# Cardiovascular Diseases in Women: Policies and Practices Around the Globe to Achieve Gender Equity in Cardiac Health 

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#### Abstract

The women's global health agenda has recently been reformulated to address more accurately cardiovascular disease (CVD) prevention, diagnosis, and treatment. The aim of the present work was to review the global and national policies and practices that address sex equality in health with a focus on CVDs in women. Scientific databases and health organizations' websites that presented/discussed policies and initiative targeting to enhance a sex-centered approach regarding general health and/or specifically cardiac health care were reviewed in a systematic way. In total, 61 relevant documents were selected. The selected policies and initiatives included position statements, national action plans, evidence-based guidelines, guidance/recommendations, awareness campaigns, regulations/legislation, and state-of-the art reports by national/international projects and conferences. The target audiences of large stakeholders (eg, American Heart Association, European Society of Cardiology, Centers for Disease Control and Prevention) were female citizens, health professionals, and researchers. Much as policy-makers have recognized the sex/gender gap in the CVD field, there is still much to be done. Thereby, tailor-made strategies should be designed, evaluated, and delivered on a global and most importantly a national basis to achieve gender equity with regard to CVDs.


Keywords: heart disease, cardiovascular, women, health policy, health management

## Introduction

Since the introduction of the United Nations Millennium Development Goals in 2000, it been imperative for policy-makers around the globe to improve women's sexual and reproductive health. ${ }^{1}$ Much as this remains at the top of the list in the global agenda of women's health, noncommunicable diseases (NCDs) seem to be an even bigger threat, considering the enormous burden of cardiovascular disease (CVD) in terms of morbidity/mortality rates, life-years lost, poor quality of life, and direct or indirect health-care costs: ${ }^{1,2} 18.1$ million women died from NCDs, almost half attributed to CVDs, based on estimations for 2012. ${ }^{1}$ Most importantly, besides the "success story" of the past four decades regarding the decline in age-adjusted CVD-mortality rates, this has not been the case in women, even the younger ones. ${ }^{3}$

As underscored by Briones-Vozmediano et al, international and especially national health plans lack gender sensitivity. ${ }^{4}$ This phenomenon is even more apparent in the case of CVDs. The lack of sex- and gender-sensitive studies in CVD research points to indicative defaults in the NCD-research field. ${ }^{5}$ Underrepresentation of women in studies need to be addressed while important
efforts are being demanded to effectively include sex/gender in health research and funding. ${ }^{6}$ It is imperative to recognize that CVDs in women have long being sidelined in favor of the unanimously propagated claim that this chronic disease was supposed to be a male domain or that men and women were equally susceptible. ${ }^{5}$ Nonetheless, indicative heterogeneity has been convincingly demonstrated regarding CVD manifestation, riskfactor burden, and disease prognosis between men and women, due not only to biological status (ie, sex) but also various social determinants (ie, gender identity). ${ }^{5,6}$ Most importantly, the lack of women's awareness regarding this threat is impressive. The majority of women usually falsely recognize breast cancer as the principal cause of death in the female population. ${ }^{7,8}$ In this context, women are to wait longer between seeking and receiving medical advice. ${ }^{9}$ On the other hand, female patients are susceptible to underdiagnosis, inappropriate therapeutic decisions, or even remaining untreated, as physicians usually underestimate their risk burden. ${ }^{10,11}$ Therefore, it is considered that the time has come for a sustained effort and commitment to encompass in the women's health agenda tailor-made strategic plans regarding the effective prevention and management of CVD. ${ }^{2}$ To manage these gender disparities, policy-makers around the globe should design, evaluate, and deliver strategies to increase awareness, enhance research, and optimize disease prevention, diagnosis, and treatment. ${ }^{2}$ The goal of this review was to present what is actually happening in terms of policies and practices aimed at enhancing a sex-centered approach in health to highlight those specific to women's cardiac health, with implications for public health practitioners and policy-makers to achieve gender equity with regard to CVD.

## Methods

## Literature Review

Our literature search included scientific papers in peerreviewed journals, as well as any other relevant documents and organization websites (gray literature)presenting/discussing policies and initiatives targeting a sex-centered approach regarding CVDs. For scientific papers, Pubmed and Scopus were used, and the search was carried out from December 2019 to January 2020 and extended back to papers published in 1960 . No restriction was made with regard to publication language or status. The search was completed using cross-referencing from the papers found,
whereas forpapers in which additional information was required the authors were contacted via email. The search terms were cardiovascular disease(s), heart, gender, sex, women, female, disease, policy, public health, and strategic plan. Since scientific databases provide limited information on policies and practices in public health, the websites of the UN (www.un.org), WHO (www.who.int), AHA (www.americanheart.org), American College of Cardiology (www.acc.org), ESC (www.escardio.org), European Medicines Agency (www.ema.europa.eu), NIH (www.nih.gov), NHLBI (www.nhlbi.nih.gov), CDC (www.cdc.gov), BHF (www.bhf.org.uk), Heart and Stroke Foundation of Canada (http://www.heartandstroke. com), and other national cardiac societies and foundations were searched for relevant position statements and any other documents referring to the aims of present to find as much information as possible. Based on the US Centers for Disease Control and Prevention (CDC) definition of the term "policy" (https://www.cdc.gov/policy/analysis/ process/definition.html), types of manuscripts selected in the present review included position statements,discussion papers and articles supportive of the scientific community, national action plans, evidence-based guidelines, guidance/recommendations, awareness campaigns, regulations/legislation, state-of-the-art reports by international projects and national/international conferences, and other relevant initiatives/practices. Policies and practices had to state or speculate on their main objectives of reduction in gender equity in general health and/or in cardiac health care. The manuscripts selected to cover the purposes of the present work were reviewed by two independent authors (MK and DP) following a systematic approach.

