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ORIGINAL ARTICLE

The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease

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ABSTRACT

Objective: To conceptualize, develop, and provide preliminary psychometric evidence for the Adherence Estimator – a brief, three-item proximal screener for the likelihood of non-adherence to prescription medications (medication non-fulfillment and non-persistence) for chronic disease.

Research design and methods: Qualitative focus groups with 140 healthcare consumers and two internet-based surveys of adults with chronic disease, comprising a total of 1772 respondents, who were self-reported medication adherers, non-persisters, and non-fulfillers. Psychometric tests were performed on over 150 items assessing 14 patient beliefs and skills hypothesized to be related to medication non-adherence along a proximal–distal continuum. Psychometric tests included, but were not limited to, known-groups discriminant validity at the scale and item level. The psychometric analyses sought to identify: (1) the specific multi-item scales that best differentiated self-reported adherers from self-reported non-adherers (non-fulfillers and non-persisters) and, (2) the single best item within each prioritized multi-item scale that best differentiated self-reported adherers from self-reported non-adherers (non-fulfillers and non-persisters).

Results: The two rounds of psychometric testing identified and cross-validated three proximal drivers of self-reported adherence: perceived concerns about medications, perceived need for medications, and perceived affordability of medications. One item from each domain was selected to include in the Adherence Estimator using a synthesis of psychometric results gleaned from classical and modern psychometric test theory. By simple summation of the weights assigned to the category responses of the three items, a total score is obtained that is immediately interpretable and completely transparent. Patients can be placed into one of three segments based on the total score – low, medium, and high risk for non-adherence. Sensitivity was 88% – of the non-adherers, 88% would be accurately classified as medium or high risk by the Adherence Estimator. The three risk groups differed on theoretically-relevant variables external to the Adherence Estimator in ways consistent with the hypothesized proximal-distal continuum of adherence drivers.

Conclusions: The three-item Adherence Estimator measures three proximal beliefs related to intentional non-adherence (medication non-fulfillment and non-persistence). Preliminary evidence of the validity of the Adherence Evidence supports its intended use to segment patients on their propensity to adhere to a newly-prescribed prescription medication. The Adherence Estimator is readily scored and is easily interpretable. Due to its brevity and transparency, it should prove to be practical for use in everyday clinical practice and in disease management for adherence quality improvement. Study limitations related to sample representation and self reports of chronic disease and adherence behaviors were discussed.

Introduction

Adherence to prescription medications has been labeled as our 'other drug problem'[1], an 'epidemic'[2], and a 'worldwide problem of striking magnitude'[3]. Research across 40 years has documented that adherence to prescription medications, regardless of diagnosis, is poor[4]. Up to 20% of patients do not fill a new prescription (primary non-adherence)[5–11]. Of those who do fill, approximately one-half discontinue therapy in the first 6 months (lack of medication persistency)[3,12–14].

Non-adherence thwarts the ability of patients to reach their clinical goals and can result in disease progression, untoward clinical sequelae, and suboptimal patient outcomes[11,14–19]. For providers, non-adherence yields frustration in clinical management and can result in economic loss for those reimbursed under pay-for-performance. Non-adherence increases healthcare costs for payers and employers[20,21] and contributes to inferior beneficiary outcomes. For pharmaceutical companies who discover and manufacture prescription medications and pharmacies who sell them, non-adherence results in significant revenue loss.

Over 32 000 articles have been published on adherence to prescription medications[22]. Much of this work has been descriptive, documenting the extent of non-adherence across disease and demographic groups. There has also been a profusion of instruments that measure adherence barriers and facilitators, including such constructs as: medication beliefs[23–28], medication concerns[29,30], perceived barriers to medication taking[31–33], perceived medication benefits[28,34], perceived need for medications[29], experience or fear of side-effects[30], perceived medication efficacy[30], regimen intrusiveness[30], and aversion to medications[34,35]. A host of other instruments measure adherence *per se* and are generic[29,36–38] as well as disease specific in content[25,31,39–44].

The National Council on Patient Information and Education, a coalition whose mission is to improve communication of information on medications to consumers and healthcare professionals, has advocated routine screening for non-adherence in clinical practice[45]. Clinical leaders have echoed this recommendation[46–53]. For example, Mitchell[51] maintains that 'more effort must be directed toward identifying those contemplating stopping medication,' and Schoberberger and colleagues argue that 'early selection of patients with higher risk for non-compliance could be important to support these patients individually'[48].

Several surveys have been developed to screen for non-adherence in specific diseases and/or specialties: three for psychotic disorders[54–56], four for antiretroviral therapy[57–60], two for antihypertensive therapy[48,61], one for rheumatologic disorders[62], one for pediatrics[63], and one for acne[64]. To the best of the author's knowledge, only four tools have been developed to screen for non-adherence across an array of chronic diseases – the Brief Medication Questionnaire[65], the Stages of Change for Medication Adherence[66], the Beliefs and Behavior Questionnaire (BBQ)[67], and the ASK-20 Survey[68,69]. The length of the BBQ (30 items), the ASK-20 (20 items), and the Brief Medication Questionnaire (minimum of 17 items) renders them less practical for use in clinical practice. The ASK-20, which was not based on a theoretical foundation, was just published in 2008, and there is no peer-reviewed experience with the survey outside of its developers. The Brief Medication Questionnaire has not enjoyed widespread use in clinical practice or research. The two-item Stages of Change for Medication Adherence poorly predicted subsequent adherence to antiretroviral therapy[70].

Herein is presented the conceptualization, development, and preliminary psychometric properties of a brief, three-item survey designed to segment patients according to their propensity to adhere to a prescription medication – the Adherence Estimator. This tool is designed as a predictive solution to adherence and is brief to easily integrate it into the office ecosystem. Given the magnitude of non-adherence, the fact that it affects all diagnostic and demographic groups, and the significant economic and clinical tolls that it renders, a brief, generic screener that provides an estimate of the likelihood of non-adherence on an individual-patient basis could make a palpable contribution to clinical practice and to population health.

Operating tenets and conceptual framework

The author's work concerns the decision to fail to purchase a newly-prescribed medication (also referred to as primary non-adherence or medication non-fulfillment) or to stop taking a medication without the advice of a healthcare provider (also referred to as lack of medication persistency). Thus, the Adherence Estimator focuses on intentional non-adherence, using the term non-adherence to reflect both non-fulfillment and lack of persistency given the prescription was initially filled. While unintentional non-adherence is common, it represents episodic, and often random, slips and lapses of medication taking, while intentional non-adherence is the eschewment of prescribed therapy.

Ten operating tenets were developed that serve to justify the development and use of the Adherence Estimator:

(1) Patients do not communicate their adherence intentions to their healthcare providers.
(2) Healthcare providers assume that *their* patients are adherent.
(3) A 'non-adherent personality' does not exist.
(4) Adherence to prescription medications behavior is largely unrelated to adherence to self-care and lifestyle recommendations.
(5) There is no consistent relationship between demographic characteristics and adherence.
(6) Patients want information about their prescription medications and feel frustrated that not enough information is provided to them.
(7) Healthcare providers are inconsistent communicators about prescription medications.
(8) Medication-taking is a decision-making process, and patients actively make decisions about their medications.
(9) Non-adherence is rational behavior – it is driven by patient beliefs about their treatment, disease, and prognosis as well as their objective experiences with their treatment and disease.
(10) Adherence represents shades of grey – patients can be faithfully adherent to one medication, non-fulfill on another, and be non-persistent to another because they hold different beliefs about medications to which they adhere, non-fulfill, and non-persist.

Tenets (1) and (2) are a clarion call for the need to screen for non-adherence because patients do not voluntarily tell their healthcare providers about their adherence intentions or behaviors[71–75]. For instance, Lapane *et al.*[74] reported that 83% of adult patients surveyed in six US states reported they would never tell their provider if they did not plan on buying a prescribed drug. Physicians, on the other hand, tend to assume that *their* patients are adherent. In two studies, from 75% to 89% of surveyed physicians believed that the majority of their patients were adherent[76,77].

