EDITORIAL

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# Health Promotion and Healthspan: Phenotypic Biomarkers Catalyzing Modern Medicine

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We write to call attention to a paradigm shift in modern medicine that is reorienting research priorities and translational practices, signaling a potential Kuhnian scientific revolution.[1] The field of medicine is amidst a pandemic of genome-lifestyle-mediated noncommunicable diseases responsible for an estimated 40–45 million annual deaths and a 9.6-year global median healthspan-lifespan gap.[2,3] Of note, the global median healthspan-lifespan gap has increased from 8.5 years in 2000 to 9.6 years in 2019, a staggering 13% increase.[3] Sex-stratified data show a 2.4 ± 0.5-year wider gap in females, associated with a disproportionately larger burden of noncommunicable diseases.[3] According to the recent statistical data, there is an urgent need for novel health promotion initiatives.[4]

Multimodal clinical diagnostics of the soma, synergized with pharmaceutical interventions, form the bedrock of modern medicine. However, rather than being confined to established clinical frameworks, we believe that mapping a multisystem profile using phenotypic biomarkers in community-based organizations will assume greater significance in future clinical practice.[5] Phenotypic biomarkers can be divided into multilayered and multifaceted molecular and physical biomarkers, such as telomere length and handgrip strength (HGS), both of which may serve as predictors of healthy aging.[6] The practicality of physical phenotypic biomarkers has the potential to reframe the centrality of preventive and adjunct therapies in the evolving healthcare landscape. In parallel, this approach represents a reconceptualization of health from a health-disease dichotomy towards a broad continuum in line with a salutogenic health model.[7]

Meanwhile, a retrospective cohort study involving 122 007 participants shows that risk-adjusted all-cause mortality was inversely proportional to cardiorespiratory fitness (CRF).[8] CRF within the sub-25$^{th}$ percentile range is associated with an almost fourfold increase in all-cause mortality risk relative to a high CRF range (75th-97.6$^{th}$ percentile).[7] A synthesis of 38 cohort studies (n = 1 907 580) indicated that higher HGS, a proxy for whole-body strength, was associated with a 31% reduction in the risk of all-cause mortality.[9] Consistent with level 2A evidence derived from cohort studies, experimental research reinforces the relevance of phenotypic biomarkers for clinical interventions. An randomized controlled trial (n = 43) investigated the efficacy of a 12-week combined aerobic-strength exercise therapy, performed three-times weekly for 60 minutes, on phenotypic biomarkers in patients with type 2 diabetes.[9] The research revealed significant improvements in muscle strength, plasma glycated hemoglobin $A_{1c}$, and other psychosocial metrics compared with the control group.[10]

Given the emerging evidence of the widening healthspan-lifestyle gap and the growing use of phenotypic biomarkers, we propose the following priorities to catalyze the evolution of modern medicine: (1) multisystem biological profiling, including measurements of CRF and HGS outside traditional hospital settings, should be integrated into the continuum of healthcare; (2) funding agencies and research institutions should allocate greater resources to investigating the use of practical phenotypic biomarkers in preventive and adjunctive therapies; and (3) a salutogenic health model must be cultivated, shifting clinical questions from "what is the diagnosis?" to "what promotes resilience in our patients?". The question is no longer whether medicine will evolve but how quickly practitioners will embrace the emerging paradigm.

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