



Women's Health: A New Global Agenda

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Executive Summary

The aims of the paper

Global efforts to improve the health of women and girls have, in the past few decades, largely focused on reducing unacceptably high levels of maternal mortality and morbidity. In large part because of these successful efforts, the global burden of disease has changed significantly in recent years, such that the leading causes of death and disability for women in almost all countries in the world are now non-communicable diseases.¹

A global agenda for women's health must, therefore, have a broadened, redefined focus to encompass not only women's sexual and reproductive health, but also the leading causes of death and disability for women.

For many years, it was widely assumed that the occurrence and outcomes of disease were the same for men and women, and that our understanding of disease processes based on studies involving only men would be equally relevant for women. An increasing body of evidence suggests that this is not the case, and that we can improve our knowledge about disease occurrence and disease outcomes – for both men and women – by undertaking analyses of health data disaggregated by sex and informed by a gender perspective,² as well as by including sufficient numbers of women in scientific studies.

A global agenda for women's health must, therefore, prioritise a gendered approach³ to the collection and utilisation of health data, whether in routinely-collected health statistics or in the creation of new scientific knowledge.

Our recommendations in summary

- We recommend that the World Health Organization, World Bank and other United Nations agencies, global non-governmental organisations, and charities and foundations consistently recognise, promote and allocate resources to address a broader, integrated women's health agenda.
- We recommend that the UK Department of Health and its agencies and public bodies recognise, promote and allocate resources, within the UK, in support of the commitment within the 2015 Global Strategy for Women's, Children's and Adolescents' Health to reducing by one-third premature mortality from non-communicable diseases and the promotion of mental health and wellbeing in women.⁴
- We recommend that the UK Department for International Development and associated agencies consistently recognise, promote and allocate resources to address a broader, integrated women's health agenda in low and middle-income countries.
- We recommend that, consistent with the 2015 World Health Organization Roadmap for Action,⁵ global and UK operatives (both governments and non-governmental) engaged in the provision of healthcare, especially in low and middle-income countries, promote, produce and report gendered analyses of healthcare statistics and ensure resources are made available to:
 - Monitor (and police) the gendered analyses of healthcare statistics;
 - Examine the *pathways and quality of care* for women within the healthcare system;
 - Determine whether these pathways differ for men and women;
 - Where needed, identify evidence-based strategies that could be implemented to ensure women receive the best available care.
- We recommend that professional and academic organisations with an interest in global health recognise, promote and address a broader, integrated women's health agenda. Consistent with the 2015 League of European Research Universities' Advice Paper,⁶ we call on global and UK-based health research funding agencies, universities and peer-reviewed journals to develop, promote and implement policies requiring that all new research is appropriately designed to facilitate the inclusion of gendered analyses and include appropriate numbers of women, and in particular provide targeted funding to support:
 - Gendered analyses of existing datasets;
 - Research to increase our understanding of the interaction of biological, sociocultural and economic factors in determining risk and outcomes for non-communicable diseases;
 - Research to examine variations in *access to care* for women and men for the prevention and treatment of non-communicable diseases and, if required, funding to determine the barriers to women seeking early care and the development, testing and implementation of strategies to improve timely access to care;
 - Research to increase our understanding of the *pathways and quality of care* for women for the prevention and treatment of non-communicable diseases within the healthcare system, determination of whether these pathways differ for women and men and the strategies that might require implementation to ensure that women receive the best available care.

Introduction

“Women and Health” was one of the key areas of action articulated at the landmark Fourth World Conference on Women held in Beijing in 1995 and in the resulting Beijing Declaration and Platform for Action, a roadmap for gender equality and the empowerment of women.⁷ Given the unacceptably high rates of maternal and infant mortality in many countries in the world at that time, the Declaration focused particularly on increasing women’s access to sexual and reproductive health (SRH) services. As a result, in the intervening 20 years, such access has increased and SRH outcomes (including maternal mortality) have improved globally.⁸

Unquestionably there remains an unfinished agenda with respect to SRH, combined with an increasing recognition of the need to address gender-based violence, especially for

women in low and middle-income countries (LMICs). However, in almost all but the poorest countries of the world, the leading causes of death and disability for women are now non-communicable diseases (NCDs),⁹ with, in many cases, higher rates for women in LMICs than in high-income countries (HICs).

From what little is known, there is emerging evidence to suggest that women (and their health providers) are often not aware of the significance of NCDs.^{10,11,12} Women do not access healthcare when they need it, do not receive the best care and, as a result, have poorer health outcomes than would be the case if they were to receive appropriate care in a timely fashion.

Why this paper is needed now

2015 marked the 20th anniversary of the Beijing Declaration and Platform for Action. While a great deal has been achieved over the past 20 years, including substantial improvements in women’s health, there is still much to be done. As a result, many governments, non-governmental agencies and multilateral organisations are asking how best to accelerate progress to ensure gender equality and the empowerment of women by 2030, if not sooner.¹³

2015 also marked the year in which the world changed focus from the Millennium Development Goals (MDGs) to the Sustainable Development Goals (SDGs).¹⁴ While the MDGs have driven important global changes, including improvements in health and gender equality, the development agenda is unfinished. Governments, non-governmental agencies and multilateral organisations are focusing on the SDGs and the policies, strategies and funding that will be required to ensure they are achieved over the next 15 years.

Also in 2015, an updated Global Strategy for Women’s, Children’s and Adolescents’ Health was launched,⁴ building on the 2010 Global Strategy for Women’s and Children’s Health. This updated strategy reflects the important gains that have been achieved in birth outcomes and child health over the past few years and the need to continue to address these issues; it also incorporates the health of adolescents and a broader range of health issues, including NCDs.

Our first focus in this paper is the importance of redefining women’s health as more than SRH, to extend the definition to include the leading causes of death and disability for women, especially NCDs. Secondly, we emphasise the value of a gendered approach to the collection and analyses of health data, so as to identify and better understand both the biological (sex) and sociocultural (gender)^{2,3} factors associated with differences and disparities in the occurrence and outcomes of health. We reflect upon current policies and practices to highlight the gaps

between current policy priorities and the reality presented by our evidence.

