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PREDICTIVE MODELING FOR EARLY DETECTION OF METABOLIC SYNDROME: MACHINE LEARNING APPROACHES AND CLINICAL TRANSLATION

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ABSTRACT

Metabolic syndrome (MetS) affects about 25% of the adult population worldwide and is a primary antecedent to cardiovascular disease and type 2 diabetes. The opportunity of early prediction through predictive modeling allows us to enable timely intervention; however, clinical adoption is stalling despite significant improvement in the algorithms. The present narrative review aims to provide an overview of the fast-evolving field of predictive modeling for early detection of MetS, scanning from basic risk scores, past machine learning models to real world clinical use cases with its current limitations. We reviewed trends in machine learning paradigms, multi-omics integration, wearable technology use, health disparities and other areas of emerging importance to the field by analyzing peer-reviewed literature and offering expert-led commentary on methodological innovations and translational hurdles. While the DL models offer significantly better discriminative ability (~AUC 0.85-0.95), interpretability becomes an even greater issue. The combination of multiple-omics and longitudinal modeling holds promise for personalized risk assessment. There are critical unmet needs in external validation, algorithmic fairness, and clinical workflow integration. Regulations for the AI-driven diagnostic tools are still in their infancy. Although prediction modeling for MetS has advanced to be technical, successful translation and implementation in clinical contexts should consider interpretability, validation quality, health disparity, and regulatory framework. Potential areas to explore include federated learning models, causal modeling techniques, and implementation of science frameworks.

KEYWORDS: *Metabolic Syndrome (MetS), Predictive Modeling, Machine Learning, Clinical Translation, Multi-Omics Integration*

1. INTRODUCTION

Metabolic syndrome (MetS) is a collection of connected cardiovascular and metabolic risk factors, central obesity, insulin resistance, dyslipidemia, and hypertension, that come together to promote the risks for cardiovascular disease (CVD), type 2 diabetes (T2D), and all-cause mortality. The prevalence of MetS worldwide is thought to be around 25% in the world's adult population, and its increasing prevalence is largely due to obesity, sedentary lifestyle and aging populations (Saklayen, 2018; Hirode & Wong, 2020). Due to its complex and gradual development, timely recognition of high-risk individuals is crucial to initiate life-style changes and pharmacologic treatments prior to establishment of subsequent complications.

The traditional MetS initial evaluation implied the use of categorical diagnostic thresholds set out by institutions, which included National Cholesterol Education Program Adult Treatment Panel III (ATP III), International Diabetes Foundation (IDF), or World Health Organization (WHO). Although these categories are used in a clinical setting, they characterize MetS as either 'yes' or 'no' and not as a continuum of risk. Current risk scores (e.g., the Framingham Risk Score or the Finnish Diabetes Risk Score) roughly correspond to expected AUC values of 0.70_0.75 and assume a linear and low-dimensional relationship for metabolic, genetic, environmental and behavioral variables (Zheng et al., 2020).

During recent years, predictive modeling for MetS has advanced rapidly as several trends converged. First, the increase in use of electronic health records (EHRs) has led to enormous longitudinal data which are an excellent fit for machine learning applications. Secondly, developments in high throughput 'omics technologies now allow full scale genomic, proteomic and metabolomic mapping. The third one regards the consumer wearable technologies and the possibility of continuous monitoring of physiological markers and activity patterns. Finally, methodological improvements in Machine Learning, namely, deep learning (DL) and ensemble methods, have increased the ability to model complex nonlinear data structures.

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Several recent reports show that state-of-the-art ML techniques can yield better prediction performance for MetS, compared to classical regression-based or rule-based systems. For instance, Lee et al.,2020) demonstrated improved discrimination by gradient boosting and random forest models with genetic as well as clinical predictors compared to logistic regression. Conversely, bulk studies of (Park et al.,2024) and (Zhang et al.,2023) found that ensemble learning and deep network model outperformed conventional risk scores with AUC often over 0.85. In an additional study (2024), BMC Medical Genomics, more demographic, clinical, and genetic markers were combined to outperform baseline models. Similar improvements were shown in other PLOS One and Scientific Reports studies, which used ML algorithms with health-check datasets (PLOS One, 2023; Kim et al., 2022).

Up to static modeling, recent efforts gradually make use of time series analysis and multi-task deep learning that can take advantage of longitudinal and multi-component data. For example, Lee et al.,2024) have developed a multi-task deep learning model for simultaneous prediction of MetS and its components, which obtained improved calibration and AUC compared to single task models. Temporal convolutional networks have also been used to study evolving metabolic risk trajectories in multi-year cohort data (Kim et al., 2022; Zhang et al., 2023). Simultaneously, progress in transfer learning and multimodal fusion methods contribute to the unified risk stratification by incorporating EHR data, clinical notes content and molecular signature altogether.

Although advances have been made in these methods, there are difficulties with their interpretability, generalization, and fairness. Although DL models have superior discriminative power (AUC 0.85–0.95), their “black-box” property restricts clinical interpretability. Further, most of the models are trained with homogeneous data, and it may raise an issue for algorithmic bias and subpopulation welfare. Reviews of fairness in medical AI draw attention to how biased data collection, labeling mistakes and sampling inadequacy risk worsening health disparities if not addressed (Rajkomar et al., 2022; Panch et al., 2023; Chen et al., 2024). As a result, there have been stronger calls for rigorous external validation, explainability and regulation scrutiny prior to clinical use (Kelly et al., 2024).

In practical applications, there are a variety of fields where we can apply predictive modeling with MetS. For early recognition and individualized prevention, risk scores are a useful tool in primary care settings. In worksite and health promotion services, predictive analytics can inform interventions aimed at high-risk employees. In research, improved risk stratification may prospectively improve clinical trial recruitment and precision medicine. In public health, predictive models can guide resource allocation and surveillance tactics. Models using non-invasive, inexpensive predictors including anthropometric and lifestyle factors are especially attractive for cost-effective screening in resource-poor environments (Lim et al., 2023; Choi et al., 2023).

The current narrative review aims at summarizing trends in up-to-date literature (from 2020 onwards) on the methodological and translational progress towards predictive model-based detection of MetS. It specifically (1) reports on recent advances in machine learning and deep learning, (2) discusses new emerging strategies for multi-omics integration and longitudinal modeling, (3) observes the gap between algorithmic innovation and real-world application, (4) addresses issues of fairness, interpretability, regulatory readiness among other topics, and lastly 5) outlines future perspectives including federated learning approaches, causal inference models, implementation science frameworks. Considering the world epidemic of metabolic diseases and increasing utilization of AI in medical research and practice, a new synthesis is crucial. The successful clinical translation of MetS predictors will require strict adherence to validation, transparency, and fair deployment so that such technologies serve further health equity, rather than challenge it.

2. EMERGING TRENDS AND THEMATIC ANALYSIS

2.1 Evolution of Machine Learning Architectures: From Classical Methods to Deep Learning

Prediction modeling for metabolic syndrome (MetS) has evolved significantly over the past decade, moving from classical statistical models to more sophisticated deep learning structures that can account for complex relationships between nonlinear and high-dimensional data. Increasingly, this development has been driven by the availability of population-based health databases endowing large-scale metabolic investigations, the omnipresence of electronic health records (EHR) and progress in computation allowing to model complex biological and behavioral antecedents to metabolic risk.

Early prediction studies are mostly based on traditional statistical and shallow machine learning algorithms including logistic regression, support vector machines (SVMs), and decision trees. Such models offered some crucial insights but were constrained in their ability to deal with interaction among variables and temporal dependence. For example, (Zhang et al.,2021) constructed a 4-year prediction model for MetS risk based on traditional ML methods in a population of large adults, and found that ensemble models (forest-like decision random and gradient rising with the foresting) had superior ability to discriminate (AUC = 0.84 vs. AUC = 0.79 of logistic regression). Similarly, (Kim et al.,2022) showed that the ensemble learners and multilayer perceptron model significantly outperformed traditional regression-based classifiers in the identification of both metabolic syndromes plus pre-metabolic syndrome, using a cohort of Korean middle-aged adults.

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Recent advancements in gradient boosting frameworks (e.g., XGBoost, LightGBM) are significantly impacting their clinical application by delivering models that are both robust and generalizable, which can be also interpreted using feature attribution methods like SHAP (SHapley Additive exPlanations) values. In a Chinese longitudinal cohort, (Li et al.,2024) built an XGBoost derived prediction model incorporating biochemical and anthropometric measurements with very good discrimination (AUC = 0.86) and even calibration across the different sexes and age groups. These models provide a compromise in accuracy and interpretability, rendering them practical for use in real-world screening tasks.

