The Medication Adherence Score: A Predictive Analytic Tool

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Research article

Keywords: adherence, medication, predictive analytic, score

DOI: https://doi.org/10.21203/rs.3.rs-48523/v1

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Abstract

Background

Poor medication adherence is widespread and associated with poor clinical outcomes. Herein, we introduce the Medication Adherence Score, a predictive analytic tool designed to provide clinicians insight into adherence behavior over the subsequent twelve months. The aim of the study was to demonstrate the feasibility of such scoring of patients at the individual level.

Methods

This is a single arm, non-randomized, 2-center, retrospective cohort study conducted among patients diagnosed with atrial fibrillation. The model, developed by Fair Isaac Corporation on pharmacy refill data, predicts adherence behavior to cardiovascular drugs using demographic, geographic and socio-economic predictors. The primary outcome was the number of patients that could be scored at the individual level without reliance on past individual refill behavior. The score was normalized between zero (lowest adherence score) and one (highest adherence score) and patients were grouped: low adherence < 0.6, intermediate adherence between 0.6 and 0.8, high adherence > 0.8. The institutional review board approved the study.

Results

A total of 1110 patients were included in the study with a median age of 71 (IQR 63, 79). Most patients (807, 73%) could be scored at the patient level, and the remaining patients (303, 27%) were scored based on characteristics associated with the geography of their home address. There were 488 patients (44%) with a high adherence score (score > 0.8), 382 (34%) with an intermediate adherence score (score between 0.6 and 0.8) and 240 patients (22%) with a low score. Younger patients had on average lower scores than older patients, and males also had higher scores.

Conclusions

The Medication Adherence Score was successfully applied to an unselected group of atrial fibrillation patients: nearly a quarter of the cohort were identified as at risk for non-adherence. Future studies are necessary to assess the association of this predictive analytic model with clinical outcomes.

Background

Medication non-adherence is defined as the extent to which a patient’s behavior in taking a drug does not correspond with agreed recommendations from a health care provider, and results in patients having incomplete treatment response and suboptimal clinical outcomes. (1) Research has shown that a quarter
of prescriptions are never filled and that over half of medications for chronic disease are not taken as prescribed.\(^{(2, 3)}\) The wide-spread presence of non-adherence makes it a major burden on society through increased medical costs and lost productivity. The annual cost to the U.S. health care system is estimated between $100 billion and $670 billion.\(^{(4–8)}\)

Non-adherence is often not correctly identified through history taking. Clinicians incorrectly predict adherence in almost half of their patients and another study found that 61% of patients report rarely or never discussing medication adherence with their physician.\(^{(9, 10)}\) The same study reported 67% of physicians not being aware of medication non-adherence among their patients, despite all physicians agreeing on the importance of discussing adherence to medication with their patients.\(^{(10)}\) Once identified by the clinician, medication non-adherence could be addressed through various evidence-based interventions: examples include simplification of the treatment regimen via polypills or daily-dose blister packaging, reducing out-of-pocket cost, addressing side-effects and improving health literacy.\(^{(11, 12)}\)

In this study, we introduce the concept and rationale behind the Medication Adherence Score, a predictive analytic tool designed to predict which patients are at risk of medication non-adherence over the subsequent 12 months. The Medication Adherence Score may help clinicians identify patients at risk for non-adherence, thereby allowing the physician to intervene both at the initiation of treatment and during follow-up. Here, we present the results of a feasibility study where atrial fibrillation patients from two clinics in the United States are scored. The study is not designed to demonstrate a correlation between the score and clinical outcomes, but rather as a feasibility study.

## Methods

### Design and setting

This is a single arm, non-randomized, retrospective cohort study conducted among patients diagnosed with atrial fibrillation and who were prescribed oral anticoagulation between January 2017 and December 2017. The two participating institutions were the Mount Sinai Hospital in New York City and CorVita Health in Chicago. The institutional review board approved the study and waived the need for informed consent due to the retrospective nature of the study and the need to collect an unbiased study sample. Patients were identified via a query in the electronic health record systems of both sites. Scores were not used in clinical care in any way and were solely obtained for the purpose of this study. The anonymized datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