Tenets (3), (4), and (5) dispel commonly-held misconceptions about adherence. First, research has not been able to substantiate the existence of an 'adherent personality'[78–81]. Hevey[80] asserts that 'there is little evidence of personality traits influencing adherence and the search for the 'non-adherent' personality type has provided limited insight.' Second, both across[82] and within[9,32,82–89] chronic diseases, there is weak correspondence between adherence to prescription medications and adherence to lifestyle or self-care recommendations. Third, as demonstrated by a rigorous meta-analysis[4], age, gender, and race are unrelated to adherence and education and income are very weakly related to adherence. In sum, neither personality traits nor self-care behaviors nor demographic characteristics yield any predictive value for screening for adherence.

Tenets (6) and (7) call attention to the discrepancy that exists between patients' desire for information about their medications and physicians' satisfying those information needs. Research has demonstrated that patients report significant unmet needs for information about the risks and benefits of their medications[73,90–98]. An equally impressive bolus of research has demonstrated that healthcare providers are inconsistent in communicating the risks and benefits of prescription medication therapy[91,92,94,99–104].

Tenets (8) and (9) reflect the accumulated knowledge about medication decision making and adherence gleaned from the past 25 years of research. Conceptual work has described adherence as a reasoned decision[72,105] and that consumers differentially value different medications[105,106]. Qualitative research has shed light on how medication taking is a decision-making process[72,97,107–111] and has illustrated how patients balance their concerns about medications against their perceived need for the therapy and its perceived benefits[72,73,97,107,108,110–120]. Quantitative research has documented that patient beliefs about their treatment, condition, and prognosis, as well as their objective experiences with their treatment and disease, predict adherence and differentiate adherers from non-adherers[10,23,27,121–154].

Finally, because adherence is neither personality, demographically, nor behaviorally driven, it is futile to label patients as 'adherers' or 'non-adherers.' Thus, as expressed in Tenet (10), adherence represents shades of grey – patients can be adherent to some medications, non-persistent to others, and fail to fill others because they make separate decisions about each prescribed medication[72,98,155]. Patients hold different beliefs about medications to which they adhere, non-persist, and non-fill because they make decisions for each medication according to their beliefs as well as the information they possess about the medication and their condition[72,98,155].

Having established from the literature that patient beliefs about their treatment, condition, and prognosis, as well as their healthcare skills and objective experiences with their treatment and condition, predict adherence and differentiate adherers from non-adherers, the author adapted Brenner's proximal–distal continuum[156] to hypothesize *which* patient beliefs, skills, and experiences may be most *proximal* to patient decision making about medications. The proximal–distal continuum holds that the strength of a relationship between a given patient belief, skill, or experience and non-adherence is related to its specificity to patients' medication decision making (see Figure 1).

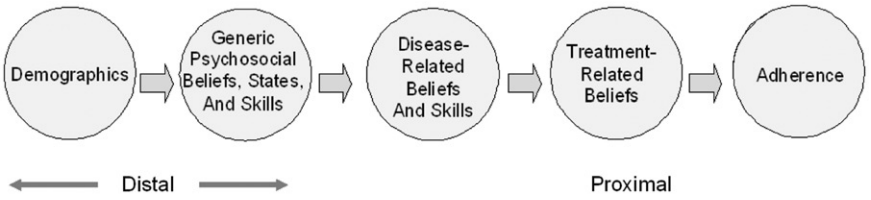

Figure 1. *Proximal–distal continuum of adherence drivers*

The closer the causal distance between patient beliefs, skills, and experiences and the decision to forgo medications, the stronger the association will be. The greater the causal distance between patient beliefs, skills, and experiences and the decision to forgo medications, the weaker the association will be.

Many of the patient beliefs tested in past research (e.g., self-efficacy and locus of control) are one or two steps causally removed from medication decision making. Insights gleaned from Horne and Weinman's Necessity-Concerns Framework[124,157]and the Beliefs about Medicine Questionnaire (BMQ)[29] have shown that proximal beliefs about the prescribed medication display a strong relationship to adherence. Across dozens of applications of the BMQ, it has become evident that perceived need for a medication[121,123–132] and perceived concerns about a medication[121,124,125,127,129–131,133–138,153,154] predict adherence and differentiate non-adherers from adherers. Research assessing medication need and medication concerns using instruments other than the BMQ also support the proximal nature of these two adherence drivers[10,23,27,122,139–152]. Owing to their demonstrated proximal nature, perceived need for medications and perceived concerns about medications are prioritized as top-level candidates for the Adherence Estimator.

In the US, up to 25% of adults engage in either cost-related non-adherence[158–162] or cost-related medication under-use[159,163–170]. Consistent with these findings, as well as past research on medication cost-sharing[171,172], prescription-drug affordability is prioritized in the proximal category. However, it was hypothesized *a priori* that perceived need for medications and perceived medication concerns should take predictive priority over medication affordability because they are more prevalent in the adult population than are drug affordability problems. Research has shown that a sizable proportion of adults with chronic disease have concerns about medications[124,125,130,133,134,151,157,173–175] and do not perceive a need for them[98,124,130,134,157,173]. Other research has substantiated drug affordability to be the lesser of the proximal drivers. For example, Doran[114], Ranji[161], and Schafheutle[113] all found cost to be a secondary factor in patients' medication decisions – secondary to a belief that the prescription was necessary.

Having hypothesized the proximal determinants, the author was left with a large array of patient beliefs, skills, and experiences which could serve as: (1) items in the Adherence Estimator or (2) external validity criteria for the psychometric analyses. The author categorized these beliefs and skills into those that are disease-specific versus those representing generic psychosocial beliefs, states, and skills (Figure 1). It is hypothesized that adherence is driven by the proximal beliefs of perceived need for medications, perceived concerns about medications, and perceived medication affordability. It is further hypothesized that perceived need and perceived concerns are determined largely by disease-specific patient skills, such as patient knowledge, disease-specific beliefs, such as perceived disease severity, as well as intermediate beliefs related to perceived proneness to side effects. It is hypothesized that disease-specific beliefs and skills are influenced largely by generic health beliefs, such as self-efficacy and locus of control, generic psychosocial states, such as social support, and generic health states, such as psychological distress. Finally, demographic characteristics are posited to be the most distal to medication decision making[4].

The purpose of the adherence proximal–distal continuum was to organize the myriad hypothesized adherence determinants on a conceptual map. Mapping the potential causal location of adherence determinants facilitated the identification of which variables could, theoretically, be most predictive for inclusion in the Adherence Estimator. The intent of this article is not to test the entire model, but to simply offer it as an organizing framework for the methodological work.

Patient and methods

Study design

Qualitative methods

The author conducted 13 focus groups with 140 adults in Chicago, IL and Atlanta, GA to understand contemporary reasons for adherence and non-adherence. Recruitment involved adults who were adherent to medications for chronic disease (five groups), as well

adults who recently stopped taking their medications without their doctor's advice (eight groups). The groups were stratified by gender to eliminate the interaction dynamics that can occur between men and women[176]. Participants were asked to silently write down their reasons for adherence and non-persistence, and they engaged in ranking and rating exercises about their reasons. Open discussions were had about the various factors that influenced medication decision making. The focus groups were used as discovery methods for developing the Adherence Estimator.

Quantitative methods

Two rounds of psychometric testing of potential items for the Adherence Estimator were conducted. The purpose of the phase I pretest was to ascertain which *domains* of patient beliefs hold the greatest predictive ability for segmenting consumers on their propensity to adhere to medications. The purpose of the phase II validity fielding was to cross-validate the pretest results in a larger independent sample of adults with chronic disease and to finalize the content of the Adherence Estimator by identifying the *specific items* to be included in the Adherence Estimator.

Study population

Both phase I and phase II sample members were part of the Harris Interactive Chronic Illness Panel (CIP), which is a nationally-representative, internet-based panel of hundreds of thousands of adults with chronic diseases. The CIP is a subsection of the Harris Poll Online Panel (HPOP), which is a multi-million panel of adults who have registered and agreed to participate in online research. During enrollment, respondents provide demographic characteristics and are screened for chronic disease.