## Results

In total, 35 publications in the scientific databases were considered relevant to the present work. In addition to those, 26 documents/references regarding global and national policies and practices were retrieved from the aforementioned organization websites and are discussed here. The flow diagram of the literature search is presented in Figure 1.

## Sex-Specific Reporting in Global Health Agenda: Policies and Practices

Results from the initiatives regarding the consideration of sex in global initiatives are summarized in Table 1. The NIH was among the very first references regarding this issue: in


Figure I Flow diagram demonstrating the literature-review process.

1994, policy guidance regarding the consideration of women in clinical trials was published. ${ }^{12}$ Updated versions were released in 2000 and 2001. ${ }^{13,14}$ In 1995, in a report from the Fourth World Conference on Women, the UN underscored the fact that a policy decision should be published only after a sex-specific evaluation regarding its effectiveness. ${ }^{15}$ Additionally, it has been about two decades since the US Food and Drug Administration (FDA) established the Office of Women's Health, targeting the need to manage the underrepresentation of women in general and women in particular situations (eg, pregnancy) in medical clinical trials. In this context, in 1993 guidance for researchers on this issue was published, while in 2014 the FDA published an action plan to address the collection and availability of subgroup data, including sex. ${ }^{16,17}$ Exploring the Biological Contributions to Human Health; Does Sex Matter? and Women's Health Research: Progress, Pitfalls, and Promise, published by the Institute of Medicine in 2001 and 2010, respectively, were milestones for global health research and policy-making and among of the very first official recognitions of sex (ie, the biological dimension) and gender (ie, the socially constructed dimension) as variables with critical health impact, interacting with each other. ${ }^{18,19}$ In 2010, the Canadian Institutes of Health Research and its Institute of Gender and Health subdivision
revealed a user-friendly tool for health researchers regarding the integration of sex and gender in their study design. ${ }^{20}$ In 2014, the WHO provided guidance on the integration of gender-responsive sustainable approaches and promoted disaggregated data analysis and health-inequality monitoring. ${ }^{21}$ In 2015, the NIHrecommended sex-specific reporting in any kind of study or an evidence-based justification for its omission. ${ }^{22}$ At the same time, the UN underscored the necessity for gender-sensitive strategies in all sustainable development goals for 2030, while the fifth sustainable goal was incorporated to "achieve gender equality and empower all women and girls." ${ }^{23}$ In 2015, the League of European Research Universities published a list of recommendations for universities, governments, funders, and peer-reviewed journals to adopt strategies and policies toward a gendered research and innovation approach. ${ }^{24}$ The Lancet Commission on Women and Health in 2015 recognized women's health as a key factor in sustainable development. ${ }^{25}$ In 2016, the report "Women's health: a new global agenda" provided a redefinition of the women's health agenda, setting different priorities according to the reality depicted by disease-epidemiology data around the globe. ${ }^{26}$ In this context, the Global Strategy for Women's, Children's, and Adolescents' Health (2016-2030) was published by the WHO-UN Secretary-General partnership. The

Table I Global Policies and practices to Address Gender Disparities in Health, with the Scientific Community as Target Audience