### The medication score model

The model for cardiovascular drugs Medication Adherence Score was developed by Fair Isaac Corporation (FICO), a predictive analytics company, and was used for this proof of concept study. The model predicts adherence behavior to cardiovascular drugs such as anti-hypertensive, anti-thrombotics and anti-coagulants, and was developed on pharmacy refill data from over one-hundred-forty thousand
individuals. The assumption is that patients cannot take prescription drugs without refills dispensed by the pharmacy. The predictors include demographic, geographic, socio-economic, and other variables available only known to FICO and proprietary. The score does not rely on past individual refill behavior. The current version of the score is based on a research model not approved by the Food and Drug Administration and can therefore currently only be used for research purposes. The output of the model is a continuous value which can be used to rank order patients according to their predicted level of adherence behavior over the subsequent twelve months for the individual patient. For the purpose of this study, the scores were normalized between 0 and 1, where 0 represents the patient with the lowest predicted adherence score in the study cohort and 1 the patient with the highest adherence score in the cohort.

**Scoring process**

In order to have patients scored at the individual level, exchange of name and address is required to be matched at the individual level to the data available to FICO. Importantly, no exchange of medical information is required. Hospitals and other care providers are allowed to exchange patient health information (PHI) such as name and address with third parties that deliver a service for which the hospital or care provider pays the third party under the Health Insurance Portability and Accountability Act (HIPAA). Within FICO, the data was handled by a dedicated team that is trained to work with PHI in compliance with HIPAA. Per the contract between the institutions and FICO, all data provided to FICO is destroyed immediately after the score has been generated and linked to the study identification number. If patients could not be scored at the individual level, they were scored based on characteristics associated with their geography. FICO provided the investigators the Medication Adherence Scores for each individual patient under a unique non personally identifiable study number. The contract enabling the exchange of data is a business associate agreement (BAA) between the institutions and FICO.

**Statistical analysis**

Baseline characteristics are presented as mean ± standard deviation or median [25th, 75th] depending on distribution, and dichotomous variables as number and percentage and compared between both centers using the Fisher exact test, Students T-test or Wilcoxon Rank sum test. Descriptive statistics are used to present the distribution of adherence scores. The primary outcome was the number of patients that could be scored at an individual level. Patients are categorized into three arbitrarily chosen adherence score groups: low when the score is < 0.6, intermediate when the score is between 0.6 and 0.8, high when the score is > 0.8. Statistical significance is accepted at the 95% confidence level (CI) (two-sided Pr ≤ 0.05) without adjustment. Data analysis is performed in R and R studio version 3.2.2, R foundation, Vienna, Austria.

**Results**

The study included a total of 1110 patients with a median age of 71 years (IQR 63, 79). For 807 (73%) patients, a Medication Adherence Score could be calculated based on the individual patients’
characteristics. The remaining patients (303 (27%)) were scored based on characteristics associated with their geography. Figure 1 presents the score distribution across the entire cohort. Baseline characteristics stratified by the Medication Adherence Score are presented in Table 1. There were 488 patients (44%) with a high adherence score (score > 0.8), 382 (34%) with an intermediate adherence score (score between 0.6 and 0.8) and 240 patients (22%) with a low score.

Table 1
Baseline characteristics stratified by Medication Adherence Score

|                      | High > 0.8 MAS | Intermediate 0.6–0.8 MAS | Low < 0.6 MAS | P-value |
|----------------------|----------------|--------------------------|---------------|---------|
| N                    | 488            | 382                      | 240           |         |
| Age (median [IQR])   | 72 [66, 78]    | 71 [61, 79]              | 68 [57, 76]   | < 0.001 |
| Male (%)             | 347 (71)       | 224 (58)                 | 151 (62)      | < 0.001 |
| Hypertension (%)     | 330 (67)       | 248 (64)                 | 163 (68)      | 0.62    |
| Diabetes (%)         | 76 (16)        | 75 (20)                  | 71 (30)       | < 0.001 |
| Height in cm (median [IQR]) | 175 [168, 183] | 173 [163, 182]       | 170 [163, 179] | < 0.001 |
| Weight in kg (median [IQR]) | 86 [73, 100] | 82 [68, 98]            | 82 [73, 97]   | 0.02    |
| History of TIA       | 7 (1.43)       | 6 (1.57)                 | 1 (0.42)      | 0.48    |
| History of Stroke (%)| 87 (17)        | 78 (20)                  | 50 (20)       | 0.49    |
| Systolic blood pressure (median [IQR]) | 127 [118, 140] | 127 [116, 140]   | 128 [118, 138] | 0.62    |
| Diastolic blood pressure (median [IQR]) | 74 [67, 81] | 75 [68, 80]           | 74 [67, 81]   | 0.77    |
| Warfarin (%)         | 127 (26)       | 98 (26)                  | 63 (26)       | 0.98    |
| Dabigatran (%)       | 24 (5)         | 26 (7)                   | 11 (5)        | 0.41    |
| Rivaroxaban (%)      | 178 (37)       | 118 (31)                 | 92 (38)       | 0.10    |
| Edoxaban (%)         | 1 (0)          | 0 (0.00)                 | 0 (0.00)      | 1.000   |
| Apixaban (%)         | 131 (27)       | 106 (28)                 | 57 (24)       | 0.56    |