Randomly-selected members of Harris' CIP were sent an e-mail invitation to participate in the surveys. Panel members were eligible for participation if they were aged 40 and older, resided in the US, and screened positive for one of six chronic diseases prevalent among US adults: hypertension, hyperlipidemia, diabetes, asthma, osteoporosis, and other cardiovascular disease. Qualified panel members were instructed to read the informed consent form, click on yes if they agreed to participate, and complete the survey. Qualified panel members could only complete each survey a single time. The protocol for both surveys was approved by the Essex IRB.

Three groups of respondents were identified for both surveys: self-reported adherers, self-reported non-persisters, and self-reported non-fulfillers to prescription medications. These groups were selected in order to test the ability and efficiency of the scales and items to discriminate between patients known to differ in their adherence behavior (i.e., known-groups discriminant validity).

During the screening portion of the survey, panel members' chronic disease status was re-confirmed. The screener solicited the number of medications respondents currently took for each disease as well as the length of time they reported taking each medication. These items were used to classify respondents as currently adherent to their medication. To identify respondents as non-persistent, they were asked if they had stopped taking a prescription medication for one of the six conditions in the past year *without* their providers telling them to do so. If respondents answered yes, they were presented with a list of 12 reasons why consumers might stop taking their medications and asked them to choose all that applied to them. To identify respondents as non-fulfillers, respondents were asked if they had received a new prescription for one of the six conditions in the past year but did not fill it. If respondents endorsed yes, they were presented with a list of ten reasons why consumers might not fill a new prescription medication and asked them to choose all that applied to them.

A sample size of at least 500 respondents was desired in order to conduct the phase I pretest psychometric analyses with sufficient precision. Specifically, principal-components analysis requires ten times as many subjects as items[177], and a two-parameter, graded-response item response theory (IRT) model requires at least 500 subjects[178]. Further, because few data are available in the literature on non-fulfillment, the author desired a sufficient number of non-fulfillers to assess their differences with non-persisters. A sampling quota for the pretest was set to obtain: (1) a 2: 1 ratio of adherers to non-persisters, (2) a 2: 1 ratio of non-persisters to non-fulfillers, and (3) a roughly equal number of persons in each chronic disease category for each adherence group. For the pretest, subjects were recruited for only one adherent behavior for a single condition. Once a given quota was met, recruitment was closed to all future potential respondents.

For the phase II study, a sample size of at least 1200 respondents was desired in order to conduct the analyses with sufficient precision. Further, because very few data are available on the beliefs of persons who are adherent to one medication while non-persistent or non-fulfilling to another, persons were sampled who reported different adherent behaviors for different diseases. A quota was set to obtain a modest sample of respondents who were: (1) adherent to a medication for one disease and non-persistent to a medication for a second, different disease, and (2) adherent to a

medication for one disease and non-fulfilling to a medication for a second, different disease. A roughly 1 : 1 ratio of adherers to non-persisters and a roughly 2 : 1 ratio of non-persisters to non-fulfillers was obtained. Once a given quota was met, phase II recruitment was closed to all further potential respondents.

Requests for the pretest survey participation were sent to 39 191 randomly-selected CIP members in November of 2007. Of these invitations, there were 3577 invalid e-mail addresses (e-mail bounce backs). Of the 35 614 invitations with valid e-mail addresses, 11 836 persons entered the survey (33.2% contact rate). Of those successfully contacted, 9689 (82%) met our study qualification criteria, and 700 persons completed the survey. The 8989 qualified persons who did not complete the pretest did not do so because the quotas were already met. Requests for Phase II survey participation were sent to 165 487 randomly-selected CIP members in the Spring of 2008. Of these invitations, there were 15 035 invalid e-mail addresses. Of the 150 452 invitations with valid e-mail addresses, 39 874 persons entered the survey (26.5% contact rate). Of those successfully contacted, 20 299 (51%) met the study qualification criteria, and 1523 persons completed the survey. The 18 776 qualified persons who did not complete the phase II survey did not do so because the quotas were already met.

Of the 1523 respondents to the phase II survey, 1072 were sampled for a single adherent behavior while 451 were sampled for more than one adherent behavior (e.g., adherent to a medication for one disease and non-persistent to a medication for a different disease). These latter sample members were not used in the analyses reported herein because of the desire to maintain symmetry with the phase I sampling design (sampled for a single adherence behavior) and because the author did not want to confound the analyses with lack of statistical independence. As described below, respondents sampled for two different adherence behaviors answered questions on perceived need for medications, perceived medications concerns, and patient knowledge specific to both of their adherence behaviors while they answered all other items only once. Analysis of these subjects, intended for the focus of a separate manuscript, would result in lack of statistical independence because their generic responses would be included in the analysis twice, resulting in correlated and dependent responses.

Survey content

Phase I pretest survey

Based on the conceptual framework, a comprehensive review of the theoretical and empirical work in adherence, and the 13 focus groups, 120 questionnaire items were developed to tap the three hypothesized proximal patient beliefs as well as selected intermediate and distal beliefs and skills. A small number of items were adapted from existing, non-copyrighted and non-trademarked surveys. A majority of items were written *de novo*. A large bolus of items was written because some items will inevitably not perform well psychometrically, and a large reserve of robust items was desired from which to select the best-performing items.

The 44 proximal items measured perceived concerns about prescription medications ($k = 13$), perceived need for prescription medications ($k = 28$), and perceived affordability of prescription medications ($k = 3$). Five intermediate patient beliefs and skills were measured using 76 items: patient knowledge of their condition and treatment ($k = 16$), perceived proneness to side effects ($k = 4$), health information-seeking tendencies ($k = 16$), patient trust in their primary provider ($k = 14$), and patient participation in their care ($k = 26$). All items had six possible response categories: 1 = agree completely, 2 = agree mostly, 3 = agree somewhat, 4 = disagree somewhat, 5 = disagree mostly, and 6 = disagree completely. For four domains of questions (perceived need, perceived concerns, perceived affordability, and patient knowledge), respondents were instructed to answer the questions specific to the adherence behavior for which they were sampled. For example, if a respondent was sampled as a non-fulfiller to an osteoporosis medication, they were instructed to answer the items in the four domains specific to the osteoporosis medication they did not fill.

Phase II survey

A total of 58 of the 120 pretest items were retained and 12 new items were developed: (1) five additional medication affordability items and (2) five items written *de novo* to assess the perceived value patients place on prescription medications versus vitamins, minerals, and supplements. In the phase II survey, respondents were directed to answer questions specific to the adherence group for which they were sampled for three domains: perceived need for medications, perceived medications concerns, and patient knowledge.

Also included in the phase II survey were well-validated, multi-item scales to serve as additional distal and intermediate adherence drivers, including psychological distress, social support, self-efficacy, and internal health locus of control. The inclusion of these constructs is supported by meta-analyses[179] and narrative literature syntheses[147,180–184]. The author measured psychological distress using the MHI-5[185], social support using a short-form of the MOS Social Support Scale[186], self-efficacy using the Generalized

Self-Efficacy Scale[187], and internal health locus of control using Wallston's measure[188].

Survey non-contact analysis and survey selection-bias analysis

Logistic regression was used to assess differences between CIP members with valid e-mail addresses who did and did not responded to the survey invitation (survey non-contact bias). Independent variables were age, gender, race, education, income, and geographic region of residence. Logistic regression was used to assess differences between CIP members who qualified for the survey but did not complete it because the preset quotas were already met (survey-selection bias). Because more CIP members who met eligibility criteria were self-reported adherers versus self-reported non-fulfillers and non-persisters, the selection-bias analyses were conducted separately by adherence status (self-reported adherers versus self-reported non-fulfillers and non-persisters combined). Independent variables were age, gender, race, education, income, and geographic region of residence.

Psychometric analysis

Unidimensionality assessment, multi-item scaling, and internal-consistency reliability

To understand the internal structure of the items (i.e., unidimensionality or the extent to which items measure just one thing in common), the ratio of the first to second eigenvalue was compared using a principal-components analysis. A 2: 1 or better ratio is supportive of unidimensionality[189]. Each multi-item scale was computed using Likert's method of summated ratings in which each item is equally weighted and raw item scores are summed into a scale score[190]. All scale scores were linearly transformed to a 0–100 metric, with 100 representing the most favorable state (or belief), 0 the least favorable, and scores in between representing the percentage of the total possible score. Cronbach's alpha coefficient was computed to estimate internal-consistency reliability.

