation.
${ }^{73}$ Royal Society of Edinburgh (2013). Women, work and care: a challenge for the $21^{\text {st }}$ century; McKinsey Global Institute (2015). The Power of Parity: how advancing women's equality can add $\$ 12$ trillion to

[^13]
## 5. Research, evidence and data

5.1. The frequent consideration of male-as-default from preclinical to clinical research puts women at risk, prevents women from accessing the benefits of research, and represents a huge opportunity cost to the UK economy. It also undermines the foundation of scientific evidence upon which the health system is built.

## Preclinical research: sex as an experimental variable

5.2. Preclinical research typically makes greater use of male animals and cells or fails to report the sex of animals and tissues used. Consideration of sex and the disaggregation of data by sex is critical to the interpretation, validation, and generalisability of research findings and may inform and undermine clinical interventions. ${ }^{81}$
5.3. Furthermore, not considering sex as an experimental variable in preclinical research prevents the identification and research of sex-specific disease mechanisms and inhibits drug discovery. For example, despite pulmonary arterial hypertension (PAH) being more prevalent in women, most PAH research has historically been conducted in male animals. The inclusion of female animals in PAH studies in recent decades has revolutionised the understanding of the disease, including sex-specific elements of disease presentation, and is aiding the discovery of therapeutics (e.g. the drug anastrozole was found to ameliorate disease in female but not male mice). ${ }^{82}$
5.4. Given the frequent failure of preclinical models to translate in clinical studies and the reproducibility crisis, it is important to design studies with sex as an experimental variable, particularly for disorders where women and men experience different symptoms. If not addressed then predictions about therapeutic intervention safety, efficacy and dosing may not be generalisable to women, and women taking part in clinical trials may experience an increased risk of adverse drug reactions (ADRs) (5.7).

## Clinical research: exclusion of women

5.5. As in preclinical research, clinical research has historically excluded women, partly due to a false assumption that drugs work similarly in both sexes and partly to avoid variability introduced by women's hormonal fluctuations.
5.6. Although international guidelines have been introduced to increase the enrolment of women, their recruitment is still often insufficient. Women are frequently only included later in the drug development process, and those from ethnic minority and low socioeconomic groups, as well as pregnant women, are typically under-represented. Furthermore, many clinical studies still fail to power and stratify their results to identify sex-specific side effects or outcomes. ${ }^{83}$ For example, despite well-known sex-differences, women comprised on average only $\sim 27 \%$ of participants in the 36 landmark trials for congestive heart failure between 1987 and 2012 and of those only $44 \%$ conducted sex-based subgroup analyses. ${ }^{84}$
5.7. This exclusion and lack of sex- and gender- disaggregated evidence endangers women's health. Indeed, of ten drugs withdrawn from the U.S. market between 1997 and 2000 because of lifethreatening health effects, eight of these posed greater health risks for women than for men, ${ }^{85}$ and a recent study showed that women are twice as likely to experience and report an ADR as men. ${ }^{86}$

