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An Engagement Model for Medication Management: From Prescription to Description and Conscription

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Abstract. Medication non-adherence is a global problem that has been studied over the past 40 years. Despite the large number of studies there is not an agreed upon definition of "adherence" in the literature. The lack of a consistent definition has resulted in issues in adherence research, clinical implementation, and HIT system development. In this paper a critical review of adherence literature is conducted. Based on this review, a new Adherence Interaction Model (AIM) is proposed and described in detail. AIM considers provider recommendations, the patient's interpretation of the recommendations, and the patient's behavior and provides the foundation for building a more objective view of adherence. AIM provides a foundation for future formalization of medication adherence concepts.

Keywords. Medication Adherence, Models, Prescriptions, Primary Care, eHealth

1. Introduction

Medication adherence, as defined by the World Health Organization (WHO), is "the extent to which a person's behaviour … corresponds with agreed upon recommendations from a health care provider"[1]. The "agreed upon recommendation" is commonly referred to as a *prescription.* In their 2003 report, the WHO highlights medication adherence as a challenge of "striking magnitude" and posits that improving adherence might have a larger impact on global health than the development of new therapies [1]. But what does adherence really mean? Reviews of adherence literature have found disparities across multiple sources and a lack of consistent means for defining and measuring adherence [2], [3]. Several models for adherence have been proposed, yet no single model has received wide adoption. This situation leads to three main challenges: 1) from a medical research perspective, numerous studies examining interventions for improving adherence have been published, yet the results are incompatible due to the variations in methods, impeding meta-analyses [2]. 2) From a clinical perspective, providers are ill-equipped to monitor, educate, and support patients with respect to adherence, and patients may not be clear on the impact of (non-)adherence on their health processes. 3) From a health information technology (HIT)

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viewpoint, it is difficult to develop evidence-based adherence-supporting technologies without a precise understanding of what adherence means at a computational level.

This paper aims to address these underlying issues by defining adherence in a way that can facilitate research, provider and patient engagement, and HIT development. First, a critical review of recent literature on adherence definitions, models, and measures is given. Second, a conceptual model for medication adherence is discussed in detail.

2. Medication adherence literature

The WHO's definition quoted above is widely referred to in the literature [4]. Historically, the term "adherence" evolved from the term "compliance", but today's concept of adherence presupposes (patient) agreement with the (provider-) recommended treatment [4]. Thus, it can be said that the concept of adherence subsumes the concept of compliance. As Vrijens *et al.* point out, the above definition of adherence implies that 1) a method exists to measure the correspondence between recommendations and patient behavior (measurement of compliance), and 2) a method exists for measuring agreement between the patient and provider [4]. Inappropriate use of the term adherence (as opposed to compliance) may be a source of confusion in the "adherence" literature.

Vrijens *et al.* also describe a taxonomy for the study of medication adherence. They distinguish between 1) *adherence*, 2) the *management of adherence*, and 3) *adherence-related sciences* [4]. According to Vrijens et al. adherence is a "process by which patients take their medications as prescribed". *Management of adherence* is the action of "monitoring and support patients' adherence". Finally, *adherence-related sciences* are "the disciplines that seek understanding of the causes or consequences" of (non-)adherence. However, Vrijens *et al.*'s taxonomy does not consider the implications of over-loading the term "adherence"; their definition of *adherence* fails to account for agreement and refers only to compliance. Further, the *adherence-related sciences* encompass the study of both compliance and adherence, but the name implies only the study of compliance once agreement has been reached and thus excludes to possibility of studying compliance alone or the process by which agreement is reached.

Cramar *et al.* provide a review of the terminology for compliance and also define the term *persistence* as: "the duration of time from initiation to discontinuation of therapy" such that time between doses does not exceed a "permissible gap" [5]. Furthermore, they state that "continuing to take any amount of medication" implies persistence [5]. This definition of the term *persistence* is unclear, as the reference to "permissible gap" overlaps with the notion of compliance, yet the second part of the definition suggests that persistence is independent from compliance.

