Risk scores in real-time: the untapped potential of mobile health

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Abstract
Risk scores are used throughout medical care to guide treatments, allocate resources, and control outbreaks of disease. Though valuable, most risk scores are limited by their basis in aging datasets and their use with patients in single, time-constrained consultations. Mobile health could collect longitudinal or even *continuous* data on patient health. Automated, dynamic, and real-time risk profiles could trigger earlier interventions, improve clinical outcomes, guide resource distribution, and preempt outbreaks. Dynamic risk profiles hold enormous potential for global health, and smartphones are now uniquely equipped and positioned to unlock that potential. We identify cough, an information-rich and readily monitored syndrome, as *the* symptom that will pioneer 'smart risk profiling' systems, prove their value in alleviating the global burden of respiratory disease, and usher in a new era of proactive mobile health.

Keywords
risk scores — mobile health – cough monitoring — proactive care

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Managing risk: proactive healthcare

A common goal across all stages of healthcare is to understand and minimize risk [1]. Assessments of risk during regular consultations allow physicians to guide preventative care [2–5]. In treating illnesses, the return to low-risk status is often an explicit treatment goal [2, 6–8], and in public health, minimizing risk across a population is the typical means of controlling disease [9–14]. It is the focus on identifying and minimizing risk that drives the difference between reactive and proactive approaches to care [1–5].

Health risk profiling saves lives and reduces the global burden of disease [15, 16]. Generating risk scores for specific illnesses help clinicians identify vulnerable populations [17], advise patients in lifestyle decisions [18], trigger early interventions [16, 19], preempt the exacerbation of symptoms [14], improve clinical outcomes [14, 15, 20], allocate limited resources in triage scenarios [21–23], and reduce the financial burden of care [24]. For these reasons, risk scores are ubiquitous in strategies for the prevention and treatment of cardiovascular disease [25–33], Chagas' heart disease [34], chest pain [16], stroke [19, 35], dementia [36], diabetes [18], kidney disease [37], childhood metabolic risk [38], asthma [14, 39, 40], oral cancer [41], lung cancer [42–46], tuberculosis (TB) [15], HIV-TB interactions [17], mental health disorders [47], repeat hospital admissions [24], acute care in emergency rooms and intensive care units [21–23], and, most recently, COVID-19 [16, 20].

Risk scores use past trials to predict future outcomes based upon a patient's preexisting and current conditions. These inputs typically include patient disabilities and comorbidities (e.g., [14, 43]), demographic factors (e.g., [38]), simple measurable features such as weight or blood pressure (e.g., [17, 38], electronic medical records [43], and, most recently, genomics (e.g., [48]). These patient characteristics are then fed to an algorithm, which is based upon a collection of past cases in which patient characteristics have been paired with disease diagnoses or treatment outcomes [49], and returns a risk score. These risk scores may be a continuous score, usually between 0 and 1, or a stratified score (low, moderate, or high risk), which are tied to recommendations for treatment, referral, and reassessment [14, 49–52] (*see Box 1 at end*).

While generally effective [15, 16], **such risk scores are inherently limited.** First, most scores are based upon archival datasets whose relevance to present-day health risks grows increasingly antiquated [28, 51]. Second, many risk scores are commercialized and distributed as products whose underlying algorithms remain proprietary and therefore difficult to evaluate [51]. Third, these scores are built for specific illnesses, making them unable to account for the interaction of multiple comorbidities [49]. Finally - and most problematically - these risk algorithms are typically applied to patients using data drawn from a single, time-constrained clinical consultation [51].

Risk scores are rarely applied to patients based upon long-term patient monitoring. Risk score algorithms are developed using the analysis of longitudinal data, in which patients are checked repeatedly throughout time to identify trends [36, 47, 53–55], but this is not how risk scores are applied. Patients are scored according to spot-sampled data, not trends from longitudinal observations, despite the latter

providing a richer picture of a patient's condition [56]. But as medical technologies advance, longitudinal data have become increasingly integral to patient monitoring, particularly for patients with cardiovascular disorders [57–61], respiratory disease [62, 63], or obstructive sleep apnea [64]. Remote sensors within pacemakers and electrocardiograph patches, for example, provide a rich time series of data that can be used to develop risk scores in near-real-time [58, 60]. These studies have demonstrated that trends in the patient's own health can be a valuable predictor of long-term risk. Longitudinal risk inputs could detect symptom exacerbations earlier, reduce clinical visits, and improve quality of life [59, 65, 66].