[^14][^15]It is estimated that ADRs account for up to $8 \%$ of unplanned hospital admissions in the UK, costing the NHS $£ 1-£ 2.5$ billion annually. ${ }^{87}$
5.8. The common practice of prescribing equal doses for men and women, generally based on malespecified dose regimens, neglects sex differences in pharmacokinetics (including changes during the menstrual cycle and across the life course), fat distribution and body weight leading to overmedication of women and women-biased ADRs. ${ }^{88}$ As there is a move towards personalised medicine in the NHS, considerations on the most effective use of existing treatments based on sex must become commonplace. ${ }^{89}$
5.9. Another consequence is that women miss out on the benefits both of participating in trials and from the outputs of research. For example, despite women making up over half of HIV patients globally, a Phase III trial of the drug Descovy for HIV-1 pre-exposure prophylaxis did not include a sufficient number of women, resulting in the FDA imposing a restricted label, preventing its use by those 'at risk from vaginal sex'. ${ }^{90}$
5.10. One issue repeatedly stressed by our Fellowship was concern about the widespread exclusion of pregnant and lactating women from clinical trials. Consequently, pregnant women can be prescribed medicines where there is no evidence of the potential harms (e.g. sodium valproate), ${ }^{91}$ or else denied access to potential life-saving medicines or vaccines entirely. Pregnant women have been excluded from $80 \%$ of COVID-19 treatment trials and all COVID-19 vaccine trials (the justification for which was unclear). ${ }^{92}$ This meant that pregnant women were initially unable to access the vaccine, despite being at a higher risk for severe COVID-19, and may have contributed to persisting vaccine hesitancy reported among young women. ${ }^{93}$ In a recent ONS survey of vaccine hesitant adults, 1 in 4 worried the vaccine was not safe and 1 in 17 were pregnant or trying to get pregnant and concerned about vaccine effects on their baby (relevance to Theme 6). ${ }^{94}$
5.11. Even medicines for complications of pregnancy can become the standard of care without full evaluation and regulatory approval. For example, although antenatal corticosteroids are used widely to improve preterm birth outcomes, no robust evaluation of dose responses was ever performed. ${ }^{95}$
5.12. The Academy supports the clinical trial and regulatory community in working towards safe inclusion of pregnant women in clinical trials as a default position. A report by Modi et al. (2021) outlined the evidence that should be collected and considered to enable such safe inclusion, including the balance of risks of exclusion from or inclusion in initial studies, patient and public perspectives, preclinical and clinical developmental and reproductive toxicity data, and approaches to collect data systematically from participants who are unknowingly pregnant at the time of exposure. ${ }^{96}$
5.13. Comprehensive post-market surveillance (PMS) should be used to monitor sex-specific ADRs, particularly in pregnant women, to develop sex-specific prescribing and dosing guidelines for HCPs

[^16]to action. Lancet Global Health 9(3), 366-371;
Vassallo A, et al. (2021). Pregnant women's appetite for risk. Lancet Global Health 9(5), P593; Modi N, et al. (2021). Equity in coronavirus disease 2019 vaccine development and deployment. Am J Obstet Gynecol 224(5), 423-427.
${ }^{93}$ Women and Equalities Committee (2021).
Government failing BAME communities and young women on vaccine take-up.
${ }^{94}$ Office for National Statistics (2021). Coronavirus and vaccine hesitancy, Great Britain: 13 January to 7 February 2021.
${ }^{95}$ Kemp M, et al. (2020). The duration of fetal antenatal steroid exposure determines the durability of preterm ovine lung maturation. Am J Obstet Gynecol 222(2), P183.
96 Modi N, et al. (2021). Equity in coronavirus disease 2019 vaccine development and deployment. Am J Obstet Gynecol 224(5), 423-427.
(e.g. Janusmed Sex and Gender knowledge bank). ${ }^{97}$ Infrastructure for PMS should be improved by addressing current data gaps, optimising data linkage, and improving data quality (e.g. standardisation of data capture using systems such as SNOMED CT). ${ }^{98}$

## Lack of research into women's health issues and sex-specific disease differences

5.14. Women's health issues are frequently understudied, and their research underfunded. For example, for every $£ 1$ spent by the NHS on reproductive care, just 1 p is spent on reproductive research in the UK, substantially less investment than for other conditions such as heart disease ( 7 p for every $£ 1$ ) and cancer ( 12 p for every $£ 1$ ). ${ }^{99}$ Throughout this response we emphasise the need for disaggregating data by sex and/or gender in all research (1.8,3.15) and identify opportunities for further research, including menstruation- and menopause- related issues (4.2), pregnancy-related issues (3.5, 3.7,5.18), and miscarriage (1.5). Other research gaps brought to our attention by our Fellows are noted below.
5.15. The lack of research and development (R\&D) in pregnancy and lactation is well documented, and is attributed to a paucity of specialised funding, the lack of a coordinated network of experienced obstetric investigators, and few incentives for pharmaceutical companies. Some key recommendations to address this are laid out in the RCOG paper 'Developing New Pharmaceutical Treatments for Obstetric Conditions'. ${ }^{100}$
5.16. Furthermore, changes in drug responses and efficacy throughout the life course are poorly studied. Despite preclinical and clinical evidence showing that oestrogen and progesterone levels affect the response of individuals to addictive drugs including nicotine, alcohol, cocaine and stimulants, ${ }^{101}$ there is a paucity of research examining the effect of menopause and menstruation on the efficacy of medical drugs.