Known-groups discriminant validity

The primary purpose of the phase I pretest was to assess known-groups discriminant validity at the *multi-item scale level*, which is the extent to which scales discriminate between mutually-exclusive groups known to differ *a priori* on the construct of interest. Our known groups were defined by self-reported adherence status: self-reported adherers, non-persisters, and non-fulfillers. General linear models and *t*-tests were used to assess discriminant validity. It was hypothesized that, compared to non-persisters and non-fulfillers, adherers would show the most favorable beliefs vis à vis perceived need for medications, perceived concerns about medications and perceived medication affordability. It was also hypothesized that adherers would express the least proneness to side effects, the most knowledge about their disease and treatment, and the most favorable perceptions about health information-seeking, trust in their provider, and participation in their care. There was no *a priori* hypothesis about differences in beliefs or skills between non-persisters and non-fulfillers.

For the phase II analyses, the author repeated scale-level tests of known-groups discriminant validity as well as assessed known-groups discriminant validity at the *item level*, which is the extent to which individual items discriminate between mutually-exclusive groups known to differ *a priori* on the construct of interest. The known groups were the same for those used for scale-level tests: self-reported adherers, non-persisters, and non-fulfillers. The item-level tests were intended to identify which specific items were the most discriminating. Such information would be used in conjunction with other psychometric criteria to select the final items for the Adherence Estimator. Item-level tests were conducted using general linear models and were cross-validated using chi-square analyses.

Logistic regression

The tests of known-groups discriminant validity were extended to a logistic regression model predicting self-reported adherence versus non-persistence and non-fulfillment combined. The independent variables were the proximal, intermediate, and distal multi-item scales. Each scale was divided into quartiles and each quartile was represented as dummy variables in order to assess scale monotonicity. The highest quartile on each scale (representing the most favorable 25% of the score distribution) was the reference group. A forward stepwise logistic regression was used with entry and retention criteria set at the 0.01 probability level. The models were repeated adding demographic variables as independent variables.

Item reduction techniques

A variety of techniques was used to achieve item reduction among the phase I pretest items as well as to select the final items for the Adherence Estimator. Item frequency distributions were examined for the range and variability of responses as well as for floor and ceiling effects. Item-total correlations were calculated to assess which items contributed the most to their respective scales. A two-parameter, graded-response IRT

model[191] from MULTILOG[192] was executed. Items were prioritized that were highly discriminating and whose boundary-location estimates were evenly spaced (indicating that each rating point contributed equally to ability). The known-groups discriminant validity of the items was examined and items were prioritized that best discriminated among the known adherence groups.

Scoring algorithm, adherence risk groups, and sensitivity and specificity

To derive the final scoring weights for the Adherence Estimator, the logistic regression was repeated using the selected individual items as independent variables. Each item was represented as dummy variables, with five dummy variables per item given that each item had six categorical responses. The total score distribution of the Adherence Estimator was cross-tabulated with self-reported adherence (self-reported adherers vs. non-fulfillers and non-persisters combined). A three-group risk classification (low, medium, and high risk of non-adherence) based on the observed adherence rates was derived. Sensitivity of the Adherence Estimator was defined as the percentage of the non-adherers (non-fulfillers and non-persisters combined) classified as medium or high risk. Specificity was defined as the percentage of self-reported adherers classified as low risk.

Characterization of adherence risk groups

The adherence risk groups derived from the scoring algorithm were characterized in terms of their demographic characteristics as well as the intermediate and distal patient beliefs and skills that were not included in the Adherence Estimator. Categorical variables were tested using chi-square analyses and interval-level variables were tested with general linear models.

Results

Survey contact and survey selection bias

A 33.2% contact rate for the phase I pretest and a 26.5% contact rate for the phase II survey was achieved. Compared to those who were invited but did not respond to the phase I pretest, those successfully contacted were more likely to be male, age 65 and older, Caucasian, and college educated (data not shown). Compared to those who were invited but did not respond to the phase II survey, those successfully contacted were more likely to be age 55 and older, Caucasian, and college educated (data not shown).

Among the qualified phase I self-reported adherers, men and those with less than a college education were more likely to not complete the full survey because the pre-set quotas were met. There was no evidence of any selection bias among the qualified phase I self-reported non-adherers. Among the qualified phase II self-reported adherers, persons with an income of $50 000 annually or greater were more likely to not complete the full survey because the pre-set quotas were met. Among the qualified phase II self-reported non-adherers, persons aged 65 and older were more likely to not complete the full survey because the pre-set quotas were met.

Sample characteristics

As shown in Table 1, respondent age ranged from 40–93 with a mean age of 59. From 60–65% of the samples were female, and 89% were Caucasian. Roughly 40% of both samples reported at least a college education, and just over one half reported an income of less than $50 000. A majority of sample members met eligibility criteria for being self-reported adherers. A symmetrical quota across the six diseases was achieved for the phase I pretest. For the phase II study, slightly more respondents with hypertension and hyperlipidemia were sampled than the other conditions.

Unidimensionality and internal-consistency analysis: phase I pretest

Appendix Table A presents data on unidimensionality and internal-consistency reliability of the pretest items. Two of the domains (information-seeking and participation) had one item each that did not load highly on the first principal component (< 0.30). The analysis was rerun excluding those two items. All of the domains were highly unidimensional. The ratio of the first-to-second eigenvalue ranged from a low of 5.2 to a high of 15.8. Cronbach's alpha coefficient ranged from a low of 0.88 to a high of 0.98. While the 13 medication concerns items met unidimensionality criteria, the rotated factor analysis suggested that two scales could be reliably derived: an eight-item scale assessing medication-safety concerns and a five-item scale assessing perceived concerns about side effects.

Bivariate, scale-level tests of known-groups discriminant validity: phase I pretest

As shown in Table 2, the scales that most powerfully differentiated the three groups were: (1) side-effect

Table 1. Sociodemographic characteristics of samples

Sociodemographic characteristic	Phase I pretest sample $n=700$		Phase II sample $n=1072$	
	n	%	*n*	%
Mean age (± SD)		59.5 (10.5)		58.2 (10.4)
Median age (± IQR)		60.0 (17.0)		58.0 (17.0)
Age 65+	245	35.0	324	30.3
Female	422	60.3	695	64.8
White	612	88.8	928	89.4
Black	30	4.4	56	5.4
Hispanic	18	2.6	30	2.9
Other race	29	4.2	24	2.3
Less than high school	7	1.0	12	1.1
High school graduate	89	12.7	167	15.6
Some college but no degree	232	33.1	343	32.0
Associates degree	81	11.6	107	10.0
Bachelor's degree	170	24.3	265	24.7
Graduate or professional degree	121	17.3	178	16.6
Income < $25 000	128	20.8	192	21.0
Income $25 000–49 999	191	31.1	309	33.8
Income $50 000–74 999	128	20.8	177	19.4
Income $75 000–99 999	75	12.2	117	12.8
Income $100 000–124 999	49	7.9	49	5.4
Income > $125 000	43	7.0	70	7.6
Asthma	117	16.7	144	13.4
Diabetes	116	16.6	157	14.6
Hyperlipidemia	124	17.7	249	23.2
Hypertension	118	16.9	257	24.0
Osteoporosis	115	16.4	180	16.8
Other cardiovascular disease	110	15.7	85	7.9
Adherer	404	57.7	434	40.5
Non-persister	193	27.6	427	39.8
Non-fulfiller	103	14.7	211	19.7

concerns ($F=56.5$, $p<0.0001$), (2) perceived medication affordability ($F=38.1$, $p<0.0001$), and (3) perceived need for medications ($F=24.5$, $p<0.0001$). While four of the five intermediate variables were statistically significant at the 0.05 level, examination of the F statistics indicated that they were less efficient at group discrimination than the proximal beliefs (range of F from 3.4 to 12.8). Differences in all of the group means were consistent with study hypotheses: for all scales, self-reported adherers held the most favorable attitudes. Examination of pair-wise means found none of the differences between non-persisters and non-fulfillers to be statistically significant at the 0.05 level. Accordingly, the analysis was re-executed using a *t*-test, and observed results mirrored those for the general linear model.