With the ultimate aim of improving women's health, we call for greater investment to: tackle the broader range of health issues of importance for women; conduct and report gendered analyses of health data; and identify and implement innovative strategies to address sex differences and reduce gender disparities in health.

Our approach recognises the continuing need to improve SRH services and outcomes for women and adolescent girls, and highlights the potential gains of integrating the latter with a greater focus on the leading causes of death and disability, especially NCDs. Our approach also recognises that gendered analyses should facilitate improvements in healthcare and health outcomes not only for women, but for all individuals. Finally, our approach especially focuses on the importance of these issues for LMICs, given that this is where the need is greatest.

Our target audience

This policy paper focuses on stakeholders both at a global level and those within the UK. It is one of a series of four related papers that will draw upon the expertise, long-term engagement and commitment of The George Institute and its collaborators to reducing the global burden of NCDs, especially for those in resource-poor countries and settings. Policy

papers are being launched in each of the four countries in which The George Institute is based: Australia, China, India and the UK. Each paper aims to make recommendations that will directly influence major international organisations, as well as governments, non-governmental organisations (NGOs) and other key stakeholders.

1. Redefining women's health

1.1 Why we need to redefine and broaden the women's health agenda

Firstly and most importantly, we believe that current practice limits the opportunities to improve the health of the maximum number of women in the most effective ways possible, and by extension the health of the communities in which they live. Secondly, we believe that an agenda with an almost exclusive focus on women of childbearing age effectively discriminates against and excludes those women who do not have children and women who are no longer of reproductive age.

To optimise the health of women globally, a women's health agenda should address those health conditions that are responsible for the greatest burden of ill health. As the next section of the paper will demonstrate, in most countries in the world, the leading causes of mortality and disability for women are NCDs.

However, to improve the health status and outcomes for mothers as well as newborns, the management of NCD risk behaviours and conditions in adolescent girls and women in their childbearing years is essential to ensuring the best birth outcomes.^{15,16} Equally,

growing evidence suggests that health status and outcomes in later life are influenced by health status in early life and pregnancy, such that a life-course approach to the control of NCDs must encompass management of both newborn infants and women before, during and immediately after pregnancy.^{16,17}

Thus, a broadened health agenda for women, that incorporates a greater focus on NCDs as well as a life-course approach, has the potential to lead to greater overall health benefits for a much larger number of women, incorporating improvements in health outcomes for mothers and their newborns.

Notwithstanding the primary focus of this paper on improving the health status of women, given the important role of women as caregivers in many communities,¹⁶ an increased focus on reducing the burden of NCDs for women will directly impact their ability to care for their families, as well as potentially indirectly facilitate reductions in the occurrence and outcomes of NCDs in other family members.

1.2 Leading causes of death and disability for women

1.2.1 The leading causes globally

In 2013, data from the Global Burden of Disease study showed that ischaemic heart disease (IHD) and stroke were the leading causes of death for women worldwide (Table One).^{9,18} Furthermore, seven of the ten leading causes of death were NCDs, including chronic obstructive pulmonary disease (COPD), Alzheimer's disease, diabetes, hypertensive heart disease, and lung cancer. By comparison, in 1990, NCDs accounted for only four of the

leading causes of death. Since 1990, maternal and infant deaths (as a result of preterm birth or low birth weight) have decreased, such that neither is now ranked in the top ten causes of death.⁹ Similarly, five of the leading causes of disability for women across the world in 2013 were NCDs, namely IHD, low back and neck pain, stroke, major depressive disorder and COPD (Table Two).⁹ Preterm birth complications continue to be ranked in the ten leading causes of disability, at number nine.

Table One: Leading causes of death for women globally, by development status and for selected countries, 2013

Rank	Global	HICs	UK	LMICs	China	India
1	Ischaemic heart disease	Ischaemic heart disease	Ischaemic heart disease	Cerebrovascular disease	Cerebrovascular disease	Ischaemic heart disease
2	Cerebrovascular disease	Cerebrovascular disease	Cerebrovascular disease	Ischaemic heart disease	Ischaemic heart disease	Cerebrovascular disease
3	Lower respiratory infections	Alzheimer's disease	Alzheimer's disease	Lower respiratory infections	Chronic obstructive pulmonary disease	Chronic obstructive pulmonary disease
4	Chronic obstructive pulmonary disease	Lower respiratory infections	Lower respiratory infections	Chronic obstructive pulmonary disease	Lung cancer	Diarrhoeal diseases
5	Alzheimer's disease	Chronic obstructive pulmonary disease	Lung cancer	Diarrhoeal diseases	Hypertensive heart disease	Lower respiratory infections
6	Diabetes	Lung cancer	Chronic obstructive pulmonary disease	HIV/AIDS	Alzheimer's disease	Tuberculosis
7	Diarrhoeal diseases	Breast cancer	Breast cancer	Diabetes	Lower respiratory infections	Asthma
8	HIV/AIDS	Colorectal cancer	Colorectal cancer	Tuberculosis	Stomach cancer	Hypertensive heart disease
9	Hypertensive heart disease	Hypertensive heart disease	Other cardiovascular and circulatory diseases	Hypertensive heart disease	Liver cancer	Diabetes
10	Lung cancer	Diabetes	Ovarian cancer	Malaria	Road injuries	Pneumoconiosis

Table Two: Leading causes of disability-adjusted life years for women globally, by development status and for selected countries, 2013

Rank	Global	HICs	UK	LMICs	China	India
1	Ischaemic heart disease	Ischaemic heart disease	Low back & neck pain	Lower respiratory infections	Low back & neck pain	Ischaemic heart disease
2	Low back & neck pain	Low back & neck pain	Ischaemic heart disease	Ischaemic heart disease	Cerebrovascular disease	Lower respiratory infections
3	Lower respiratory infections	Cerebrovascular disease	Cerebrovascular disease	Cerebrovascular disease	Ischaemic heart disease	Diarrhoeal diseases
4	Cerebrovascular disease	Depressive disorders	Alzheimer's disease	Low back & neck pain	Chronic obstructive pulmonary disease	Chronic obstructive pulmonary disease
5	Depressive disorders	Alzheimer's disease	Chronic obstructive pulmonary disease	Diarrhoeal diseases	Depressive disorders	Neonatal preterm birth complications
6	Diarrhoeal diseases	Sense organ diseases	Depressive disorders	HIV/AIDS	Sense organ diseases	Neonatal encephalopathy
7	HIV/AIDS	Other musculoskeletal disorders	Breast cancer	Malaria	Diabetes	Tuberculosis
8	Malaria	Diabetes	Lung cancer	Neonatal preterm birth complications	Other musculoskeletal disorders	Cerebrovascular disease
9	Neonatal preterm birth complications	Chronic obstructive pulmonary disease	Sense organ diseases	Depressive disorders	Skin diseases	Iron-deficiency anaemia
10	Chronic obstructive pulmonary disease	Breast cancer	Road injuries	Chronic obstructive pulmonary disease	Road injuries	Depressive disorders

Disability-adjusted life years refers to the number of years lost due to ill-health, disability or early death.