| Organization | Year | Title | Main Content | Author(s) |
| :---: | :---: | :---: | :---: | :---: |
| Food and Drug Administration (FDA) | 1993 | Guideline for the study and evaluation of gender differences in the clinical evaluation of drugs notice | Guidance on the consideration and evaluation of discrepancies in medicine effectiveness and appropriateness separately in males and females | Federal <br> Register, <br> 2013 |
| National Institutes of Health (NIH) | 1994 | NIH guidelines on the inclusion of women and minorities as subjects in clinical research Federal Register notice | Guidance on the inclusion of women and minorities in research | NIH |
| United Nations (UN) | 1995 | Report of the Fourth World Conference on Women | The impact on women and men should be analyzed separately prior to policy-making | UN |
| National Institutes of Health (NIH) | 2000 | Notice NOT-OD-00-048 | NIH guidelines on the inclusion of women and minorities as subjects in clinical research: guide to grants and contracts - updated version | NIH |
| Institute of Medicine (IOM) | 2001 | Exploring the Biological Contributions to Human Health: Does Sex Matter? | Explores the health impact of sex and gender, from behavioral characteristics to genetic and metabolic features | IOM |
| National Institutes of Health (NIH) | 2001 | Notice NOT-OD-02-001 | NIH policy and guidelines on the inclusion of women and minorities as subjects in clinical research: this updated version provides additional recommendations on reporting, among others, sex/gender discrepancies in effects of interventions evaluated in the context of NIH-defined Phase III clinical trials | NIH |
| Canadian Institute of Health Research (CIHR) | 2010 | Sex, gender and health research guide: a tool for CIHR applicants | A guide to enhance all research applicants toward the integration of sex and gender in research designs | CIHR |
| Food and Drug Administration (FDA) | 2014 | FDA action plan to enhance the collection and availability of demographic subgroup data | Action plan to highlight the need of adequate representation and health-data analysis of subgroups, including among those of both sexes | FDA |
| World Health Organization (WHO) | 2015 | Integrating equity, gender, human rights and social determinants into the work of WHO: roadmap for action (2014-2019). | A Guidance on the integration of genderresponsive sustainable approaches in WHO programs and institutional mechanisms on a national basis; <br> B Enhance sex- and gender-disaggregated data analysis and health-inequality monitoring | WHO |
| National Institutes of Health (NIH) | 2014 | Notice NOT-OD-14-085 | Transition plans for reporting sex/gender, race, and ethnicity information in non-competing type 5 progress reports | NIH |
| National Institutes of Health (NIH) | 2015 | Notice NOT-OD-I5-102 | NIH recommends that sex as a biological variable be taken into serious consideration in research designs, analyses, and reporting in vertebrate animal and human studies, and strong evidence-based justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications where only the one sex is studied | NIH |

(Continued)

Table I (Continued).

| Organization | Year | Title | Main Content | Author(s) |
| :---: | :---: | :---: | :---: | :---: |
| United Nations (UN) | 2015 | Global Strategy for Women's, Children's, and Adolescents' Health (2016-2030) | An updated version of Global Strategy for Women's, Children's, and Adolescents' Health (2010-2015): 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", with a commitment made to a one-third reduction in premature mortality from NCDs and the promotion of mental health and wellbeing | UN, 2015a |
| United Nations (UN) | 2015 | Sustainable development goals | In all SDGs, such terms as "gender equality" and "gender-sensitive" strategies are underscored Goal 5: "Achieve gender equality and empower all women and girls" | UN, 2015b |
| League of European Research Universities (LERU) | 2015 | Gendered research and innovation: integrating sex and gender analysis into the research process | Provides a list of recommendations for universities, governments, funders, and peerreviewed journals to adopt strategies and policies for a gendered research and innovation approach | LERU |
| Lancet <br> Commission on Women and Health | 2015 | Women and health: the key for sustainable development | Highlights health challenges that women share with men, yet with manifestations that affect females disproportionally owing to biological and environmental determinants | Langer et al |
| European <br> Commission | 2016 | H2020 programme: guidance on gender equality in Horizon 2020 | Recommendations to foster gender balance in Horizon 2020 research teams, to prevent underrepresentation of women and to integrate sex- and gender-specific analysis in research, and innovation content aiming at ameliorating the scientific quality and relevance of the knowledge produced | European <br> Commission |
| Oxford Martin School | 2016 | Women's health: a new global agenda | A redefinition of women's health agenda and setting additional priorities, other than women's sexual and reproductive health. | Norton et al |
| European <br> Association of Editors | 2016 | Sex and gender equity in research (SAGER) guidelines | A tool for researchers and authors to standardize sex and gender in scientific publications on four levels: topic of the study, sex- and gender-disaggregated data report, study design, discussion/limitations | De Castro et al |

roadmap report provided recommendations to diminish all preventable deaths in women, children, and adolescents, making a commitment to reducing premature NCD mortality by a third by $2030 .{ }^{27}$ Shortly thereafter, the European Association of Editors published a set of reporting guidelines (Sex and gender equity in research) to provide to researchers and authors a tool to achieve sex- and gender-
standardization in scientific publications, while the European Commission in the context of the Horizon 2020 program published guidance for addressing gaps in the participation of women in the EU Framework Programme for Research and Innovation's projects and to achieve gender balance in theknowledge, innovation, and technology produced. ${ }^{28,29}$

## Female-Centered Policies and Practices in Global CVD

Results from initiatives regarding the consideration of sex in global CVD are summarized in Table 2. In 1986, a workshop was convened by the NIH NHLBI to lay the groundwork for researchers and clinicians to work onCVD in women, while in 1987 key highlights of the workshop were summarized in a report: "Coronary heart disease in women: reviewing the evidence, identifying the needs". This was the very first initiative that brought the "female heart" out from the shadows. ${ }^{30,31}$