Recent progress in deep learning (DL) has further extended predictive potentials by capturing high-dimensional and nonlinear dependencies present in challenging health data. Deep architectures (e.g., Multilayer perceptron, Convolutional neural Networks and Recurrent Neural Networks) can learn complex latent features from raw or multimodal input sources. In an investigation among National Health and Nutrition Examination Survey (NHANES) participants, (Peng et al., 2022) proposed an MLP model with an AUC of 0.91 outperformed that of logistic regression and random forest in detecting correlation between lipid markers, inflammatory indices, and anthropometric factors in which deep learning can capture weak relationship for T2DM early diagnosis prediction as considered in this study.

Temporal modeling has also become a crucial novelty, especially for chronic and progressive pathologies such as MetS. (Kim et al., 2021) applied long short-term memory (LSTM) networks on five-year longitudinal health records data for the prediction of MetS onset and found modeling temporal dependencies (AUC = 0.89) significantly outperformed static baseline models (AUC = 0.84). Imaging-based methods, such as (Park et al., 2020) utilized CNNs for the assessment of visceral adipose tissue (VAT) from abdominal CT images, estimating MetS with AUC = 0.90, surpassing conventional anthropometric indices (AUC = 0.78).

In more recent years, hybrid deep learning models that leverage multimodal inputs (combining tabular, imaging, and temporal data streams) have been proposed. For example, (Wang et al., 2023) developed a multimodal deep neural network of clinical factors, physiological signals, and retinal images with strong external validity (AUC = 0.93). Although predictive, these models are hardly explainable, compute-intensive, and may have limited real-world deployment feasibility. (Rufo et al., 2021) suggested a two-stage solution where risk is stratified with a random forest model before selectively applying a deep learning model on cases of uncertainty. This method enabled high accuracy to be achieved and simultaneously enhanced interpretability and efficiency.

These advances bring to light a fundamental tension between model complexity and clinical applicability. Although deep learning models show statistical advantages over their interpretative ensemble counterparts, the marginal clinical values in practice are still limited (Zhang et al., 2022). As a result, selecting context-relevant models for reconciling predictive performance, interpretability, and operational practicality was identified as a major challenge for translating into practice.

What this progression from classical to deep learning has done is "trade accuracy for feasibility". Large scale population screening initiatives may be gained from simpler models with long-term risk interpretation, while multimodal data in specialist clinics could justify greater complexity of deep architectures.

2.2 Multi-Omics Integration and Personalized Risk Assessment

Integration of multi-omics data stands as the most promising and challenging frontier in metabolic syndrome prediction. Taking advantage of molecular-level data across genomics, transcriptomics, proteomics, metabolomics and metagenomics, multi-omics strategies target underlying biological mechanisms and inter-individual diversity that can't be identified in clinical or anthropometric measurements alone. This approach is fundamentally congruent to those of precision medicine that aims at individualizing treatment and risk assessment based on biological profiles (Pan et al., 2023).

Recent large-scale studies have already started to quantify the degree of MetS variance explained by the various molecular layers. In a pioneering investigation with 62,822 UK Biobank participants, the phenotypic variance of MetS and its components was systematically decomposed throughout the genome, transcriptome, metabolome and exposome. In an interesting parallel, the metabolome layer contributed in a significant way to disease variance and in many cases more than genetic or transcriptomic layers. Previous observations confirm and emphasize that metabolic intermediates are more proximal reflections of the cardiometabolic dysfunction than heritable genetic susceptibility, integrating effects of genes along with environmental and lifestyle influences on these pathways (Amente et al., 2024).

Genomic studies have yielded initial findings on the heritable component of MetS that family and twin investigations put at 40-60%. Hundreds of genetic loci have been identified by genome-wide association studies (GWAS) for the individual components of MetS; however, these usually explain a small proportion of heritability and generally exhibit modest effect sizes. Polygenic risk scores (PRS)

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sum multiple genetic variants into summary risk measures and provide a logical way to integrate genetic data into prediction models. However, despite theoretical appeal, PRS have not consistently exhibited significant additional predictive value beyond clinical information alone in the majority of populations. The strength of genetic information is not in immediate risk-discrimination, but rather its durability over the life course, facilitating early-life risk-stratification prior to clinical risk factors emerging and theoretically informing prevention strategies during important windows of development.

Metabolomics profiling has been identified as a particularly powerful omics modality to predict MetS. Metabolites are direct biomarkers of metabolic disturbance, combining genetic risk with environmental influences and lifestyle. Numerous extensive studies showed that metabolite panels, in particular the dyad of branched-chain amino acids (BCAAs), acylcarnitines, and glycerophospholipids, lead to a substantial enhancement to discrimination over clinical models. (Cheng et al., 2021) performed untargeted metabolomics profiling on plasma from 1,448 individuals in the Framingham Heart Study and identified a panel of 23 metabolites that significantly associated with incident MetS in an AUC of 0.831 and a net reclassification improvement of 12.4% ($p < 0.001$) when added to traditional clinical factors. This was even more marked for those at intermediate risk, where clinical decision-making is least clear-cut, and improved stratification would be expected to have the greatest potential impact on intervention decisions.

The biological interpretability of metabolite associations leads to mechanistic insights that support clinical plausibility. Increased BCAAs have been repeatedly associated with induction of insulin resistance via activation of the mTOR pathway and interference in glucose homeostasis. Acylcarnitines also rise, which represents incomplete fatty acid oxidation and is a sign of mitochondrial health problems, evidence of metabolic inflexibility. Changes in the glycerophospholipid signature are related to membrane composition, lipid signaling, and cellular inflammation. These mechanisms are not only validating models that may be based on metabolomics but also informative of potential therapeutic targets, and it is therefore suggested that metabolomics have predictive and explanatory power.

Networking: Proteomics approaches furnish orthogonal information (most biological activities are protein based, and proteins can represent more directly actionable drug targets or biomarker candidates than metabolites or SNPs). (Cai et al., 2023) constructed predictive models of incident MetS based on high-throughput serum proteomics, revealing proteomic signatures that could predict future disease onset many years prior to appearance of the disease. Similarly, Carrasco-Zanini et al., 2024) showed that plasma proteomic signatures improved the prediction of common diseases compared with genetic risk scores, highlighting their translation into gene-cardiometabolic medicine. (Gao et al., 2023) used an aptamer-based proteomics platform to quantify 1,305 plasma proteins of 4,067 subjects in the EPIC-Norfolk study and identified a 15-protein signature associated with 10-year risk of MetS (AUC = 0.842). Prominent proteins were inflammatory markers (IL-6, CRP), lipid metabolite controllers (APOC3, PCSK9), and endothelial function mediators (VEGF, ICAM1). The protein panel contributed additional predictive value compared to clinical models and substantially improved the risk stratification up to ≈10 years prior to MetS diagnosis, which would expand the time for preventive intervention.

The gut microbiome is an important environmental factor influencing metabolic health through mechanisms such as the production of short-chain fatty acids, transformations in the bile acid profile, function of the intestinal barrier, and systemic inflammation. Microbe-metabolite interactions are especially relevant for lipid metabolism and immune programming. (Bishehsari et al., 2023) performed an integrative multi-omics analysis, including fecal microbiota composition, plasma metabolomics, inflammatory cytokines, and dietary data in obese individuals. As shown in Table 1, 37 characteristics linked to MetS component burden were found, and they created a combined “metabolic-inflammatory” index that was highly associated with both microbial dysbiosis and poor diet quality. These studies illustrate how the microbiome can modulate risk prediction, while providing mechanistic insights into disease pathways that link diet, socioeconomic status, and metabolic disease. (Liu et al., 2021), who sequenced the 16S rRNA gene and characterized gut microbiome composition in 1020 Chinese adults (both upper and lower tertiles) showing that metrics of microbiome diversity, as well as looking at two beneficial commensals, Akkermansia muciniphila and Faecalibacterium prausnitzii among others, and found that resulting metrics reflected (and were alone associated with) prevalent MetS and incident (coupled metrics representing it). A random forest model combining clinical factors and microbiome features had AUC =0.873, significantly higher than that of the models including only clinical factors (AUC 0.802), indicating a substantially improved risk stratification by incorporating microbiome profiling.

Although individual omics modalities look promising, the true potential lies in their integration. Multi-omics integration is challenging from a methodological standpoint because of the heterogeneity in nature and characteristics of different data types (dimensionality, measurement scales, biological relationships, and noise profiles). Sophisticated analytical methods are needed to successfully integrate such diverse sets of data.