1.2.2 The leading causes in HICs

In HICs, all but one of the leading causes of death (lower respiratory infections) amongst women were NCDs, with Alzheimer's disease listed as number three (following IHD and stroke) and three cancers (breast, lung and colorectal) also listed in the top ten (Table One). In the UK, similarly, all but one of the leading causes of death were NCDs, including Alzheimer's disease, with four cancers (lung, breast, colorectal and ovarian) listed in the top ten.

NCDs were responsible for all ten leading causes of disability in women in HICs, dominated by cardiometabolic conditions, musculoskeletal conditions, and neurological and mental health disorders (Table Two). In the UK, similarly, NCDs were responsible for the ten leading causes of disability among women, led by low back and neck pain and including both breast and lung cancers.

1.2.3 The leading causes in LMICs

In LMICs, stroke, IHD and COPD accounted for three of the four leading causes of death for women in 2013, and NCDs for five of the top ten causes, with diabetes ranked seventh and hypertensive heart disease ranked ninth (Table One). Unlike in 2010, preterm birth complications were no longer ranked in the top ten causes of death, with lower respiratory infections, diarrhoeal diseases, HIV/AIDS, tuberculosis and malaria accounting for the other leading causes of death.

For women in India, seven of the leading causes of death were NCDs, led by IHD and stroke. Three of the leading causes of death were chronic respiratory-related conditions, namely COPD, asthma and pneumoconiosis. Diarrhoeal diseases, lower respiratory infections and tuberculosis were the other leading causes of death. Unlike in 2010, preterm birth complications were no longer ranked amongst the leading causes of death.⁹

In China, NCDs and injuries accounted for nine of the ten leading causes of death for women, led by stroke, IHD and COPD. Lung, stomach

and liver cancers ranked in the top ten causes of death, and Alzheimer's disease was ranked at number six.

Lower respiratory infections were the leading cause of disability amongst women in LMICs (Table Two). However, NCDs, comprising IHD and stroke, low back and neck pain, major depressive disorders and COPD were responsible for five of the ten leading causes. Preterm birth complications were ranked number eight.

In India, while IHD now ranks as the leading cause of disability for women, three of the leading causes of disability are still associated with pregnancy and birth outcomes, namely preterm birth complications, neonatal encephalopathy and iron-deficiency anaemia.

In China, the leading causes of disability were low back and neck pain, stroke, IHD, COPD and major depressive disorders. Neither birth complications nor any of the major communicable diseases were ranked in the top ten leading causes of disability.

1.3 Current policies and practices

A Global Strategy for Women's and Children's Health was first launched by the United Nations Secretary-General, Ban Ki-moon, in 2010, because of his belief that the global community should do more to save the lives and improve the well-being of women and children.¹⁹ The Global Strategy was complementary to the MDGs and so almost exclusively focused on improving maternal and newborn health.

The influence of the Global Strategy was substantial, leading to the establishment of the Every Woman Every Child²⁰ movement and multiple commitments by many countries, UN agencies and NGOs. Most recently, this included the establishment of the Global Financing Facility, a fund to support these activities coordinated by the World Bank.²¹

As a consequence, over the past five years an estimated 2.4 million deaths of women and children have been averted and financial commitments for the Global Strategy have reached nearly US\$60 billion.²² Notably, while official development assistance for health has grown only modestly in recent years, funding for reproductive, maternal, newborn and child health has risen sharply, increasing by 25%.²²

The World Health Organization (WHO), as the lead public health arm of the UN, is a significant player in directing the global agenda on health, including women's health. While clearly supporting the strategic direction of the Global Strategy, more recently the WHO has been at the forefront of calls to move the women's health agenda beyond a primary focus

on reproductive health issues to ensure that health systems have the capacity to provide for women at all stages of life and in particular to address the control of NCDs.

In September 2013, a theme issue of the *Bulletin of the World Health Organization* was devoted to this topic,²³ with the WHO leadership outlining the changing nature of the health problems facing women, especially in LMICs, and highlighting the significance of a life-course approach to women's health. Specifically, they outlined the interrelationships between both maternal and infant health and health problems, especially NCDs, in later life, and the potential value of integrating maternal and child health services with those that identify and manage women at high risk of NCDs.¹⁷

In June 2015, the Lancet Commission on Women and Health reported their findings, echoing many of the calls by the WHO.¹⁶ The Commission noted in particular that the global response to NCDs was not commensurate with their burden amongst women and highlighted the importance of a life-course approach to women's health, to show the breadth of women's health issues beyond their reproductive years.

In September 2015, The Global Strategy for Women's, Children's and Adolescents' Health (2016–2030) was launched by the UN Secretary-General, in partnership with the WHO. The strategy outlined what countries and health partners need to do to end “all preventable

deaths of women, children and adolescents by 2030 and improve their health”.⁴ A commitment was made to a one-third reduction in premature mortality from NCDs and to the promotion of mental health and wellbeing.

Concurrent with the release of the updated Global Strategy in New York, the UN General Assembly hosted the “Global Leaders' Meeting on Gender Equality and Women's Empowerment: A Commitment to Action”.¹³ The meeting sought to build support, consensus and renewed political commitment, at the highest possible level, for the full implementation of the Beijing Declaration and Platform for Action. It also focused attention on realisation of the gender equality goals and targets in the SDGs and mobilisation of concrete new commitments and financial contributions by UN Member States (governments) to eliminate gender inequality and discrimination against women.