The potential of mobile health

Mobile health technology has made risk easier to assess longitudinally. The use of mobile wireless technology for public health – known as mHealth [67] – has been transforming health services across the globe [67–69]. Smartphones are in the pockets and purses of nearly half the world population [70], and there are more phones than people in some Western developed nations [70, 71]. In high-income areas, up to half of smartphone owners use their devices to manage their health [72–74]. For individuals in remote settings and areas of high deprivation, smartphones connect users to information and care that were previously unavailable [75–77], and equip frontline health workers with digital tools that compound their local impact [33, 41]. MHealth is widely considered a key pathway for reducing socioeconomic disparity in global health [69, 78–81]. Though still in its infancy, mHealth has already yielded benefits for patients with diabetes [82, 83], obesity [84, 85], atrial fibrillation [78, 86], pregnancy complications [50], asthma [87–89], chronic obstructive pulmonary disorder (COPD) [89], substance abuse issues [90], mental health disorders [91–94], and cancer [95–97]. Messaging services, client portals, self-reporting surveys, and reminders for appointments and medications have all improved longitudinal care [74, 83, 86, 87, 89, 91, 95, 98, 99].

Most importantly, smartphones bring *continuous* risk monitoring within reach. These devices come with built-in sensors and satellite links that allow for data collection of unprecedented volume and dimensionality [100]. In principle, smartphones are capable of monitoring health indicators on a continuous longitudinal basis, without the need for clinical outreach or proactive self-reporting on the part of the patient. Moreover, the algorithms that generate these scores no longer need to depend upon archived data; as more and more real-time, high-resolution data are collected from the population of users, risk scores can be continually improved through machine learning techniques [49, 77, 101, 102]. If risk scores were updated in real-time and increasingly personalized according to individual baselines, they would allow for even earlier clinical interventions [52, 86], better prioritization of diagnostic testing resources [52, 103], more effective in-person consultations [19], rapid response to disease outbreaks [104], and detailed outpatient monitoring throughout the course of illness [52].

That potential, however, remains largely untapped. Most mHealth interventions have taken the form of SMS messages or apps that provide appointment reminders [78, 86, 90, 95, 105], instructions for managing prescriptions [89, 106–108], health education [89], guided self-care activities [77, 92, 109], daily logs (e.g., *Blood Pressure Log*), symptom surveys [77], interactive tools for self-diagnosis [69, 73, 77, 109], and encouragement towards exercise-, diet-, and addiction-related goals [89, 106]. These services have facilitated and emulated clinical care in important ways (*see above*), but mixed results in several areas have underscored the fact that mHealth will never replace in-person care [87, 110–113].

Smartphones: the key to dynamic risk profiling

But the value of smartphones in mHealth lies not in their comparability to a doctor, but in the services they might offer that no clinician ever could. Unlike doctors, smartphones are uniquely able (1) to follow patients wherever they are carried, (2) to measure vital signs and other indicators of health quantitatively in real-world scenarios, (3) to store long-term time series of such data for review at a later date, and (4) to integrate data across users to train dynamic models of risk assessment – all on a continuous basis. This enormous potential for mobile-device biosensing has been anticipated for several years [77, 78, 87, 101, 102], and the concept has been proven through various controlled and retrospective studies (e.g., [43, 104, 114]).

No clinically validated mHealth service has yet to implement dynamic risk profiling based upon continuous syndromic monitoring. Several mHealth apps allow users to interact with risk algorithms by manually entering data [94, 115, 116], and others have used built-in or auxiliary sensors to screen for risk during guided exercises (e.g., [50, 117]). But the demand of mHealth for objective, quantitative, continuous risk profiling remains to be met [69, 86], even as the global prevalence and severity of respiratory, cardiovascular, and mental illnesses continue to increase [86, 118, 119].

Cough: the ideal syndrome to pioneer dynamic risk

Certain indicators of health, such as cough, are particularly ideal for 'smart risk profiling'. Unlike other diagnostic signs such as blood pressure, body temperature, heart rate, and blood oxygen levels, cough can be measured remotely without specialized sensors [102, 120]. Coughs are a conspicuous and common symptom of many respiratory illnesses that span the full range of prevalence, morbidity and lethality, from asthma and COPD to COVID-19, lung cancer, and TB [62, 63, 104]. Coughs have acoustic signatures that contain important diagnostic information, and equally telling is the frequency and severity of cough production [121–123]. All of these attributes can readily be monitored using the microphones that are built into smartphones [123]. For decades, cough counting has been an important tool in the screening,

diagnostics, and monitoring of respiratory disease within clinical settings [120, 122–128]. Now smartphones are poised to scale the value of cough monitoring to entire populations [123]. With phones as a platform, cough data can be readily combined with other continuous sensors, e.g., accelerometry, as well as push surveys to improve risk score accuracy and actionability. And, by integrating cough monitoring data streams into medical records, primary care providers would have access to a rich diagnostic picture of the patient's condition [123]. Cough appears to be the biomarker of choice to pioneer the age of dynamic, smartphone-based risk profiling.