(Zhang et al., 2023) developed an end-to-end deep learning approach to combine clinical data, genotypes and metabolomics and gut microbiome profiles of 2,156 individuals enrolled in the Multi-Ethnic Study of Atherosclerosis (MESA). Multi-omics model (AUC 0.907) for MetS prediction performed significantly better than clinical-only (AUC 0.814), genetics-only (AUC 0.742), metabolomics-

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only (AUC 0.846), or microbiome-only models (AUC = 0.768). Notably, when attention mechanisms were implemented in the neural networks, we observed how different omics layers contribute to a variable extent across individuals, with metabolomics being most informative in individuals close to early metabolic dysregulation and clinical factors dominating for those near full-blown disease. This finding is in line with the model of "precision risk assessment" where optimal feature combinations depend on patient and stage specific conditions.

Network-based integration methods provide an alternative approach that directly models connections between multi-omics characteristics. (Hasin et al., 2020) developed integrated molecular networks based on multi-omics and clinical parameter profiles of 1,012 individuals and found several functionally coherent modules related to different MetS traits. This systems biology analysis demonstrated that insulin resistance and dyslipidemia implicated predominantly different molecular networks and therefore generalized MetS criteria might mask underlying biological heterogeneity, with component-based prediction models being potentially more biological appropriate.

There are immense challenges to the practical realization of multi-omics strategies. High-throughput omics profiling is still costly, costing hundreds to thousands of dollars per sample (depending on platform and depth of sequencing). The analytical pipelines demand expertise in specialized bioinformatics and significant computation infrastructure. A lack of full standardization in sample collection, processing and measurement protocols between laboratories still exists raising issues of reproducibility and cross-platform comparability.

Most importantly, we do not know if multi-omics models can be useful in the clinic. Statistically significant increases in AUC are of scientific interest, but whether they translate to any meaningful difference in patient outcomes by prompting more timely interventions or better treatment selection needs to be tested prospectively in clinical trials at a great cost and time investment. The requirement for clinical applications should be more than just statistical superiority or an observed gain that would warrant the additional expense and difficulty.

A promising pragmatic alternative is the targeting of omics profiling in selected use cases rather than universal screening policies. Thus, some approaches (such as metabolomics) could be saved for people with disparate clinical risk factors or family histories suggesting genetic predisposition. Microbiome profiling could also inform choice of intervention (e.g. dietary modification approaches) rather than risk prediction per se. Such a tiered approach may enhance cost-effectiveness by making better use of the distinctive information delivered through multi-omics approaches.

Future directions of multi-omics integration Merely moving toward higher levels of automation, reduced cost as well as point-of-care or near-patient technologies that simplify the complexity of sample-handling and manipulation techniques will most likely further shape multi-omics integration in the future. The simultaneous development of large-scale biobanks with integrated clinical, genetic, and molecular phenotyping data may help facilitate more comprehensive model construction and validation. In the end, the impact of multi-omics will not be measured in terms of how much technical wizardry we generate but rather by whether our efforts result in better clinical decisions and patient outcomes out there in the real world.

Table 1: Multi-Omics Data Categories in the Metabolic-Inflammatory Score (Bishehsari et al., 2023)

Data Categories

Category	Description	Examples of Measured Parameters
Fecal Microbiota	Gut Microbial Composition and Diversity	Microbial taxa abundance, alpha/beta diversity metrics
Systemic Inflammation Markers	Inflammatory Cytokines and Immune Activation Markers	IL-6, TNF-α, CRP, other pro-inflammatory cytokines
Plasma Metabolites	Small Molecule Metabolites in Circulation	Lipids, amino acids, organic acids, bile acids
Plasma Glycans	Glycosylation Patterns of Plasma Proteins	N-glycan profiles, glycoprotein modifications
Intestinal Permeability	Gut Barrier Function Assessment	Sugar permeability test results (lactulose/mannitol ratio)
Dietary Quality	Nutritional Intake Assessment	Diet quality scores, nutrient composition

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2.3 Wearable Technology and Continuous Monitoring

The commercial emergence of wearable consumer products and remote monitoring technology is driving unprecedented potential for continual longitudinal assessment of physiological kinetic measurements and behavioral traits associated with metabolic syndrome. In contrast to traditional clinical evaluations that offer snapshots at relatively sparse time-points, wearables afford high-frequency temporal sampling for the capture of dynamic signatures, diurnal fluctuations, circadian rhythms and early deviations from healthy states. This transition from episodic to continuous surveillance paradigm is a good fit with the progressive, multifactorial nature of metabolic dysregulation and should allow for entirely new strategies in early diagnosis.

Today, wearables incorporate many sensing modalities to capture a wide variety of physiological signals. PPG sensors are capable of detecting heart rate, HRV, and also can estimate blood pressure and vascular tone. Accelerometers and gyroscopes measure patterns of physical activity, sedentary time, and sleep-wake cycles. Electrodermal activity sensors measure sympathetic nervous system activation and stress. More sophisticated devices may include thermal sensors, electrocardiography (ECG), and increasingly more recently, non-invasive continuous glucose monitoring. Integration of these multi-modal sensor streams enables a holistic view of an individual's physiological and behavioral status outside the laboratory settings.

Recent studies have empirically shown that it is possible and clinically relevant to predict the metabolic risk from wearable data. (Bent et al., 2020) published a landmark study that used data from consumer, wearable fitness trackers for 5,609 participants of the health eHeart Study. Machine learning models using continuous HR, physical activity, and sleep as features to predict prevalent MetS had an AUC of 0.811 which was like that attained by models employed with conventional clinical metrics. Resting heart rate, heart rate variability, sedentary time, and sleep disruption were reported as important discriminative features of the model based on wearables. These prospectively monitored measures capture autonomic dysfunction and metabolic stress while they are ongoing before clinical manifestations become overt.

Based upon such pillars, (Kim et al., 2024) also carried a specialized cross-sectional study in which 272 (88 MetS, and 184 non-MetS) participants were tracked using Fitbit devices to obtain the data for 26 digital biomarkers comprising features from step count, HRV, and sleep-wake cycle. By applying interpretable machine learning models, Garaulet and colleagues found circadian rhythm metrics, particularly the continuous wavelet circadian rhythm energy (CCE) and heart rate-based relative amplitude, to be powerful predictors of MetS, independent of age and BMI. This observation highlights the potential of circadian biomarkers from wearables to capture early (preclinical) autonomic-metabolic changes preceding later disease, and that disruption in that timing may serve as an early warning index measurable via passive sensing.

The temporal variability of wearable data opens the door for new analysis methods that leverage dynamic trends beyond single-point summary statistics. Mun et al. (2024) analyzed continuous heart-rate data from 564 middle-aged adults obtained by commercial wearable fitness trackers and demonstrated that heart-rate indices derived from wearables, including all-day, sleeping, minimum, and inactive heart rate as well as nighttime HR dip were significantly associated with PreMetS/MetS and provided better model fitness than clinical resting heart rate. These findings suggest that problems with metabolism may not just be altered in baseline physiology, but also an outcome reflected in real-time data. Gaur et al. (2024) investigated this through an 8-month observational study, tracking HRV, step counts, and PPG signals continuously via wearables in 59 individuals. The authors showed that long-term HRV trajectories and signal stability could be reliably estimated from real-world wearable-based data, providing physiological variability patterns potentially indicative of subclinical metabolic stress. Effective time series modeling is needed to discern clinically meaningful trends from normal physiological variability captured by these dynamic signatures.

Disturbed sleep is especially critical, yet a frequently overlooked risk factor for metabolic syndrome. Low quality of sleep, short duration of sleep and circadian desynchronization are known to causally affect insulin resistance, appetite increase and weight gain through pathways which include cortisol imbalance, glucose metabolism malfunction and leptin-ghrelin imbalance. We showed that sleep regularity can be objectively quantified using them, giving opportunity to estimate continuous/discrete and up to a minute sleeping exposure rather than solely from sleep diary (subjective).

Recent studies have focused on the potential of wearable devices to improve prediction and prevention of metabolic diseases. For instance, Liang et al. (2023) employed Mendelian randomization in a sample of 335,727 UK Biobank participants and showed that genetically predicted 1-hour longer self-reported sleep duration was related to approximately 13% reduced risk for MetS. While the present investigation was not conducted using wearable sleep measures, it reinforces that sleep duration is significant for metabolic health. One of the major advantages of (wearable) sleep monitoring over self-report measures is that they provide an objective and

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continuous measurement of sleep-wake patterns, meaning wearable devices may help to identify individuals at increased risk for MetS before traditional risk factors manifest themselves.

For physical activity, strain et al. (2023) used UK Biobank wrist-worn accelerometers to produce estimates in the use of data from 90,096 participants. Their results showed that for higher PAEE, there was a linear relation with the risk of type 2 diabetes, a major part of MetS. Even getting some exercise, say a 20-minute brisk walk each day, was associated with a 19 percent decrease in diabetes risk. These findings lend support for the relevance of wearables in capturing subtle activity patterns beyond step-based metrics such as identifying sedentary behavior and ultimately fostering interventions that facilitate frequent activity across the day.

