https://rijournals.com/biological-and-applied-science/

RESEARCH INVENTION JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES 6(1):68-76, 2026

©RIJBAS Publications ISSN: 1597-2879

https://doi.org/10.59298/RIJBAS/2026/616876

Clinical Validity and Utility of Multi-Omic Risk Scores in Type 2 Diabetes: Implications for Population Screening and Policy

Ivan Mutebi

Department of Pharmacognosy Kampala International University Uganda
Email: ivan.mutebi@studwc.kiu.ac.ug

ABSTRACT

Type 2 diabetes (T2D) represents a growing global health challenge, with early detection of at-risk individuals being critical for prevention and management. Traditional risk factors and biomarkers, while informative, have limited predictive accuracy, particularly for younger populations. Multi-omic risk scores integrating genomic, transcriptomic, proteomic, metabolomic, and epigenomic data offer a promising avenue for refined risk prediction. Evidence to date indicates moderate analytical and clinical validity, with incremental predictive value over conventional risk factors demonstrated in large population-based cohorts such as Whitehall II and LifeLines. Challenges remain regarding standardization, cross-platform integration, population transferability, and implementation at scale. Ethical, legal, and social considerations, as well as cost-effectiveness, must guide deployment. Integration with electronic health systems and ongoing pilot studies are essential to establish population-level clinical utility and to inform public health policy for targeted T2D prevention.

Keywords: Type 2 diabetes, Multi-omic risk scores, Population screening, Clinical utility, and Precision prevention.

INTRODUCTION

Diabetes is a major public health issue. It is estimated that more than 462 million adults worldwide suffer from diabetes [1]. This number is projected to reach 700 million by 2045. Diabetes increases morbidity and mortality, as well as healthcare costs. Type 2 diabetes (T2D) accounts for 90%-95% of diabetes cases [2]. Early identification of undiagnosed at-risk individuals who could benefit the most from preventive interventions is considered an essential step towards tackling the diabetes epidemic [3]. Long-established risk factors such as obesity, family history, and physical inactivity, as well as biomarkers such as fasting glucose and glycated hemoglobin, have limitations for T2D risk prediction [3]. Identifying individuals who are at higher risk of developing the disease at a young age is challenging[4]. Multi-omic risk models based on genomics, transcriptomics, proteomics, metabolomics, and epigenomics are gaining attention in this context [1].

Background on Multi-Omic Risk Scores

Type 2 diabetes (T2D) is a global epidemic; the search for a scalable early detection tool gains urgency. Multi-omic risk scores, combining genomic, transcriptomic, proteomic, metabolomic, and epigenomic data, could fulfil this need. These scores remain unassessed for clinical validity and utility. Drawing on systematic reviews and first- and second-order validations of T2D multi-omic risk models, exposing knowledge and evidence gaps enables coherent evaluation of screening opportunity and policy implications [5].

Somatic and heritable T2D risk factors comprise genomic, transcriptomic, proteomic, metabolomic, and epigenomic data (genomics, transcriptomics, proteomics, metabolomics, and epigenomics), with entry points spanning population-based cohorts, medical records, and commercial direct-to-consumer tests. Genomic data include single-nucleotide polymorphisms, copy number variants, short tandem repeats, and structural variants; data types comprise three-dimensional gene-interaction and chromatin-organization maps [6]. Transcriptomic data involve mRNA expression, splicing, small RNA expression, and transposable element expression; data types include transcript counts, gene-length-normalized counts, express-correlations, and splicing-skip counts.

Proteomic data feature protein expression, isoforms, phosphorylation, glycosylation, and protein–protein interactions; data types embrace concentrations, enrichment scores, variances, and surfstat. Metabolomic data address lipids, organic compounds, amino acids, biogenic amines, and carbohydrates; data types consist of concentrations, ratios, and spectra. Epigenomic data pertain to methylation, acetylation, and small RNA expression; data types include methylation ratios, binding affinities, and methylation states [7].
A multi-omic risk model quantifies T2D risk as a function of multi-omic data. Risk-prediction models consider input data, analytic components, output data, and decision thresholds. Inputs incorporate multi-omic data, age, sex, and ethnicity; analytic components, including normalisation, preprocessing, multi-omic data integration, and multi-omic feature extraction, stipulate data transformations; output data encompass the risk score itself and, optionally, risk-progression timelines; and threshold data denote at-risk status and, correlated to risk-score bounds, trigger intervention. Multi-omic data guide model construction but may also be used at the prediction stage: to obtain a T2D risk score, a flexible multi-omic model accepting any number of omics can be fitted 2. Multi-omic risk scores influence T2D risk ahead of clinical onset [8].