Commitments totaling US\$25 billion were made by 88 UN Member States, regional organisations, NGOs, charities and foundations.²⁴ Yet, despite this level of political support, a full appreciation of women's health, in its broader sense, was lacking. In fact, a consistent theme of speeches pledging support for these efforts in relation to women's health was an almost exclusive focus on SRH, with the occasional reference to violence against women and female genital mutilation. The broader women's health agenda was not in evidence.

1.4 Implications for future policies and practices

Importantly, the updated Global Strategy for Women's, Children's and Adolescents' Health (2016–2030), supported by the WHO, firmly commits to a one-third reduction in premature mortality from NCDs and a greater focus on a broader life-course approach to addressing and improving the health of women and girls. The documentation that was produced leading up to the 20th anniversary of the Beijing Declaration and Platform for Action reinforces the latter approach as do the targets for the new SDGs.

However, as articulated above, much of the focus and resources of governments, UN agencies (including UN Women) and NGOs continues to be narrowly defined. This clearly impacts the delivery of care, for both prevention and treatment of NCDs; unless their focus can be broadened to include health issues relating to NCDs, health investments will likely lead to decreasing returns for women's health overall and will not benefit the greatest number of women. Genuine progress in women's health

will only be realised, and the 2030 targets achieved, if there is concerted, systematic engagement with UN agencies, governments and NGOs to ensure they address these targets.

Awareness about the significance of NCDs and strategies to reduce them are already high on the agenda of most governments and NGOs in HICs. But gender disparities in awareness, access and quality of care are not well known and should be on the agendas of governments in HICs. By comparison, awareness of the significance of NCDs and strategies to reduce them are low both in LMICs and amongst those agencies and NGOs, charities and foundations based in HICs with a focus on improving health or the empowerment of women in LMICs.

It may be that there is a need for greater promotion of the persuasive data summarised above. It is certainly true that there is a need to provide further evidence showing the benefits to women's health of greater investment in addressing a broader life-course agenda, and there is a need to provide evidence that such investment is able to address the current SRH agenda better, compared with a sole focus on the latter. Nevertheless, the data on the contribution of NCDs to the global burden of death and disability for women worldwide is compelling; despite the political commitments laid out above, it is yet to lead to changes in practice.

An example of the type of evidence required to show the benefits of integrating a focus on SRH and NCDs to improve health outcomes for women in South Asia

In August 2015, an award was made by the Global Alliance for Chronic Diseases, with funding from the Indian Council of Medical Research and the National Health and Medical Research Council of Australia, to support a lifestyle intervention programme for the prevention of Type II diabetes mellitus amongst South Asian women with gestational diabetes mellitus.

Primary research aim: To determine whether a resource- and culturally-appropriate lifestyle intervention programme in South Asian countries (Bangladesh, India and Sri Lanka), provided to women with gestational diabetes mellitus (GDM) after delivery, will reduce the incidence of Type II diabetes mellitus (T2DM), in a manner that is affordable, acceptable and scalable.

Research methodology: A new lifestyle intervention programme is being developed that will be delivered by auxiliary nurse midwives or their equivalent in each participating hospital, representing a strategy of within-system task-shifting. The intervention will be evaluated in a randomised controlled trial (1414 women from 24 centres) to determine whether it will reduce the incidence of T2DM at a median of 20 months follow-up. This project focuses on generating new knowledge around implementation of a preventive strategy embedded within existing health systems, using mixed-methods evaluation to inform on cost-effectiveness, acceptability and scalability.

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2. A gendered approach to health analyses

2.1 Why we need a gendered approach

Increasing evidence suggests that a gendered approach to the analyses of health data, whether for routinely collected health data or data collected for research purposes, has the potential to improve the health of women (and men) substantively. A gendered approach involves identifying sex differences and the biological explanations for these differences, as well as gender disparities and the sociocultural factors, including health system responses, which might account for these disparities. The identification and examination of sex differences and gender disparities, and if and how they interact, has the potential to facilitate the discovery and implementation of preventive and treatment strategies to respond to these differences and to reduce disparities and thereby improve the health of women.

Until recently, there was little recognition that differences and disparities might exist in the occurrence, management and outcomes of health conditions in men and women. Consequently, data and research findings involving only men were assumed to be relevant for all. Not only is such an assumption highly prejudiced, it has the potential to lead to detrimental effects on the health of women. For example, between 1997 and 2000, ten drugs were withdrawn from the US market because of life-threatening health effects; eight of these posed greater health risks for women than for men.¹²

Until recently, also, the potential influence of social and economic factors in disease presentation and outcomes – such as the organisation of

An example of the type of evidence required to better understand whether and why access to healthcare might be different for women and men with hip fractures in Odisha, India

Primary research aim: Worldwide, as the population ages, the incidence of hip fractures, particularly amongst older women, is increasing. Half the projected burden, of over six million fractures annually by 2050, is expected to occur in Asia and especially in India and China. Access to safe, affordable surgical and anaesthesia care in a country like India is a huge challenge, where nine out of ten people cannot access basic surgical care. However, availability and timely access to surgical care is essential if mortality, morbidity and disability from hip fractures are to be minimised. The aim of this study is to determine the processes in decision-making following a hip fracture, identify the causes of delay in obtaining care and the potential barriers and facilitators to seeking appropriate, timely care.

Research methodology: Women and men aged 50 years and older who sustain a hip fracture are being recruited to the study from seven healthcare facilities (four public, two private and one traditional bone setter) in two administrative districts of the state of Odisha, India. Key informant interviews will be conducted with individuals and their caregivers. This study is being conducted by The George Institute for Global Health, India, in collaboration with the Indian Institute of Public Health in Bhubaneswar.

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health systems – was not recognised; nor was there general awareness of the potential impact of wider gender inequalities and lack of empowerment on women's access to healthcare and resulting health outcomes, especially for the management of NCDs. Consequently, the benefits of addressing these factors as a means to improve the health of women has not been widely nor systematically examined.

