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Commentary

Addressing the Bias in Cardiovascular Care: Missed & Delayed Diagnosis of Cardiovascular Disease in Women

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1. The Problem

In January 2021, at the *Convening on Missed and Delayed Diagnosis of Heart Disease in Women*, national experts and healthcare stakeholders heard the personal journeys shared by WomenHeart Champions – women living with heart disease. There was a distinct pattern in each story, years of “normal results”, being told “it is all in your head”, incorrect diagnoses of “asthma” or “anxiety”; all resulting in missed and delayed diagnoses of heart disease among women.

Cardiovascular disease (CVD) is the leading cause of mortality among women in the United States (US), resulting in more deaths than all forms of cancer combined.[1] Over the past 20 years, transdisciplinary research made advances to better understand CVD in women.[2] There is an increased awareness that conventional atherosclerotic CVD (ASCVD) risk factors, such as hypertension, tobacco use and diabetes mellitus, impact women differently than men.[2–4] Unique to women are also the female-specific and female-predominant risk enhancers that should be considered in the ASCVD risk assessment of women,[5] which have the ability to further refine the risk assessment based on biological sex.[6]

Despite these advances, the prevalence of traditional ASCVD risk factors including diabetes mellitus, obesity, and hypertension has increased among women younger than 55 years old over the past decade.[7,8] Ad-

ditionally, the rate of decrease in CVD-related deaths has plateaued and unfortunately increased in younger women, with approximately one-third of CVD events among women less than 65 years old.[7,8] Despite almost two decades of national efforts to increase women's awareness of heart disease as the leading cause of death, awareness has decreased from 65% in 2009 to 44% in 2019 among all women across race/ethnicities, and most notably among 25-64 year-olds.[9] Additionally, only 22% of primary care physicians and 42% of cardiologists felt adequately prepared to assess CVD risk in women.[10] This likely contributes to the noted underutilization of preventive therapies in women, when compared to men.[11,12]

Once women have CVD, there are continued sex disparities in their diagnosis, treatment, and management, resulting in worse outcomes for women. Such sex differences have been demonstrated across CVD diagnoses including acute coronary syndromes, heart failure, and valvular disease with delays in care,[13] underutilization of guideline directed medical therapies and cardiac rehabilitation,[2] and less aggressive treatment,[14–16] when compared with men. As a result, we continue to see higher mortality rates and rehospitalizations in women, compared with men.[17] Additionally, women remain underrepresented in clinical cardiovascular trials, making it difficult to fully appreciate sex differences in novel medical therapies, devices, or other interventions.[18]

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1.1. Finding Solutions

To directly address these issues, WomenHeart: The National Coalition for Women with Heart Disease in partnership with the Society to Improve Diagnosis in Medicine (SIDM), was awarded funding from the Patient-Centered Outcomes Research Institute (PCORI) to host a convening of diverse stakeholders to specifically address missed and delayed diagnosis of heart disease in women. In preparation for the convening, a steering committee of WomenHeart and SIDM leadership, WomenHeart Champions (patient leaders), clinicians, and policy stakeholders met virtually throughout 2020. The objective of the steering committee was to conduct a rigorous environmental scan with compilation of the literature to identify research gaps in the diagnosis of cardiovascular disease in women. The steering committee identified gaps along the diagnosis spectrum defined by The National Academy of Medicine's conceptual framework for diagnosis.[19] For these objectives, the selected CVD in women were heart failure, spontaneous coronary artery dissection [SCAD], hypertension, microvascular disease, valve disease, epicardial obstructive disease, and pregnancy-related cardiovascular disorders.