Collectively, these studies indicate that wearables can supply valuable information about sleep and activity behavior to non-invasively stratify individuals according to metabolic risk as well as support early lifestyle interventions.
With the development of sensor technology, there are more possibilities for sophisticated physiological monitoring, among which continuous glucose monitoring (CGM) seems particularly promising. CGM technologies, pioneered for diabetes care, are increasingly being studied in non-diabetic and prediabetic populations as measures of metabolic health. CGMs show postprandial glycemic responses, GV, and TIR that offer a finer detailed assessment of glucose homeostasis compared to intermittent fasting measurements. Recent developments in continuous glucose monitoring (CGM) offer insight into marked heterogeneity of glycemic responses among non-diabetic adults. In a Science Advances paper, Zeevi et al. (2023) monitored glucose levels in an extensive cohort using CGMs and demonstrated that people react distinctly at the same meals, which illustrates a restriction of fasting glucose or HbA1c to estimate metabolic health. These individualized glycemic profiles were then employed to train machine learning models that can predict postprandial glucose responses with clinically useful accuracy, providing evidence that data collected from CGMs could identify early biomarkers of dysregulated glucose metabolism prior to reaching diagnostic thresholds.

The study was not designed to directly predict MetS, but does lend support for the use of CGM data in defining those at risk for metabolic derangement more generally. The opportunity to identify the abnormal glucose responders among healthy individuals creates opportunities for focused lifestyle interventions and personalized nutrition approaches to prevent this metabolic deterioration.

Scaling up the findings on a larger and diverse cohort, The Ultrahuman M1 study (Chaudhry et al., 2024) performed a multiple-arm observational study that involved 105 nondiabetic and prediabetic Indian adults and included continuous glucose monitoring (CGM) in combination with wearable activity tracker. The study identified wide individual variability of GV, and it also found high associations between the CGM-derived parameters and insulin resistance (HOMA-IR), dysglycemia (OGTT glycemia, HbA1c) or lipid disturbances. Hs-CRP was strongly associated with GV in prediabetics and there were modest relationships between the sleep-activity patterns and CGM parameters for non-diabetic participants. These results highlight the power of CGM and wearables in early identification of metabolic dysfunction, which is not obvious with periodic glucose measurements, thus enabling earlier lifestyle interventions.

Another field of continuous cardiovascular assessment is the cNIBP technology, which relies on PPG waveform analysis as well as pulse transit time (PTT) for cuffless blood pressure monitoring. Although accuracy limitations have precluded widespread clinical application, these technologies may allow the assessment of blood pressure trends and patterns of variability not observed in isolated clinic readings. White coat hypertension and masked hypertension remain diagnostic challenges that continuous ambulatory monitoring may be possibly addressed but require further investigation (Choi et al., 2023).

And in the realm of wearable technology, while there is great potential, a number of obstacles hinder use in predicting MetS. Accuracy and reliability of devices vary widely amongst manufacturers, as well as sensor modalities, with numerous consumer-level devices not having been adequately validated to gold-standard measurement techniques. PPG-based heart rate measurements are relatively accurate at rest and not reliable during peak activity. Sleep-staging algorithms, although constantly evolving, still perform less than polysomnography (Schyvens et al., 2025). Device location, individual biomechanics and environmental conditions may complicate activity classification. Variability of different brands adds problem difficulty for cross-study comparison and model generality.

There are continued difficulties with data quality. Data loss related to non-wear time, battery drain and connectivity issues can be considerable, especially in free-living with minimal level of participant involvement. The quality and completeness of the data is likely to differ per person, as some people wear the devices for several days consistently whereas others are only sporadically using them. Most studies find that a significant proportion of users stop using them within six months, with 30-50% eventually abandoning their devices, and engagement decreases over time (Van Der Donckt et al., 2024). Predictive models must treat missing data carefully since patterns of missingness themselves can be informative (e.g., lower device adherence may be associated with lower health engagement and/or negative health outcomes).

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The ever-growing amount and dimensionality of data from wearables pose significant computational and analytics challenges. A single person wearing a device every day for a year will produce millions of data points. The scale at which we process, store, and analyze these data already creates a significant need for infrastructure and technical skills. Feature engineering about the transformation of raw sensor streams into interpretable summary statistics is a labor-intensive process that depends on domain knowledge, and it can have a notable impact on system performance. Standardized feature-engineering pipelines remain underdeveloped. An alternative is deep learning, which provides an automated feature-learning procedure, but it has higher demand for data and computing resources (Hong, Dai, & Zheng, 2025).

The issue of providing privacy and data security is fundamental to continuous physiological and behavioral monitoring. Wearable data reflects private information of people's real life such as their daily activities, locations routine and health conditions. Data breach, unauthorized access or misuse could lead to discrimination by insurers or employers, unwanted monitoring of individuals' behavior, and sensitive health information being made public. All those guidelines are violated by a consumer wearable ecosystem, which often lacks strong data governance frameworks, secure transmission and storage protocols, privacy preserving analytics techniques or transparent consent mechanisms (Bouderhem, 2023; Doherty et al., 2025).

Generalizing across devices and populations is even more challenging. The device (model version and specific sensor specifications) as well as proprietary algorithms are also used in various studies, making it unclear whether results can be translated to other devices. Socioeconomic, demographic, and health-related selection biases are apparent in possession of wearables which may affect the representativeness of samples. Most existing datasets represent segments of the population that have higher income, education, and health literacy that may limit the generalizability of predictive models to more robust and diverse populations. These biases may have implications for algorithmic fairness and could even worsen inequalities in health if wearable-based risk estimation is rolled out without due regard to equity (Chaturvedi et al., 2025).

Despite these limitations, wearable technologies may provide distinct advantages that are not achievable by traditional clinical measurement. Nature vs Nurture Factors such as capturing free-living behavior in ‘real’ environments provide ecological validity that laboratory measures do not. Continuous monitoring allows for early identification of deviations from individualized baselines before crossing population thresholds, which could support "n-of-1" precision medicine paradigms. Inclusion of a large number of timepoints along the task allows for exploring temporal dynamics and causal context with time-lagged analyses. Moreover, the scalability and low technology cost of sensor monitoring after initial infrastructure has been put in place would provide an opportunity for population-level surveillance and screening programs that could not be done with conventional clinical-based assessment approaches (Ghadi et al., 2025). This trend of finding deeper ways to blend wearable data with other sources is consistent with earlier developments. Hybrid dynamics models, which blend periodic clinical testing and wearable monitoring, might balance the trade-off between accuracy of measurement and practical considerations. Contextual data collected from smartphones, such as location and indoors/outdoors state, screen time, food logging by taking pictures of meals, and passively sensed social interactions (and other mobile source) can complement physiological wearables with behavioral and environmental context. Linkage to electronic health records allows combination of longitudinal sensor data with medical diagnoses, laboratory results and medication use to develop holistic longitudinal profiles (Ghadi et al., 2025).

The wearable-based prediction of the future of MetS may rely on personalized adaptive models that teach individuals inter-visit baselines and monitor deviations using individually defined thresholds instead of aggregate ones. Such “n-of-1” strategies are consistent with concepts of precision medicine and may provide a sensitivity advantage for early detection. But they need prolonged baseline monitoring periods for a stable individual pattern and complex algorithms to detect small changes that are clinically relevant instead of being due to normal physiological variations. Important next steps for research on these remote monitoring technologies should include efforts to validate measurements across populations, standardize analytic approaches, and evaluate the clinical utility of the data as well as whether wearable-driven interventions result in significant improvements in metabolic outcomes and quality of life.

2.4 Health Disparities and Algorithmic Fairness Addressing health disparities using AI is also related to algorithmic fairness.
The potential of machine learning for early detection of MetS needs to be carefully examined in terms of health equity. Metabolic syndrome varies greatly along racial, ethnic, socioeconomic, and geographical lines. Among adults in the US, Hispanic/Latino adults have high MetS prevalence (about 36.3%), followed by non-Hispanic white (36%) and non-Hispanic black (32.3%) adults and lower MetS prevalence among Asian American/PI groups (24%); but there is substantial variation within these broad racial/ethnic categories (Hirode & Wong, 2020). These inequities are borne of complex interplay between genetic factors, and environmental exposures; structural racism; differences between people in both the likelihood of exposure to risk-factors or hazards that can harm health (like pollution or work-related stress); access to the resources necessary compare food environment, neighborhood walkability), chronic physical and social conditions across urbanicity further compound these disparities(Cacciatore et al., 2025).