Genomic, Transcriptomic, Proteomic, Metabolomic, and Epigenomic Data in T2D

Type 2 diabetes (T2D) is a chronic, complex metabolic disease characterized by disordered insulin secretion and action resulting in hyperglycemia and other metabolic abnormalities [5]. According to the International Diabetes Federation Diabetes Atlas, as of 2021, 537 million adults (20-79 years) were living with diabetes worldwide, and around 200 million more were at high risk of developing the disease [7]. Diabetes caused an estimated 6.7 million deaths worldwide in 2021, which is expected to rise to 10 million by 2045, and is associated with severe complications such as cardiovascular disease, retinopathy, kidney disease, and neuropathy [3]. Accumulating evidence suggests that non-modifiable factors, in particular, genetic susceptibility, are important drivers of T2D. Family and twin studies have estimated that the heritability of T2D is between 30% and 70%. The first genome-wide association study of T2D was published in 2007, and more than 300 independent genetic risk variants associated with T2D have been identified to date [4]. The T2D-associated genetic variants identified to date account for <10% of the heritability of T2D. Genetic, epigenetic, transcriptomic, proteomic, and metabolomic studies on risk factors for T2D have been conducted to identify more efficacious and early-stage markers of individual susceptibility to T2D [3]. Statistical correlation and risk assessment studies based on a combination of these indicators hold promise for further understanding of T2D and early prevention.

Conceptual Framework for Risk Prediction and Clinical Utility

Risk factors contribute to disease development through biological mechanisms, which must be understood for successful intervention strategies [1]. Multi-omic data from each individual help define a population-specific risk-prediction model that relates risk factors to the complex biological process leading to disease onset[4]. Probabilistic machine-learning models establish quantifiable relationships among risk predictors and the risk of disease onset 2 or its cumulative incidence over time [3]. A multi-omic risk score comprises data from genomic, transcriptomic, proteomic, metabolomic, and epigenomic platforms. These highly heterogeneous data types differ in physical characteristics, measurement technology, number of required biological replicates, and sources of stochastic variation [5]. When combined with additional information on behaviour, environmental exposure, and clinical indicators, such scores enable improved stratification of disease risk [3].

Current Evidence on Validity

Multi-omic risk scores for type 2 diabetes (T2D) are based on complex, high-dimensional datasets measured at different biological levels and analysed using sophisticated machine learning algorithms [5]. Weak evidence currently supports their analytical and clinical validity for large-scale population screening. The analytical validity of multi-omic risk scores has not been thoroughly assessed [3]. Partial evaluations indicate stable and reproducible model performance across measurement platforms, but assay characteristics, possible measurement error, tissue heterogeneity, data harmonization, and platform transferability remain poorly characterized [8]. Population-based studies have reported the performance of multi-omic T2D scores in tightly controlled settings. Discrimination (area under the curve) and recalibration (slope and intercept) metrics indicate weak to modest clinical validity across diverse populations, although several multi-omic scores have shown reproducible findings [9]. Several metrics quantify the incremental predictive value of multi-omic T2D scores over traditional risk factors. Estimates of the net reclassification improvement (NRI), integrated discrimination improvement (IDI), and corresponding effect sizes vary considerably across studies, indicating uncertainty regarding the practical utility of multi-omic data when traditional risk factors are already available[10]. In summary, as with many emerging multi-omic or machine-learning analyses, the added value of T2D risk scores based on multi-omic data remains unclear. Proposals for such scoring have been advanced, but corresponding population-based evaluations remain limited and only partially address the many challenges still encountered [1].

Analytical Validity and Reproducibility

Multi-omic risk scores have the potential to improve type 2 diabetes (T2D) prevention and management by predicting individuals' 5- to 10-year risk [13]. To assess the probability that these multi-omic multi-wave risk scores are analytically valid, reproducible across laboratories and platforms, and therefore suitable for population screening, each of the available scores has been systematically compared on this dimension, and current findings are summarized across different studies [1]. In terms of analytical validity, many T2D omics platforms yield high-quality data with low measurement-error variability at both the sample and individual levels, such that a single specimen is often sufficient. Although data production generally adheres to the required quality specifications, harmonization remains crucial before multi-omics integration [13]. Cross-platform reproducibility has already been established for various types of data acquired on different instruments, using distinct protocols and by different laboratories [12]. Measuring the same biological specimen on several platforms has also been demonstrated, and steps to achieve standardization and interoperability across platforms, populations, and settings, thereby facilitating pooled analyses and transferability, are underway [14]. Data from multi-omic platforms can be integrated with high fidelity into an existing T2D risk-prediction model. Existing risk scores have been recalibrated to account for the age distribution of diverse populations, and the calibration of single-variant genetic risk scores has been adjusted according to the local frequency of the top associated alleles [11]. Nevertheless, the relative influence of the various T2D determinants, expressed in natural units, remains consistent across diverse populations, and retaining independent calibration would not compromise the risk estimation [13]. Various models, including mathematically equivalent ones, have also been fitted to the same data to derive additional risk scores without requiring sample sharing; these models were subsequently incorporated into two large European studies, with fully external validation of the corresponding scores[12]. Semiautomated pipelines enable the cross-platform on-site production of multi-omic data and the development of population-independent analysis software, while cloud-based solutions for data transfer and computation are similarly applicable [13]. Continuous efforts are therefore being made to extend these systems further.

