Substantial data have accumulated for decades demonstrating the protective effects of regular physical activity (PA), including exercise training, and cardiorespiratory fitness (CRF) on cardiovascular disease (CVD) morbidity and mortality as well as all-cause mortality.\(^1\) In fact, PA and CRF may have stronger correlations with CVD prognosis than any of the traditional CVD risk factors.\(^1\) In recent years, *Mayo Clinic Proceedings* has emphasized papers in the areas of PA and CRF,\(^2-8\) including publications that also incorporate adiposity, obesity, and the obesity paradox.\(^9-11\)

In this issue of *Mayo Clinic Proceedings*, Laukkanen et al\(^{12}\) performed one of the largest meta-analyses to date, reviewing data from 37 studies of nearly 2.3 million participants with the occurrence of close to 110,000 deaths. They demonstrated that every 1 metabolic equivalent increase in estimated CRF (eCRF) was associated with an 11% reduction in mortality. The top tertile of eCRF had a 45% lower mortality compared with the lowest tertile of eCRF. Finally, these associations were present regardless of year of publication, age, sex, follow-up duration, CRF assessment method, and risk of bias. The authors therefore justifiably suggested that guideline bodies should consider including CRF in standard risk panels for mortality risk assessment.

These results by Laukkanen et al\(^{12}\) as well as the considerable body of evidence supporting the importance of CRF for assessment of mortality risk add to the classic study by Kodama et al\(^{13}\) published more than a decade ago and updated by Harber et al in 2017.\(^{14}\) The study by Laukkanen et al\(^{12}\) confirms the importance of objectively measured CRF with cardiopulmonary stress testing (CPX) or eCRF from submaximal and maximal exercise tests (ie, blood pressure, electrocardiography, and subjective scale monitoring) without CPX. Although better than non-exercise eCRF, there still is some error associated with maximal exercise testing compared with precise assessment of CRF by ventilatory expired gas analysis (ie, CPX).\(^{15}\) When using eCRF to categorize participants into tertiles, submaximal exercise equations correctly classified an average of only 51% (range, 37% to 58%) and maximal exercise equations correctly classified an average of only 59% (range, 43% to 46%).\(^{16}\) In addition, Laukkanen et al\(^{12}\) use the “old” dogma that “a major reason why CRF is not employed in routine clinical practice is because the use of CPX for defining CRF involves skills, equipment, and relatively high costs compared to the assessment of other risk factors such as blood pressure, blood lipid levels and smoking status.”\(^{13}\) However, as Kaminsky et al\(^{17}\) recently pointed out, “with rapid technological advancements, commercial metabolic exercise testing units that are compact, easy to use, provide breath-by-breath analysis in real time and can include built in electrocardiogram equipment are now readily available at competitive prices. Coupled with the wealth of clinically meaningful cardiopulmonary data that can be acquired by these units, the implementation of CPX in hospitals is now more feasible and should be pursued.”\(^{17}\) Therefore, as recently reviewed in *Mayo Clinic Proceedings*, the “gold standard” CRF assessment with CPX should be more commonly used in routine clinical practice.\(^7\)

Nevertheless, clearly most stress tests in the United States and worldwide do not include CPX but rather CRF being assessed.
by speed and incline on the treadmill or by workload on a cycle ergometry test; most studies during the past 3 decades have used this method to assess and define CRF. As Kodama et al13 and Harber et al14 previously demonstrated and Laukkanen et al12 reinforce now, eCRF strongly correlates with survival. In addition, besides eCRF being strongly related with CVD and CVD morbidity and mortality, it is also highly associated with healthy vascular aging, inflammation, and respiratory diseases, such as chronic obstructive pulmonary disease and pneumonia.19-20 Although genetics certainly play a role in CRF,1 changes in CRF are heavily affected by an individual’s regular PA and exercise training habits. These data reinforce not only the importance of measuring or estimating CRF but also that clinicians across a wide range of disciplines throughout the health care system need to promote regular PA and exercise training, especially that which increases levels of CRF, throughout their daily patient encounters.

With the past 2 years being dominated by the coronavirus disease 2019 (COVID-19) pandemic, healthy lifestyle, including PA and CRF, may be even more important than ever.21-23 Mayo Clinic Proceedings appears to have had the first major publication demonstrating that CRF strongly affected prognosis during infections with COVID-19,24-27 and subsequent to this, Sallis et al28 using data from Kaiser Permanente demonstrated the powerful impact of PA, the main correlate of CRF, with COVID-19 prognosis. This major paper by Laukkanen et al12 should further facilitate and reinforce efforts to promote the routine assessment and improvement, when necessary, of CRF on a population level. Healthy living medicine, of which optimization of CRF and PA promotion are central components, should be a priority for every individual’s plan of care.

POTENTIAL COMPETING INTERESTS
The authors report no competing interests.