As an example of the benefits of a gendered approach to the analyses of health data, in the next section we provide an overview of recent research that has deepened our understanding of the occurrence, management and outcomes of

cardiovascular disease (CVD) in women, and led to consideration of the implications for prevention.²⁵

We have focused on CVD in large part because there is a growing body of research (mostly in HICs) that has explored sex differences and gender disparities in the occurrence, management and outcomes of CVD, including a major programme of research undertaken by The George Institute, which has included data from LMICs. By comparison, there is a dearth of similar research for most of the leading causes of NCDs, although increasing recognition exists of the need for, and potential benefits of, undertaking gendered analyses.^{26,27}

2.2 A gendered approach to addressing CVD

For many years, there has been a widespread perception that CVD, including IHD and stroke, is predominantly a male disease. This assumption has stemmed largely from observations that women, at any given age, have a lower risk of CVD than men and the misperception that, if a woman develops CVD, it typically will not be as serious as it would be for a man. Consequently, CVD in women was not widely discussed and, as a result, the role of sex differences and gender disparities in the pathophysiology, risk factors, outcomes and treatment of CVD are still relatively poorly acknowledged, explored and understood.

Although awareness of the importance of CVD in women is increasing in HICs, there remains a significant gap between perceived and actual risk of CVD in women, and few women see it as a paramount threat to their health.¹² This is despite the fact that CVD causes more deaths than any other cause for women in almost all countries in the world, and the numbers of deaths from CVD amongst women have outnumbered men for over three decades, due to women living longer than men.

2.2.1 Sex differences in the presentation of CVD

In recent years there has been a greater representation of women in medical studies

than previously, including clinical trials.^{28,29,30} Results from these studies have challenged the conventional wisdom that women are protected from CVD, and have provided convincing evidence of sex differences in CVD over the life course. For example, even when women and men have similar risk factors, considerable differences exist in the occurrence of the manifestations of CVD.^{31,32}

Men generally develop CVD at a younger age and are more likely to develop IHD than women. Women, in contrast, are at a higher risk of developing stroke, which occurs most often in older age. Also, haemorrhagic stroke (bleeding in the brain) is more frequent in women than men.

Despite the fact that CVD presents differently in men and women,^{33,34} the clinical definition of symptoms classically associated with CVD, particularly IHD, is based on the characteristics of those reported in men. Warning signs in women are therefore often regarded as 'atypical' and thus tend to go ignored, unrecognised or misdiagnosed, leading to under-treatment of women.

2.2.2 Sex differences and gender disparities in access, diagnosis and treatment of CVD

Access to healthcare services for the management of CVD is different for men and women.

Compared to men, women are less likely to receive pharmacological treatment for the management of cardiovascular risk factors or to be referred for diagnostic and therapeutic procedures.^{35,36,37,38} Suboptimal access to healthcare services leads to delays in medical diagnosis and the start of effective treatment, and consequently worse prognosis for women with CVD. This is despite evolving evidence suggesting that the majority of recommendations to prevent CVD should be similar for women and men,^{39,40} with few exceptions.

For instance, aspirin is routinely recommended for the primary prevention of IHD in men but not women.⁴¹ Such recommendations are generally based on cost/benefit trade-offs related to average risk, yet the CVD risk profile for women and men overlaps considerably. Moreover, sex differences may be present in the magnitude of the relative and absolute potential benefits and risks of preventive interventions. This might largely be a consequence of the later age at initiation of preventive interventions and the higher rates of comorbidities in women, rather than any inherent biological differences in the efficacy of evidence-based interventions *per se*.

2.2.3 Sex differences and gender disparities in the effects of risk factors on CVD

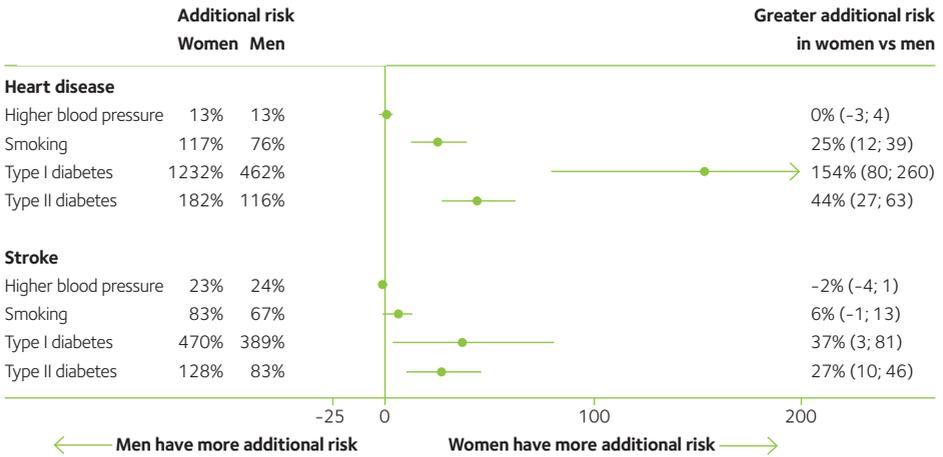
Elevated blood pressure, cigarette smoking, diabetes mellitus, excess weight and raised cholesterol are the most important, widely prevalent and yet largely preventable risk factors for CVD.^{42,43} It is commonly assumed that these risk factors have a similar effect on CVD outcomes in women as in men. This assumption neglects significant anatomical, physiological, and behavioural differences between men and women, as well as potential gender disparities in health system responsiveness.

A reliable determination of clinically meaningful sex differences in associations between risk factors and CVD outcomes is important, not solely to better understand the etiology of CVD, which could help in the development or improvement of new interventions and screening strategies, but also from a population and public health vantage. Robust evidence of any important sex differences and gender disparities in the link between prominent risk factors and CVD outcomes could act as an impetus for the more efficient tailoring of specific interventions aimed at the treatment and management of these risk factors, for both men and women.

Sex differences in the risk of CVD are also likely to occur for major demographic factors, such as age, ethnicity and social status. The evidence for the latter is particularly persuasive. Markers of low socio-economic status are associated with CVD in both sexes, but several studies have found a stronger association amongst women, most often for coronary heart disease (CHD).^{44,45} When seeking to reduce socioeconomic inequalities in CHD, it is thus likely that different approaches will be required for men and women.

