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## VIEWPOINT

## Advancing Our Understanding of Women's Cardiovascular Health Through Digital Health and Artificial Intelligence

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rtificial intelligence (AI) involves the application of algorithms to structured and unstructured data to make accurate and reliable predictions or classifications through the identification of patterns that might be unrecognizable by the clinician's expert eye.1 The ideas and mathematical calculations behind machine learning, a form of AI, are not new. However, recent advances in computer chip technologies, data storage, and retrieval have dramatically improved computing power and reduced the computational cost of machine learning-based predictions, while the availability of big data has created the essential input needed to train AI models. AI surrounds our daily lives and is present in everyday applications, commonly going unnoticed by end users. The personalized options offered by smartphones, social platforms, streaming services, online shopping, and home appliances such as smart vacuums represent common practical applications of machine learning.

Since the 1970s, AI has been steadily advancing into health care scenarios,<sup>2</sup> and in recent years it has regained popularity as a tool with huge potential to augment medical care and improve patient outcomes. The digitization of health care systems can facilitate the incorporation of AI into clinical practice by providing sources of big data for the development, testing, and validation of predictive algorithms in multiple domains. In particular, AI models have been explored with multiple cardiovascular imaging modalities and disease prediction algorithms to improve diagnostic accuracy and guide treatment decisions.<sup>3</sup>

Cardiovascular disease (CVD) is the leading cause of death among women, responsible for 35% of deaths in the United States in 2019.<sup>4</sup> Despite the high prevalence, CVD is often underrecognized and understudied among women.<sup>4</sup> Among 740 cardiovascular clinical trials registered on ClinicalTrials.gov between 2010 and 2017, only 38.2% of participants were women, with lower percentages seen in clinical trials that involved an intervention, including the use of a drug, device, or procedure.<sup>5</sup> These trends are a contributing factor to the lack of evidence-based guidelines specific to women.

Despite the pressing need to improve the diagnosis and treatment of CVD among women, as well as include more women in cardiovascular research studies, there are multiple individual, systemic, and cultural barriers that need to be addressed.<sup>6</sup> Furthermore, long-term data collection has become increasingly difficult to implement and undertake due to the inherent challenges of running a traditional clinical trial.<sup>7</sup>

With the benefits of technological advancements, novel digital health technologies (DHTs) and AI can be harnessed to improve our understanding of CVD in women and enhance women's cardiovascular health through the following mechanisms.

- Facilitating the participation of women, including those from racial and ethnic minority groups, in cardiovascular research studies.
- 2) Identification of novel disease pathophysiology through curation of robust longitudinal datasets and explainable AI; and

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3) Advancing precision cardiovascular care for women through the development of sex-specific clinical decision support tools.

Leveraging AI and digital biometric monitoring technologies to track and collect physiological data could provide a viable solution to expand the availability of cardiovascular data sets among women.8 Incorporating this data collection into daily life or routine clinical encounters can facilitate data acquisition for research purposes through convenience as well as enable diverse participant recruitment.<sup>9</sup> Some research studies have demonstrated the feasibility of employing DHTs to facilitate data collection among women-such as the use of a hip-worn accelerometer to examine associations between physical activity, mortality,<sup>10</sup> and coronary heart disease.<sup>11</sup> Personalized DHTs, such as smartwatches, smartphones, and other biosensors, can also be used to monitor women's health over time. The data acquired from these tools can be incorporated into targeted interventions in the workplace, primary care and subspecialty clinics, emergency departments, inpatient settings, and through telehealth modalities. A large prospective study demonstrated the feasibility and effectiveness of using an AI-enabled digital stethoscope for point-of-care cardiovascular screening in hospitals and community health centers in the United Kingdom.<sup>12</sup> More recently, a Mayo Clinic study demonstrated that the use of a consumer smartwatch to obtain electrocardiograms (ECGs) was effective for identifying patients with left ventricular dysfunction in non-clinical environments.<sup>13</sup> The smartwatchbased study successfully enrolled study participants across 46 US states and 11 countries, acquiring over 125,000 ECGs over a 5-month period. Members of our team are currently conducting a clinical trial of an AIbased intervention to screen for cardiomyopathy among pregnant and postpartum women in Nigeria (NCT05438576). Study visits and data collection efforts were designed to be incorporated into routine prenatal and postpartum appointments at obstetrics clinics to minimize the burden related to research study visits. Additionally, the use of portable digital technologies has also facilitated follow-up ECG data acquisition in clinical and home settings, and surmounted challenges related to unstable power supply in a developing country. These examples highlight the utility of DHTs and AI to improve cardiovascular research among women.

In addition to ensuring transparency and trust, explainable AI (XAI) can also provide novel insights into disease pathology among women. One study demonstrated that using XAI with skin microbiome samples provided accurate phenotypic predictions.<sup>14</sup> This is especially important for specific cardiovascular conditions disproportionately affecting women, where disease pathophysiology may be poorly understood and treatment options are limited. XAI could enable the identification of sex-specific biomarkers and potential therapeutic targets to guide novel drug development and therapeutic interventions for women. Remote data acquisition using mobile and wearable devices can also be used to track health data over time and may provide additional diagnostic information by monitoring physiological changes related to disease progression. With more comprehensive data sets, AI-based algorithms can be trained to detect subtle changes over time and identify previously unrecognized disease patterns and novel phenotypes, as demonstrated in a study utilizing unsupervised learning to identify unique heart failure subgroups.<sup>15</sup> Additionally, mobile devices can capture data during routine day-to-day activities, providing additional information on the impact of lifestyle behaviors on cardiovascular health. This continuous and longitudinal data collection approach contrasts with traditional clinical trials where study participants are followed at prespecified timepoints, often resulting in limited data due to missed windows, non-adherence, and loss to follow-up. It has been suggested that a metaverse approach could have a positive impact on health care and clinical practice. The development of new medical technologies and an AI metaverse will allow for the incorporation of AI into multiple health care virtual domains for real-time data collection and secure data sharing.<sup>16</sup> Implementing AI technology into a wide digital network could enhance patient care by reducing associated health care costs related to delayed diagnosis and multiple testing. Furthermore, the development and validation of AI algorithms using digital data from portable devices can support remote care options. Physician access to remote sensor data and the potential provision of near realtime AI predictions using devices with edge computing capabilities can provide an additional tool to enhance health care decisions, allowing care to be expanded into areas where women may have limited access to basic and specialty care..

Lastly, the use of DHTs and AI can be harnessed for developing sex-specific risk prediction algorithms and clinical decision support tools. Studies have demonstrated multiple non-traditional risk factors for CVD among women, including adverse pregnancy outcomes, chronic inflammatory conditions, and menopause, but these have yet to be incorporated into existing clinical risk prediction tools (such as the atherosclerotic cardiovascular disease risk estimator & SCORE-2). Also, the identification of breast arterial calcification has been shown to be associated with adverse cardiovascular outcomes, and with AI, these can be automatically quantified during routine mammography<sup>17</sup> and leveraged to improve cardiovascular risk prediction among women. The incorporation of female-specific factors using AI approaches can allow for improved cardiovascular risk stratification, enable the development of preventive strategies tailored to the specific needs of women, and could be utilized to streamline care management processes, ultimately resulting in more efficient, cost-effective, and precision-based care.<sup>18</sup>

In conclusion, the use of AI and DHTs has immense potential to improve cardiovascular health among women. The daily advancements in health care technologies continue to expand the scope of these possibilities as we usher in the digital era in the field of cardiology and women's health.

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