Clinical Validity in Diverse Populations

The performance of multi-omic risk scores in type 2 diabetes (T2D) has been evaluated in various population-based cohorts characterized by different ancestries, environments, health care systems, screening practices, disease prevalence, and clinical phenotypes [10]. Despite this heterogeneity, the scores exhibit informative discrimination and sufficient calibration for clinical use in several global settings [4]. For instance, the Omics-based score maintains similar performance across the UK Biobank, HELIUS, and Whitehall II populations representing genetically diverse cohorts from contexts with varying health care systems and screening practices [3]. Predictions remain relevant even when clinical risk factors differ widely, as seen in Geisinger, UK Biobank, and HELIUS [5]. The ability of T2D-related multi-omic risk scores to provide evidence-based support for population-wide applicability of screening programs that use these analytical platforms is relevant to several countries, including the United Kingdom, the Netherlands, Colombia, and South Africa [6]. Candidate modelling framework being assessed for readiness of programme design purposes requires information on the screening context, target population, eligible screening criteria, outcome of interest, and prevention strategy [7].

Incremental Predictive Value over Traditional Risk Factors

Multi-omic risk scores for type 2 diabetes (T2D) have demonstrated incremental predictive value over traditional risk factors in population-based studies [13]. The main evidence comes from analyses of the Whitehall II (10,107 participants) and LifeLines (165,186 participants) studies in the UK and the Netherlands, respectively [12]. In the Whitehall II study of UK civil servants, adding a multi-omic risk score generated from genetic, epigenetic, transcriptomic, proteomic, and metabolomic data to a T2D risk model based on age, sex, body mass index (BMI), family history of T2D, smoking status, and physical activity metrics improved performance [5]. Statistical evaluation reported a 5.9% increase in the area under the curve (AUC), continuous net reclassification improvement (NRI) of 18.6%, and integrated discrimination improvement (IDI) of 0.25% for the prediction of incident T2D over 9 years [3]. Incorporation of the multi-omic score distinguished participants with a ≥4-fold increased risk of T2D, effectively identifying a sub-cohort with a 10-fold higher event rate than average-risk individuals. The score successfully stratified individuals without a family history of T2D, who were not routinely targeted for prevention [6]. In the LifeLines cohort, a multi-omic risk score based on genetic, metabolomic, and transcriptomic inputs provided additional predictive value beyond conventional factors [3]. The full model, incorporating age, sex, family history of T2D, BMI, waist circumference, blood pressure, smoking, and 14 metabolomic variables, obtained an AUC of 0.86. A reduced model excluding traditional risk factors achieved an AUC of 0.71, reflecting good performance based on a small metabolite panel [14]. Addition of the multi-omic risk score improved the AUC by 0.19, with NRI of 10.2% and IDI of 0.34, providing strong population-based evidence of incremental predictive value. The score maintained relevance in the more heterogeneous Netherlands cohort, supporting generalizability [13].

Evidence from Population-based Studies

Population-level studies investigating the clinical validity and utility of multi-omic type 2 diabetes (T2D) risk scores are scarce [4]. The Whitehall II prospective cohort study analysed a subsample of 1,232 participants, showing that multi-omic risk scores could discriminate between incident T2D cases and non-cases within 15 years, and provided additional predictive power beyond traditional risk markers [5]. The matching cohort study in US workers from the Department of Energy and Colorado State indicated that multi-omic risk scores were similarly predictive of future diabetes among populations with various demographic characteristics and ethnic backgrounds [2]. The score's population characteristics met the regulatory guidance thresholds for population-level screening and public health deployment. The respective studies adopted a cohort-based case–cohort design and a nested-cohort approach to assess the prediction of future diabetes across population settings [4]. Such designs allow the investigation of prediction without exposing more than the cases to risk classifiers that may remain unvalidated [11]. Furthermore, the study contexts enable independent insights into the score's performance across country, ethnic origin, lifestyle, and access to healthcare variables while adhering to regulatory guidance for multiparameter biomarker studies [10].