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Algorithmic Bias and Performance Differences: The Sources

Health outcome inequalities span a continuum of dimensions and complex group interactions inherent in healthcare. Making inequality assumptions explicit during predictive modelling is practically challenging but becomes unavoidable. Algorithmic bias can be created by several sources. One of the main sources is data imbalance, meaning if the training data does not contain enough samples from a certain population, models could fail when tested on this group. Bias can also occur when historical disparities in access to care, diagnostic or treatment decisions are encoded in training labels that models learn and perpetuate. Moreover, predictors included in models are frequently social determinants or structural inequalities, which have themselves been influenced by social factors, such that models may be relying inadvertently on proxies for race or socioeconomic status rather than biological risk.

Recent substantial reviews have also described the scope and mechanisms of bias in healthcare AI.

A systemic review of fairness in AI for medicine and healthcare underscored that AI models stratified at the subpopulation level frequently also display strikingly different diagnostic accuracies, treatment recommendations, or prognosis predictions across patient populations unless steps are taken to mitigate bias during model development (Ueda et al., 2024). A scoping review on clinical AI fairness (Liu et al., 2025) highlighted that while algorithmic equity is receiving increasing recognition, a substantial chasm still separates theory from practices in health-care ML, with numerous deployed models lacking subgroup performance reporting or systematic bias assessment.

To robustly investigate algorithmic fairness, evaluating model performances among sub-populations and analyzing the source of any observed differences are crucial. (Gianfrancesco et al., 2020) investigated a range of machine learning models for different clinical prediction tasks and showed that there were consistent performance differences across racial groups. In the context of MetS, models developed primarily in whites may have diminished predictive ability among Black, Hispanic or Asian subjects. These performance disparities were attributed to differences in feature distribution between populations as well as the lack of representation in training data. The notion of fairness in machine learning is ill-defined, and there exist many different competing mathematical definitions often conflicting with one another (Gao et al., 2024; Chakradeo et al., 2025). Demographic parity imposes that positive prediction rates are the same for all groups. It needs equal, true, and false positive rates for all classes. For calibration, PPV must be the same among groups. Those criteria can conflict and lead to hard trade-offs (Barr et al., 2024; Chakradeo et al., 2025). In predicting MetS, should models strive for racial parity in sensitivity (which may require specific probability to cut points), specificity or overall accuracy?

(Chen et al., 2021) explored equity in the MetS prediction assortment among racial and ethnic populations based on NHANES data. In standard machine learning models, AUC varied considerably, 0.883 in non-Hispanic white participants and 0.824 in Hispanic subjects. The paper investigated fairness-aware training methods such as adversarial debiasing and re-weighting. Although these methods mitigated performance disparities (AUC gaps were decreased to 0.02-0.03), they degraded the models' overall accuracy or suppressed majority groups in extremes. A relevant empirical analysis by (Pfohl et al., 2020) showed that many of the fairness- penalizing methods (e.g., constraints for equalizing the performance with respect to different groups) lead to poor performance across all groups and may result in trade-offs over calibration or ranking accuracy. These are findings that capture an age-old tradeoff in optimizing performance (overall) for aggregate behavior and distributive justice (among subpopulations).

Feature Selection and the Structural Confounding Problem

Feature selection is critical for fairness but often an underestimated component. Many of the clinical features that we use are affected by social determinants and structural realities. For example, body mass index has varying implications for metabolic risk in different racial groups: Asians, for instance, have higher risk at lower levels of BMI. Thus, the application of race-agnostic BMI cutoffs may lead to underestimation of risk for Asian populations (Zhu et al., 2021). Socioeconomic predictors such as insurance status or neighborhood may be predictive but ethically challenging to include, since they may cause a model to reproduce current disparities rather than facilitate the identification of biological risk (Colacci et al; 2025). This being the case, the decisions involved in feature selection determine fairness of a model. Several works have put forth fairness-aware feature-selection methods that optimize jointly the predictive performance and demographic parity (Zawad & Washington, 2024; Belitz et al., 2021).

Incorporating race or ethnicity into the model features provokes a special controversy. Race is a social construct with a little clear biologic foundation; however, race-based disparities in health exist. Some suggest that the addition of race to the model can increase calibration and account for unmeasured aspects of social experience, environmental exposures or structural racism (Were et al., 2025). Others argue that the role of race in classification risks reinforcing racial categories, masking underlying causes, and supporting substantive measures for race-based medicine (Barton et al., 2023; Jain et al., 2024). Antiracism efforts in the era of genomic medicine and 'big data' Recent trends in precision medicine promote discarding crude racial categories for more nuanced information on genetic ancestry, environmental exposures or the social determinants that are more proximate to causal mechanisms (Bains et al., 2024; Poduval et al., 2025).

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(Vyas et al., 2020) performed in-depth analysis of race-based correction factors in clinical algorithms, suggesting that many reinforce racial health disparities under the pretext of correcting biological variations. For MetS risk assessment, they suggest it is inappropriate to provide a race-specific adjustment for risk unless the biological mechanisms can be identified and stated. Alternatively, they propose models that integrate social determinants, environmental exposure, and structural factors that causally determine metabolic health.

Strategies for Equity-Aware Model Development

Various interrelated strategies are suggested in the AI ethics and medical ML fairness literature to mitigate such algorithmic bias, for the sake of fairness. The JAMA Network Open guiding principles for addressing algorithm bias (2023) describe a lifecycle approach, requiring that equity considerations be integrated into the entire development life cycle from initial problem statement to deployment and monitoring (Chin et al., 2023).

Diverse Data Curation and Representation: Having adequate representation of underserved populations in the training datasets serves to mitigate bias at its origin. Representativeness of data is a significant challenge, and many large clinical datasets are known to over-represent certain populations while underrepresenting others (Kurapati et al., 2025; Chinta et al., 2025). There are well-documented recruitment issues for cohort studies in minority and underserved communities, which can result in datasets that do not represent the demographics of the populations on whom models will be applied (Rambabu, 2025). EHR data overrepresent people with access to healthcare, leaving uninsured and underserved populations (Getzen & Long, 2023; Chen et al., 2024).

Approaches to data representation include focused oversampling of underrepresented populations, collaboration with community health centers treating diverse individuals, and conducting multisite studies across geography and demographics. (Goff et al., 2021) constructed MetS prediction models from pooled data sources representing multiple health care systems serving diverse populations including federally qualified health centers and safety-net hospitals. The models produced more equitable predictions between racial and socioeconomic groups than those trained on data from individual academic medical centers, highlighting the value of diverse data sources in creating fair algorithms.

Serious Audit and Subgroup Review: Models should be assessed both in the aggregate and among subgroups for race, sex, socioeconomics, and other protected categories. Sensitive, specificity of false-positive and false-negative rates of disparities should be reported systematically and resolved. External validation in varying populations is necessary but has been underutilized. A meta-analysis conducted by (Wynants et al., 2020) demonstrated that less than 15% of the published clinical prediction models are externally validated, and validation among populations with different demographics from training data is even scarcer. In the absence of rigorous external validation, performance discrepancies across populations are unknown, and there is a substantial risk for deploying biased algorithms.

Fairness-Aware Learning: Methods like adversarial debiasing, sample reweighting, or constrained optimization to match parity with respect to groups can mitigate group-level inequality but can lead to loss of overall performance and lack of calibration (Raftopoulos et al., 2025; Petrović et al., 2020; Zhang et al., 2024). Such methods must account for which fairness definition is contextual, and stakeholder-value appropriate.

Causal and Counterfactual Modeling: Incorporating causal thinking at the modeling level can protect against unfair proxying as well as disentangle true risk associations from structural effects (Joshi et al., 2025; Tian et al., 2024; Robertson et al., 2025). Causal fairness frameworks seek to remove associations between predictions and protected attributes that are mediated by inequitable causal pathways, while maintaining those through fair biological pathways.

Transparent Reporting and Community Involvement: It is important to involve patient/ community stakeholders in algorithm development as well as share limitations, fairness tradeoffs to build trust and accountability (Rice et al., 2025; Akintobi et al., 2025). Community-based participatory research approaches, including patients, community advocates, and diverse stakeholders in developing and evaluating models can help ensure that priorities for fairness align with those of the community, and that performance measures are calibrated to reduce rather than perpetuate inequities *(Gupta et al., 2025; Farmer et al., 2022)*.

Continuous Monitoring and Mitigation: After deployment, models need to be carefully monitored for drift in performance, biased subgroups, etc. If differences across groups appear or increase over time, algorithms might require retraining, recalibration or retirement (Chakradeo et al., 2025; Bamiro, 2025). Surveillance after deployment is vital but rarely carried out in an organized way.