Conceptual definitions provide philosophical guidance, however there remains the need to measure the correspondence between patient behavior and recommendations, especially when interventions to improve behaviour are being considered. To date many different methods of measurement have been used and have been categorized by Osterberg and Blaschke as either *direct* (e.g. observed pill taking, measuring blood levels of a substance) or *indirect* (e.g. pill counts, patient diaries) [6]. However, Osterberg and Blaschke's notion of direct v. indirect only accounts for the concept of compliance, not of adherence and is therefore a misnomer w.r.t. WHO's

definition. They have not suggested "direct" measures for patient agreement with provider recommendations.

The literature on adherence measurement has been focused on two aspects: 1) methods of patient behavior and agreement *data capture*, and 2) calculating a degree of compliance (agreement is not considered in the reported calculation methods). Methods of data capture are as follows. *Self-reporting* consists of questionnaires, surveys, and/or discussion with health care providers. Though there are known issues with patient self-reports, including patient misrepresentation and provider perception, this method has been the primary means of adherence measurement [2]. *Pill Counting and Refill Counts* requires patients, providers, or researchers to count the number of doses remaining at a given point in time and/or the frequency of medication refills at pharmacies. These approaches, while more reliable than self-reporting, due to the added objectivity, still require the assumption that patients execute the prescribed behavior between measurements [2]. *Electronic Devices* measure the time at which a is medication administered. These devices more accurately approximate patient behavior by recording times at which doses are removed from the device. However, these methods suffer from the same issue (though somewhat less dramatically) as pill/refill counting [2].

Once data on patient behaviors is captured, calculation of the degree of compliance is often required. Reported methods of calculation are varied [3]. Many calculations are *sparse*; they consider behavior over an extended period of time. One such method is the *Mean Possession Ratio* (MPR), which is calculated as the number of days in which doses are available over the total number of days. However, several variations of MPR have been used which count "days" differently leading to incompatible measurements across studies. Unfortunately, these sparse calculations do not consider the timing of doses [4].

More detailed calculations consider doses taken "on time", but inherently impose the challenge of defining what "on time" means [7]. Additionally, reported calculation methods tend to assume that medications are prescribed with a periodic schedule and may not be able to accommodate for concepts such as *take as needed* or more complex dosing/timing regimes.

3. The Adherence Interaction Model - AIM

Based on the above review, we propose a conceptual model (the *Adherence Interaction Model – AIM*) for defining and relating the major concepts related to medication adherence. AIM suggests that *compliance*, *agreement* and *persistence* are "distance measures" between provider-recommended, patient-adopted, and patient-enacted medication plans, which we refer to as *prescription*, *conscription*, and *description* respectively. The AIM can most intuitively be visualized as a triangle, as depicted in Fig. 1.

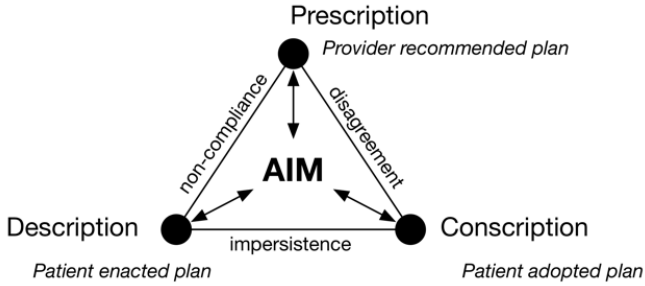

Fig. 1. Adherence Interaction Model (AIM)

In this model, measuring (non)*compliance* entails determining a "distance" between the provider-recommended medication plan (*prescription*) and the patient-enacted medication plan (*description*). The closer the *description* is to the *prescription*, the higher degree of compliance. Measuring (dis)*agreement* entails determining a distance between a provider-recommended plan (*prescription*) and the patient-adopted plan (*conscription*). The patient agrees completely with the provider's recommendation if and only if the *conscription* is a *refinement* of the *prescription*, in which case the disagreement distance is zero. Note that the patient-adopted plan (*conscription*) does not necessarily need to be identical to the *prescription*, rather it must be a refinement of the *prescription*, meaning that it may be more specific, while still satisfying the prescription. For example, a provider may recommend a once daily medication and the patient may take the medication once a day in the mornings. Finally, (im)*persistence* is defined as a distance between the patient-adopted plan (*conscription*) and patient-enacted plan (*description*).