Multivariate, scale-level tests of known-groups discriminant validity: phase I pretest

The bivariate, scale-level tests of known-groups discriminant validity were cross validated using logistic regression (Table 3). Only the three hypothesized proximal scales were predictive of self-reported adherence. None of the intermediate variables entered into the model. There was a monotonic association between increasing side-effect concerns and increased likelihood of non-adherence. Compared to adherent respondents, those who were non-adherent had 3.6 times the odds of having high affordability concerns (Q1) and 2.3 times the odds of having modest affordability concerns (Q2). Non-adherent respondents had 1.7 times the odds of reporting low perceived need for medications (Q1).

Table 2. *Summary of bivariate, scale-level known-groups discriminant validity: phase I pretest sample* (n = *700)*

Multi-item scale*	Mean for adherers	Mean for non-persisters	Mean for non-fulfillers	*F*-test: three-group discrimination†		*T*-test: two-group discrimination‡	
				F	*p*-value	*t*	*p*-value
Hypothesized proximal beliefs							
Perceived medication concerns							
Side-effect concerns	82.5	64.7	62.0	56.5	< 0.0001	10.1	< 0.0001
Medication-safety concerns	63.3	50.4	55.0	20.7	< 0.0001	6.2	< 0.0001
Perceived need for medications	73.8	64.9	63.1	24.5	< 0.0001	6.5	< 0.0001
Perceived medication affordability	51.4	32.5	28.9	38.1	< 0.0001	8.7	< 0.0001
Hypothesized intermediate beliefs and skills							
Knowledge	79.3	75.6	77.1	3.4	0.033	2.5	0.012
Perceived proneness to side effects	61.7	54.9	53.7	6.2	0.002	3.5	0.0005
Patient trust	79.2	71.5	70.7	12.8	< 0.0001	4.8	< 0.0001
Patient participation	76.4	69.2	68.8	10.5	< 0.0001	4.4	< 0.0001
Health information-seeking	75.8	74.9	74.2	0.5	0.624	0.9	0.373

*Higher scores represent more favorable beliefs: fewer side-effect concerns, fewer medication-safety concerns, stronger perceived need for medications, better perceived medication affordability, more knowledge, less perceived proneness to side effects, more trust, more participation, and more health information-seeking

†Three-group discrimination was self-reported adherers vs. non-persisters vs. non-fulfillers

‡Two-group discrimination was self-reported adherers vs. non-persisters and non-fulfillers combined

Table 3. *Summary of multivariate, scale-level known-groups discriminant validity: phase I pretest sample* (n = *700)*

	Adherence vs. non-persistence/ non-fulfillment Odds ratio and CI	*p*-value
Side-effect concerns (reference = Q4, least side-effect concerns)		
Q3	2.75 (1.66–4.55)	< 0.0001
Q2	3.70 (2.17–6.29)	< 0.0001
Q1 (most side-effect concerns)	7.77 (4.39–13.77)	< 0.0001
Perceived need for medications (reference = Q4, most perceived need for medications)		
Q3	0.62 (0.38–1.03)	0.065
Q2	0.79 (0.48–1.31)	0.368
Q1 (least perceived need)	1.71 (1.01–2.88)	0.045
Perceived medication affordability (reference = Q4, most perceived affordability)		
Q3	0.85 (0.52–1.38)	0.515
Q2	2.31 (1.42–3.74)	0.0007
Q1 (least perceived affordability)	3.61 (2.22–5.88)	< 0.0001

Q = quartile

Odds ratios for each proximal belief are adjusted for the other two proximal beliefs in the model

Bivariate, item-level tests of know-groups discriminant validity: phase I pretest

Appendix Table B presents a gestalt summary of the item-level tests of known-groups discriminant validity. Consistent with the scale-level results, the proximal items were the most differentiating (highest median F statistic and highest median chi-square). However, within most domains, there was great variability in

Table 4. Summary of bivariate, scale-level known-groups discriminant validity: phase II sample (n = 1072)

Multi-item scale*	Mean for adherers	Mean for non-persisters	Mean for non-fulfillers	F-test: three-group discrimination†		*T*-test: two-group discrimination‡	
				F	*p*-value	*t*	*p*-value
Hypothesized proximal beliefs							
Perceived medication concerns							
Side-effect concerns	76.6	54.4	55.0	178.2	< 0.0001	19.6	< 0.0001
Medication-safety concerns	58.8	49.4	48.1	28.6	< 0.0001	7.5	< 0.0001
Perceived need for medications	77.7	60.3	60.8	143.2	< 0.0001	17.8	< 0.0001
Perceived medication affordability	59.7	46.9	46.4	21.2	< 0.0001	6.6	< 0.0001
Hypothesized intermediate beliefs and skills							
Knowledge	83.4	75.5	76.4	36.8	< 0.0001	8.8	< 0.0001
Perceived proneness to side effects	62.9	50.7	48.5	35.7	< 0.0001	8.5	< 0.0001
Patient trust	78.8	64.5	64.8	58.7	< 0.0001	11.5	< 0.0001
Patient participation	77.8	66.2	67.9	35.1	< 0.0001	8.7	< 0.0001
Health information-seeking	76.4	75.6	76.2	0.2	0.802	0.5	0.589
Value of supplements	28.8	43.7	45.1	50.7	< 0.0001	10.5	< 0.0001
Hypothesized distal beliefs							
Psychological distress	74.1	66.7	67.7	16.5	< 0.0001	6.1	< 0.0001
Social support	69.4	60.9	63.0	8.5	0.0002	4.1	< 0.0001
Internal locus of control	66.9	63.9	66.8	3.5	0.031	2.1	0.040
Self-efficacy	73.6	71.2	70.6	3.3	0.037	2.6	0.009

*Higher scores represent more favorable beliefs: fewer side-effect concerns, fewer medication-safety concerns, stronger perceived need for medications, better medication affordability, more knowledge, less perceived proneness to side effects, stronger trust, more participation, more health information-seeking, higher value on supplements, less psychological distress, more social support, more internal locus of control, and better self-efficacy

†Three-group discrimination was self-reported adherers vs. non-persisters vs. non-fulfillers

‡Two-group discrimination was self-reported adherers vs. non-persisters and non-fulfillers combined

item differentiating ability, with some items being highly discriminating (large value of F and chi-square) while others were not at all.

Item reduction

The author reduced the number of perceived need items from 28 to 14 and the number of medication concern items from 13 to 10. One medication affordability item was eliminated. The number of patient trust items was reduced from 14 to 7, participation items from 26 to 7, knowledge items from 16 to 9, side-effect proneness items from 4 to 3, and information-seeking items from 16 to 5. Items were retained in the following priority: (1) performance in item-level, known-groups discriminant validity, (2) highest item and category information from the two-parameter IRT model (available upon request), and (3) least skewed item score distributions.

Unidimensionality and internal-consistency analysis: phase II

As shown in Appendix Table C, all of the proximal, intermediate, and distal scales were highly unidimensional. The ratio of the first-to-second eigenvalue ranged from a low of 4.3 to a high of 21.7. Cronbach's alpha coefficient ranged from a low of 0.87 to a high of 0.97.

Bivariate, scale-level tests of known-groups discriminant validity: phase II data

Consistent with the phase I results, the scales that most powerfully differentiated the three groups were side-effect concerns and perceived need for medications (F = 178.2 and F = 143.2, respectively, Table 4). For both scales, self-reported adherers had the fewest side-effect concerns and the most perceived need. Several additional scales were also highly differentiating, including perceived medication affordability,

Table 5. Summary of multivariate, scale-level known-groups discriminant validity: phase II sample (n = 1072)

	Adherence vs. non-persistence/ non-fulfillment Odds ratio and CI	*p*-value
Side-effect concerns (reference = Q4, least side-effect concerns)		
Q3	1.98 (1.42–2.78)	< 0.0001
Q2	4.41 (3.01–6.46)	< 0.0001
Q1 (most side-effect concerns)	12.73 (7.76–20.87)	< 0.0001
Perceived need for medications (reference = Q4, most perceived need)		
Q3	1.19 (0.87–1.64)	0.273
Q2	1.94 (1.39–2.70)	< 0.0001
Q1 (least perceived need)	6.27 (4.12–9.55)	< 0.0001
Perceived medication affordability (reference = Q4, most perceived affordability)		
Q3	0.91 (0.65–1.27)	0.589
Q2	0.97 (0.68–1.38)	0.847
Q1 (least perceived affordability)	2.33 (1.65–3.28)	< 0.0001

Q = quartile
Odds ratios for each proximal belief are adjusted for the other two proximal beliefs in the model

patient trust, perceived value of supplements, patient participation, and perceived proneness to side effects. There were no observed differences between self-reported non-persisters and non-fulfillers on any of the proximal, intermediate, or distal scales. Observed results for the two-group discrimination (*t*-test) mirrored those for the general linear model.