Due to the coronavirus disease 2019 (COVID-19) pandemic caused by the SARS-CoV-2 virus the *Convening on Missed and Delayed Diagnosis of Heart Disease in Women* occurred virtually on January 27, 2021.[20] The convening engaged patients (WomenHeart Champions), primary care, emergency department and other specialty clinicians (including cardiologists, nurses, physician assistants), hospital leaders, healthcare advocates, policy makers, and experts from the Centers for Disease Control and Prevention and the National Institutes of Health. Members of the steering committee presented findings from the environmental scan, delivered state-of-the-art-reviews, and led interactive discussions. The presentations highlighted important gaps in patient-centered research, implicit bias, deficiencies in medical and lay community knowledge, in addition to inertia in clinical implementation of US guidelines, and gaps in US medical training; each believed to be important contributors to delayed and missed diagnosis of CVD in women.

A summary of the environmental scan process and literature findings is available on-line.[20] The environmental scan was the blueprint to guide small group discussions during the convening to provide granular recommendations of patient-centered outcomes research, using comparative effectiveness research. The groups used the PICOTS framework (Patient Population, Intervention, Comparator, Outcome, Timing, Setting).[21] There were four areas addressed to improve diagnostic rates, treatment, and clinical outcomes for women with heart disease: i) provider education, ii) patient-provider communications, iii) social determinants of health and iv) pregnancy-related diagnostic challenges.

The participants of the convening highlighted patient, provider, and system-level barriers along the diagnostic journey for women with heart disease as summarized in the final report.[20] Some important factors are summarized in [Table 1](#):

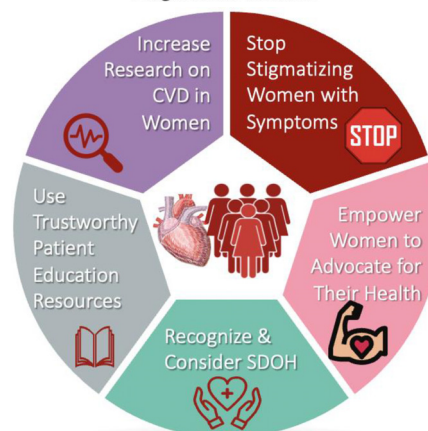
1.2. Action Steps

In response to the identified barriers, the convening progressed to the critical step of recommending feasible, comparative effectiveness research questions to develop tangible, sustainable interventions. Extensive details of the recommended research studies, including a review of potential feasibility are in the convening's publication.[20] A brief summary is in [Table 2](#).

1.3. Using the Blueprint

The environmental scan and convening provided the necessary foundation to take the next action steps to decrease adverse CVD events among women. Now is the time to reinvest in solutions and efforts to improve the awareness of CVD risk factors that affect women among the lay population and across primary care and specialty care within

Steps to Reduce Delayed & Missed Cardiovascular Disease Diagnosis in Women



Central Figure. CVD= Cardiovascular Disease; SDOH= Social Determinants of Health

the medical community. Education goals should reach beyond traditional CVD risk factors, but also highlight pregnancy-related and other female-specific risk factors. The interventions identified during the convening[20] highlight the importance of multidisciplinary, multi-level, collaborations to improve clinical outcomes, to support more timely and accurate diagnosis of heart disease in women, and to further decrease CVD-related deaths. The urgency and feasibility of new interventions need to be addressed in the context of the COVID-19 pandemic, incorporating its additional longitudinal adverse effects on clinical care, clinical outcomes, and social determinants of health. While acknowledging current challenges and strains to health systems, there are actions that can be started today (also see [Central Figure](#)):

- It is time to destigmatize women presenting with shortness of breath, chest discomfort, or other potential CVD-related symptoms
- Support and empower women to advocate for their healthcare and be part of the solution. A patient resource (https://www.womenheart.org/wp-content/uploads/2021/08/Misdiagnosis_Patient-Resource_FINAL.pdf) was created as an accompaniment to the report,¹⁸ which encourages women living with heart disease to take their own actions in support of better outcomes for their peers.
- Recognize and consider the impact of social determinants of health throughout the diagnostic and treatment process
- Continue to educate every woman on their primary or secondary CVD risk factors
- Refer women to WomenHeart for educational resources and access to peer support through the WomenHeart Champions – women heart disease patient leaders: <https://www.womenheart.org/>.
- Encourage your hospital to provide gender-sensitive cardiac care. Consider joining WomenHeart's National Hospital Alliance to collaborate with colleagues across disciplines (ex: obstetrics/gynecology, rheumatology) to address female-specific and female-predominant risk factors.
- Do the research – identify one or more of the patient-centered outcomes research questions proposed in the convening report²⁰ and help build an evidence-base of solutions that improve the diagnostic process for women
- Increase representation of women in clinical cardiovascular trials
- Use resources from the American Society of Preventive Cardiology for patient and clinical education: <https://www.asponline.org/clinical-resources/provider-tools/infographics/>

