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A Biomarker Signature Associated With Future Functional Decline And Outcomes On The Frailty-Disability Cascade

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Background: Biological ageing is a dynamic and heterogeneous process that occurs due to dysregulation at the molecular, cellular, physiological and functional level, manifesting in functional decline. We investigated whether biomarker data across a range of biological systems predicted incident functional decline and frailty-disability cascade outcomes.
Methods: Secondary data analyses were performed on n=4,961 participants aged 50+ years from waves 1-5 of The Irish Longitudinal Study on Ageing (TILDA). We examined 18 blood biomarkers representing key systems that become dysregulated with ageing (inflammatory, cardiovascular, metabolic, renal, cognitive, musculoskeletal and senescence). Model-based clustering classified participants as belonging to one of three biomarker signatures - low, medium and high risk. These biomarker signatures were utilized to predict 4-year functional decline (grip strength, timed up and go test (TUG) and gait

speed) using mixed effect models; 8-year frailty and disability using logistic regression models; and 12-year mortality using Cox-Proportional Hazard models. All models were adjusted for age, sex, education, smoking history, lipid lowering and anti-hypertensive medications.

Results: The prevalence of the low, medium and high-risk groups was 58.5%, 9.2% and 32.3%. Medium and high-risk biomarker signatures had progressively increased hazard of 12-year mortality (HR:1.54, 95%CI:1.13-2.10) and (HR:1.89, 95%CI:1.53-2.34) respectively. Participants with the high-risk signature also had significantly higher odds of 8-year incident frailty (OR:2.1, 95%CI:1.60-2.74) and disability (OR:1.72, 95%CI:1.30-2.29), with the medium-risk group showing attenuated associations. The biomarker signatures had a dose response relationship with functional decline; with the high-risk group having lower grip strength, slower walking speed and higher time to complete the TUG over 4-year follow-up ($p<0.01$). Findings were replicated in a US cohort.

Conclusion: We report a unique biomarker signature that was consistently associated with mortality, incident frailty and disability, and functional decline. This signature may be a useful early indicator and risk stratification tool to predict future functional decline and frailty-disability cascade outcomes.