Multivariate, scale-level tests of known-groups discriminant validity: phase II data

The bivariate tests of known-groups discriminant validity were cross validated using logistic regression (Table 5). Only the three hypothesized proximal scales were, once again, most predictive of self-reported adherence. None of the intermediate or distal scales entered into the model. There was a monotonic association between increasing side-effect concerns and increased likelihood of non-adherence. Compared to adherent respondents, those who were non-adherent had 6.3 (Q1) and 1.9 (Q2) times, respectively, the odds of having lower perceived need for medications. Non-adherent respondents had 2.3 times the odds of reporting the most affordability concerns (Q1).

Item selection for the adherence estimator

Across two waves of data analysis, the three hypothesized proximal beliefs proved to be the most efficient and powerful at discriminating between groups known to differ in self-reported adherence. Once the predictive domains were identified and cross-validated, it was time to select the single best item from each domain for inclusion in the Adherence Estimator. The author repeated tests of known-groups discriminant validity at the item level. Appendix Table D summarizes the data.

There were seven affordability items to select among. COST8 performed the best in both the three- and two-group discrimination. In individual regressions predicting adherence, COST8 also exhibited the highest Wald statistic. Examination of item frequency distributions showed COST8 to have the most even distribution across the six categorical rating points. Finally, item information curves from the graded-response IRT model indicated COST8 to assess a wider range of the latent construct of affordability than the other six items. For these reasons, COST8 ('I feel financially burdened by my out-of-pocket expenses for my prescription medications') was selected for inclusion in the Adherence Estimator.

There were five side-effect concern items to select among. CONCERN11 and CONCERN13 performed similarly in item-level tests of known-groups discriminant validity. However, the IRT analysis showed the category information curves to be more informative for CONCERN11 than CONCERN13. Additionally, CONCERN11 exhibited a less skewed item distribution than did CONCERN13. For these reasons, CONCERN11 ('I worry that my prescription medication will do more harm than good to me') was selected for inclusion in the Adherence Estimator.

*Table 6. Self-scoring algorithm for the Adherence Estimator**

	Agree completely	Agree mostly	Agree somewhat	Disagree somewhat	Disagree mostly	Disagree completely
I am convinced of the importance of my prescription medication	0	0	7	7	20	20
I worry that my prescription medication will do more harm than good to me	14	14	4	4	0	0
I feel financially burdened by my out-of-pocket expenses for my prescription medication	2	2	0	0	0	0

ADD UP THE TOTAL NUMBER OF POINTS FROM THE CHECKED BOXES	
Score	Interpretation
0	Low risk for adherence problems (> 75% probability of adherence)
2–7	Medium risk for adherence problems (32–75% probability of adherence)
8+	High risk for adherence problems (< 32% probability of adherence)

There were 15 items assessing perceived need for medications to select among. Five items were top candidates (NEED6, NEED25, NEED16, NEED15, and NEED12). All of them performed well in discriminant-validity tests. However, NEED6 yielded the most item and category information and it had the highest item-total correlation, which suggests it was the best single-item measure of the underlying construct. Thus, NEED6 ('I am convinced of the importance of my prescription medication') was selected for inclusion in the Adherence Estimator.

Scoring algorithm and characterization of the adherence risk groups

Table 6 presents the self-scoring algorithm for the Adherence Estimator. The item category weights were derived from a logistic regression equation with the items represented as dummy variables. The obtained c statistic from the equation was 0.834 and the Hosmer and Lemeshow goodness-of-fit test was 9.22 ($p = 0.33$). The author stayed true to the magnitude of the obtained odds ratios except when it was necessary to make slight proportionate amendments in order to have each final score be derived in one and only one possible way. As the table shows, one sums the three numbers to obtain the Adherence Estimator score. Because each score can be obtained in one and only one way, they are easily interpretable. For example, there is only one way to obtain a score of 7 – a patient scoring 7 has a modest perceived need for medication, but no issues with side-effect concerns or medication affordability. A patient scoring 22 has a very low perceived need for medication as well as medication affordability issues.

The total score of the Adherence Estimator was cross-tabulated with self-reported adherence (non-fulfillers and non-persisters combined) and a three-group risk classification (low, medium, and high risk of non-adherence) was derived. The low-risk group comprised 31% of the sample and had an observed self-reported adherence rate of 76%. The medium-risk groups comprised 30% of the sample and had an average self-reported adherence rate of 39% (range of 32–45%, median = 40%). The high-risk groups comprised 39% of the sample and had an average self-reported adherence rate of 8% (range of 0–25%, median = 7%). Sensitivity was 88% – of the non-adherers, 88% would be accurately classified as medium or high risk by the Adherence Estimator. The false negative rate was 12% – 12% of non-adherers would be classified as low risk. Specificity was 59%. Of the adherers, 59% would be classified as low risk by the Adherence Estimator. The false positive rate was 41% – these are adherent patients who would be falsely classified as medium or high risk.

Table 7 presents a characterization of the three risk groups by demographic characteristics and the intermediate and distal scales. The low-risk group was characterized by the oldest mean age and the largest percentage with persons age 65 and older. The low-risk group was under-represented by females relative to the medium- and high-risk group. There were no differences across the groups in race. The medium- and high-risk groups had the highest percentage with income less than $35 000 annually. These same two

Table 7. Characterization of adherence risk groups by demographics and intermediate and distal beliefs: phase II sample (n = 1072)

	Low risk for non-adherence 31% of the sample	Medium risk for non-adherence 30% of the sample	High risk for non-adherence 39% of the sample	Chi-square or F	*p*-value
Demographic characteristics					
Mean age	61	58	56	25.6	< 0.0001
Age 65+	43%	25%	24%	37.8	< 0.0001
Female	59%	67%	68%	8.2	0.017
Caucasian	92%	86%	90%	5.8	0.056
Income < 35K	31%	45%	36%	11.2	0.004
College educated	49%	37%	39%	11.6	0.003
Intermediate beliefs and skills*					
Medication-safety concerns	70	52	42	153.6	< 0.0001
Knowledge	88	83	68	179.6	< 0.0001
Perceived proneness to side effects	67	54	46	74.8	< 0.0001
Patient trust	82	75	57	171.8	< 0.0001
Patient participation	81	75	60	114.7	< 0.0001
Health information-seeking	77	77	74	2.7	0.068
Perceived value of supplements	25	35	51	116.1	< 0.0001
Distal beliefs*					
Psychological distress	77	66	66	36.9	< 0.0001
Social support	71	62	62	9.2	0.0001
Internal locus of control	67	65	65	2.2	0.106
Self-efficacy	75	70	71	7.7	0.0005

*Higher scores represent more favorable beliefs: fewer medication-safety concerns, more knowledge, less perceived proneness to side effects, stronger trust, more participation, more health information-seeking, higher value on supplements, less psychological distress, more social support, more internal locus of control, and better self-efficacy

groups also had the lowest percentage of college graduates.

For all of the intermediate and distal scales, the low-risk group scored the best and the high-risk group scored the worst. The greatest differences between the risk groups were observed for patient knowledge (F = 179.6), patient trust (F = 171.8), and medication-safety concerns (F = 153.6). The weakest observed associations between the risk groups (F < 10.0) were for health-information seeking tendencies and the more distal beliefs (locus of control, self-efficacy, and social support).