Implementation Equity and Regulatory Considerations

The future of algorithmic fairness regulation is still in its infancy. The FDA has started to publish guidance on AI/ML medical devices with best practices for bias assessment and real-world performance monitoring (FDA, 2025). Yet, the exact criteria for assessing fairness, thresholds for acceptable performance biases and means of monitoring post-market remain to be prescribed. Several jurisdictions have

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introduced or enacted algorithmic accountability laws that would mandate impact assessments, transparency reports and/or remediation processes for biased algorithms (Kumar et al., 2025; Wyden, 2025).

The context of implementation exerts a profound effect on the distribution of fairness. Even well-calibrated models can create disparities if they are used in ways that differentially impact subgroups within the population (Gupta et al., 2025; Gustafson et al., 2023). For example, targeted enrollment in prevention programs using prediction models of MetS risk may unintentionally filter out underserved subpopulations if model thresholds are based on enriched majority populations or not culturally sensitive outreach efforts. It is imperative to pay attention to implementation equity including targeted outreach, language access, cultural appropriateness, and reducing access barriers (Nong et al., 2022).

Novel strategies for fairness also involve training independent models for S demographic subgroups, with potentially different subsets of the input features used, and a distinct threshold optimized. Although such a strategy might enhance intragroup care, its potential for promoting "segregated medicine" and for sanctioning between-group differences is somewhat troubling (Chen et al., 2023; Anderson & Visweswaran, 2025). An alternative perspective foregrounds frameworks that focus on causal fairness and intersectional analyses, which address how different forms of identity and disadvantage intersect (Lett & La Cava, 2023; Gohar & Cheng, 2023).

Beyond Technical Solutions: Addressing Root Causes

Finally, it is important to note that algorithmic fairness is not a replacement for underlying drivers of health inequity. Conversations about algorithmic fairness in health care ultimately need to shift beyond measures of technical fairness towards broader conversations addressing the upstream social, economic, and environmental determinants that generate the very health disparities we seek to mitigate (Chin et al., 2023; El-Azab & Nong, 2023; Tang et al., 2025). Yet no amount of fairness modeling can erase health disparities based in poverty, food insecurity, environmental toxins, lack of access to health care and structural racism. Those tools should exist not as techno-fixes to fundamentally social problems, but within larger health equity work focused on addressing the underlying causes.

2.5 Clinical Application and Decision Support Incorporation

The journey from algorithm creation to clinical application is a key, but frequently neglected, stage of the translation pipeline. Although a large number of studies have reported that the predictive performance of ML models is superior to traditional statistical models in research, their clinical adoption has been limited (Watson et al., 2020; Yan et al., 2025). It was a dominant and counterintuitive approach which often led to almost no one attending the meeting. Understanding and overcoming the multi-factorial barriers to implementation is important to realize the potential benefits of predictive modeling for early identification of MetS.

Barriers to Implementation

Recent systematic reviews have compiled the identified obstacles to AI implementation in health. (Nair et al., 2024), there are institutional, workflow-related, educational and ethical barriers that range from scarce leadership backing deep complexity of integration vague regulation sustainability barriers. Similarly, (Petersson et al., 2022) suggested that technical, organizational and human factors interplay to block the successful deployment of AI in clinical practice. (Hassan et al., 2024) noted that clinician trust, interpretability, perceived usefulness and alignment with institutional priorities were the most important predictors of adoption. A scoping review of Scipion et al. (2025) synthesized clinician viewpoints, and noted that workflow interference, lack of clarity around what to do with predictions, and skepticism of “black box” algorithms were prevalently cited barriers.

Workflow Integration and Clinical Utility

One of the pressing challenges is to integrate into clinical workflows. Healthcare is a time-intensive activity; primary care consultations have been shown to the last minute. To achieve this, such predictive tools need to be easily incorporated into the framework of existing EHR systems, or other databases and data registries, extracting data, calculating risk scores, and presenting results in a user-friendly manner.

(Yang et al., 2022) described a pilot deployment of an EHR-embedded machine learning driven MetS risk calculator in three primary care centers. While technically successful, acceptance was mixed due to alarm fatigue, lack of time, and doubts about follow-up. These results emphasize that technology is not enough; successful implementation requires an organizational context, clinician education, and fit with reimbursement and quality-metric systems.

AUC performance is insufficient to test clinical benefits. DCAs provide net benefit estimation of a model under different risk thresholds. (Kerr et al., 2021) further presented that ML-derived MetS models have the most clinical utility in intermediate risk populations (20%–50% predicted probability), implying concentrated value where decision uncertainty is highest.

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Interpretability, Trust, and Explainable AI

Clinician trust hinges on interpretability. Although they are more accurate than traditional methods, we also have a problem explaining their black-box nature. (Markus et al., 2020) stated that trustable AI in medicine must necessarily be explainable and transparent.

Explainable AI (XAI) tools like SHapley Additive exPlanations (SHAP) may be used to illustrate the contribution of certain features to an individual's risk prediction. (Lundberg et al., 2020) demonstrated that predictions with SHAP-based feature importance led to significantly better clinicians' confidence and intention to use the AI systems. Nevertheless, explanations need to strike a balance between thoroughness and accessibility by eschewing technical overload but focusing on risk factors that are clinically well known. On the other hand, simpler and more interpretable models (e.g., decision trees or weighted risk scores) could facilitate adoption by sacrificing some predictive accuracy for transparency.

From Prediction to Action

Prediction without subsequent action tends not to lead to better outcomes. (DeFilippis et al., 2020) showed that automated CV risk calculators improved rates of documentation of preventive counseling but did not improve metabolic outcomes at 1 year. This proposal linking predictive models to actionable interventions such as automated referrals to weight loss or exercise programs could further increase clinical impact. Incorporation of predictive outputs with decision-support systems that connect to evidence-based frameworks (e.g., Diabetes Prevention Program) improves clinical attainability.

Governance, Regulation, and Reimbursement

Feasibility is highly affected by regulation and payment schema. In the U.S., clinical decision-support systems could be regulated by the FDA as a medical device and may require evidence of this technology is safe and effective. Dynamic Adaptive algorithms for continual learning from new data, challenging current validation paradigms. In addition, relatively low payment for preventive counseling or risk-stratification tools acts as a disincentive to uptake. Other value-based payment models, including population health contracts or pay-for-performance programs, may provide greater rewards for prevention of results.

Monitoring, Maintenance, and Education

Post-deployment monitoring remains underdeveloped. Models can become outdated as population attributes, quality of data, and treatment practices change. Perpetual monitoring, re-calibration, and version control are vital points to maintain reliability. Equally critical is clinician training; clinicians need to know the capabilities and limitations of a model to either interpret predictions or override recommendations as appropriate.

Patient-Facing Tools and Ethical Considerations

New patient-facing tools, like mobile risk assessment tools or EHR-tethered patient portals, can support shared decision-making and promote behavior change. However, such a tool must be accompanied by transparent communication of uncertainty, culturally sensitive framing, and protections for data privacy (Weiner et al., 2025; Kelkar et al., 2025; Shah, 2025). There are also ethical issues to be considered, among those: Lack of an informed consent process; propensity for stigmatization and algorithmic misuse by insurers or employers (Corfmat et al., 2025). The resolution of these questions must be based on a continuing dialogue among the clinicians, ethicists, and policymakers (Goktas & Grzybowski, 2025).

Future Directions

Models like the PREVENT equations (2023) that substituted race-based coefficients for physiological parameters and multi-stakeholder validation show possible ways to update clinical risk scores. Finally, rigorous prospective validation, stakeholder engagement and algorithm integration into the care pathway will be required to translate the algorithm performance gains into real-world clinical impact.

3. CLINICAL APPLICATIONS AND REAL-WORLD IMPACT

With the emergence of multi-modal data streams (wearable sensors, continuous glucose monitors, and mobile apps) in metabolic syndrome (MetS), we are well poised to transition predictive modeling tools from bench to bedside (Dehghani Zahedani et al., 2023; Park et al., 2025). When we move from developing proof-of-concept algorithms into the clinical domain of delivering healthcare, what changes is that the focus is less on technical performance and more on clinical validity, usability and impact (Schouten et al., 2024; Du et al., 2025). Emerging standards for data interfaces facilitate predictive modeling as the underpinning technology of new paradigms in population health screening, clinical decision support and remote patient monitoring, which close the loop between continuous data acquisition and an actionable intervention (Osamika et al., 2025).

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3.1 Community-Based Health Screening and Risk Stratification

Risk-modeling for metabolic syndrome (MetS) is not limited to individual patients' visits but also facilitates population-based screening and risk stratification. Such approaches use scalable algorithms to contact-trace high-risk individuals throughout large populations but can be more efficient and lead to the way for proactive prevention.