Table 1
Diagnostic Challenges for Women with Heart Disease

Diagnostic Barrier	Patient Level	Provider Level	Health System Level
Access	Financial barriers; Distrust/avoidance of medical care	Limited preventive and chronic care tailored to women with CVD	Limited public health outreach to women about CVD; Limited provider availability
History	Language/cultural barriers; Unaware of family history; Unaware of need to report all symptoms	Limited time and/or attention; Limited knowledge of symptoms among women with CVD	Medical training insufficiently addresses CVD presentation differences between women and men
Physical Examination	Concerned about disrobing; Anxious or embarrassed about body habitus	Clinical signs of CVD are misinterpreted (i.e., wheezing); Limited knowledge of cultural/religious background	Limited visit time; insufficient training and/or comfort regarding physical examinations in women
Clinical Testing	Financial barriers to additional testing; "No news is good news"	Insufficient CVD evaluation for women; Lack of result communication	Barriers transitioning within and across systems; prior authorizations/referrals
Assessment	Misdiagnosed (e.g., anxiety); Lack of empowerment to request additional evaluation	Symptoms attributed to non-cardiac diagnosis (i.e., anxiety); Implicit bias based on patient's sex, gender, age, race, ethnicity, appearance	Limited CVD research in women for guideline recommendations
Specialist Referral	Limited time (i.e., work, caregiver); financial barriers; unclear why referral is needed	Lack of communication/closing loop with specialist	Long wait for initial visit; Geographic disparities in specialty access
Follow-up	Misunderstanding of CVD diagnosis; Feels abandoned	Limited staff, appointments, community resources	Inability to track patients lost to follow-up; Geographic disparities in longitudinal medical access

Table 2
Summary of Potential Comparative Effectiveness Research Questions and Interventions in Women with CVD

Patient Level	Provider Level	Health System Level
<p>Research Question: Do women who self-assess heart rhythm, blood pressure or other biofeedback using wearable devices receive an earlier, accurate diagnosis of CVD than women who do not?</p> <p>Intervention: Evaluate the role of wearable devices in CVD diagnosis and treatment among women.</p>	<p>Research Question: Are obstetricians/gynecologists (OB/Gyn) who receive dedicated training about CVD in women more likely to make accurate and timely diagnoses of heart disease?</p> <p>Intervention: Provide focused education and training to OB/GYN about CVD.</p>	<p>Research Question: Do women seen in health systems that use telehealth-enabled remote cardiology consultations during the diagnostic process experience more timely and accurate diagnosis of heart disease than women seen in health systems without this virtual capacity?</p> <p>Intervention: Initiate/expand telehealth cardiovascular consultation services.</p>
<p>Research Question: Are women who access information or support from other women with heart disease more likely to be accurately diagnosed with CVD compared to those who do not?</p> <p>Intervention: Provide support groups and/or patient advocates for women with CVD.</p>	<p>Research Question: Does including women with heart disease in simulation training programs improve the diagnostic accuracy of clinicians, compared to clinicians who do not receive such training?</p> <p>Intervention: Increase representation of women in clinical and procedural medical simulation education.</p>	<p>Research Question: Do women seen in hospitals that require admission after repeated emergency department visits have more timely and accurate diagnosis of heart disease than those seen in hospitals without this policy?</p> <p>Intervention: Evaluate the role of dedicated CVD diagnostic pathways for women presenting to the emergency department.</p>