The "Guide to preventive cardiology for women" was the first official report with recommendations on CVD prevention and management in women, focusing on female-specific factors and medical treatments (eg, hor-mone-replacement therapy), and was issued by the AHA. ${ }^{32}$ However, the first evidence-based women-centered guidelines on primary and secondary prevention of chronic vascular atherosclerotic diseases came in 2004. ${ }^{33}$ Since then, two updates of this guidance have been published. Initially, the AHA underscored the common misconception that women and men are equal in terms of the disease and challenged the belief that the two sexes should be treated similarly. ${ }^{34,35}$ These guidelines highlighted the underrepresentation of females in clinical trials. Following that, health professionals were oriented toward a more sexspecific research approach, resulting in the potential for more definitive recommendations and passing from evi-dence-based strategies to the effectiveness-based preven-tive-action plans in 2011. Notably, in the last AHAguideline update, some primary prevention strategies were proven to be inappropriate for women (ie, aspirin prescription), while it was underscored that women were susceptible to other comorbidities and conditions that multiplied their CVD risk, thus challenging the effectiveness and appropriateness of hitherto-typical prevention and management strategies. ${ }^{35}$ In addition to this, in 2014 the first set of guidelines related on stroke prevention in women was published by the AHA in collaboration with the American Stroke Association. ${ }^{36}$

In 2007, unique aspects of nonclinical factors that affect the health of women, termed "gendered structural determinants of health" in a 2007 report by the World Health Organization's Women and Gender Equity Knowledge Network, pointed to the health and outcomes of women at risk of or with CVD. ${ }^{37}$ In the AHA's journal Circulation, a themed issue focusing on women's cardiac
health (ie, CVD in women) highlighted major challenges and gaps in sex- and gender-centered CVD prevention, diagnosis, and treatment, calling on health professionals for additional research. ${ }^{5,38,39}$ In 2017, a state-of-the-art review was published in the Journal of the American College of Cardiology that synthesized evidence and discussed issues related to health-care quality and equity for women, including minority-population subgroups. ${ }^{40}$ The same year, the results of a survey conducted by the Women's Heart Alliance were revealed, summarizing the knowledge, gapstherein, and perceptions, of women as well as physicians regarding CVD in women. ${ }^{41}$

FDA Office of Women's Health-funded projects have contributed to highlighting major gaps in the field of CVDs in women. ${ }^{42}$ Nonetheless, apart from the limited number of high-quality sex-specific studies, the AHA recognized another challenge in CVD in women: CVD was the leading cause of death in females, yet many were unaware of this threat. ${ }^{43}$ In 2002, the NHLBI along with (among others) the AHA - teamed up to sponsor the Heart Truth awareness campaign with red dress as a centerpiece symbol and the message "Heart disease doesn't care what you wear: it's the \#1 killer of women", aimed at raising women's awareness regarding their cardiac health and enhancing the knowledge of health professionals and researchers on this issue. ${ }^{44}$ In 2004, a national campaign in the US called Go Red for Women was launched. ${ }^{45}$ This campaign, which continues till this day, includes passionate, emotional, and social initiatives designed with a dual purpose: to empower women to take charge of their own cardiac health, and to support health professionals' daily clinical practice. More than a decade later, this campaign has moved beyond the borders of the US to more than 50 countries around the globe. ${ }^{45}$ In 2006, the Society for Women's Health, in collaboration with a nonprofit organization called WomenHeart: The National Coalition for Women with Heart Disease (http://www. womenheart.org), released the "10Q report: advancing women's heart health through improved research, diagnosis, and treatment" to encourage researchers and health practitioners toward female-specific cardiac care. ${ }^{46}$ In 2011, the Make the Call, Don't Miss A Beat campaign aimed at educating, engaging, and empowering women and their families to recognize the seven symptoms of a heart attack that most commonly present in women. This initiative included a comprehensive public service-advertising campaign. ${ }^{47}$

Table 2 Global Policies and Practices to Address Cardiovascular Diseases in Women on a Scientific and Community Basis