## The role of science policy in promoting research that supports gender equity

5.17. To help address the systemic male-as-default bias in research, we recommend that research funders in the UK require and support all grant applicants to factor sex and gender as experimental variables into preclinical/clinical research designs, analyses, and reporting, in line with similar requirements by other major funding agencies across the globe, including U.S. National Institutes of Health and Horizon Europe. ${ }^{102}$ Subgroup analyses will become increasingly important if the healthcare system is to achieve the goal set out in the NHS Long Term Plan to make personalised care 'business as usual' and take advantage of the benefits offered by precision prevention medicine. ${ }^{103}$
5.18. Neglect of women in research means that many aspects of women's physiology are poorly understood, preventing medical progress; for example, we have heard that poor understanding of placental development presents a barrier to the advance of pre-eclampsia interventions. There is currently a lack of women's health-specific research streams of funding in the UK, meaning women's health is often grouped into broader fields that are dominated by non-sex-specific diseases (e.g. maternal health topics like placental biology into endocrine/physiology). There is concern that resulting interdisciplinary competition is leading to women's voices and issues being side-lined,
https://janusinfo.se/beslutsstod/janusmedkonochgenus Ljanusmedsexandgender/inenglish/workingprocess.5.7 28c0e316219da8135e7339.html
${ }^{98}$ Commission on Human Medicines (2021). Report of The Commission on Human Medicines Expert Working Group on Optimising Data on Medicines Used During Pregnancy
${ }^{99}$ Guthrie S, et al. for RAND (2020). Preqnancy research review: Policy report.
${ }^{100}$ RCOG (2015). Scientific Impact Paper No. 50: Developing New Pharmaceutical Treatments for Obstetric Conditions.
${ }^{101}$ Moran-Santa Maria M, Flanagan J \& Brady K (2014). Ovarian Hormones and Drug Abuse. Curr. Psychiatry

Rep 16(11), 511; Yum SK, Yum YK \& Kim T (2019). The problem of medicating women like the men: conceptual discussion of menstrual cycle-dependent psychopharmacology. Translational and Clinical Pharmacology 27(4), 127-133.
102 https://orwh.od.nih.gov/sex-gender/nih-policy-sex-biological-variable; European Union (2021). Gender Equality: a strengthened commitment in Horizon Europe.
${ }^{103}$ NHS (2019). NHS Long Term Plan; Academy of Medical Sciences (2021). Precision prevention for modifiable health risks: Steps to achieving personalised preventive healthcare workshop.
https://acmedsci.ac.uk/file-download/48790754
particularly those that affect sub-groups of women such as faecal and urinary incontinence. It has been suggested that this could be addressed by women's health-specific funding streams and by funders acknowledging the importance of women's health issues during prioritisation exercises.
5.19. One reason for the neglect of women's health issues in research is a lack of women in decisionmaking roles in the research workforce; despite making up 49\% of entry level positions, women make up only $24 \%$ of executive level and $14 \%$ of board level positions in the life sciences industry. ${ }^{104}$ We have heard that the increasing gender diversity of funding panels has promoted the inclusion of women's health issues in research prioritisation exercises. As such, continuing to appoint and support women in decision-making roles within research and the health system is essential (4.1). Innovative initiatives, such as the Academy's SUSTAIN programme, ${ }^{105}$ are valuable in supporting women to thrive in their independent research careers and could be replicated by other institutions to improve retention of women in the workforce.