Notably, the term "adherence" does not appear in the AIM as a primitive measure. As discussed in the previous section, the WHO defines the term *adherence* only for the case where the patient agrees to the provider's prescription, i.e. disagreement distance is zero; otherwise, the concept of adherence remains undefined.

We suggest that the AIM is valuable not only for defining and relating the major concepts in medication adherence, but also as a basis for developing and comparing means of quantitative and qualitative measurements.

The use of AIM as a theoretical framework for developing measures for medication adherence (and systems), requires a means to *formally express* medication plans and actions, i.e. must be based in mathematics; this permits the measurement of *compliance*, *persistence*, and *agreement*. From an abstract point of view, a medication management system is just another type of system; numerous formalisms have been developed for modelling the behaviour of systems. Our ongoing research focuses on exploring the potential application and adaptation of these formalisms in the context of medication management systems and adherence.

Directly above, we described medication prescriptions, conscriptions and descriptions as three types of plans (prescriptions, descriptions, and conscriptions). That was actually not quite correct: only prescriptions and conscriptions should be considered as *plans*, a *description* in AIM is a record of events that occurred. Such a record is commonly referred to as a *trace* in systems engineering. Moreover, plans (planned system behaviour) are usually referred to as *specifications*. Formalizing prescriptions and conscriptions as mathematic-based specifications requires a formalism capable of modelling planned behavior over time (e.g. temporal logic). Such

methods are usually endowed with precise conditions that must be met for a system behaviour (trace) to satisfy a specification (plan). However, in contrast to other types of systems (e.g., computer systems), medication adherence systems impose special challenges with respect to modelling the *imprecision* inherent to human behavior and medication plans. For example, consider a prescription specification with an administration time at 12:00pm, an administration at 12:05 pm is likely acceptable, even though the specification was not strictly satisfied. Therefore, traditional "crisp" specification formalisms should be extended to allow for a more gradual notion of plan satisfaction.

Formalizing a measure of *agreement* requires measuring the difference between two plans, the *prescription* and *conscription*; complete agreement requires that the conscription specification *refines* the prescription specification. Many formalisms provide means to verify refinement; however, they usually lack a means of quantifying distances in the case where one specification is found not to refine another, i.e. there is disagreement between the prescription and conscription. We propose two approaches for measuring (dis)agreement. 1) By *approximate triangulation* based on measurements of compliance and persistence wherein complete persistence is assumed and then the ratio of persistent and compliant doses to persistent doses is calculated. 2) By *trace enumeration* wherein all traces that satisfy the prescription specification and all traces that satisfy conscription specification are enumerated, the two sets of traces are compared and a ratio of equivalent to all total traces is calculated. The *approximate triangulation* method has the advantage of being relatively easy to compute, however requires the assumption that the patient is persistent and at least to some degree compliant. The *trace enumeration* method is very precise and would provide a definitive measure of agreement between the two specifications, however it may be computationally intensive, especially in cases where the number of traces is very large.

4. Conclusion

We have provided a critical review of the medication adherence literature and highlighted concerns related to terminology and measure of measurement. Until definitions are standardized, issues will continue to persist in research, clinical, and HIT aspects of medication adherence. To this end, we suggested an Adherence Interaction Model (AIM) that aims to provide a conceptual foundation for terminology in the domain. AIM uses *prescription* (provider plan), *description* (patient behavior), and *conscription* (patient's plan) and distances between them to describe concepts previously discussed in literature. Formalizing the concepts in AIM provides concrete measures of compliance, agreement, and persistence; some directions for future work to this effect were discussed.

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