

Grip strength and mortality: a biomarker of ageing?



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See [Articles](#) page 266

Grip strength is a simple but powerful predictor of future disability, morbidity, and mortality. The relation between grip strength and future mortality has been shown, not only in older people¹ but also in middle-aged² and young people.³ The evidence has been summarised in systematic reviews⁴ and in a meta-analysis.⁵ However, important questions remain, such as whether the association between grip strength and future mortality is generalisable across countries of widely varying socioeconomic circumstances and, particularly, what might explain the associations. In *The Lancet*, Darryl Leong and colleagues⁶ address the first question comprehensively and provide clues as to how the second question might be further explored.

Leong and colleagues⁶ investigated the relation between grip strength, cause-specific mortality, and incident disease in 139 691 participants aged 35–70 years from three high-income, ten middle-income, and four low-income countries during a median follow-up period of 4 years. This work forms part of the Prospective Urban Rural Epidemiology (PURE) Study, designed to investigate societal effects on chronic non-communicable diseases in 17 countries. The international breadth and methodological rigour of the undertaking has already led to a series of high-impact articles, one of which described cardiovascular risk and events.⁷ Leong and colleagues now show⁶ that grip strength predicts not only all-cause mortality (hazard ratio for every 5 kg decrease in grip strength 1.16, 95% CI 1.13–1.20) but also cardiovascular mortality (1.17, 1.11–1.24), non-cardiovascular mortality (1.17, 1.12–1.21), and cardiovascular disease occurrence (myocardial infarction [1.07, 1.02–1.11], and stroke [1.09, 1.05–1.15]) across a range of country and income settings. These findings seem relatively specific because no association was found with incident diabetes, cancer, pneumonia, hospital admission for respiratory illness, injury from a fall, or fracture. Furthermore, case-fatality rates in incident cases of cardiovascular disease were higher in people with low grip strength.

How should these findings be interpreted? First, the scale and scope of the study provide definitive replication: there can be no doubt that grip strength predicts future all-cause mortality across a range of populations. Second, that grip strength is related

specifically to cardiovascular mortality and morbidity suggests a potential mechanistic explanation. Third, the finding that grip strength is a more powerful predictor of cardiovascular outcomes than systolic blood pressure raises important questions about risk prediction and why these cause-specific associations exist.

The work has some limitations. Leong and colleagues⁶ highlight the limitations of observational epidemiology to address causal pathways. In terms of specificity of the findings, issues of ascertainment bias might be relevant; identification of mortality might be less problematic than determination of incident disease. With respect to the morbidity data, cases of cardiovascular disease can be more straightforward to identify than falls and related injuries, perhaps explaining the absence of an association between grip strength with the latter outcome. The investigators noted an unexpected association between low muscle strength and low risk of cancer in high-income countries, but not in low-income countries. This association warrants further investigation, although in the context of multiple analyses and absence of consistency with a previous study,⁸ the association might have arisen by chance. The ability to explore mechanisms underlying the associations with cardiovascular disease was limited because, understandably, the breadth of the data collection in PURE came at the expense of depth. Future rounds of data collection will have the potential to address these mechanisms. The investigators did consider the possibility of reverse causation, but the associations between grip strength and mortality were robust to exclusion of participants who died within 6 months of grip-strength measurement, and exclusion of participants with pre-existing cardiovascular disease or cancer.

The findings from this study add to the growing evidence that skeletal muscle function is an important component of health, ageing, and disease. Poor muscle strength has been proposed to directly affect mortality through its association with increased disability. However, the findings from PURE suggest that associations with cardiovascular disease and its risk factors might be an additional pathway. Of course, this association does not explain why grip strength should be related to cardiovascular disease, and Leong and colleagues⁶ proffer only the non-specific, though

plausible, suggestion that low grip strength represents poor health. This explanation is not entirely consistent with the findings of other studies³ that show long-term associations between grip strength in young people and subsequent mortality.

An intriguing implication is that grip strength might act as a biomarker of ageing across the life course.⁹ This is not a new idea, but findings from PURE add support. Loss of grip strength is unlikely to lie on a single final common pathway for the adverse effects of ageing, but it might be a particularly good marker of underlying ageing processes, perhaps because of the rarity of muscle-specific diseases contributing to change in muscle function. Interestingly, similar age-related changes have been reported in other species, such as *Caenorhabditis elegans*.^{10,11} Life-course normative data¹² have been described in a UK setting, and birth and ageing cohort studies, particularly those with long-term longitudinal data,¹³ provide ideal opportunities to explore this hypothesis. Furthermore, linkage of epidemiological findings to new approaches in muscle biology could yield informative insights into the nature of human ageing.

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Universal health coverage: progressive taxes are key

On Dec 12, 2012, a UN General Assembly Resolution was passed unanimously which called on all countries to move their health systems towards universal health coverage (UHC).¹ Interestingly, this resolution was cosponsored by the USA—a country not known for having achieved this goal.

With UHC now a common objective for all health systems, the debate is shifting to how countries should achieve it. Particularly since publication of the 2010 *World Health Report*,² there has been growing interest in how countries should finance their health systems to reach the twin goals of universal coverage of effective health services and financial protection from the costs of these services. Most recent research evidence in this area is now showing that public

financing is the key to achieving UHC.³ For example, in the 2012 *Lancet* Series on UHC, Moreno-Serra and Smith⁴ showed that pooled public financing resulted in improved health outcomes; private voluntary insurance had no effect on indicators, and a greater share of out-of-pocket expenditure was associated with higher mortality rates.

In *The Lancet*, Aaron Reeves and colleagues⁵ reinforce these findings on the benefits of public financing, but now provide new research evidence on which specific public financing mechanisms have the greatest effect on UHC indicators. Using longitudinal data from 89 low-income and middle-income countries from 1995 to 2011, they show that increasing general taxation financing was associated with increased



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See [Articles](#) page 274