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Precision Medicine and the Biomarker Revolution: Bridging the Non-Communicable Diseases Gap in Low- and Middle- Income Countries

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The global health landscape is currently defined by rise of non-communicable diseases (NCDs), a silent but devastating crisis. NCDs accounted for roughly 43 million deaths in 2021 alone, that represents 75% of all non-pandemic mortality. Although generally perceived as "diseases of affluence," the reality is quite different as 75% of these deaths occur in low- and middle-income countries (LMICs) [1]. This place burden on the fragile health systems of these countries. The traditional way to control NCD relies on population-level screening and symptom-driven diagnosis. This approach results in quite delayed detection, that causes significant organ damage till the diagnosis is reached. Precision medicine has evolved to combat this, resulting in a revolutionary shift for cost-effective laboratory innovations in the form of biomarkers and transition from reactive to proactive care.

Precision medicine aims to customize the management i.e. prevention and treatment based on individual clinical, biological, and environmental differences [2]. The main emphasis is on biomarkers, the diagnostic sentinels that are able to capture subclinical pathophysiological manifestations before actual symptoms appear. The healthcare resources are scarce in LMICs, that requires an integration of these biomarkers into clinical workflows. This will result in an accurate risk stratification, distinguishing patients with a more gradual trajectory from those who experience rapid disease progression.

Inflammatory markers, have emerged as powerful predictors of cardiovascular events such as interleukin-6 (IL6) and high-sensitivity C-reactive protein (hsCRP). It has been shown in meta-

analytic data that even in asymptomatic adults, elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) and hsCRP are associated with incident cardiovascular disease (CVD) with hazard ratios of 1.22 and 1.19 respectively [3]. Similarly, NT-proBNP remains a gold standard for heart failure as a twofold increase in this marker is linked to a 1.47-fold increase in heart failure risk. Furthermore, cost effective markers like platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) help in discriminating CVD risk, marginally improving classical models without the need for high-cost assays. HbA1c remains a cornerstone for metabolic health as evidence suggests that a lower baseline threshold of 5.7% can be used to predict future diabetes (with 85% specificity and 62% sensitivity). This calls for intervention during a "high-risk state" rather than waiting for full-blown clinical manifestation. Combination of these metabolic markers with organ-specific and inflammatory signals such as renal markers like urine albumin-to-creatinine ratio and cardiac troponins improves predictive accuracy for CVD to an AUC as high as 0.89.

Multi-omics frameworks (MOF) are required to understand the complexity of NCDs, which often requires a more holistic view. MOF integrate proteomics, genomics, metabolomics, and transcriptomics that provide a comprehensive molecular portrait of disease biology. Proteomics reflects functional changes, genomics identifies inherited predisposition, and metabolomics captures the current biochemical phenotype. Literature supports that specific molecular signatures, such as the CPS1 genetic variant, provides targets for managing T2D-related cardiovascular risk as it links genomic predisposition to urea cycle-related metabolites. Similarly, integrated metabolomic and proteomic profiling in heart failure with preserved ejection fraction (HFpEF), has revealed 124 metabolites and 46 plasma proteins and that distinguish patients from healthy controls, highlighting an activated immune profile. Advanced technologies currently face multiple challenges in LMICs especially computational complexity and standardized analytics, but these represent the future of targeted therapeutic strategies [4].

Centralized laboratories with high tech tests are often inaccessible and unaffordable to rural populations, which requires decentralization and affordable point of care (POC)testing. POC diagnostics testing if conducted at or near the site of patient care can shorten turnaround times and enable immediate clinical action. Studies have provided evidence that POC platforms for creatinine, HbA1c, lipid panels, correlate strongly with centralized laboratory assays, which makes them ideal for LMIC environments. These are proved by implementation studies in Peru and India., where the use of multiparameter POC devices in primary care at PERU, significantly increased the diagnosi of new diabetes and high-cholesterol cases. Similarly, combination of it with digital health technologies in India, achieved early and new cases identification of chronic kidney disease (CKD) [5]. Continuous

monitoring of glucose or cardiac markers can be done by wearable diagnostics and smart sensors. This data can be linked to digital laboratory networks, and can be transmitted to centralized systems for remote interpretation and population-level surveillance. This "connected diagnostic ecosystem" allows clinicians to detect deviations from a patient's health baseline at the earliest stages [6].

Non-invasive imaging technologies as part of precision medicine and point-of-care testing ultrasound (POCUS) is a transformative tool for visualization of cardiac and renal pathology at the bedside by the clinicians. [7]. It can change clinical management decisions in resource-limited settings up to 50% of cases. Similarly, carotid intima-media thickness (CIMT) assessment serves as an imaging biomarker, which is validated for subclinical atherosclerosis. CIMT correlates strongly with renal dysfunction and blood pressure and provides a nuanced view of vascular remodeling in high-risk individuals [8].

The ultimate goal is to create epidemiological surveillance systems by integrating individual clinical data into precision public health framework. Health systems can construct population-level risk maps to identify geographic hotspots of NCDs by harmonizing data from electronic health records, laboratory results, and digital diagnostics. These digital platforms enable real-time visualization of disease prevalence, allowing for data-driven distribution of healthcare resources [9].

There are several challenges for the transition to precision medicine in LMICs. These include Infrastructure gaps, like lack of trained personnel, unreliable supply chains and limited use of advanced molecular platforms. Financial constraints are equally challenging with limited health budgets in LMICs that are focused on infectious disease management. Moreover, frequent stockouts of essential diagnostics exacerbate health inequities. These challenges need solutions, like strengthening community-based POC testing through pharmacy-led models and investing in workforce development. There is a need to validate these biomarkers in diverse populations, as most predictive models are derived from homogenous cohorts in high-income countries..

The way forward is to integrate precision medicine by linking NCD diagnostics into primary care and national health information systems. Effective implementation depends on an integrated primary care model that can reduce fragmentation, strategic financing, including pooled procurement and domestic budget allocations, and multi-stakeholder governance, such as the "NCD Policy Lab," which bridges the gap between researchers and policymakers.

Precision medicine, powered by cost-effective biomarkers and digital innovations, is the way forward to reduce the global burden of NCDs in LMICs. Data-driven model, in contrast to symptom-driven model, is the need of the hour in LMICs through which these countries can achieve better patient

outcomes even within resource constraints. However, the key to success lies in ethical governance, equitable access, and the rigorous validation of technologies within the diverse populations they are meant to serve. The integration of clinical, laboratory, and public health systems is a necessity for sustainable healthcare delivery in the 21st century.

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