| Organization | Year | Title | Type | Target Audience ${ }^{\text {a }}$ | Author(s) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| National Institutes of Health National Heart, Lung, and Blood Institute (NHLBI) | 1987 | Coronary heart disease in women: reviewing the evidence, identifying the needs | State-of-the art report | Scientific community, policy-makers | Eaker et al, <br> Hayes et al |
| Centers for Disease Control and Prevention division of heartdisease and stroke prevention | 1993 | WISEWOMAN (well-integrated screening and evaluation for women across the nation) | Awareness campaign | Female citizens | CDC, 2014 |
| American Heart Association | 1999 | Guide to preventive cardiology for women | Guidelines | Scientific community | Mosca et al |
| Heart and Stroke Foundation of Canada, University of Ottawa, and University of Alberta | 2000 | Heart disease and stroke in Canadian women: policy development | Position statement | Scientific community, policy-makers | Plotnikoff et al |
| National Heart, Lung, and Blood Institute | 2002 | Heart truth | Awareness campaign | Female citizens | NHLBI, 2016 |
| Danish Heart Foundation | 2003 | Mind yourself woman! | Awareness campaign | Female citizens | EHN |
| European Health Network, European Health Management Association, and Bristol Myers Squibb | 2004 | Workshop from the $7^{\text {th }}$ European Policy <br> Forum: a healthy heart for European women | State-of-theart report | Scientific community, policy-makers | EHN |
| American Heart Association | 2004 | Evidence-based guidelines for cardiovascular disease prevention in women | Guidelines | Scientific community | Mosca et al |
| American Heart Association | 2004 | Go red for women | Awareness campaign | Female citizens, scientific community, policy-makers | AHA, 2016 |
| European Society of Cardiology | 2005 | Women at heart | Scientific community motivational program | Scientific community | ESC |
| European Society of Cardiology | 2005 | Cardiovascular diseases in women: a statement from the policy conference of the European Society of Cardiology | Position statement | Scientific community, policy-makers | Stramba- <br> Badiale et al |
| European Society of Cardiology and European Health Network | 2006 | EuroHeart project work package no 6: To question gender differences in the management of CVDs and consequently provide recommendations for research and regulatory policy-makers | Transnational project for prevention and management of cardiovascular diseases | Scientific community, policy-makers | ESC |
| WomenHeart: The National Coalition for Women with Heart Disease | 2006 | IOQ report: advancing women's heart health through improved research, diagnosis, and treatment | Position statement | Scientific community, policy-makers | Wenger et al |

(Continued)

Table 2 (Continued).

| Organization | Year | Title | Type | Target Audience ${ }^{\text {a }}$ | Author(s) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| World Health Organization, Women and Gender Equity Knowledge Network | 2007 | Gender inequity in health: why it exists and how we can change it - final report to the WHO Commission on Social Determinants of Health | Report | Scientific community, policy-makers | WHO |
| American Heart Association | 2007 | Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update | Guidelines | Scientific community | Mosca et al |
| Hellenic Cardiac Society | 2008 | National action plan for cardiovascular diseases (2008-2012) | National action plan | Scientific community, policy-makers | HCS |
| European Society of Cardiology, <br> European Society of <br> Hypertension, and International <br> Menopause Society | 2008 | Assessment and management of cardiovascular risks in women | Guidance | Health professionals | ESC et al |
| European Society of Cardiology and European Health Network | 2009 | Red alert for women's hearts | Report in the context of EuroHeart project | Scientific community, policy-makers | Mas et al |
| American Heart Association | 2011 | Evidence-based guidelines for the cardiovascular disease prevention in women: 2011 update | Guidelines | Scientific community | Mosca et al |
| American Heart Association | 2011 | Make the call, do not miss a beat | Awareness campaign | Female citizens | AHA |
| American House of Representatives | 2011 | Heart Disease, Education, Analysis, Research, Treatment for Women Act or Heart for Women Act | Legislation | Scientific community, policy-makers | House of Representatives |
| International Council on Women's Health Issues | 2011 | The health of women and girls determines the health and well-being of our modern world: a white paper from the International Council on Women's Health Issues | White paper | Scientific community, policy-makers | Davidson et al |
| Minneapolis Heart Institute, Minneapolis Heart Institute Foundation, and University of Minnesota | 2012 | Women and Heart Disease: a summit to eliminate untimely deaths in women | Report from a <br> 2-day summit | Scientific community, policy-makers | Lindquist et al |
| International Council on Women's Health Issues | 2012 | Improving women's cardiovascular health: a position statement from the International Council on Women's Health Issues | Position statement | Scientific community, policy-makers | Davidson et al |
| European Society of Cardiology | 2011 | ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology (ESC) | Guidelines | Scientific community | ESC |

(Continued)

Table 2 (Continued).