Population-health workflows now often include risk stratification based on machine learning within health systems. (Kramer et al.,2021) reported EHR-based predictive model implementation in 127 primary-healthcare practices that serve more than 450,000 patients. The system identified high Met S risk individuals who had not been screened metabolically, and detected 5.3% of eligible adults as high-risk, doubling the pick-up rate from opportunistic screening.

Predictive analytics has been used in workplace wellness programs as well, to help determine the intensity of an intervention. (Mattke et al., 2020) demonstrated that machine-learning-assisted stratification enabled a large employer to provide intensive coaching to the highest-risk 15% of workers, with more significant improvements in waist circumference (−3.2 cm for tailored vs. standard care), and systolic/diastolic blood pressure (−5.4/–3.1 mmHg).

Field-based outreach is a critical adjunct to facility screening. Despite a paucity of evidence, (Lee et al., 2022) found that digital health-facilitated lifestyle interventions delivered through general-practice units yielded improvement in metabolic factors, thus it seemed likely that mobile or tablet-based risk assessment tools could be utilized to extend screening directly into underprivileged communities.

Predictive models also serve as the basis for geospatial risk mapping to pinpoint areas with dense populations at high metabolic burden. (Biello et al., 2020) constructed a spatial model of metabolic-risk factors by neighborhood in Chicago that revealed substantial overlap between areas with high predicted MetS prevalence and structural inequities, including food deserts and historic redlining. These analyses illustrate how machine learning could inform resource allocation and measure health disparities.

3.2 Clinical Decision Support to Promote Prevention and Early Intervention

Predictive models may also be used to encourage the best clinical decision after screening, once preventive treatment is considered. Intensive lifestyle intervention delivered by the Diabetes Prevention Program (DPP) reduced diabetes incidence by 58%, but scaling these programs is challenging. (Sussman et al., 2021) applied prediction modeling to identify who is most likely (versus least likely) to benefit from participating in the DPP and found that targeting the top-benefit one-third of participants captured >70% of preventable cases, suggesting a much more cost-effective approach.

Responsiveness to lifestyle modification or pharmacologic interventions can also be predicted by machine-learning models. (Bae et al., 2023) on a personalized, digital health solution for people at risk of metabolic syndrome that utilized AI-driven feedback regarding diet, exercise, and vitals. Subjects showed a significant reduction in weight, blood pressure, and fasting glucose levels highlighting the potential for personalized digital interventions for MetS prevention.

(Shin, Shim, & Oh, 2023) also built an independent non-invasive machine-learning model that only utilized anthropometric and lifestyle information to predict MetS risk, AUC 0.88. These models may facilitate early preventive counselling without relying on laboratory testing, which is especially important in resource-limited settings.

Though predictive models improve accuracy, ethical and practical concerns remain, particularly algorithmic transparency, bias, and inappropriately deferring to model results without clinical judgment.

3.3 Interfacing with Remote Patient Monitoring and Digital Health Platforms

The blending of predictive modeling, wearable monitoring and digital health platforms is changing how we manage MetS. Today's platforms provide dynamic tracking rather than just static risk scores, and continuous adjustment of risk.

(Dunn et al., 2021) also detailed how smartphone-connected wearables monitoring sleep, activity and heart-rate-variability can power AI algorithms to identify early metabolic decline. Feedback from adaptive algorithms led to higher engagement in preventive behavior for a pilot cohort, when compared to typical fitness tracking.

Utilization of telehealth, which had been growing slowly before COVID-19, has exploded in the past year and offers opportunities for managing metabolic risk remotely. (Lee et al., 2022) reported that a combination of connected blood-pressure monitors, smart scales, and app-based coaching decreased multiple MetS components. Likewise, (Yang et al., 2022) demonstrated that a longitudinal machine-learning model with three-year EHR data led to better accuracy in predicting incident MetS cases (AUC 0.91).

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These are examples of predictive models that can transform episodic point-of-care medicine into systems of continuous care. Even so, providing fair access to digital infrastructure and literacy is still crucial to prevent gaps from growing.

4.BENEFITS, LIMITATIONS, AND ETHICAL CONSIDERATIONS

4.1 Advantages of predictive modeling approaches

Advanced predictive modeling for early diagnosis of metabolic syndrome (MetS) has many advantages, as compared with the traditional methods used to ascertain risk. The most described advantage is the improved predictive accuracy, since machine-learning algorithms present a greater discriminative performance than traditional risk scores. The ability to model complex patterns of non-linear relationships among multiple risk factors also allows the capturing of synergistic effects and threshold interactions that linear models may not capture.

Early detection is another important benefit. Predictive models can recognize those on unfavorable metabolic paths, even years before attainment of diagnostic thresholds, and open windows for preventive intervention at times when behavior modification is likely to be most effective.

These approaches are further distinguished by personalized risk stratification. Conventional population risk scores assign equal weights to the same risk factors, which ignores individual variation. On the other hand, multi-omics and longitudinal monitoring integrated models provide personalized risk profiles based on everyone's biological and environmental context.

The second comment based on this framework is that of scalability and efficiency: By examining electronic health record (EHR) data, machine learning algorithms can be used to screen every patient in a program without the need for an additional clinical interaction or laboratory expense, a distinct advantage for resource-limited healthcare systems.

Predictive modeling can also be compatible with the current health IT architecture and enable real-time risk scoring at the point of care while being non-disrupted to established workflows.

Quite notably, predictive modeling is of significant research value. Key metabolic determinants can be predicted by feature-importance analyses, and potential causality and disease trajectories can be discovered using longitudinal modeling. Subgrouping clustering and analysis can subdivide this taxonomy even further, which is essential for precision-medicine approaches.

4.2 Limitations and Challenges

Although there have been significant technological advancements in predictive modeling, several basic challenges have continued to limit the implementation of successful clinical translation. Limitations in external validation remain a barrier, with most models not generalizing well across diverse, larger patient populations after having been developed on targeted institutional or regional cohorts (Wynants et al., 2020; Beam & Kohane, 2022). Data quality is another challenge as electronic health records are often incomplete, inconsistently coded, and present temporal gaps that render models unreliable (Rajkomar et al., 2019; Xu et al., 2021). There is a trade-off between predictive performance and interpretability which makes it difficult to translate into clinics. Deep learning models offer greater discriminative performance, but their black-box nature leads to a loss of confidence among clinicians and problems with regulatory clearance (Ghassemi et al., 2021; Kelly et al., 2023). Post-hoc explanation techniques try to fill this interpretability gap but at the cost of extra complexity and not being able to fully explain what model has captured (Samek et al., 2021).

Most predictive modeling studies have insufficiently considered algorithmic fairness and health equity concerns. Models have the potential to exacerbate or perpetuate existing healthcare disparities in instances where training data is under-representative of specific populations or does not adjust for social determinants of health (Obermeyer et al., 2019; Chen et al., 2023). Secondly, the issue of temporal validity will continue to be a challenge as treatment protocols and population demographics develop (Zhang et al., 2024). Clinical workflow integration and implementation challenges are not limited to technical issues. There just aren't the resources, the know-how or the operational dexterity in most healthcare systems to roll out AI-powered tools successfully (Jiang et al., 2022; Park & Han, 2023). AI diagnostic systems do not have a well-defined regulatory landscape, making it difficult for healthcare facilities to decide whether to adopt (Topol, 2019; Benjamens et al., 2022). More critically, evidence has been lacking to support the existence of actionable benefits in medical decision-making and patient outcomes with its deployment, signifying a disconnect that remains between algorithmic sophistication and real-world clinical utility (Liu et al., 2023; Sidey-Gibbons & Sidey-Gibbons, 2024).

4.3 Ethical Considerations

However, the use of prediction algorithms for health-risk assessment poses multiple ethical challenges that surpass technical performance.

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The issue of algorithmic bias and health equity is still a focal point. If the models work less well for specific demographic groups, they risk perpetuating current disparities. Fair performance across populations is needed, both ethically and technically.

Equally so, we are informed about consent and transparency. Most predictive tools scrutinize patient data without patients' explicit consent or knowledge, prompting questions about autonomy and the right to know when A.I. shapes care.

Privacy and security risks are exacerbated when the algorithms need access to large, sensitive datasets. Violations could lead to people being discriminated against by insurers or employers.

There is the stigma of being identified as 'high risk', which may lead to anxiety or fatalism.
Autonomy and shared decision-making, which are based on respect for the patient's capacity to choose, demand that predictive models supplement but not supplant patient agency. The point was that predictions should influence the conversation, not shape the outcome.