MAS – Medication Adherence Score, TIA – transient ischemic attack, cm – centimeter, kg - kilogram

On average, men had higher Medication Adherence Scores than women, 0.78 versus 0.74 (p-value < 0.001). Patients with scores < 0.6 had a 10% greater likelihood of diabetes mellitus. Figure 2 demonstrates that the model on average scores younger patients lower than older patients. Both median
systolic blood pressure and diastolic blood pressure did not differ between patients with a high, intermediate or low score (systolic blood pressure: high 127, intermediate 127, low 128 \( P = 0.62 \) and diastolic blood pressure: high 74, intermediate 75, low 74 \( p = 0.77 \)).

Between the two participating centers, the median Medication Adherence Score was not significantly different with a median score at CorVita (Chicago) of 0.79 (IQR 0.65, 0.87) and 0.75 (IQR 0.61, 0.87) at Mount Sinai (New York), \( p \)-value of 0.06.

**Discussion**

**Main findings**

This study introduces the Medication Adherence Score and demonstrates that it is feasible to score approximately three quarters of patients at the individual patient level. The score aims to enhance awareness of non-adherence at the individual level, assist clinicians with diagnosing likelihood of non-adherence and allow them to intervene when non-adherence is present. Importantly, the score enables identification of patients with a risk of low adherence – in our population, this accounted for 22% of the full cohort, with another 34% displaying an intermediate level of adherence. This provides clinicians the opportunity to potentially tailor treatment to the needs of the individual patient.

**Diagnosing non-adherence**

Accurate and timely assessment of adherence behavior is the crucial first step when addressing non-adherence with medical therapy. Current subjective assessment instruments are flawed as patients can deny their failure to adhere and report their behavior inaccurately during history taking or in self-reported questionnaires.\(^{13}\) Objective methods such as counting the remaining pills at office visits are considered tedious, after the fact and insufficiently reliable.\(^{14}\) Counting medications might also result in patients feeling policed by their physician. The benefits of the Medication Adhere Score are that it is simple to obtain, immediately available (e.g. if incorporated in the local electronic health record) and provides clinicians an estimate of the adherence behavior preceding the initiation of treatment. This may direct clinicians as to when to discuss with the individual patient the obstacles to full adherence that may be present and how these can be addressed.

Creating a single analytic from multiple socio-economic-geographic metrics can provide strong and objective predictive information for patient care. Indeed, predictive analytics have been successfully used in clinical care by the United States Department of Veterans Affairs in the REACH-VET program to identify veterans at high-risk of suicide not previously identified, and to guide the delivery of preventive interventions.\(^{15}\) The initial implementation of REACH-VET resulted in more (mental) health care appointments and less all-cause mortality.\(^{16}\)

**Treatment differentiation**
The current strategy to improve adherence often follows a one-size-fit-all approach where every patient, irrespective of their (future) adherence behavior, is subjected to the same intervention. This approach differs from other medical problems where first the diagnosis is established before treatment commences. With the Medication Adherence Score, we propose an approach of treatment differentiation where the score, in conjunction with the findings during history taking, help dictate whether interventions to improve adherence are needed.

**Interventions to improve adherence**

Lower pill burden and simplification of the treatment regimen have repeatedly been demonstrated to improve adherence in multiple conditions, and the effect might be greatest in underserved patients. Adherence to cardiovascular drugs has been shown to improve in patients whose medication copayments were reduced or whose coverage improved. Physicians can incorporate these evidence-based strategies by reducing the number of daily doses, prescribing fixed-dose combinations or have presorted medications in daily blister packaging, actively describing non-essential medication, and when financial barriers are present seek cheaper drug regimens.

Additionally, alternatives to daily drugs in the form of devices or very long-acting drugs can potentially help mitigate non-adherence. For example, intrauterine devices (IUDs) provide highly effective, long-term contraception with failure rates between 0.1 and 0.8% compared to 9% of first-time users of combined oral contraceptive pills in the first year. For patients with atrial fibrillation, left atrial appendage closure might replace a daily oral anticoagulant, and in dyslipidemia, a once a month and soon semiannual subcutaneous injection can potentially replace a daily drug.