2. Summary

Cardiovascular disease is the leading cause of morbidity and mortality in women, with increasing prevalence of cardiovascular risk factors, and disturbing changes in trends of CVD-related death, especially among younger women. Collaborative efforts of WomenHeart: The National Coalition for Women with Heart Disease in partnership with the Society to Improve Diagnosis in Medicine, with funding from PCORI advanced our knowledge of patient, provider, medical training, and health system research gaps needed to decrease missed and delayed diagnoses of CVD in women. This collaboration highlighted important next steps for patient-centered comparative effectiveness research to directly address the defined gaps. Now is the time for us all to follow the blueprint.

Declaration of Competing Interest

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gagement Award (EACC-18922). Dr. Johnson served as a WomenHeart Steering Committee Member for the convening, is an American Society of Preventive Cardiology Board Member and co-chair of the American Society of Preventive Cardiology - Women in Preventive Cardiology Working Group. The remaining authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Given her role on the Editorial Board, Heather Johnson had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to [NAME of delegated editor].

CRedit authorship contribution statement

Heather M. Johnson: Conceptualization, Visualization, Writing – original draft, Writing – review & editing. **Celina E. Gorre:** Writing – review & editing. **Amy Friedrich-Karnik:** Writing – review & editing. **Martha Gulati:** Writing – original draft, Visualization, Writing – review & editing.