Discussion

Non-adherence to prescription medications is a problem of international importance. Non-adherence is an equal opportunity epidemic – it knows no demographic, geographic, or political boundaries. It is equally prevalent in acute and chronic conditions as well as symptomatic and asymptomatic conditions and is equally prevalent across different healthcare financing arrangements in the US and abroad[162,193–195]. It is with these facts in mind that the author set out to conceptualize, develop, and provide preliminary psychometric evidence on the Adherence Estimator – a brief, three-item, self-scoring instrument that segments patients on their propensity to adhere to prescription medications for chronic disease.

The author deemed it essential to ground the work on the Adherence Estimator in a cogent theoretical framework. Brenner's proximal–distal continuum[156] was adapted to prioritize which of the myriad hypothesized adherence drivers hold the greatest predictive promise for screening on adherence. Work by Horne and Weinman on the Necessity-Concerns Framework[124,157], as well as countless others, have identified two proximal patient beliefs about prescription medications that predict adherence and differentiate adherers from non-adherers – perceived need for medications and perceived concerns about medications. Specific instruments have copyrighted individual items to tap these unobservable constructs. The author developed her own items to assess these constructs as

well as added perceived medication affordability as a high-priority proximal driver. To fill out the proximal–distal continuum, the predictive ability of 11 other adherence drivers was tested.

The *a priori* prioritized proximal determinants were confirmed across two phases of psychometric research. Out of 14 constructs measured with highly-reliable, multi-item scales, only perceived need for medication, perceived medication concerns, and perceived affordability of medications strongly differentiated adherers from non-persisters and non-fulfillers in both bivariate and multivariate tests. The finding that perceived medication concerns and perceived need for medications were the most predictive of the three proximal beliefs is consistent with Tenets (6) and (7) – patients have unmet needs for information about medication risks and benefits and providers communicate such risks and benefits inconsistently.

No differences between non-fulfillers and non-persisters were observed on any of the 14 scales. There were also no statistically significant differences between non-fulfillers and non-persisters in mean age, age defined categorically, gender, race, income, and education. From the two sets of data, it is posited that the only differentiating factor between non-persisters and non-fulfillers is the timing and decisiveness with which they eschew prescription medication therapy.

The Adherence Estimator yields an immediately-interpretable and completely-transparent score. By simple summation of the weights assigned to the category responses of the three items, a total score is easily obtained. Patients can be instantaneously placed into one of three segments based on their total score – low, medium, and high risk for non-adherence. Because each total score can be obtained in one and only one way, healthcare providers and researchers will unmistakably know how each possible obtained score is achieved vis à vis the individual item responses. In the developmental work to date, a slip cover has been created into which the completed Adherence Estimator is placed. The overlaying slip cover is color coded in white (satisfactory response), yellow (medium-risk response), and red (high-risk response).

On the battlefield or in natural emergencies, persons placed in the same 'triage' group should have similar medical needs to one another but different needs from those in other triage groups. Analogously, patients within a given adherence segment should resemble one another but should be qualitatively and quantitatively different from patients in other adherence segments. The profiles of patients classified as low, medium, and high risk were consistent with the proximal–distal continuum. Low-risk patients had the best scores on all of the intermediate adherence drivers, high-risk patients the worst score, and medium-risk patients in between. The patient beliefs classified as generalized psychosocial states (distal beliefs) least differentiated the three risk groups. Patient knowledge, patient trust, and medication-safety concerns best differentiated the three adherence risk groups.

Research has shown that physicians poorly predict patients' adherence[196,197], so poorly that Turner and Hecht[198] assert that 'clinicians would do better to toss a coin than to try to predict non-adherence.' As depicted by Tenets (1) and (2), a 'don't ask, don't tell' standoff about adherence exists in clinical practice because patients do not volunteer information about their adherence intentions and behaviors and providers assume that *their* patients are adherent. The need for a tool to estimate patients' propensity to non-adhere to medications is analogous to clinicians managing hypertension without a sphgymomanometer[50]. Like adherence, clinicians cannot assess the level of systolic and diastolic blood pressure by knowledge of a patient's demographic characteristics (Tenet (5)) or their lifestyle behaviors (Tenet (4)).

The sensitivity of the Adherence Estimator was excellent at 88% – the tool accurately identified nearly everyone who is at risk for non-adherence. Specificity was acceptable at 59%. Compared to other adherence screeners[56,62,65], the Adherence Estimator's sensitivity was very similar but its specificity was slightly lower. The author believes that there is minimal risk to patients being identified as false positives because such patients would no doubt benefit from supportive communication about the risks and benefits of their medications and strategies to make their medications more affordable.

There are both strengths and limitations to the study. In terms of strengths, a large, internet-based panel of adults with chronic disease was accessed with representation from 47 of the 50 US states for both the phase I and phase II surveys. Two independent studies were conducted with separate samples large enough to confidently conduct and interpret the psychometric tests. The psychometric evaluation used techniques from both classical and modern test theory. Numerous sensitivity tests were conducted using alternative methods. For example, for item-level, known-groups discriminant validity, tests were based on both interval and categorical levels of measurement. Item selection for the Adherence Estimator was re-confirmed using regression tree and classification analysis. These results (not reported here but the subject of a future publication) corroborated those reported herein. The author repeated the analysis including chronic disease as dummy variables in the logistic-regression models and reached the exact same conclusions. Finally, the

analyses were repeated using the enhanced sample, including the additional 451 respondents who were sampled for dual adherence behaviors, and the exact same conclusions were reached.

The study is not without limitations. The internet-based samples were slightly under-represented by adults with income less than $25 000 annually compared to the US adult population[199]. Also relative to the US adult population aged 25 and older[200,201], the obtained samples had under-representation of adults with less than a high school education, over-representation of adults with a college education, and over-representation of Caucasians. Some differences were observed between those who were successfully and non-successfully contacted for survey participation in terms of age, race, and education. Small demographic differences were observed between those who qualified for the surveys but did not complete them because the sampling quotas were met. The literature provides little guidance as to whether perceived need for medication and side-effect concerns vary as a function of sociodemographic characteristics and whether different results might have been obtained with a more diverse sample. It is likely that the slight income bias would provide a *lower-bound* estimate on the results observed for perceived medication affordability.

The study involved adults with self-identified chronic disease. None of the six study conditions were substantiated with medical records. On the other hand, a well-defined, chronic disease panel was accessed and the six conditions were re-verified using a separate, independent screener than that used to enroll the CIP. Only six conditions were studied, although they are highly prevalent in the US adult population. No psychiatric conditions were studied.

Another limitation of this study is that the tests of known-groups discriminant validity, and ultimately domain and item selection, were based solely on self-reported adherence status – no external indicators of adherence (such as pharmacy claims, refill records, pill counts, or electronic monitoring) were available. However, every direct and indirect method of assessing adherence has its limitations, and none are measured without error[202,203]. A prospective study has been launched to assess the predictive validity of the Adherence Estimator with regard to adherence measured using pharmacy claims. Thus, additional validity evidence using methods other than self-report will be forthcoming in subsequent publications.

The author explicitly asked about non-fulfillment and non-persistence, and all patients provided reasons for their behaviors using a standardized checklist. Past research has demonstrated that patients reliably report non-adherence[204,205]. Thus, the author is confident in the classification of non-persisters and non-fulfillers. However, it is conceivable that some post-hoc rationalization may have occurred among the non-persisters and non-fulfillers. It is possible that these respondents justified their non-adherence behaviors with their survey responses. However, the purpose of the survey was blinded to respondents. It is also equally likely that all of the proximal–distal constructs would have been susceptible to post-hoc rationalization, not just the three proximal drivers. Further, due to recall bias, it is likely that some degradation in memory occurred, which would have served to attenuate reports on the proximal–distal constructs. Such degradation would serve to act as a lower bound on our observed results.