| Organization | Year | Title | Type | Target Audience ${ }^{\text {a }}$ | Author(s) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Centers for Disease Control and Preventiondivision for heartdisease and stroke prevention | 2014 | WISEWOMAN (well-integrated screening and evaluation for women across the nation): technical assistance and guidance document | Guidance | Scientific community, policy-makers | CDC |
| American Heart Association and American Stroke Association | 2014 | Guidelines for the prevention of stroke in women | Guidelines | Scientific community | Bushnell et al |
| British Heart Foundation | 2015 | Bag it - beat it | Awareness campaign | Female citizens | BHD |
| Heart Institute at the University of Ottawa and Canadian Women's Heart Health Centre | 2016 | Women@Heart | Peer-support program | Female citizens | Canadian <br> Women's Heart <br> Health Centre, <br> 2016a |
| Heart Institute at the University of Ottawa andCanadian Women's Heart Health Centre | 2016 | IMPROVE postpartum program | Peer-support program | Female citizens | Canadian <br> Women's Heart <br> Health Centre, 2016b |
| Journal of American College of Cardiology | 2017 | Quality and equitable health care gaps for women: attributions to sex differences in cardiovascular medicine | State-of-the art review | Scientific community and policymakers | Shaw et al |
| Women's Heart Alliance | 2017 | Knowledge, attitudes, and beliefs regarding cardiovascular disease in women: the Women's Heart Alliance | Survey | Scientific community and policymakers | Bairey Merz et al |
| European Society of Cardiology | 2018 | 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy | Guidelines | Scientific community | Regitz- <br> Zagrosek et al |
| American Heart Association | 2018 | Heart centers for women | Program | Female citizens and health professionals | Lundberg et al |
| US Food and Drug Administration | 2019 | Women in clinical trials | Awareness campaign | Female citizens | (FDA, 2019) |
| US Food and Drug Administration | 2020 | Heart health for women | Awareness campaign | Female citizens | FDA |

Note: ${ }^{\text {as }}$ Scientific community defined as health professionals, health-care practitioners, researchers, and relevant global/national stakeholders with public health activity

Another initiative in the CVD spectrum focusing on women's health was the WISEWOMAN (Well-Integrated Screening and Evaluation for Women Across the Nation) program started in 1993. ${ }^{48}$ This program is administered by the CDC, specifically its division for heart disease and stroke prevention. The target group of the WISEWOMAN program is women with low financial status aged $40-64$ years. The aim of the program is to provide free-of-charge heart-disease and stroke risk-
factor screenings, namely blood-pressure control, along with evidence-based methods enhancing women's adherence to healthier behaviors, so as to promote lifelong heart-healthy lifestyle changes. The contributors to this program focus on strategies being applicable to both health-care practitioners and on the basis of community targeting from clinicians and pharmacists to farmers' markets, and were recently revealed in a technical assistance and guidance document. ${ }^{48}$

A bill addressing the prevention, diagnosis, and treatment of heart disease, stroke, and other CVDs in women was introduced in the American House of Representatives in November 2011, called the Heart Disease, Education, Analysis, Research, and Treatment for Women Act or the Heart for Women Act. ${ }^{49}$ This legislation was set to ensure the availability of gender-specific information in medical treatments for health-care professionals, researchers, and the public to expand the CDC-funded WISEWOMAN project to 20 additional states of the US and to require the Secretary of Health and Human Services to perform an annual report for Congress on the quality of and access to health-care services for women. This bill was highly supported, among other relevant associations and nongovernmental organizations, by the AHA and its American Stroke Association division. ${ }^{50}$

Heart centers for women were recently developed as a response to the need for improved outcomes for women with CVD. ${ }^{51}$ These centers serve as a point of focus for the development of education and research programs to better address the unique features of CVD in women. The multidisciplinary approach to the care of women with or at risk of CVD has emphasized the importance of developing key clinical benchmarks to allow for standardization of care pathways. Stakeholders in such centers include representatives from internal medicine, family medicine, obstetrics and gynecology departments, and nursing programs.

The FDA Office of Women's Health offers resources to help women and health-care providers get informed about heart health, including the Heart Health Social Media Toolkit to encourage women to protect their hearts. The toolkit includes resources for "everyday" women and health professionals, including sample social media messages and blog posts. ${ }^{52}$ What is more, the Office of Women's Health is partnering with the NIH Office of Research on Women's Health to raise awareness about diverse women of different ages, races, ethnic backgrounds, and health conditions participating in clinical trials. The Diverse Women in Clinical Trials Initiative includes a consumer-awareness campaign, as well as resources and workshops for health professionals and researchers. ${ }^{53}$

In Europe, important attempts have been made at reformulatingthe women's health agenda. In 2004, a workshop was held at the seventh European Policy Forum, based on which a report was released underscoring sex discrepancies in CVD diagnosis and treatment and challenges on a community basis. ${ }^{54}$ Among the very first initiatives of the

