Normative Values for Cardiorespiratory Fitness: 45 Years after Bruce

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COMMENTARY

Cardiorespiratory fitness powerfully predicts outcomes in health and disease (1–5). Normative data from cardiopulmonary exercise testing (CPX), especially peak oxygen uptake ($\dot{V}O_2$peak) are imperative for the proper interpretation of CPX, both in terms of prognosis and clinical decision making (6). Since 1973 and the seminal work from Bruce et al., there have been numerous normative values for $\dot{V}O_2$peak suggested (7,8). In 1984, the most widely used normative values for exercise testing were updated (9,10). The resulting "Wasserman equations," based on a small sample of homogeneous subjects were originally presented in the first edition of the textbook *Principles of Exercise Testing and Prescription* and further modified to its current version by Wasserman et al. (11).

Compared to other available equations, the equations from Wasserman et al. have been observed to be superior for the prediction of clinical outcomes in patients with heart failure and are the most widely cited (6). They are a series of 6 equations, incorporating age, sex, body weight, "ideal weight" (based on height), and include a correction factor for mode of testing (treadmill or cycle ergometer). However, the relatively small and homogeneous sample, along with their complexity, has made the equations difficult to apply consistently and has limited their application. Although current technology has largely eliminated the problems of complexity, the generalizability of the Wasserman equations remains a concern. Furthermore, normative data must be specific and sensitive to changes within a population, including changes in disease status, percent female, and body weight. Lastly, exercise testing is mostly performed using 1 of 2 different modes, the treadmill or cycle ergometer, and there are significant differences between the 2 in oxygen consumption. These factors in part were the motivation behind the recent American Heart Association (AHA) initiative to support the Fitness Registry and the Importance of Exercise (FRIEND) database (1). Briefly, the FRIEND registry is a consortium of 10 CPX labs and >80,000 subjects designed to enhance the value of fitness across environments, including the clinical setting and workplace as well as the public, to better inform national policy efforts on physical fitness, activity, and health. Published analyses on FRIEND include tests from the 10 participating CPX laboratories (see Acknowledgments) with geographical representation from 27 states, including Indiana, Louisiana, North Carolina, Oregon, Pennsylvania, Tennessee, Texas, and 1 lab with tests from multiple states (1).

In the past, patients referred to CPX were largely male, middle-aged, and presented with traditional coronary artery disease (CAD) risk factors [e.g. smoking/alcohol, visceral adiposity, hypertension (HTN)] and symptoms (e.g. chest pain, dyspnea). Population level changes in anthropometry as well as the CPX referral base have changed substantially since the 1980s. An increase in patients with undiagnosed disease (12), CPX screening for inherited cardiovascular disease (13), unexplained dyspnea, and the "exercise is medicine" initiative (14) are examples of factors that have transformed the CPX referral base. Considering the population being referred for exercise testing has changed substantially, the derived exponents of $\dot{V}O_2$peak embedded within commonly used equations may not truly represent the population being screened.

Contemporary efforts have been made to optimize prediction equations in subpopulations (15). An optimal

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Conflicts of Interest and Source of Funding: None.

long-term strategy would be to invest in the development of a set of large multicenter, regional databases incorporating real-time data to generate a constantly improving equation. Current examples that may provide such a platform include the FRIEND (1) and Helseundersøkelsen i Nord-Trøndelag Study (HUNT, 16) registries in the US and Norway, with approximately 83,530 (personal correspondence with R Arena on July 31, 2017) and 5,000 exercise tests, respectively. Arising from the human genome project, outsource data has become common practice in genomics (17); however, challenges in clinical testing exist in terms of protecting patient privacy and separating those patients who are healthy from those with disease, particularly when patients are often referred for CPX as part of the diagnostic pathway.

Both the FRIEND and HUNT registries have provided equations which seem to predict $\dot{V}O_2$peak in their respective populations more accurately than existing equations. Having access to these different registries and technology that allows great connectivity supports a multimodal approach applying multiple prediction equations. As these large registries continue to grow and develop, studies are necessary to assess their ability to predict outcomes and to apply these equations in additional datasets in clinical and research settings. To maximize the utility of these equations, CPX testing systems need to be updated, preferably through an automated system to reflect the models on an ongoing basis. Considering these factors, after 30 years, it may be time to update what we consider "normal" in clinical exercise testing.

Acknowledgments: FRIEND Consortium Contributors: Ball State University (Leonard Kaminsky, PhD), Brooke Army Medical Center (Kenneth Leclerc, MD), Cone Health (Paul Chase, PhD), East Carolina University (Joseph Houmard, PhD), Pennington Biomedical Research Center (Timothy Church, MD), MET-Test (Nick Menasco, BS), Taylor University (Erik Hayes, PhD), University of Oregon (Andrew Lovering, PhD), Translational Research Institute for Metabolism and Diabetes (Bret Goodpaster, PhD), and University of Tennessee, Knoxville (David Bassett, PhD).

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