Current estimates of the burden of CVD used to inform public health policy assume that preventable risk factors increase the risk of CVD in women and men in a similar manner. This assumption is likely to be false for at least two of the key risk factors. Recent systematic reviews of the literature, and new analyses of the totality of data, have provided reliable evidence that women are impacted more by smoking⁴⁶ and diabetes^{47,48,49} than men, in terms of their relative chance of developing CVD (Figure One). We consider these risk factors specifically in the following two sub-sections.

Figure One: The additional risks of ischaemic heart disease and stroke associated with higher blood pressure, smoking, Type I and Type II diabetes in women compared with men



The additional risk of ischaemic heart disease and stroke for (1) those with a 10 mmHg higher value of systolic blood pressure; (2) smoking compared to not; (3) Type I diabetes compared to not; (4) Type II diabetes compared to not. Results are shown as the additional risk for women and men and (plotted results and right-hand column) the extra additional risk for women compared to men (e.g. smoking confers 25% more risk of heart disease for women than it does for men). 95% confidence intervals are shown as horizontal lines around the estimates on the graph, and in parentheses in the right-hand column. Additional risk = 100 x (Relative risk - 1); greater additional risk = 100 x (Female: male ratio of relative risks - 1).

The ‘catching up’ process in risk – women who smoke or have diabetes are more like men than other women, in terms of CVD risk – does not appear to occur for all risk factors. For example, a higher level of systolic blood pressure⁵⁰ has the same deleterious effect on IHD and stroke in both women and men (Figure One) and anti-hypertensive medication has a similarly beneficial cardiovascular effect in both.³⁹ There is also no evidence of any difference in the effect of body mass index (BMI) on CHD between the sexes.⁵¹ These null differences make the excess risks from smoking and diabetes more likely to be ‘real’, and not just a consequence of the way risk is compared between the genders in standard analyses.

2.2.3.1 Smoking

In the 20th century, an estimated 100 million deaths were due to smoking,⁵² and it has been

predicted that there will be one billion deaths attributable to tobacco in the current century.⁵³ It is anticipated that there will be an increasing relative burden amongst women due to two factors: more women are now starting to smoke and a higher proportional risk of IHD attributed to smoking for women than men.⁴¹

The smoking epidemic amongst women in HICs reached its peak several decades later than amongst men, and the effects of accumulating risk are still ‘working through’.^{54,55} Women who do start smoking are increasingly taking it up at a younger age, converging on the age that has been historically associated with men, although women still tend to smoke in somewhat lower quantities than men.⁵⁶

In LMICs, typically more than ten times as many men as women smoke cigarettes. This contrasts

with HICs where current smoking rates are virtually the same in women and men, such as in the UK where 19% of women and 20% of men currently smoke.⁵⁷ But things seem to be changing.

Unfortunately, girls and women are a prime target for the tobacco industry, particularly in LMICs.⁵⁸ Tobacco products are increasingly affordable to women, and marketing campaigns often present smoking to women, particularly those of young age, as a manifestation of empowerment, independence, beauty, femininity and sex appeal.

Many women (and men) remain unaware of the health risks of tobacco use and believe that its use relieves tension and facilitates weight loss. Women's health is also jeopardised by exposure to second-hand smoke, especially in countries and cultures where many women do not have the power to negotiate smoke-free spaces, including in their own homes. Additionally, women in LMICs are at greater risk of exposure to smoke from biomass fuels used for cooking, compared with men.

The second reason why the future health burden of smoking can be expected to affect women disproportionately is that female smokers have a 25% greater relative risk of IHD, compared with their male counterparts, independent of other cardiovascular risk factors (Figure One).⁴¹ This is despite the lower cumulative exposure to smoking in women than in men due to the relative immaturity of the smoking epidemic in women, and the generally lower number of cigarettes smoked per day by women, suggesting that this estimate of 25% extra risk conferred on women could represent an understatement.

Since smoking is such a major risk factor for many chronic diseases in addition to CVD – such as COPD and lung cancer – as well as being associated with adverse birth outcomes and the health of newborns, it is critical that strategies to reduce smoking have a clear understanding of, and can take into consideration, the beliefs, concerns and attitudes of women.^{25,48}

2.2.3.2 Diabetes

Strong and consistent evidence exists for a substantial sex difference in the effects of diabetes on the risk of CVD, to the detriment of women.^{25,47,48,49} Women with diabetes have a 44% higher excess risk of IHD, and a 27% higher excess risk of stroke compared to similarly affected men (Figure One). Additionally, a 37% higher excess risk of all-cause mortality in women as compared with men associated with Type I diabetes has been reported.⁴⁷ This was predominantly driven by a higher excess risk for CVD in affected women.

Gender disparities in cardiovascular risk factor management, to women's disadvantage, have often been suggested to underpin women's greater excess risk of CVD associated with diabetes.⁵⁹ A recent report from the UK National Diabetes Audit found that women with diabetes were 15% less likely than affected men to receive the care recommended by national guidelines or to meet treatment targets.⁶⁰

However, the biological changes associated with the metabolic transition to diabetes may also be more detrimental in women than men,^{61,62} especially in relation to excess body weight. Women generally have a higher BMI than men when first diagnosed with diabetes,^{63,64} suggesting that women may have more cardiometabolic reserves, requiring greater deterioration than men, before being diagnosed with diabetes.

Consequently, the diabetes-related excess risk of CVD in women may not be solely due to significant sex differences in the effects and complications of diabetes itself, but rather the result of the combination of both a greater deterioration in cardiovascular risk factor levels and a chronically elevated, but undiagnosed and untreated, cardiovascular risk profile in the pre-diabetic state.

Diabetes develops over decades, which presents an opportunity to identify individuals at high risk for diabetes and, subsequently, for timely intervention to prevent or delay the

onset of the condition. The pathogenesis of diabetes is complex and incorporates genetic, physiological, psychological, sociological and wider environmental influences that play out differently for individuals in different settings.