## Women's health R\&D: an opportunity not to be missed

5.20. Women's health research presents a significant opportunity for both the UK economy, in terms of cost savings and health benefits (3.3), and the UK R\&D sector. The global women's health market was valued at $£ 23$ billion in 2019 and is projected to be worth $£ 37$ billion by $2025 .{ }^{106}$ In particular, investments in women-focused digital therapeutics have surged as the pandemic pushed services online. Despite this recent increase in investor interest, women's health technology start-ups still only accounted for 3\% of overall digital health funding in 2020. ${ }^{107}$
5.21. Most digital health start-ups focus on applications associated with fertility, meaning significant unmet need remains in conditions more stigmatised by society such as menopause, pelvic pain and menstrual disorders. Of the top 39 women's health start-up companies (of which $15 \%$ were UKbased), $54 \%$ focus on reproductive health whereas only $5 \%$ focus on menopausal symptoms. ${ }^{108}$

## How research is used by healthcare professionals and patients

5.22. Scientific evidence should be at the heart of decisions made about the use of drugs and other therapeutic interventions. However, only around a third of the public trust evidence from medical research. ${ }^{109}$ To tackle this and enable shared decision-making in a healthcare setting, evidence generation must be robust, reliable and relevant to patients, in this case women but also ageappropriate; the evidence must be disclosed in an accessible, assessable and usable manner such that it is trusted; and the communication of evidence should be clear, accurate and actionable. ${ }^{110}$ More information and resources to achieve this can be found on the Academy's microsite dedicated to enhancing the use of scientific evidence. ${ }^{111}$
5.23. While some patients may conduct personal research and self-advocate, not all patients have this skill. Therefore, tools to support decision-making should be used, such as the 'pocket guide to helping you decide whether to take a medicine' developed by the Academy. ${ }^{112}$ We also heard that improvements to the NHS website could make it a better source of information; for example, by

[^17][^18]signposting to relevant evidence from experts and patient groups and creating age-appropriate content for young people (2.5).
5.24. National patient-focused digital platforms, such as Patients Like Me (which has a women's health section), take evidence and present it in an accessible format to enable patients and HCPs to make healthcare decisions together. ${ }^{113}$ They can also be used to gather data from patients and involve them in research.

## The importance of embedding research in the NHS

5.25. As stated in the recent Academy report on integrating the NHS and academia, the widening gap between the NHS and academia is preventing the translation and implementation of research into improved patient and population health. ${ }^{114}$ This is no less an issue affecting women's health.
5.26. There are also challenges in implementing novel therapeutic interventions that improve on the current standard of care. For example, remifentanil significantly out-performs the standard of care, pethidine, in terms of reducing pain and numbers of instrumental deliveries (associated with perineal trauma and long-term morbidity) during childbirth. ${ }^{115}$ However, we heard that lack of funding for pumps and an insufficient number of midwives prevents the adoption of remifentanil by many NHS Trusts.
5.27. By creating an implementation- and innovation- positive climate, embedding research in the NHS will expedite the uptake of innovation. ${ }^{116}$ Research-active NHS staff would also have increased interaction with basic scientists and knowledge of new research (2.1). There is increasing evidence that research-active healthcare settings have improved patient health outcomes and staff recruitment and retention. ${ }^{117}$ Therefore, embedding research into the NHS is essential to ensure that women's health research is translated into benefits for patients.
5.28. However, NHS staff increasingly lack the capacity to engage with and in research. The Academy's report recommended a pilot scheme in which $20 \%$ of consultants have $20 \%$ of their time protected for research in ten NHS trusts to determine the costs and the impact on various factors - including research activity, staff recruitment and retention, and patient outcomes. ${ }^{118}$

This response was prepared by Alice Fletcher-Etherington, Policy Intern, and Dr Anna Hands, Policy Officer, and informed by members of the Academy's Fellowship and previous policy work in this area. For further information, please contact Dr Anna Hands, Policy Officer (anna.hands@acmedsci.ac.uk; +44(0)20 3141 3200).