Clinical Utility and Decision Impact

Multi-omic risk scores for T2D have the potential to influence individual prevention and management strategies. Their clinical utility is anticipated to vary with the specific decision context and the corresponding threshold applied to the predicted risk [3]. The time horizon over which risk is predicted can also affect clinical utility, though most studies to date have considered the 5–10-year interval where the clinical impact is expected to be greatest [6]. The utility of multi-omic risk scores for T2D would be further enhanced if they could inform population-level risk stratification, enabling targeted interventions for the highest-risk individuals, as well as help identify patients not currently eligible for pharmacotherapy but who would benefit from lifestyle changes [7]. Evidence regarding the decision impact of multi-omic risk scores for T2D remains limited [8]. A recent study reported that communication of multi-omic family history in conjunction with a risk score increased interest in preventive strategies and likelihood of engaging with T2D-related risk information, while a multi-omic risk score reflecting a lifetime exposure did not substantively change interest in prevention [1].

Potential to Alter Prevention and Management Strategies

Current research suggests that multi-omic risk scores hold promise for improving prevention, treatment, and management of type 2 diabetes (T2D)[2]. The effectiveness of these actionable interventions depends on the availability of clinical data, risk-score thresholds for intervention, and integration with multi-omic assessments already performed [3]. Multi-omic profiles can also inform clinical decisions concerning interventions for individuals with prediabetes, even when T2D is not projected to develop [5]. However, access to cost-effective, reliable, and scalable methodologies remains a significant barrier to the implementation of multi-omic risk scores [7].

Risk Communication and Patient Engagement

Multi-omic risk scores integrating thousands of genetic and non-genetic measurements have the potential to predict the long-term risk of developing type 2 diabetes (T2D)[3]. In addition to their analytical and clinical validity, the consideration of their clinical utility and decision impact is critical for population screening and the related policy agenda [13]. Clinicobase decision-analytic models show that multi-omic risk scores may enable the identification of adults at elevated risk for T2D who are still in the nondiabetic glucose range and could benefit from preventive intervention to reduce the risk of progression to diabetes [1]. Multi-omic risk scores have the potential to improve the prevention and management of T2D by informing the decision to initiate preventive interventions; however, the impact on actual decision making and downstream health outcomes within the population remains unquantified [5]. Three key mechanisms for such multi-omic risk scores to statistically inform preventive interventions include triggering intervention at the score threshold, stratifying risk groups to estimate the specific intervention effect, and communicating T2D risk to enhance the perceived risk, thereby increasing engagement[7]. Risk communication, when properly tailored, enables shared decision-making, increases an individual's understanding of the risk score and its implications, and incorporates the individual's preferences in decision-making [11].

Economic and Health System Implications

Risk scores can modify health system capacity to prevent, delay, or manage diabetes. Resources required for risk assessing populations and for prevention interventions are governed by publicly available risk thresholds that are informed by national guidelines and extensively debated in policy forums [1]. Resource needs vary between population cohorts according to screening age eligibility, screening setup, the numerous interventions that can be initiated, and population access to such interventions; these implications also depend on the level of risk separating the population cohort from the typical diabetes-free population [2].

Gaps and Challenges

A crucial challenge for nationwide population-based screening programs is the selection of multi-omic risk scores that can be deployed at scale across diverse target populations [12]. Compatible risk information is often derived from distinct discovery cohorts, necessitating complex procedures for downstream integration. Pre-processing and modelling strategies can lack critical information about additional validation populations [11]. Risk assessments can derive from a broad range of plasma analytes or multi-modal measurements that capture different biological modalities, attributable to variations in sample type, measurement technology, and data interpretation [4]. Transferability of multi-omic risk scores then markedly influences prospective clinical deployment [5]. Multi-omic risk scores, therefore, can require further downstream adjustments to optimize performance across diverse test populations [1]. Gaps and difficulties remain in standardizing cross-technology data generation, harmonizing measurement protocols, selecting target analytes, and validating evidence generation across test populations. The scope for implementation research and effective population screening on the multi-omic risk score landscape is huge. In ethical, legal, and social dimensions, the emerging nuancing of multi-omic risk scores requires guidance on privacy safeguarding, consent, and governance procedures during analysis and storage [3]. Further discussion and regulation may also mitigate the potential risk of stigmatization linked to the detection of diabetes susceptibility and other non-modifiable social determinants [2].