Moreover, increased awareness of the magnitude and timing of the risk of diabetes after gestational diabetes, which disproportionately affects Asian women and

increases the risk of diabetes sevenfold,^{65,66} could provide an opportunity to facilitate lifestyle interventions that might prevent or delay the onset of Type II diabetes in affected women. Such interventions would of course dovetail with those aimed at pregnant women with existing Type II diabetes, in whom the risk of adverse pregnancy outcomes are increased.⁶⁷

2.3 Current policies and practices

2.3.1 A gendered approach to the analyses of routine health data

The 1995 Beijing Declaration and Platform of Action, building on previous initiatives in a range of countries, promoted the need to ensure that before policy decisions are taken, the effects on women and men should be analysed separately.⁷ Subsequently, many governments, UN agencies and NGOs have committed to “gender mainstreaming”. With the launch of the SDGs, gender-sensitive and disaggregated data were recognised as essential and integral to the attainment of the SDGs.¹⁴

The importance of collecting, analysing and reporting disaggregated data in the health sector has been specifically recognised. The WHO has produced a Roadmap for Action, 2014–2019, aimed at ensuring the integration of equity, human rights, gender and social determinants across all WHO programmes and in all Member States.⁵ The promotion of disaggregated data analysis and health inequality monitoring is one of the three key directions of this report.

However, the implementation of these policies into practice, especially across Member States, still has some way to go, even in HICs.⁶⁸ The 2008 UK Gender and Access to Health Services Study,⁶⁹ for example, highlighted the limited availability of data on the link between gender and use of health services. Specifically, the report showed that little is known about

whether men and women use health services with different degrees of effectiveness, and whether they receive different kinds of service from the National Health Service (NHS). Only 18% of local health authorities in the UK provide data disaggregated by sex.

Similarly, the 2009 European Commission report on Access to Healthcare and Long-Term Care⁷⁰ concluded that little is known about gender disparities in accessing healthcare and long-term care, plus if and how these are taken into account in service delivery. The report also concluded that there is a need to adopt a gender perspective in healthcare policies, in order to improve their effectiveness. Additionally, the report stated there is an increased need for sex and gender-based health research to increase knowledge about the complex ways in which biological, social, cultural and environmental factors interact to affect the health of women and men.

Arguably, the situation is worse in LMICs, although data providing evidence of disparities in both access to and quality of care are limited. The 10,000 women Arogya survey, for example, suggested that access to NCD care for women in Asian countries, in particular, was challenging, as a result of care facilities being too far away and transportation being limited.¹⁰ However, no comparative data were available for men.

An example of the type of analyses of large healthcare databases required to better document sex-specific utilisation and sex differences in the use of hospital care among the poor in Andhra Pradesh, India

Primary research aim: The Rajiv Aarogyasri Community Health Insurance Scheme (RACHIS) was launched in 2007 by the state government of undivided Andhra Pradesh, India, to provide access to hospital care for poor households. By 2012, RACHIS covered 19 million households, thereby extending its benefits to 81% of the population of undivided Andhra Pradesh. De-identified claims data published by RACHIS are publicly available and provide an opportunity to document the leading causes of disease accounting for hospital use by women. They also allow determination of whether use of hospital care differs for women and men, in an environment where cost should not be a barrier to use.

Research methodology: Data will be accessed for the four years from mid 2008 to mid 2012. The numbers of unique beneficiaries, numbers of hospitalisation events, numbers of bed-days and expenditure in US dollars will be accessed and mapped to the leading disease categories, as outlined in the International Classification of Diseases, version 10. Data for women and men will be compared for sex-neutral conditions.

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2.3.2 A gendered approach to the conduct of health research

A gendered approach to the creation of new knowledge in science, including health and medicine, has been gaining momentum.⁷¹ In the EU, UK, and US, for example, policies have been implemented to support the incorporation of gendered approaches into the conduct of research. Major science funding bodies, such as Horizon 2020, have started to request that researchers explicitly identify how they will promote gendered analyses in their research and especially show that their studies have been designed to facilitate such analyses. Likewise, an increasing number of major peer-reviewed journals, such as *The Lancet*, have developed policies requiring that women are routinely included in clinical trials and that authors report gendered analyses in their publications.

Substantial, but not sufficient, progress has been made in increasing the involvement of women in large-scale population studies and clinical

trials and there has been an increase in studies undertaking *a priori*, gender-specific analyses. Nevertheless, a recent US publication provides sober reading; it showed that the majority of applications for high-risk cardiovascular devices to the US Food and Drug Administration (FDA) were lacking sex-specific data and that women were still underrepresented in clinical trials.¹²

In September 2015, the League of European Research Universities (LERU) published an Advice Paper, outlining the case for “gendered research and innovation” (GRI), and provided case studies showing how a gendered approach to science has contributed to increased excellence in science and the production of new knowledge.⁶ The paper makes recommendations to members of LERU and to other universities, encouraging them to engage with governments, funding agencies and peer-reviewed journals to highlight the importance of GRI, so as to ensure that sufficient funds are being allocated to it.

2.4 Implications for future policies and practices

The comprehensive application of a gendered approach to the reporting and analysis of healthcare data has substantial support from many governments and global and regional organisations. However, its implementation will only be realised if there is systematic engagement with and monitoring of healthcare providers, including both governments and the private sector. Engagement is required in both HICs and LMICs. To facilitate a greater understanding of the value of such data by healthcare providers, there will be a need to show how investments in gendered analyses can provide new knowledge and lead to health improvements especially for women.

As proposed by the LERU Advice Paper, the consistent application of a gendered approach to the conduct, analysis and reporting of health research needs to be led by the university sector, in both HICs and LMICs. Governments, funding agencies and peer-reviewed journals also need to be engaged. To facilitate change, there will be a need to show how investments in gendered research can provide new knowledge and can lead to health improvements, including reductions in gender disparities in health.

An example of the type of evidence required to determine whether and why sex differences exist in the management and outcomes of acute coronary syndromes in China

Primary research aim: Variations in care and outcomes by sex in patients with acute coronary syndrome (ACS) have been reported worldwide. However, little is known about whether similar disparities exist in contemporary China. The Clinical Pathways for Acute Coronary Syndromes – Phase 2 (CPACS-2) study was a cluster randomised trial of a clinical pathways-based quality improvement initiative for ACS in China. Data were used from this trial to establish whether sex differences in ACS care and outcomes exist in China.