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- Dr Pauline Williams CBE FMedSci, Senior Vice President and Head of Global Health R\&D, GlaxoSmithKline.


[^0]:    ${ }^{1}$ The concepts of sex and gender are inextricably linked but not equivalent, and both impact health. Throughout this response, we will be using the ONS definitions of 'sex' and 'gender'.
    ${ }^{2}$ Academy of Medical Sciences (2021). Precision prevention for modifiable health risks: Steps to achieving personalised preventive healthcare workshop. https://acmedsci.ac.uk/filedownload/48790754
    ${ }^{3}$ Academy of Medical Sciences (2021). Response to the House of Commons' Health and Social Care Select Committee inquiry into the DHSC's White Paper on

[^1]:    ${ }^{5}$ The core themes are 1) Women's voices; 2) Information and education on women's health; 3) Women's health across the life course; 4) Women's health in the workplace; 5) Research, data and evidence; 6) Impacts of COVID-19 on women's health. https://www.gov.uk/government/consultations/women s-health-strategy-call-for-evidence/written-submissionguidance
    ${ }^{6}$ All websites were last accessed 21/05/21.
    ${ }^{7}$ Davies SC (2014). Annual Report of the Chief Medical Officer, The Health of the 51\%: Women.
    ${ }^{8}$ The Independent Medicines and Medical Devices Safety Review (2020). First Do No Harm.
    ${ }^{9}$ Clark M (2012). Experiences of women with endometriosis: an interpretative phenomenological 1022 analysis [thesis]: Queen Margaret University;

[^2]:    ${ }^{14}$ National Perinatal Epidemiology Unit (2014). Safely delivered: a national survey of women's experience of maternity care.
    ${ }^{15}$ RCOG (2017). Maternal Mental Health - Women's Voices.
    ${ }^{16}$ Thomas SL \& Ellertson C (2000). Nuisance or natural and healthy: should monthly menstruation be optional for women? Lancet 355(9207), 922-4.
    ${ }^{17}$ Rodriguez MB, et al. (2018). Interventions for the treatment of heavy menstrual bleeding. Cochrane Database Syst Rev 11.
    ${ }^{18}$ The Lancet (2021). Miscarriage: worldwide reform of care is needed. Lancet 397(10285), P1597.
    19 PHE (2018). What do women say? Reproductive health is a public health issue.
    ${ }^{20}$ Critchley H, et al. (2020). Menstruation: science and society. Am J Obstet Gynecol 223(5), 624-664; Plan International UK (2018). Break the Barriers: Girls' Experiences of Menstruation in the UK.
    ${ }^{21}$ Field N, et al. (2013). Associations between health and sexual lifestyles in Britain: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). Lancet 382(9907), 1830-1844.
    22 Davies SC (2014). Annual Report of the Chief Medical Officer, The Health of the $51 \%$ : Women.

[^3]:    ${ }^{23}$ MacArthur C, et al. (2016). Urinary incontinence persisting after childbirth: extent, delivery history, and effects in a 12-year longitudinal cohort study. BJOG 123(6), 1022-1029.
    ${ }^{24}$ Dolman C, Jones I \& Howard LM (2013). Preconception to parenting: a systematic review and meta-synthesis of the qualitative literature on motherhood for women with severe mental illness. Arch Womens Ment Health. 16(3), 173-96; RCOG (2017). Maternal Mental Health - Women's Voices. 25 NHS Digital (2014). Adult Psychiatric Morbidity Survey: Survey of Mental Health and Wellbeing, England.
    ${ }^{26}$ Memon A, et al. (2016). Perceived barriers to accessing mental health services among black and minority ethnic (BME) communities: a qualitative study in Southeast England. BMJ Open 6(11), e012337.
    27 Academy of Medical Sciences \& MQ Mental Health Research (2021). Progress and priorities for mental health sciences research since COVID-19 workshop, April 23.
    https://acmedsci.ac.uk/more/events/Progress-and-priorities-for-mental-health-sciences-research 28 NHS Digital (2021). Detentions under the Mental Health Act.