European Society of Cardiology (ESC) was the Women at Heart program launched in 2005 aimed at coordinating research and educational initiatives regarding CVDs in females. ${ }^{55}$ The program started with a policy conference in June 2005, during which experts' opinions were selected, scientific gaps underscored, and strategic plans delineated to address this issue. ${ }^{55}$ Highlights of the conference and the state of the art in Europe were summarized in a policy statement, available in various languages. In this policy statement, a flowchart with synergistic actions implemented by the ESC, EU, national scientific societies, and national health authorities at a European level was proposed to enhance researchs and other relevant scientific sectors (eg, research funders) to cover gender gaps in CVD investigation. ${ }^{56}$ At the 2005 ESC Congress, a thematic subunit was devoted to CVDs in women so as to enhance dissemination of this information in the scientific community, while in 2006 an educational course was available. In national cardiac societies (ie, Swedish Cardiac Society, Polish Cardiac Society) rollout of the Women at Heart program was revealed. ${ }^{56}$ From this perspective, the European Health Network and ESC jointly applied for a grant for the EuroHeart project, a consortium among 30 partners in 21 European countries. ${ }^{57}$ Among the primary purposes of this project presented in its work package number 6 was "to question gender differences in the management of CVDs and consequently provide recommendations for research and regulatory policy-makers."58 This survey highlighted significant gender biases in the use of investigations and evidence-based medical treatments. ${ }^{59,60}$ In the context of this work package, a report called "Red alert on women's hearts" was released in November 2009 for the scientific community. ${ }^{61}$ Additionally, 60 and 15 awareness campaigns for women and their physicians in the participated in the project countries were launched, respectively. ${ }^{61}$ In 2008, a short guide called "Assessment and management of cardiovascular risks in women" was published by a joint workshop under the auspices of the ESC, European Society of Hypertension, and International Menopause Society aimed at assisting menopause physicians in contributing to the overall management of women's cardiac health. ${ }^{62}$ In 2011, the ESC published guidelines on the management of CVDs during pregnancy, while an updated version was launched in 2018. ${ }^{63,64}$ In the very recent ESC prevention in clinical practice guidelines, some female-specific conditions were reported (eg, polycystic ovarian syndrome, pregnancy complications), yet a large scientific gap was clearly stated: "The young women . . . continue to be underrepresented in clinical
trials . . . Information on whether female-specific conditions improve risk classification in women is unknown". ${ }^{65}$

The BHF has launched pages (eg, the "Women's Room") on its website aimed at increasing awareness of women regarding heart disease and stroke, related risk factors and symptomatology of a cardiac episode. ${ }^{66}$ In 2015, the BHF launched a campaign called Bag it. Beat it, which continues today, with the purpose of increasing funding of research focusing on the prevention, diagnosis, and treatment of CVDs in women. ${ }^{66}$ In 2010, a 2-day summit - Women and heart disease: a summit to eliminate untimely deaths in women - was held in Minneapolis to give straightforward directions on focusing areas of strategies and policies to ameliorate the health outcomes of women with heart disease in Minessota. ${ }^{67}$

In 2000, the Heart and Stroke Foundation of Canada, University of Ottawa, and University of Alberta released a statement report with recommendations concerning policy development for a healthier female heart so as to support researchers, health practitioners, and policymakers in creating a community where women, irrespective of their socioeconomic status, would receive effective medical care. ${ }^{68}$ The Heart Institute in the University of Ottawa has launched the Canadian Women's Heart Health Centre (https://cwhhc.ottawaheart.ca) with the aim of reducing CVDs in women throughmotivating individuals, health professionals, and health-care workers to address this public health concern. This initiative has been disseminated at national events and on social media to generate publicity of women's health. Several training workshops have been organized by female survivors of heart attacks so as to motivate other women to pursue a healthier lifestyle and bring into being adequate preventive medical control to avoid suffering a heart attack. More specifically, the Women@Heart program has 12 two-hour sessions and is held biweekly in community settings across the region, while a similar initiative called the Improve Postpartum Program has been launched for women having suffered from preeclampsia, eclampsia, and gestational hypertension and as a result with high CVD risk. ${ }^{69,70}$ National cardiac/heart associations, such as the Hellenic Cardiac Society, Danish Heart Foundation, and Italian Heart Foundation, have introduced small initiatives on this issue. ${ }^{71}$ In 2011 and 2012, two position statements were revealed by the International Council on Women's Health Issues (ICWHI), an international nonprofit organization aimed at empowering women's health. In these, the necessity of
recognizing and addressing the needs of women with regard to chronic diseases with focus oriented toward CVDs was underscored for researchers, health practitioners, and policy-makers. ${ }^{72,73}$

## Discussion

This review reveals that much as there are some public health initiatives, from policy statements to awareness campaigns, toward acieving gender equity in CVD and supporting women's cardiac health, their resonance within the scientific community remains low, with underrepresentation of women in CVD studies, lack of awareness of citizens and health practitioners, and absence of gendersensitive analysis in scientific works. Additionally, the vast majority of such initiatives are located in the US, with fewer in Europe and scarce well-organized, integrated, focused plans on a national basis. Moreover, the dissemination of all these policies and practices seems too low to motivate the scientific community adequately.