Methods and results: The study enrolled patients from 75 hospitals throughout China between October 2007 and August 2010. Key performance indicators and in-hospital clinical outcomes were compared between 4,632 women and 10,508 men. After adjustment for baseline characteristics, women compared to men had a longer length of hospitalisation stay (mean difference [95% CI] 0.51 [0.18 to 0.83] days, $P=0.002$), were less likely to undergo coronary angiography when indicated (HR 0.88 [0.85 to 0.92], $P<0.001$) and were less likely to be discharged on appropriate secondary prevention medical therapy (HR 0.94 [0.91 to 0.98], $P=0.003$). In-hospital clinical outcomes did not differ by sex.

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3. Recommendations

3.1 Recommendations to global stakeholders, including leaders within the UN system, global NGOs, charities and foundations with a focus on women's empowerment and the health of women and adolescent girls

- It is imperative that global stakeholders consistently recognise, promote and allocate resources to address a broader health agenda for women and adolescent girls, with a focus on the established leading causes of death and disability for women and adolescent girls, namely NCDs. Particular leadership must be exercised by the UN Secretary-General as well as the leaders of the WHO, UN Women, United Nations Development Programme (UNDP), United Nations Children's Fund (UNICEF), United Nations Population Fund (UNFPA) and the World Bank.
- Furthermore, we recommend that these stakeholders consistently recognise, promote and allocate resources to support an integrated, life-course approach to addressing SRH issues, recognising that such an approach has the potential to lead to reductions in both SRH issues and NCDs.
- Consistent with the WHO Roadmap for Action, we call on the UN system, as well as global private sector health operatives and global NGOs, charities and foundations engaged in the provision of healthcare, especially in LMICs, to promote, produce and report gendered analyses of healthcare statistics. We particularly call on them to ensure resources are made available to:
 - Monitor (and police) the gendered analyses of healthcare statistics;
 - Examine the *pathways and quality of care* for women within the healthcare system;
 - Determine whether these pathways differ for men and women;
 - Identify evidence-based strategies that could be implemented to ensure women receive the best available care.

3.2 Recommendations at a national level, using the UK as an illustrative example

- The UK Department of Health and its agencies and public bodies, including Public Health England, NHS England and the National Institute for Health and Care Excellence (NICE), should recognise, promote and allocate resources, within the UK, in support of the 2015 Global Strategy's commitment to reducing by one-third premature mortality from NCDs and the promotion of mental health and wellbeing in women.
- The UK Department for International Development (DFID), and government agencies such as NICE International, should play a strong leadership role and consistently recognise, promote and allocate resources to address a broader, integrated women's health agenda in LMICs, with a focus on the established leading causes of death and disability for women, namely NCDs.
- Consistent with the WHO Roadmap for Action, the UK Department of Health

(and its agencies and public bodies); DFID (and government agencies such as NICE International); private sector health operatives; and NGOs, charities and foundations engaged in the provision of healthcare, especially in LMICs, should promote, produce and report gendered analyses of healthcare statistics and ensure resources are made available to:

- Monitor (and police) the gendered

analyses of healthcare statistics;

- Examine the *pathways and quality of care* for women within the healthcare system;
- Determine whether these pathways differ for men and women;
- Identify evidence-based strategies that should be implemented to ensure women receive the best available care.

3.3 Recommendations to academia, including universities, professional and academic organisations and journals

- We call on professional and academic organisations with an interest in global health to recognise, promote and address a broader, integrated women's health agenda.
- We recommend that, consistent with the LERU Advice Paper, universities take a leadership role in developing, promoting and implementing policies requiring that all new research is appropriately designed to

facilitate the inclusion of gendered analyses and involve appropriate numbers of women.

- We recommend that, consistent with the LERU Advice Paper, UK-based peer-reviewed medical research journals develop, promote and implement policies requiring that all new research papers submitted for publication include gendered analyses.

3.4 Recommendation to research funding agencies

- We recommend, consistent with the LERU Advice Paper, that health research funding agencies develop, promote and implement policies requiring that all new research is appropriately designed to facilitate the inclusion of gendered analyses and involve appropriate numbers of women and, in particular, provide targeted funding to support:
 - Gendered analyses of existing datasets;
 - Research to increase our understanding of the interaction of biological, social and economic factors in determining risk and outcomes for NCDs;
 - Research to examine variations in *access to care* for women and men for

the prevention and treatment of NCDs and, if required, funding to determine the barriers to women seeking early care and the development, testing and implementation of strategies to improve timely access to care;

- Research to increase our understanding of the *pathways and quality of care* for women for the prevention and treatment of NCDs within the healthcare system, determination of whether these pathways differ for men and women and the strategies that might need to be implemented to ensure women receive the best available care.

Notes

- 1 The *Global Burden of Disease (GBD)* study (see endnote 9) categorises the leading causes of death into three main groups: Group I – communicable, maternal, perinatal and nutritional conditions; Group II – non-communicable diseases; and Group III – injuries. Non-communicable diseases or chronic diseases are those conditions that are not passed from person to person and are usually of long duration and slow progression.
- 2 “Sex” refers to the biological and physiological characteristics that define men and women. “Gender” refers to the socially constructed roles, behaviours, activities and attributes that a given society considers appropriate for men and women. <http://apps.who.int/gender/whatisgender/en/> (accessed 4 December 2015).
- 3 In referring to a “gendered” approach, we refer collectively to the use of sex and/or gender disaggregated analyses. Sex disaggregated analyses enable the identification of biological “differences” between males and females. Gender disaggregated analyses facilitate the identification of “disparities” between men and women that relate to the impact of sociocultural and economic factors.
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The focus of 'women's health' interventions has traditionally been sexual and reproductive health. In almost all but the poorest countries of the world, however, the leading causes of death and disability for women are now non-communicable diseases (NCDs). This paper calls for the global women's health agenda to prioritise NCDs, and goes on to emphasise the value of a gendered approach to the analysis of health data, so as to identify and better understand the factors associated with disparities between women and men in health outcomes.

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