[^4]:    ${ }^{29}$ Criado Perez C. (2019). Invisible Women: Data Bias in a World Designed for Men. Chatto \& Windus, London.
    ${ }^{30}$ Kleinman Z (2020). PPE 'designed for women' needed on frontline. BBC News, April 29; Chaklader A \& Ascott A (2021). Personal protective equipment is sexist. The BMJ Opinion; Prospect (2016). Women's PPE: One size does not fit all.
    ${ }^{31}$ British Heart Foundation (2019). Bias and Biology. ${ }^{32}$ Lee K. et al. (2019). Sex-Specific Thresholds of HighSensitivity Troponin in Patients with Suspected Acute Coronary Syndrome. J Am Coll Cardiol. 74(16), 20322043.
    ${ }^{33}$ British Heart Foundation (2019). Bias and Biology.

[^5]:    ${ }^{34}$ APPG on Women's Health (2017). Informed Choice? Giving women control of their healthcare.; Critchley H, et al. (2020). Menstruation: science and society. Am J Obstet Gynecol 223(5), 624-664.
    ${ }^{35}$ APPG on Endometriosis (2020). Endometriosis in the UK: time for change.
    ${ }^{36}$ ActionAid (2017). 1 in 4 UK women don't understand their menstrual cycle.
    ${ }_{37}$ APPG on Women's Health (2017). Informed Choice? Giving women control of their healthcare.
    ${ }^{38}$ Critchley H, et al. (2020). Menstruation: science and society. Am J Obstet Gynecol 223(5), 624-664.

[^6]:    ${ }^{39}$ AbbVie (2021). Empowering conversations: Making shared decision making a reality for patients in an evolving NHS.
    ${ }^{40}$ Menstrual Health Coalition (2020). Heavy Menstrual Bleeding - breaking silence and stigma; RCOG (2019). Better for women; Tanton C, et al. (2015) Patterns and trends in sources of information about sex among

[^7]:    young people in Britain: evidence from three National Surveys of Sexual Attitudes and Lifestyles. BMJ Open 5(3), e007834.
    ${ }^{41}$ Plan International UK (2018). Break the Barriers:
    Girls' Experiences of Menstruation in the UK.
    ${ }^{42}$ https://www.pocketalk.com/

[^8]:    ${ }^{43}$ Jayatunga W (PHE) (2018). Contraception: Economic Analysis Estimation of the Return on Investment (ROI) for publicly funded contraception in England About Public Health England.
    ${ }^{44}$ Cameron et al. (2017). Feasibility and acceptability of introducing routine antenatal contraceptive counselling and provision of contraception after delivery: the APPLES pilot evaluation. BJOG, 124(13); Personal communication with Dr Edward Mullins (Annex 1).
    ${ }^{45}$ The Faculty of Sexual and Reproductive Healthcare, the Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives (2020). FSRH, RCOG \& RCM statement provision of postpartum contraception during Covid-19.
    ${ }^{46}$ Vazquez-Vazquez A, et al. (2021). The impact of the COVID-19 lockdown on the experiences and feeding practices of new mothers in the UK: Preliminary data from the COVID-19 New Mum Study. Appetite 156.

[^9]:    ${ }^{47}$ MacArthur C, et al. (2003). Redesigning postnatal care: a randomised controlled trial of protocol-based midwifery-led care focused on individual women's physical and psychological health needs. Health technology assessment 7(37), 1-98.
    ${ }^{48}$ https://www.england.nhs.uk/mentalhealth/perinatal/; NHS (2021). New dedicated mental health services for new expectant and bereaved mums.
    ${ }^{49}$ Academy of Medical Sciences (2017). Personalised psychiatry meeting, September 6.
    https://acmedsci.ac.uk/file-download/16107617 ${ }^{50}$ Ibid.
    ${ }^{51}$ The Health Foundation (2020). Health Equity in England: The Marmot Review 10 Years On.
    ${ }^{52}$ Academy of Medical Sciences \& The Royal Society (2020). Healthy Ageing. https://acmedsci.ac.uk/filedownload/35061800