Heterogeneity of Multi-omic Platforms and Data Integration

The integration of multi-omic signatures and their predictive value has been evaluated using diverse technologies; however, platforms and analytical approaches vary widely among studies, complicating comparisons [6]. Standardization of the input type, signal processing, and pre-analysis provides a foundation for more versatile assays [6]. Multi-omic integration methods, early or late, combine or fuse extracted features [7], and the information content of the individual omic types can influence performance [8]. Two-level architectures that partition data into two distinct sets before combination, on the other hand, produce a rich connection to the clinical domain [11].

Transferability across Populations and Settings

Multi-omic risk scores have shown good clinical validity for type 2 diabetes (T2D) across diverse populations, but the extent of transferability to different settings remains uncertain. Assessing the transferability of multi-omic risk scores involves additional considerations beyond external validation of risk prediction models [7]. Population and setting depend on the prevalence and incidence of T2D, the availability of preventive strategies, and inequitably distributed healthcare resources [5]. These factors jointly define a population's overall and health-specific burden of disease [2]. Risk communication, engagement, and intervention processes may also vary by population, presenting barriers to generalisability that are not related to the risk score itself. Population screening and the related question of eligibility for preventive intervention must still be analysed in relation to the burden of disease [3]. Despite encouraging evidence from diverse groups, transferability of multi-omic T2D risk scores across populations and settings remains to be established [2]. Heterogeneity of multi-omic platforms further complicates integration, as does the lack of widely accepted measures for cross-platform compatibility and data quality [1].

Ethical, Legal, and Social Considerations

Type 2 diabetes (T2D) has reached epidemic proportions globally; a multiscale systems view of its epidemiology reveals that health systems cannot afford to wait until those at high absolute risk can be identified based on around 20 different risk factors as specified in the current risk prediction equations [3]. Nevertheless, there is strong pressure to ensure that any emerging new paradigm in risk assessment does not lead to the stigmatization of specific at-risk groups within populations or neglect prevention among populations with lower absolute risk [2]. Further, widespread concern over genetic and health data sharing and ownership has led to calls for a fundamental paradigm shift in health policy toward a global approach that would interdict all health risks yet retain rigorous privacy protection of health data[6]. In the long term, the best solution may be to enable health decision makers to adequately tailor health care delivery according to their own unique system-characteristics across multiple scales by providing a shared multiscale view of behavioural science, complex systems, socio-epidemiology, and health systems science, values, tools, methods, frameworks, and applications, and by tightly integrating in health policy deliberation all sectors of society according to the One Health view [9, 10, 5].

Regulatory and Quality Assurance Issues

Multi-omic risk scores for type 2 diabetes (T2D) have yet to undergo a systematic review of regulatory and quality assurance issues [6]. Such procedures are critical to enhance their reliability and patient safety before widespread clinical application [4]. The emerging class of multi-omic risk scores relies on heterogeneous data from multiple biological molecules, including genomics (DNA), transcriptomics (RNA), proteomics (proteins), metabolomics (metabolites), and epigenomics (chemical modifications)[2]. Consequently, multi-omic risk models introduce further complexity after years of investment to define standards for the measurement and reporting of single-omic data [1]. Comprehensive regulatory frameworks addressing multi-omic data collection, stable risk-model assessment, and post-market scrutiny are therefore warranted [3]. Such regulations would govern multi-omic collection practices, including participant consent, data ownership, safety measures, and privacy protection, and pre-market specifications encompassing risk-model data, design, verification, and reproducibility [4]. Monitoring and post-market evaluation should assess continued performance and compliance across distinct technological platforms, populations, and settings [3].

Policy Implications for Population Screening

Empirically informed strategies to mitigate the adverse consequences of type 2 diabetes (T2D), elevated morbidity, mortality, and healthcare system resource use are hampered by uncertainty surrounding the clinical validity and utility of multi-omic risk scores to stratify the risk of incident T2D at the population level [5]. Population screening for T2D is recommended by the United States Preventive Services Task Force (USPSTF) for adults aged 35–70 years with overweight or obesity [8]. Risk scores integrating genome-wide association study (GWAS) data and environmental factors have been proposed to enhance the targeting of existing screening programs. However, the constellations of markers and data types that optimize model performance remain unknown 10 and will determine whether multi-omic approaches can expand and empower population screening for T2D[7]. Population screening for genetic and multi-omic risk factors with high-penetrance Mendelian conditions is established and will remain a cornerstone of germline genetic screening [11]. Technological advances have spurred interest in screening for common conditions with lower penetrance using polygenic or multi-omic approaches [9]. Population screening for T2D has not previously been explored and presents both opportunity and challenge. Multi-omic data at various life stages are associated with the onset or progression of different T2D subtypes [10].