**Effect adherence in clinical trials**

Adherence in the setting of clinical trials is often better than during routine clinical care – but is even present in trials, thereby significantly affecting outcomes. In superiority trials aiming to demonstrate a benefit of one drug over another, the treatment effect in both studies arms is attenuated by non-adherence. Selecting patients with high predicted adherence may allow smaller and more efficient superiority studies. In non-inferiority trials, where the goal is to demonstrate that the new treatment is not significantly worse than an existing therapy, the effect of non-adherence may be even more impactful. In the hypothetical situation where all patients in both study arm are completely non-adherent, the “treatment” effect will be identical to control, leading to the inappropriate conclusion that the strategies are equal. The Medication Adherence Score can help identify patients who have a higher chance of demonstrating good adherence and thus increase the power of non-inferiority trials.

**Ethical and privacy consideration**

In the research setting of the current study, the institutional review board approved the study and waived the need for informed consent which allowed us to obtain an unbiased sample. In the future, when the Medication Adherence Score may be used to guide therapy, the score should only be obtained with the consent of the patient as with any medical diagnostic test or intervention. It should be explained that the
score estimates adherence behavior and can help the clinician understand whether a patient would benefit from additional interventions that aim to improve adherence. Ideally, the consent question starts a conversation between the patient and clinician regarding adherence and which boundaries may apply to the patient's situation.

To obtain the Medication Adherence Score for an individual patient, name and address need to be exchanged, but no other information from the patients' medical file. The objective of the exchange in the context of the Medication Adherence Score is to improve treatment at the individual level, resulting in an immediate benefit for the patient whose information has been exchanged. FICO destroys the exchanged data immediately after the score has been generated and returned to the requestor. From a financial perspective, there is a charge per generated score.

**Limitations**

One of the limitations of the current study is that not all patients could be scored at the individual level because patients could not be matched by FICO. Therefore, approximately a quarter of patients could only be scored based on characteristics associated with their geography. In those instances, the averaged characteristics for the zip code area were entered into the model to generate scores. Scoring success at the individual level is related to the quality of the input data, proportion of patients that move and proportion of patients that live “off the grid”. Additionally, this was a feasibility study introducing the concept of the Medication Adherence Score and assessing the potential to generate a score in individual patients from two different US institutions.

In this study, there was no difference in the last recorded blood pressure observed between the adherence score groups (high vs. intermediate vs low). However, a better comparison would have been to compare the delta blood pressure between treatment naïve and on treatment patients, but those data were not available for this study. Future studies must study the association of the Medication Adherence Score with clinical outcomes, and whether interventions based on the Medication Adherence Score improves adherence and results in improved outcomes.

**Conclusions**

The Medication Adherence Score is a predictive analytic model that aims to assist clinicians in identifying patients at risk for non-adherence – thereby potentially allowing them to intervene both at the initiation of treatment and during follow-up. In this study, proof of feasibility was successfully demonstrated.

**Abbreviations**

MAS  
Medication Adherence Score
Declarations

Acknowledgements: We thanks Betsy Ellsworth for her assistance during the study. We thank Fair Isaac Corporation, in particular Andrea Richardson and Angela Waller, for their cooperation during the study and providing scores. We thank Boston Scientific Incorporation for funding this study.

Funding: This study was supported by an unrestricted grant from Boston Scientific Incorporation through the investigator sponsored research program. The funder had no role in the design, execution and reporting of the study.

Author Contributions:
TFB – was responsible for design, data collection, data interpretation, drafting of the manuscript. REK was responsible for data interpretation and critical review of the manuscript. MCB was responsible for data collection, data interpretation and critical review of the manuscript. VYR was responsible for data collection, data interpretation and critical review of the manuscript. All authors read and approved the final manuscript.

Ethics declarations

Ethics approval and consent to participate
The study protocol was reviewed and approved by the Biomedical Research Alliance of New York (BRANY registration number: 17-02-444-05) and granted a HIPAA and consent waiver.

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Figures

Figure 1

Title: Medication adherence score distribution of the combined cohort Legend: MAS – Medication Adherence Score
Figure 2

Title: Age stratified by Medication Adherence Score Legend: MAS – Medication Adherence Score. High >0.8, intermediate 0.6-0.8, low <0.6