[^10]:    ${ }^{53}$ Hägg S \& Jylhävä J (2021). Sex differences in biological aging with a focus on human studies. eLife 10.
    ${ }^{54}$ Academy of Medical Sciences (2018). Multimorbidity: a priority for global health research.
    https://acmedsci.ac.uk/file-download/82222577; Salisbury C, et al. (2011). Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. British Journal of General Practice. 61(582). ${ }^{55}$ Cassell A, et al. (2018). The epidemiology of multimorbidity in primary care: a retrospective cohort study. British Journal of General Practice 68 (669).
    ${ }^{56}$ Academy of Medical Sciences (2021). Response to the House of Commons' Health and Social Care Select Committee inquiry into the DHSC's White Paper on

[^11]:    health and social care. https://acmedsci.ac.uk/filedownload/17381964
    57 http://www.exppectedinburgh.co.uk/
    ${ }^{58}$ Academy of Medical Sciences (2016). Improving recognition of team science contributions in biomedical research careers. https://acmedsci.ac.uk/filedownload/6924621
    59 The Lancet (2021). Miscarriage: worldwide reform of care is needed. Lancet 367(10285), P1597.
    ${ }^{60}$ Academy of Medical Sciences (2021). Precision prevention for modifiable health risks: Steps to achieving personalised preventive healthcare workshop. https://acmedsci.ac.uk/filedownload/48790754

[^12]:    ${ }^{61}$ Public Health England (2019). Cervical screening: implementation guide for primary HPV screening
    62 Tanton C, et al. (2015) High-Risk Human
    Papillomavirus (HPV) Infection and Cervical Cancer Prevention in Britain: Evidence of Differential Uptake of Interventions from a Probability Survey. Cancer Epidemiology, Biomarkers and Prevention 24(5), 842853.

    63
    https://www.who.int/social determinants/themes/wom enandgender/en/
    ${ }^{64}$ Payne S. (2009). How can gender equity be addressed through health systems?
    65 The Health Foundation (2020). Health Equity in England: The Marmot Review 10 Years On.

[^13]:    global growth; Alzheimer's Research UK (2015). Women and Dementia: A Marginalised Majority.
    ${ }^{74}$ Corfe S (2020). The parenthood penalty?
    ${ }^{75}$ Ibid.; Slater and Gordan (2014). Slater and Gordon highlights maternity discrimination.
    ${ }^{76}$ van de Ven P, Zwijnenburg J \& De Queljoe M (2018). Including unpaid household activities: An estimate of its impact on macro-economic indicators in the G7 economies and the way forward. OECD Publishing.
    ${ }^{77}$ Royal Society of Edinburgh (2013). Women, work and care: a challenge for the $21^{\text {st }}$ century; Critchley J, Schwarz M \& Baruah R (2021). The female medical workforce. Anaesthesia 76(S4), 14-23.
    ${ }^{78}$ https://sdgs.un.org/goals/goal5
    ${ }^{79}$ Rieger P, Bird G \& Farrer M for the Government Equalities Office (2018). Employer research on returner programmes: research report.
    ${ }^{80}$ RCOG (2019). Better for women

[^14]:    ${ }^{81}$ https://orwh.od.nih.gov/sex-gender/nih-policy-sex-biological-variable; Pollitzer E (2013). Cell sex matters. Nature 500, 23-24; Wellcome Sanger Institute (2017). Study reveals how sex 'blindspot' could misdirect medical research.
    82 Mair K, et al. (2014) Sex-dependent influence of endogenous estrogen in pulmonary hypertension Am J Respir Crit Care Med 190(4), 456-67.
    ${ }^{83}$ Zucker I \& Prendergast B (2020). Sex differences in pharmacokinetics predict adverse drug reactions in women. Biology of Sex Differences 11, 32.