References

- [1] Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, et al. Heart Disease and Stroke Statistics-2021 Update: A Report from the American Heart Association. *Circulation*. 2021;143:e254–743. doi:10.1161/CIR.0000000000000950.
- [2] Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular Disease in Women: Clinical Perspectives. *Circ Res* 2016;118(8):1273–93. doi:10.1161/CIRCRESAHA.116.307547.
- [3] Cho L, Davis M, Elgendy I, et al. Summary of Updated Recommendations for Primary Prevention of Cardiovascular Disease in Women: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020;75(20):2602–18. doi:10.1016/j.jacc.2020.03.060.
- [4] Brown HL, Warner JJ, Gianos E, Gulati M, Hill AJ, et al. Promoting Risk Identification and Reduction of Cardiovascular Disease in Women Through Collaboration With Obstetricians and Gynecologists: A Presidential Advisory From the American Heart Association and the American College of Obstetricians and Gynecologists. *Circulation* 2018;137:e843–52. doi:10.1161/CIR.0000000000000582.
- [5] Elder P, Sharma G, Gulati M, Michos ED. Identification of Female-specific Risk Enhancers Throughout the Lifespan of Women to Improve Cardiovascular Disease Prevention. *American Journal of Preventive Cardiology* 2020;2:100028 doi.org/. doi:10.1016/j.ajpc.2020.100028.
- [6] Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in *Circulation*. 2019 Jun 18;139(25):e1182–e1186]. *Circulation* 2019;139(25):e1082–143. doi:10.1161/CIR.0000000000000625.
- [7] Vikulova DN, Grubisic M, Zhao Y, Lynch K, et al. Premature Atherosclerotic Cardiovascular Disease: Trends in Incidence, Risk Factors, and Sex-Related Differences, 2000 to 2016. *J Am Heart Assoc* 2019;8:e012178. doi:10.1161/JAHA.119.012178.
- [8] Ritchey MD, Wall HK, Georgea MG, Wright JS. US trends in premature heart disease mortality over the past 50 years: Where do we go from here? *Trends in Cardiovascular Medicine* 2020;30:364–74. doi:10.1016/j.tcm.2019.09.005.
- [9] Cushman M, Shay CM, Howard VJ, Jiménez MD, Lewey L, et al. on behalf of the American Heart Association. Ten-Year Differences in Women's Awareness Related to Coronary Heart Disease: Results of the 2019 American Heart Association National Survey: A Special Report from the American Heart Association. 2021; 143: e239–e248. <https://doi.org/10.1161/CIR.0000000000000907>.
- [10] Bairey Merz CN, Andersen H, Sprague E, Burns A, Keida M, et al. Knowledge, Attitudes, and Beliefs Regarding Cardiovascular Disease in Women: The Women's Heart Alliance. *J Am Coll Cardiol* 2017 Jul 11;70(2):123–32 Erratum in: *J Am Coll Cardiol*. 2017 Aug 22;70(8):1106–1107. doi:10.1016/j.jacc.2017.05.024.
- [11] Mosca L, Linfante AH, Benjamin EJ, Berra K, Hayes SN, et al. National Study of Physician Awareness and Adherence to Cardiovascular Disease Prevention Guidelines. *Circulation* 2005;111:499–510. doi:10.1161/01.CIR.0000154568.43333.82.
- [12] Peters SAE, Muntner P, Woodward M. Sex Differences in the Prevalence of, and Trends in, Cardiovascular Risk Factors, Treatment, and Control in the United States, 2001 to 2016. *Circulation* 2019;139:1025–35. doi:10.1161/CIRCULATION-AHA.118.035550.
- [13] Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, et al. on behalf of the American Heart Association Cardiovascular Disease in Women and Special Populations Committee of the Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Cardiovascular and Stroke Nursing, and Council on Quality of Care and Outcomes Research. Acute Myocardial Infarction in Women: A Scientific Statement From the American Heart Association. *Circulation*. 2016;133:916–47. doi:10.1161/CIR.0000000000000351.
- [14] Peters SAE, Colantonio LD, Zhao H, Bittner V, Dai Y, et al. Sex Differences in High-Intensity Statin Use Following Myocardial Infarction in the United States. *J Am Coll Cardiol* 2018;71:1729–37. doi:10.1016/j.jacc.2018.02.032.
- [15] Breathett K, Yee E, Pool N, Hebbon M, et al. Association of Gender and Race With Allocation of Advanced Heart Failure Therapies. *JAMA Network Open* 2020;3(7):e2011044. doi:10.1001/jamanetworkopen.2020.11044.
- [16] Kisilitsina ON, Zareba KM, Bonow RO, et al. Is mitral valve disease treated differently in men and women? *European Journal of Preventive Cardiology* 2019;26(13):1433–43. doi:10.1177/2047487319833307.
- [17] Smilowitz NR, Mahajan AM, Roe MT, Hellkamp AS, Chiswell K, Gulati M, Reynolds HR. Mortality of Myocardial Infarction by Sex, Age, and Obstructive Coronary Artery Disease Status in the ACTION Registry–GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines). *Circ Cardiovasc Qual Outcomes* 2017;10:e003443. doi:10.1161/CIRCOUTCOMES.116.003443.
- [18] Steinberg JR, Turner BE, Weeks BT, Magnani CJ, Wong BO, et al. Analysis of Female Enrollment and Participant Sex by Burden of Disease in US Clinical Trials Between 2000 and 2020. *JAMA Network Open* 2021;4(6):e2113749. doi:10.1001/jamanetworkopen.2021.13749.
- [19] Committee on Diagnostic Error in Health Care. Board on Health Care Services; Institute of Medicine; The National Academies of Sciences, Engineering, and Medicine Improving Diagnosis in Health Care. Balogh EP, Miller BT, Ball JR, editors editors, WashingtonDC: National Academies Press (US); 2015 Dec 29. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK338596/>doi: 10.17226/21794.
- [20] From Errors to Solutions: Building a Research Agenda to Improve Diagnosis of Heart Disease in Women – A Report from a Convening on Missed and Delayed Diagnosis of Heart Disease in Women. <https://www.womenheart.org/from-errors-to-solutions/>. Last accessed 8/29/2021.
- [21] Butler M, Epstein RA, Totten A, Whitlock EP, Ansari MT, et al. AHRQ Series on Complex Intervention Systematic Reviews - Paper 3: Adapting Frameworks to Develop Protocols. *J Clin Epidemiol* Oct 2017;90:19–27 DoiEpub 2017 Jul 15. PubMed PMID: 28720510. doi:10.1016/j.jclinepi.2017.06.013.