'Smart risk profiling' can address the growing global burden of respiratory disease. Respiratory diseases account for one-quarter of all deaths worldwide, and they are the leading cause of death in developing nations [129]. Hundreds of millions endure chronic respiratory conditions that reduce quality of life [129], and pandemic respiratory diseases have depressed economies and exacerbated social inequalities globally [130, 131]. These diseases – and the cough syndromes that come with them – will increase in the years to come [130, 132]. But the growing relevance of cough has coincided with the proliferation of smartphones [70], presenting mHealth with an urgent opportunity. Dynamic risk profiles, informed by smartphone-based cough monitoring, could alleviate the global burden of respiratory disease and lead mobile health into a new era of proactive care.

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Box 1. Calculating risk scores

To review standard methods for constructing health risk scores, we reviewed a range of risk scores developed for various diseases and medical outcomes, including asthma [14, 39], lung cancer [43], COVID-19 hospitalization/mortality [16], TB [15, 17], cardiovascular disease [32, 49], chest pain [16], Chagas' heard disease [34], diabetes [18], childhood metabolic risk [38], and mortality probability upon admission to emergency rooms [22] and ICUs [23].

Risk scores are usually stratified using three-tiers: low-, intermediate-, and high-risk.
Continuous risk scores (i.e., a value between 0 and 1) are quite rare (e.g., [14]) compared to the strategy of risk stratification (i.e., low-, intermediate-, and high-risk; e.g., [15–18, 20, 38, 49].

Most studies adhere to the same general procedure for risk score development.

1. Statistical models are fit to variables that may be predictive of a patient's clinical outcomes.
2. The best-fit model is used to cull the set of variables to important predictors only.
3. Those predictors are assigned weighted points in proportion to their Beta correlation coefficients within the model [16, 17, 22, 32, 34]. This is typically a linear transformation that is then scaled and rounded. For example, Nguyen *et al.* [17] divided all coefficients by the smallest coefficient, multiplied by an arbitrary constant, then rounded to the nearest integer. In another instance, Abdelbary *et al.* [15] rounded coefficients to the nearest 10th and multiplied by 10.
4. Patients are given a score based on the sum total of their predictor variable weights.
5. Patient scores are then sorted into deciles (quantile 0.0 – 0.09, 0.10 – 0.19, etc.) (e.g., [17, 18, 49]).
6. These scores are then collapsed into terciles (deciles 0.0 – 0.3, 0.3 – 0.6, 0.7 – 1.0) to assign low-, medium-, high-risk (e.g., [17, 18]).
7. Total performance for the algorithm is based upon the Area Under the Curve (AUC) for the pooled receiver operating characteristic (ROC), which describes trade-offs between the sensitivity and specificity of the model [15–17, 20, 34, 38, 43].

Other methodologies include the following:

1. When only two risk strata are used (i.e., low- and high-risk), the risk score can be calibrated by finding the threshold that maximizes the area under the curve [38]
2. Inclusion of other performance metrics such as positive predictive value, negative predictive value, the positive probability ratio, and the negative probability ratio [22]. AUC confidence intervals have been assessed using standard techniques such as leave-one-out cross-validation [16] and bootstrapping [18].
3. When presumptive risk indicators were used instead of outcomes (e.g., cardiovascular fitness), a patient's risk was assigned based on its sample quantile [38].
4. Three-tier risk profiles have also been based simply upon the number of known risk factors present (Low = 0, Intermediate = 1 – 2, High = more than 2) [35]
5. Risk profiles have also been validated using the coefficient of correlation between predicted and observed outcomes [14].

Most risk scores are based upon multivariate logistical models.
The vast majority of studies reviewed here based risk scores upon multivariate logistic regression models [14–17, 20, 23, 34, 39]. Less common methods include Kaplan-Meier survival curves [34, 49], Cox proportional hazard rate models [18, 32], generalized linear mixed models [16], machine learning [43], and simple sums of questionnaires [40]. Nearly all studies trained their models upon a 'learning' cohort or subsample of their data, then validated their model using a testing cohort.

Data for most studies are drawn from retrospective longitudinal studies.
All of these risk score algorithms were developed using archival datasets in which patient characteristics were assessed during a baseline period and then paired with known clinical outcomes at later dates, based upon either longitudinal monitoring or the examination of medical records.

We were unable to find any studies pertaining to dynamic risk scores based on continuously collected data, e.g., from mobile devices. However, recent studies have incorporated continuous data streams from mobile devices into correlations with health outcomes such as influenza [114] and COVID-19 [104]. In these studies, predictor variables are derived from data streams based upon anomalies. The mean value during a rolling window is compared to the overall mean value for a user; if that rolling mean exceeds a threshold deviation from the overall mean (e.g, 1.5 standard deviations) for a threshold period of time (e.g., 4 days), the time period is categorized as anomalous.