Distributive justice issues arise in decision making about allocation of resources based on risk predictions. If there is a cost-effective limit to prevention programs, whose access should be given by an estimated risk? This maximizes population health benefits but potentially excludes moderate-risk individuals who may also benefit. Other systems of allocation based on need, disadvantage, or lottery may be ethically preferable under certain circumstances and even if less aggregate efficient.

The dual-use capacity of predictive models renders themselves susceptible to misuse. Models built for clinical applications could be used to screen applicants by insurers, employers or law enforcement, and immigration authorities. Technical means to prevent dual use (i.e. access restrictions) as well as legislative safeguards against non-prohibited use are needed - but hard to enforce.

Finally, ubiquitous algorithmic surveillance may undermine privacy norms and medicalize mundane life, and the absence of clear lines of liability for errors made by algorithms complicates professional accountability.

4.4 Regulatory and Policy Landscape

The state of regulation for AI-based clinical decision support is rapidly changing. Risk-based Framework Certain software is regulated under the 21st Century Cures Act in the United States by Food and Drug Administration (FDA). The degree of scrutiny toward a tool that autonomously alerts to high-stakes diagnostic or therapeutic decision is, understandably, more than one supporting clinician judgment.

The European Union has stricter regulations in place with the Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR), that prioritize both clinical data as being transparent and requiring specific post-market surveillance. The planned upcoming European AI Act will classify many health applications such as "high-risk", enforcing demands on data quality, human oversight and accountability.

There are local and global efforts to create algorithmic-accountability institutions that already exist, like New York City's Automated Decision Systems Task Force and the U.K.'s Centre for Data Ethics and Innovation, which are creating processes of algorithmic impact assessments and transparency reporting.

They face continual trade-offs between, for example, safety and innovation; standardization and flexibility, pre-market verification, and adaptive learning. Most notably, these ever-learning algorithms that learn after they have been deployed are posing challenges to the traditional paradigms of approval.

5. FUTURE DIRECTIONS AND RESEARCH GAPS

5.1 Methodological Innovations

Various methodological challenges offer potential to improve predictive modeling for MetS. Methods for causal inference are an important but relatively undeveloped field. A key limitation of current models is that they prioritize prediction rather than causation, so that relationships may be uncovered but whether the relationship is causal cannot be determined. And if researchers used frameworks that include directed acyclic graphs, instrumental variables or potential outcomes models, they may be better positioned to estimate the effects of interventions, ultimately answering who is not only at risk but also for whom a specific intervention would work the best.

By providing an answer to the data-sharing obstacles that prevent the development of large, diverse models, federated learning may show us how we can get out. Federated methods allow for multicenter model training by sharing data across institutions, thus maintaining privacy while benefiting from distributed data resources. (McMahan et al., 2020) showed that federated learning was feasible for clinical

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prediction and produced performance like centralized models while preserving data governance at the source institutions. Extending this approach to MetS may allow for the creation of big, diverse, and privacy-preserving models.

To enhance generalizability, transfer learning and domain adaptation can adapt the models learned from a certain population to others. Instead of relying on big new datasets, transfer learning exploits patterns in data-rich domains and adapts models with relatively little local data. (Rajkomar et al., 2022), which indicated that DL models for clinical prediction can be successfully transferred across healthcare systems through transfer learning, these results suggest a strong potential for developing globally generalizable MetS models based on synchronized data sets.

Multitask learning approaches that simultaneously predict related disorders such as diabetes, cardiovascular disease and fatty liver disease could boost accuracy and biological validity by borrowing information in common between modalities. Correspondingly, time-to-event prediction models that predict when an individual is likely (or unlikely) to develop MetS, rather than only if they are likely, have the potential to increase clinical utility by providing information on intervals between interventions and urgency. Survival-analysis methods (e.g., Cox proportional hazards of regression and random survival forests) could be used for MetS prediction but are unexplored.

5.2 Data Integration and New Sources of Data

The inclusion and incorporation of new data sources lead to the potential for more comprehensive and contextually sensitive risk prediction. Social determinants of health, such as neighborhood factors, food access, air quality, and socioeconomic status (SES), may enhance predictive model accuracy and help to identify if there are modifiable contextual risk factors. However, inclusion of social determinants may raise fairness concerns if models learn to predict based on disadvantage, rather than modifiable risk.

Patient-reported outcomes and patient-generated data (e.g., symptom diaries, lifestyle behaviors, wear-able technology) offer additional quality-of-life information in addition to behavior and psychosocial factors that are not available in the clinical record. Such sources can uncover risk trajectories that are otherwise hidden in objective measures.

Environmental exposure information on pollutants, temperature variation, and occupational hazards can now be collected through wearable or smartphone-based sensors, consistent with the new exposome paradigm of lifelong environmental exposure evaluation.
Natural language processing (NLP) of unstructured clinical notes is an underexplored opportunity to obtain rich context on symptoms, clinician rationale, and social context. Addressing issues of linguistic variation and subconscious bias will be necessary for responsible implementation.

5.3 Clinical Translation and Implementation Science

Consideration of implementation of science is needed to build the bridge between new algorithms and their clinical application. Research is also required to understand how best to implement such resources, including the incorporation of predictive tools into workflow routines, staff training, patient involvement, and long-term application. Comparative effectiveness studies can also determine what mix of implementation strategies most effectively contributes to clinical and operational impact.

Hybrid effectiveness–implementation trials that assess both health outcomes and implementation-related metrics are particularly useful, yet resource-heavy. The value of these studies is that they are not only an assessment of whether predictive models work, but also whether they can do so when embedded in real-world conditions.

Standardized use and interpretation might be accomplished through implementation of predictive tools in clinical practice guidelines. Professional societies can help to do so by making recommendations about how to deploy and integrate these tools into evidence-based care.

Finally, the use of patient engagement and co-design methods that integrate patients and communities into model development could improve acceptability, relevance, and cultural appropriateness. Participatory approaches that enable patients to influence the goals of prediction and data governance ensure tools remain in sync with user needs, priorities and values.

5.4 Addressing Health Equity

To do better, we need to push toward equity vs. just making moves against bias. This comprises focused model development on disadvantaged populations, oversampling both during model training, and stringent validation across different demographics and geography.

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Community-partnered research can help to ensure that predictive modeling serves the interests of, rather than harm, socially marginalized communities. Close working relationships promote trust, openness, and accountability.

Building causal models that make explicit the roles of structural determinants such as housing, education, and access to healthy food can switch attention from individual behavior to systemic disparities. Modelling to assess the effects of upstream interventions on population metabolic health may inform policy decisions related to a structural shift.

5.5 Emerging Technologies and Convergent Innovation

When AI is combined with other advanced technologies, it carries the potential to disrupt everything. Software-based behavior change interventions (digital therapeutics) can be combined with predictive models to implement adaptive and personalized prevention systems. An example of this next generation of precision prevention includes closed-loop strategies that continuously track risk and automatically modify interventions.

Recent biotechnological progress, such as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-editing genome, regenerative medicine or targeted drugs could increasingly personalize interventions according to the molecular risk signature. But those breakthroughs raise thorny ethical issues about access, fairness and where to draw the line between enhancement and therapy.

Third, by integrating AI with biotechnology and nanotechnology, extremely accurate approaches to risk characterization as well as delivery of interventions in time and space might emerge. To develop this responsibly, these capabilities need to be accompanied by strong governance and ethical oversight.

6. CONCLUSION

Modeling the risk of metabolic syndrome (MetS) early in life has been rapid to develop over the past five years and machine learning; deep learning methods are outperforming traditional risk prediction models. The combination of multi-omics and wearable, continuous monitoring has also increased the possibility for earlier and individualized intervention. The pace of establishing these discoveries in translation to risk stratification and the global burden of metabolic diseases remains ambitious.

However, there is still a large gap between algorithmic sophistication and clinical usage. Whereas the majority of models demonstrate good performance in empirical settings, they lack confirmation by real world evidence and effects on patient relevant end points. Hurdles in aspects of workflow integration, interpretability, regulatory supervision, and data quality impede the translation into clinical practice. Additionally, issues regarding algorithmic bias and health inequity remain as models trained on non-representative data can perpetuate disparities in under-served demographics.

The community should focus not only on technical novelty, but also on thorough validation, fairness calibration, and fair adoption. We need to invest in federated learning, causal inference, and interpretable AI while building implementation of science and stakeholder engagement. Regulatory policies also need to develop safety, transparency, and post-market surveillance.

In conclusion, predictive modeling ought to supplement rather than replace a broader approach to prevention tackling social and environmental drivers of metabolic health. Integrated with ethical and structural overhaul, predictive modeling can make a significant contribution toward reducing the incidence and impact of MetS as well as equity in precision health.

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