[^15]:    ${ }^{84}$ Vitale C, et al. (2017). Under-representation of elderly and women in clinical trials. Int J Cardiol 232, 216-221.
    ${ }^{85}$ United States General Accounting Office (2001).
    Druq Safety: Most Druqs withdrawn in Recent Years had Greater Health Risks for Women.
    ${ }^{86}$ Zucker I \& Prendergast B (2020). Sex differences in pharmacokinetics predict adverse drug reactions in women. Biology of Sex Differences 11, 32.

[^16]:    ${ }^{87}$ Frontier Economics for the Department of Health (2014). Exploring the costs of unsafe care in the NHS.; Kongkaew C, Noyce P \& Ashcroft D (2008). Hospital admissions associated with adverse drug reactions: A systematic review of prospective observational studies. Annals of Pharmacotherapy 42(7-8), 1017-1025.
    ${ }^{88}$ Zucker I \& Prendergast B (2020). Sex differences in pharmacokinetics predict adverse drug reactions in women. Biology of Sex Differences 11, 32.
    ${ }^{89}$ Academy of Medical Sciences (2017). Personalised psychiatry. https://acmedsci.ac.uk/filedownload/16107617
    ${ }^{90}$ FDA (2019). FDA approves second druq to prevent HIV infection as part of ongoing efforts to end the HIV epidemic.
    ${ }^{91}$ The Independent Medicines and Medical Devices Safety Review (2020). First Do No Harm.
    92 Taylor M, et al. (2021). Inclusion of pregnant women in COVID-19 treatment trials: a review and global call

[^17]:    104 Liftstream (2017). Opening the Path to a Diverse Future.
    ${ }^{105}$ Limb M (2015). Barriers facing female researchers are tackled by Academy of Medical Sciences scheme. The BMJ 350.
    ${ }^{106}$ Grand View Research (2020). Women's Health Market Size, Share \& Trends Analysis Report By Application (Postmenopausal Osteoporosis, Infertility, Endometriosis, Contraceptives, Menopause, PCOS), By Region, And Segment Forecasts, 2020-2027; Bhong S (2018). Women's Health Market to Cross US $\$ 50$ Billion Mark by 2025. Healthcare Business Today, October 6.
    107 Davalos J (2021). Women's Digital Health Startups Reap Record VC Funding on COVID Surge. Bloomberg Technology, April 19.

[^18]:    108 https://www.medicalstartups.org/top/womenhealth/ (accessed 11/05/21)
    ${ }^{109}$ Academy of Medical Sciences (2016) Medical
    Information Survey. https://acmedsci.ac.uk/filedownload/59091244
    ${ }^{110}$ Academy of Medical Sciences (2017) Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines. https://acmedsci.ac.uk/filedownload/44970096
    ${ }^{111}$ http://acmedsci.ac.uk/policy/how-can-we-all-best-use-evidence
    ${ }^{112}$ Academy of Medical Sciences. A pocket guide to Helping you decide whether to take a medicine.
    https://acmedsci.ac.uk/file-download/53013414

[^19]:    ${ }^{113}$ https://www.patientslikeme.com/
    ${ }^{114}$ Academy of Medical Sciences (2021) Transforming health through innovation: Integrating the NHS and academia. https://acmedsci.ac.uk/filedownload/23932583
    ${ }^{115}$ Wilson M, et al. (2018). Intravenous remifentanil patient-controlled analgesia versus intramuscular pethidine for pain relief in labour (RESPITE): an openlabel, multicentre, randomised controlled trial. Lancet 392, 662-672;

[^20]:    ${ }^{116}$ Jacobs S, et al. (2015). Determining the predictors of innovation implementation in healthcare: a quantitative analysis of implementation effectiveness. BMC Health Services Research 15(6).
    ${ }^{117}$ Academy of Medical Sciences (2021). Transforming health through innovation: Integrating the NHS and academia. https://acmedsci.ac.uk/file-
    download/23932583
    118 Ibid.