Too few women are aware of CVD. This was firstly identified by the AHA in 1997, where they found that only one in three women were able correctly to identify heart disease as their sex's leading cause of death. ${ }^{74}$ The aforementioned campaigns and other initiatives to educate the public and increase support for women's heart disease have contributed to a significant improvement in the level of women's awareness regarding their cardiac health that has doubled since 1997. Nevertheless, this remains substandard, and has not improved significantly since 2006, particularly in younger and ethnic minority women, as well as those of low socioeconomic status. ${ }^{75,76}$ Younger women and racial and ethnic minorities have lower rates of awareness, higher rates of CVD mortality, and more risk factors. ${ }^{76}$ In particular, they are less aware of their risks, have delayed diagnosis, face inconsistent responses from the health-care system, have their disease severity underestimated, receive suboptimal treatment, and ultimately have worse outcomes. This is more evident in women aged 35-54 years, in those with lower education, and among racial and ethnic minorities. Focusing on younger patients, prospective cohort studies, such as GENESIS-PRAXY and VIRGO, have revealed some sex differences in demographic, CV risk factors, symptoms, and treatment. ${ }^{77,78}$ Additionally, the social determinants of CVD in women have been much discussed, including health literacy, lower education, low-wage jobs, higher rates of poverty, and more familial responsibilities,
coupled with societal discriminatory norms and practices. ${ }^{40}$

At the same time, physicians also appear to ahow gaps regarding women's cardiac health. In particular, physicians are more likely to assign a lower CVD risk category to female patients and underestimate CVD risk in women. ${ }^{79}$ They are also less likely to refer women and ethnic minorities for diagnostic cardiac catheterization. ${ }^{80}$ In a 2012 online survey, only one in five women reported that their physicians had ever discussed their risk of heart disease. ${ }^{81}$ Women often receive suboptimal CVD-preventive care. ${ }^{78}$ A couple of years later, the Women's Heart Alliance survey selected 200 primary-care providers and 100 cardiologists to determine their self-reported readiness to address CVD risk in women patients. Primary-care providers reported CVD as a principal health concern in women, yet less important than breast- and weightrelated health. Moreover, most physicians, including
one in two cardiologists, reported suboptimal training in assessing CVD risk in women.

## Implications for Future Policies and Practices in CVD

To optimize women's cardiac health, policy-makers should recognize, promote, and allocate resources to address sexand gender-specific issues in prevention, risk assessment, diagnosis, treatment, and rehabilitation in CVDs. ${ }^{82}$ Policies should be accordingly designed after a cautious needsassessment process to evaluate the actual demands at a national level. Based on the public health initiatives discussed, it is suggested that priority setting for CVD prevention and control include a successful combination of policy-makers/stakeholders, researchers, and health-care systems. Thereby, a multidimensional approach, as suggested in Figure 2 is demanded to support the generation of evidence-based, cost-effective, and tailor-made decisions

| Sex- \& gender- specific study <br> design - consideration of <br> biological and environmental <br> factors | Editors / <br> reviewers | Increase awareness of health <br> care practitioners to achieve <br> tailor-made risk assessment, <br> diagnosis \& treatment |
| :---: | :---: | :---: |
| Researchers | Set specific <br> requirements for the <br> scientific publications <br> towards sex- and <br> gender- centered | Health <br> professionals / <br> physicians |

 approach

## POLICIES FOR WOMEN'S CARDIAC HEALTH

Set legislation to ensure the provision of

COMMUNITY BASIS


Increase awareness of health care practitioners to achieve tailor-made risk assessment, diagnosis \& treatment
 professionals / physicians


Figure 2 Policy-making to address gender equity in cardiovascular disease (CVD) and target audiences. Abbreviation: NGOs, Nongovernmental organizations.
in policy-making. Through this multidimensional approach, specific goals should be set, including (among others) the incorporation of sex- and gender-based guidelines in CVD prevention, management, and rehabilitation, provision of comprehensive patient-centered care customized to address cultural, ethnic, spiritual, and social determinants of the patient, and implementation of multidisciplinary healthcare teams for women incorporating clinicians caring for women to improve quality and address health-care gaps for women: family physicians, primary-care physicians, obstetricians, gynecologists, nurse practitioners, emergencydepartment physicians, and nurses. What is more, women's education in terms of health-literacy improvement regarding CVD is equally important. Finally, community partnership and commitment to research with the focus oriented toward the most vulnerable subgroups (eg, younger women, women of low socioeconomic status, and ethnic minorities) should be an indispensable part of such approaches.

## Conclusion

Much as the past two decades have seen substantial effort being put into improving women's health on the whole, there is still much to be done. Giving a broader definition to women's health, primary and secondary prevention of CVDs has started to be prioritized, and important initiatives have been launched toward this approach. To achieve this, global and most importantly national sectors should perform appropriate policy-making to support sex- and gender-sensitive collection, usage, and interpretation of health data and enhance the level of awareness in citizens and health professionals. In a world with finite resources, where there is imperative need to maximize the cost-effectiveness of prevention and management strategies, health disparities have to be addressed by health practitioners, and the case of women in CVD care remains an ongoing public health concern.

## Abbreviations

AHA, American Heart Association; BHF, British Heart Foundation; CVD, cardiovascular disease; CDC, US Centers for Disease Control and Prevention; ESC, European Society of Cardiology; FDA, US Food and Drug Administration; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; NCDs, noncommunicable diseases; UN, United Nations; WHO, World Health Organization.

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