Research has suggested that patients over-estimate adherence when measured by self-report[204,206]. It is widely asserted[207–209], although rarely documented with any breadth or depth, that such over estimates result from social-desirability bias. It is plausible that there may be some classification error among the self-reported adherers. In both of our surveys, data were collected among the self-reported adherers on current medication usage and length of use. Also included in both surveys were additional items on intentional and non-intentional non-adherence that the self-reported adherers completed. All tests of known-groups discriminant validity were repeated in both datasets using 'perfect adherers' as the known group (albeit with a smaller sample size). All observed results were maintained in direction, magnitude, and statistical significance. Thus, by conducting sensitivity tests and cross-validating our results using a purer adherent group, criticism is minimized about possible biases in adherence self reports.

Adherence to prescription medications is well-recognized as an essential component of chronic illness quality improvement. Adherence lies at the heart of patient-centered care because it is patients themselves who decide to forego prescription medication therapy. The availability of a predictive adherence screener is just one step toward adherence quality improvement. In addition to a rapid, easily-interpretable adherence screener, there must be in place appropriate decision-support and clinical-information systems for providers to meaningfully act on the Adherence Estimator. Our current, incentive-based, healthcare reimbursement system perversely works against improving adherence. Given that non-adherence is an epidemic that knows no boundaries, it may be necessary for all of the major adherence stakeholders to initiate and sustain a public-education campaign to elevate adherence as the sixth vital sign so that providers are reimbursed

for their adherence screening and communication efforts.

Given the rapid and precipitous drop-off in medication persistency rates observed in the first 6 months of therapy, it is recommended that the Adherence Estimator be administered shortly after the initiation of new therapy. Others have likewise recommended that suboptimal adherence should be identified shortly after the initiation of new therapy[53,210]. The Adherence Estimator should be completed for each new medication prescribed. Ideally, the Adherence Estimator should be completed by the patient by pencil and paper, computer, personal digital assistant, or kiosk rather than directly administered via interview format to the patient by a healthcare provider. The Adherence Estimator can also be used to screen patients for eligibility for adherence intervention trials. Research has found that adherence interventions that target persons with poor adherence have stronger effects than those with unrestricted eligibility[211].

Conclusions

Preliminary psychometric evidence was provided on the Adherence Estimator. The author offers the instrument to healthcare providers and researchers to screen patients on their propensity to adhere to prescription medications for chronic disease. The three-item, self-scoring tool is theory-based, evidence-based, and patient-centered, can be completed in less than one minute, and can be immediately interpreted to identify specific proximal adherence drivers, or combinations thereof, that are most problematic to patients so that issues related to intentional non-adherence can be addressed in a timely and supportive manner. Ongoing work is developing and validating motivational adherence communications consonant with perceived need, side-effect concerns, and perceived medication affordability that will hopefully yield tailored and actionable solutions that address these three proximal adherence determinants.

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Appendix

Appendix Table A. *Summary of unidimensionality and internal-consistency analyses: phase I pretest sample* (n = *700)*

	K	Ratio of 1st to 2nd eigenvalue	Range of loadings with the first principal component	Median loading with the first principal component	Cronbach's alpha
Hypothesized proximal beliefs					
Perceived medication concerns					
Side-effect concerns	5	6.3	0.79–0.85	0.83	0.88
Medication-safety concerns	8	6.2	0.65–0.84	0.81	0.91
Perceived need for medications	28	5.2	0.32–0.87	0.74	0.96
Perceived medication affordability	3	6.0	0.84–0.94	0.94	0.90
Hypothesized intermediate beliefs and skills					
Knowledge	16	9.8	0.63–0.85	0.77	0.95
Perceived proneness to side effects	4	11.8	0.90–0.92	0.92	0.94
Patient trust	14	14.5	0.76–0.92	0.87	0.97
Patient participation	25	15.8	0.77–0.93	0.86	0.98
Health information-seeking	15	8.4	0.69–0.87	0.77	0.95

Appendix Table B. *Summary of item-level known-groups discriminant validity: phase I pretest sample* (n = *700)*

	K	Range of F	Median F	Range of chi-square	Median chi-square
Hypothesized proximal beliefs					
Perceived medication concerns					
Side-effect concerns	5	20.9–49.8	34.7	51.3–107.3	81.9
Medication-safety concerns	8	3.6–18.8	13.7	14.0–46.8	35.7
Perceived need for medications	28	1.1–38.0	17.0	6.3–92.2	43.5
Perceived medication affordability	3	25.4–46.9	25.6	60.9–103.5	61.4
Hypothesized intermediate beliefs and skills					
Knowledge	16	0.1–9.07	3.3	7.8–31.4	21.8
Perceived proneness to side effects	4	3.4–7.1	5.3	18.4–30.2	22.8
Patient trust	14	1.3–19.9	10.0	8.4–62.7	29.5
Patient participation	25	2.6–13.3	7.9	14.6–42.1	26.7
Health information-seeking	15	0.1–2.1	0.5	7.6–19.2	13.5

Appendix Table C. *Summary of dimensionality and internal-consistency analyses: phase II sample* (n = *1072)*

	K	Ratio of 1st to 2nd eigenvalue	Range of loadings with the first principal component	Median loading with the first principal component	Cronbach's alpha
Hypothesized proximal beliefs					
Perceived medication concerns					
Side-effect concerns	5	5.5	0.74–0.85	0.84	0.87
Medication-safety concerns	5	4.5	0.77–0.86	0.82	0.87
Perceived need for medications	15	6.4	0.48–0.88	0.80	0.95
Perceived medicine affordability	7	21.7	0.87–0.96	0.93	0.97
Hypothesized intermediate beliefs and skills					
Knowledge	9	5.6	0.69–0.87	0.79	0.92
Perceived proneness to side effects	3	8.7	0.90–0.94	0.92	0.91
Trust	7	17.2	0.88–0.93	0.92	0.97
Participation	7	14.5	0.82–0.93	0.89	0.96
Health information-seeking	5	7.9	0.79–0.89	0.87	0.91
Perceived value of supplements	5	16.9	0.90–0.93	0.92	0.95
Hypothesized distal beliefs					
Psychological distress	5	5.1	0.70–0.88	0.84	0.88
Social support	8	8.7	0.82–0.90	0.88	0.96
Internal locus of control	10	4.3	0.56–0.82	0.76	0.90
Self-efficacy	10	7.9	0.55–0.82	0.81	0.92

Appendix Table D. *Summary of item-level known-groups discriminant validity: phase II sample* (n = *1072)*

	F from three-group test*	Chi-square from three-group test*	T from two-group test†	Chi-square from two-group test†	Wald from logistic regression†
COST8	20.2	52.5	6.6	48.2	43.9
COST3	20.0	43.7	6.6	44.0	39.7
COST7	19.9	46.5	6.5	42.0	38.6
COST4	17.6	37.6	6.2	38.7	33.9
COST6	17.2	42.7	6.1	40.3	35.9
COST2	16.3	37.0	5.9	35.7	32.7
COST9	12.1	38.6	5.1	35.6	31.1
CONCERN13	163.7	295.3	18.8	290.0	249.9
CONCERN11	133.4	248.6	16.8	243.4	219.2
CONCERN5	118.9	234.0	16.1	229.5	206.6
CONCERN2	107.7	208.4	15.2	202.9	182.5
CONCERN1	52.4	122.4	10.2	99.6	95.1
NEED25	168.1	318.1	19.1	305.1	259.3
NEED16	156.1	304.2	18.8	289.5	228.7
NEED15	149.0	282.5	18.2	301.2	214.1
NEED12	145.6	291.1	18.1	285.1	227.4
NEED6	144.2	286.9	17.9	261.1	210.4
NEED11	133.7	259.1	17.3	250.4	204.2
NEED5	96.6	202.6	14.4	188.3	171.4
NEED17	78.4	157.7	12.8	149.4	138.6
NEED2	77.2	155.4	12.8	150.3	140.4
NEED18	75.8	167.8	12.8	157.8	139.6
NEED26	74.5	149.2	12.7	139.4	120.6
NEED7	66.4	145.9	11.9	131.4	121.4
NEED21	46.3	108.4	9.7	99.8	95.0
NEED23	5.7	14.8	3.4	12.2	12.1
NEED1	2.8	23.2	2.2	10.5	10.5

*Three-group discrimination was self-reported adherers vs. non-persisters vs. non-fulfillers;
†Two-group discrimination was self-reported adherers vs. non-persisters and non-fulfillers combined

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