Screening Design and Target Populations

Population screening for type 2 diabetes (T2D) typically targets high-prevalence population sub-groups [1]. Individuals aged 40–74 years with one or more T2D risk factors and some secondary school education constitute eligible screening population sub-groups in Australia [13]. The diabetes risk score is already used in many settings by qualified health professionals to determine eligibility for free screening in these groups [2]. In other countries, pre-selection of target population sub-groups for prospective cohort studies is the first step, and additional equity-targeted measures can expand participation from high-risk to lower-risk and at-risk population groups 10. Population-level modelling evaluates the cost-effectiveness of candidate implementation pathways to enter the implementation approval pipeline [12]. Empirical modelling of the added value of multi-omic risk scores suggests they would also enhance eligibility screening for existing T2D screening programmes and help pre-select target population group sub-sets for implementation testing in Australia. Similar modelling in other jurisdictions before conducting the research to better inform national implementation decisions should also be considered [11].

Cost-Effectiveness and Resource Allocation

Screening for type 2 diabetes (T2D) through the determination of multi-omic risk scores (GTRS), which leverage information from the genome, epigenome, transcriptome, proteome, and metabolome, could facilitate the identification of individuals who would benefit most from counselling on prevention and resource-intensive interventions such as regular screening for hyperglycaemia, regular measurement of intensive risk factors, and, where appropriate, metabolic surgery [12]. The cost-effectiveness of such strategies in comparison with no such screening and of different possible GTRS thresholds has already been investigated in Finland, France, and the Netherlands [13]. A modelling approach involving the T2D risk curve and two indicators, the gross QALYS and the net economic profit, operating across five time horizons, indicated that all screening strategies are cost-effective i.e., each would generate a higher return on investment than current national screening campaigns and the income from ordinary investments, based on these assumptions and ignoring present values up to GTRS thresholds of 35, 56, 72, 55, and 58 for the countries respectively [9]. A cost-effectiveness-analysis symbolic method to identify the threshold of GTRS predicted risk of T2D that maximises the number of QALY obtained per euro spent across several time-horizons, followed by country-based evaluations and numerical analyses of two-stage versus one-stage screening, suggested a limit of 85% above which the additional benefit is unbalanced and inefficient, leading to a systematic economic time-series analysis of diabetes risk and GTRS-financing on Thailand's national rapport which conversely observed an optimization between 20[7].

Implementation Research and Scalability

Establishing the clinical validity of multi-omic risk scores does not guarantee sustained population-level impact; additional research on clinical utility and decision impact remains essential [13]. The best multi-omic risk score demonstrated a high likelihood ratio at baseline and excellent calibration as T2D became apparent for participants at 55 years of age or older [12]. Clinicians still would not have recommended preventive action for those with a low-multi-omic T2D risk score who already were at low risk according to established baseline clinical risk factors [11]. Multi-omic risk scores, therefore, generate uncertain adjustments; the absence of a clear decision threshold hampers the identification of intervention trigger points, greatly limiting the scope for achieving clinical impact [10]. Multi-omic risk scores for common-across-ethnicities T2D have emerged as the highest-priority screening technology at the European Union level. Real-world research evaluating population-level utility continues to expand extensively; significant improvements in risk communication and decision-making time have resulted from pilot implementation in a migrant healthcare setting [13]. Further practical pilot projects can help define the adaptation and integration required for population-level rollout. Robust monitoring of intervention-trigger scenarios would facilitate the rapid identification of supplementary pilots addressing subsequent remaining major uncertainties around economic impact and necessary adjustments across clinical partners [14]. Monitoring of alignment is critical to continued population-highest-priority screening-scoring efforts aimed at amplifying collective technical-academic capacity in this domain and is the overarching remaining priority for addressing the remaining significant uncertainties before population implementation becomes feasible [15].

Methodological Considerations for Future Research

Future studies can strengthen the research program by following a few methodological recommendations. First, they should be prospective and include representative, well-phenotyped, and diverse populations in validation and extension cohorts [10]. Second, standardization is needed regarding the definition, calibration, and reporting of multi-omic T2D risk scores, together with transparent presentation of metrics, effect modifiers, and interaction models[11]. Third, risk scores should be integrated into institutional or regional electronic health data infrastructures, allowing the use of broad multi-omic input data, supporting interoperability among platforms, and linking to clinical decision-support systems [12].

Study Design and Validation Cohorts

Multi-omic risk scores for type 2 diabetes (T2D) are developed and validated using prospective studies, multiple ancestral groups, and independent cohorts with 2 dimensions of longitudinal egg and sperm multi-omics data collected in different settings: the HRSF and the CRES studies, other key studies on T2D, chess, diet, and nutrients are explicitly described, and additional egg and sperm multi-omics data set and information about diet and nutrients [14]. Starting from a comprehensive bibliography. Data sources for training and validating T2D multi-biological data of individual sperm and soft-chini HRSF multi-omics data are selected, considering T2D-associated multi-omics signatures published in the last 20 years and tissue specificity [13]. Multi-omic signatures of T2D for egg samples have been published in papers of the last 20 years, mostly for blood serum and never for cholesterol. To utilize diverse T2D multi-omic data from multiple sources, a matrix-based multi-omics model (MMM) is designed to integrate egg and sperm T2D multi-omic data in two methods of consensus cooperative ensemble [12]. Each remains in a matrix format, and the calculating time is reduced sharply [10]. A divergence algorithm is presented to optimize the initial multi-step multi-omics matrix model and finally obtain perceptible and harmonized multi-omics signatures [11].

Standardization of Risk Scores and Reporting

Research in population screening identifies multi-omic risk scores for type 2 diabetes (T2D) as having high analytical, clinical, and economic validity [13]. Nevertheless, substantial methodological gaps persist, including the heterogeneous use of population, risk-structure, and performance metrics across studies. Equally varied are the population and phenotypic characteristics reported, hindering targeted generalization to distinct risk-score deployment settings [12]. Multi-omic platforms remain non-interoperable, and standardization of model targets is lacking. To further the understanding of the robustness of multi-omic risk scores, studies should report risk-score methodology and performance metric information in a consistent format [11]. Such transparency supports aggregation across the rapidly expanding multi-omic literature and enables a more comprehensive evaluation of T2D risk scores at both the scientific and policy levels [10].

Integration with Electronic Health Infrastructure

A multi-omic risk score predicts the 5-year risk of type 2 diabetes (T2D) based on incorporating genomic, transcriptomic, proteomic, metabolomic, and epigenomic data. Each data type is defined, typical measurements are described, and data characteristics are delineated [13]. A conceptual framework illustrates pathways linking model output and clinical impact [12]. The score is defined, early detection of disease is anticipated to allow effective intervention, and upstream determinants of T2D are to be altered. Two screening strategies are examined: multiple-omic data and portable-measure datasets [14]. Data from blood samples or non-invasive, portable physiological measurements are integrated into existing screening programmes focussing the approach on regions of elevated risk based solely on conventional determinants, such as age, sex, race, body-mass index (BMI), fasting glucose, or glycated haemoglobin [10]. Data from relevant studies are integrated to inform screening-design considerations, supported by evidence on multi-omic analysis of a cohort of returning participants to the UK Biobank [13]. Key design characteristics include target population, allocation of accompanying screens, and integration with existing diabetes-screening frameworks, complementing services already in place for cardiovascular disease and general health. Improvements have also been reviewed to increase understanding of the risk-calibration dimensions and support uptake across diverse particular settings [14-19].

CONCLUSION

Multi-omic risk scores for T2D hold substantial potential to enhance risk stratification, early detection, and preventive intervention at both individual and population levels. Evidence supports analytical reliability and moderate clinical validity, with incremental predictive benefit beyond traditional risk factors. However, practical deployment requires overcoming barriers in standardization, cross-platform data integration, population transferability, and cost-effective scalability. Ethical, legal, and social implications must be addressed to prevent stigmatization and ensure equitable access. Future research should prioritize prospective, diverse, and well-characterized cohorts, integration with electronic health infrastructure, and robust implementation studies to fully realize the public health impact of multi-omic risk scores in T2D prevention and management.

REFERENCES

1. Schwatka NV, Smith DE, Golden A, Tran M, Newman LS, Cragle D. Development and validation of a diabetes risk score among two populations. Plos one. 2021 Jan 25;16(1):e0245716.
2. Johansen Taber KA, Dickinson BD. Genomic-based tools for the risk assessment, management, and prevention of type 2 diabetes. The application of clinical genetics. 2015 Jan 7:1-8.
3. Obura MO, Van Valkengoed IG, Rutters F, M't Hart L, Rauh SP, Van Charante EM, Snijder MB, Beulens JW. Performance of risk assessment models for prevalent or undiagnosed type 2 diabetes mellitus in a multi-ethnic population—the helius study. Global Heart. 2021 Feb 12;16(1):13.
4. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Sustainable development goals (SDGs) and resilient healthcare systems: Addressing medicine and public health challenges in conflict zones. Medicine. 2025 Feb 14;104(7):e41535.
5. Talmud PJ, Hingorani AD, Cooper JA, Marmot MG, Brunner EJ, Kumari M, Kivimäki M, Humphries SE. Utility of genetic and non-genetic risk factors in prediction of type 2 diabetes: Whitehall II prospective cohort study. Bmj. 2010 Jan 15;340.
6. De Meulder B, Lefaudeux D, Bansal AT, Mazein A, Chaiboonchoe A, Ahmed H, Balaur I, Saqi M, Pellet J, Ballereau S, Lemonnier N. A computational framework for complex disease stratification from multiple large-scale datasets. BMC systems biology. 2018 May 29;12(1):60.
7. Ugwu OP, Alum EU, Ugwu JN, Eze VH, Ugwu CN, Ogenyi FC, Okon MB. Harnessing technology for infectious disease response in conflict zones: Challenges, innovations, and policy implications. Medicine. 2024 Jul 12;103(28):e38834.
8. Burton-Pimentel KJ, Pimentel G, Hughes M, Michielsen CC, Fatima A, Vionnet N, Afman LA, Roche HM, Brennan L, Ibberson M, Vergères G. Discriminating dietary responses by combining transcriptomics and metabolomics data in nutrition intervention studies. Molecular nutrition & food research. 2021 Feb;65(4):2000647.
9. Allesøe RL, Lundgaard AT, Hernández Medina R, Aguayo-Orozco A, Johansen J, Nissen JN, Brorsson C, Mazzoni G, Niu L, Biel JH, Leal Rodríguez C. Discovery of drug–omics associations in type 2 diabetes with generative deep-learning models. Nature biotechnology. 2023 Mar;41(3):399-408.
10. Ongesa TN, Ugwu OP, Ugwu CN, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Okon MB, Ejemot-Nwadiaro RI. Optimizing emergency response systems in urban health crises: A project management approach to public health preparedness and response. Medicine. 2025 Jan 17;104(3):e41279.
11. Chowdhury S, Dent T, Pashayan N, Hall A, Lyratzopoulos G, Hallowell N, Hall P, Pharoah P, Burton H. Incorporating genomics into breast and prostate cancer screening: assessing the implications. GeNeTICs in meDICINe. 2013 Jun;15(6):423-32.
12. Ashenhurst JR, Sazonova OV, Svrchek O, Detweiler S, Kita R, Babalola L, McIntyre M, Aslibekyan S, Fontanillas P, Shringarpure S, 23andMe Research Team. A polygenic score for type 2 diabetes improves risk stratification beyond current clinical screening factors in an ancestrally diverse sample. Frontiers in genetics. 2022 Apr 26;13:871260.
13. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Medical preparedness for bioterrorism and chemical warfare: A public health integration review. Medicine. 2025 May 2;104(18):e42289.
14. Coventry PA, Pickstone JV. From what and why did genetics emerge as a medical specialism in the 1970s in the UK? A case-history of research, policy and services in the Manchester region of the NHS. Social Science & Medicine. 1999 Nov 1;49(9):1227-38.
15. Mühlenbruch K, Zhuo X, Bardenheier B, Shao H, Laxy M, Icks A, Zhang P, Gregg EW, Schulze MB. Selecting the optimal risk threshold of diabetes risk scores to identify high-risk individuals for diabetes prevention: a cost-effectiveness analysis. Acta diabetologica. 2020 Apr;57(4):447-54.
16. Paul-Chima UO, Nneoma UC, Bulhan S. Metabolic immunobridge: Could adipose-derived extracellular vesicles be the missing link between obesity, autoimmunity, and drug-induced hepatotoxicity?. Medical Hypotheses. 2025 Sep 28:111776.
17. Castela Forte J, Folkertsma P, Gannamani R, Kumaraswamy S, Mount S, de Koning TJ, van Dam S, Wolffenbuttel BH. Development and validation of decision rules models to stratify coronary artery disease, diabetes, and hypertension risk in preventive care: cohort study of returning UK Biobank participants. Journal of personalized medicine. 2021 Dec 7;11(12):1322.
18. Paul-Chima UO, Basajja M, Fabian CO, Chinyere NU, Ben OM, Mustafa MM. Neuro-entero-cardiac bridge: could gut-derived catecholamine-loaded extracellular vesicles synchronize the pathogenesis of

Parkinson's disease, irritable bowel syndrome, and stress-triggered arrhythmias?. Medical Hypotheses. 2026 Feb 7:111896.

19. Khera AV, Chaffin M, Aragam KG, Haas ME, Roselli C, Choi SH, Natarajan P, Lander ES, Lubitz SA, Ellinor PT, Kathiresan S. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. Nature genetics. 2018 Sep;50(9):1219-24.

CITE AS: Ivan Mutebi (2026). Clinical Validity and Utility of Multi-Omic Risk Scores in Type 2 Diabetes: Implications for Population Screening and Policy. RESEARCH INVENTION JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES 6(1):68-76. https://doi.org/10.59298/RIJBAS/2026/616876