




BMJ Open Patient-reported outcome measures to detect intentional, mixed, or unintentional non-adherence to medication: a systematic review

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ABSTRACT

Objective To categorise patient-reported outcome measures (PROMs) into their propensity to detect intentional and/or unintentional non-adherence to medication, and synthesise their psychometric properties.

Design Systematic review and regression analysis.

Eligibility Medication adherence levels studied at primary, secondary and tertiary care settings. Self-reported measures with scoring methods were included. Studies without proxy measures were excluded.

Data sources Using detailed searches with key concepts including questionnaires, reliability and validity, and restricted to English, MEDLINE, EMBASE, CINAHL, International Pharmaceutical Abstracts, and Cochrane Library were searched until 01 March 2022. Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA-2020) checklist was used.

Data analysis Risk of bias was assessed via COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN-2018) guidelines. Narrative synthesis aided by graphical figures and statistical analyses.

Outcome measures Process domains [behaviour (e.g., self-efficacy), barrier (e.g., impaired dexterity) or belief (e.g., perception)], and overall outcome domains of either intentional (I), unintentional (UI), or mixed non-adherence.

Results Paper summarises evidence from 59 studies of PROMs, validated among patients aged 18–88 years in America, the United Kingdom, Europe, Middle East, and Australasia. PROMs detected outcome domains: intentional non-adherence, n=44 (I=491 criterion items), mixed intentionality, n=13 (I=79/UI=50), and unintentional, n=2 (UI=5). Process domains detected include belief (383 criterion items), barrier (192) and behaviour (165). Criterion validity assessment used proxy measures (biomarkers, e-monitors), and scoring was ordinal, dichotomised, or used Visual Analogue Scale. Heterogeneity was revealed across psychometric properties (consistency, construct, reliability, discrimination ability). Intentionality correlated positively with negative beliefs ($r(57)=0.88$) and barriers ($r(57)=0.59$). For every belief or barrier criterion-item, PROMs' aptitude to detect intentional non-adherence increased by $\beta=0.79$ and $\beta=0.34$ units, respectively ($R^2=0.94$). Primary care versus specialised care predicted intentional non-adherence (OR 1.9; CI 1.01 to 2.66).

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ While the processes leading to the final classification can be subjected to individual interpretation of the items' construct and consequences to treatment default, the twofold approach to first, classify every PROM item, and second, to classify the overall PROMs into outcome domains depending on the dominance of item type, demonstrated good inter-rater reliability.
- ⇒ Using regression analysis of process and outcome domains, some insights were gained on the reasons for non-adherence. However, for future studies, further analysis with greater sample sizes are recommended.
- ⇒ The process domains of behaviour (habitual), barrier (tangible impediment), or belief (mindset) were not only difficult to assess by means of self-reported outcome measures, but were also revealed as the real challenges to fostering adherence.
- ⇒ While we had juxtaposed scores against proxy measures, as with any self-reported data, limitations existed with the accuracy of recall and fair reporting of events.

Conclusions Ten PROMs had *adequate* psychometric properties. Of the ten, eight PROMs were able to detect total, and two PROMs were able to detect partial intentionality to medication default. Fortification of patients' knowledge and illness perception, as opposed to daily reminders alone, is most imperative at primary care levels.

INTRODUCTION

The act of taking medication is deemed fitting when it is done in accordance to instructions given by healthcare professionals. In general, the patient is instructed to take an accurate dose, at a predetermined time interval. Poor medication adherence poses a serious and expensive challenge to patients and healthcare systems. The Centers for Disease Control estimated that each year, the death of 125,000



persons in the USA alone was caused by treatment failure for chronic diseases and default in taking prescribed medications regularly and accurately. In addition, \$300 billion USD (approx. £228 billion) was spent on hospitalisation, emergency admissions and clinic visits.¹

Intentional and unintentional non-adherence are usually distinguished by patients' medication-taking conduct, which is influenced by, firstly, processes such as pre-emptive thoughts or behavioural aspects, which eventually lead the patients to take their medication (e.g., to get better, habitual, or due to medication stock availability). Secondly, medication-taking conduct is distinguished by the outcome or action, i.e., patient ended up forgetting, skipping a dose, changing the amount, or delaying the time at which a medication should be taken, or did not take medication on purpose.² As the nature of instructions for medication-taking is often complex and varied depending on an individual's pre-existing medical conditions and concomitant medications, the criteria for adherence assessment are also subjective. Ideally, an adherence measure is developed to detect common predictors that may influence adherence for a diseased population.

Existing measures have commonly explored forgetfulness as an obstacle to adherence and subsequently identified instances where forgetting may be more frequent, such as, when away from home, during weekends, or when travelling for work.³ Intuitively, many measures also explored psychosocial aspects, such as, attitudes and perceptions associated with belief (e.g., their medication is not working, they do not need to take 'too much of' the medication). Nevertheless, users have critiqued that although such patient-administered questionnaires addressed specific obstacles to medication adherence, they were disease-specific, and hence had limited use in the general clinical care setting.⁴ In addition, the vulnerable older adults, who most require the assessment, were often excluded from the surveys as they presented with visual or cognitive impairment, and could not communicate effectively.

Several self-reported adherence measures, such as the Morisky scale,⁵ were established to screen for the possibility of missed doses or timings, and have been widely incorporated in clinical practice because of their ease of use. However, measures that assess only the instances of non-adherence offer little insights into the myriad of possibilities contributing to such misconduct, such as, the lack of motivation or specific difficulties encountered that could impact one's adherence.⁶ To the best of our knowledge, this is the first systematic review that characterises patient-reported outcome measures (PROMs) of medication non-adherence, and distinguishes between intentional and unintentional causes. For the purpose of this review, intentional non-adherence is defined as instances when a patient is in a conscious and aware state of mind, and subsequently decides against following the recommendations of healthcare professionals.⁷ The patient is mindful of his or her decision, and had consciously

weighed the pros and cons of adhering to treatment. Unintentional or sporadic non-adherence, in contrast to intentional causes, is consequential to a passive process i.e., unlikely associated with one's implicit judgement.⁸ Patients can unintentionally non-adhere to their medication, i.e., when forgetful, careless, or have limited physical dexterity.

The aim of the systematic review was to critically appraise and synthesise PROMs in order to categorise their data into intentional and unintentional non-adherence to medication for chronic illnesses. The scope of this review is threefold: first, to establish studies where the level of non-adherence to medication was scored using validated and published self-reported measures (where adherence was reported, the scoring was reversed); second, to categorise each of the measure's items/criteria (adherence related) to one of the three process domains: *behaviour*, *barrier* or *belief*, and to one of the three outcome domains: intentional, unintentional, or mixed; third, to categorise every measure into intentional, unintentional or mixed, based on the dominance or leading domain of its criterion item.

The term, 'medication-taking conduct' shall be used henceforth, and is defined as whether or not a patient is capable of taking medication in a manner judged to be congruent with the governing norms.

METHODS

Design

This review was developed and reported considering the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA-2020) checklist⁹ (checklist in online supplemental appendices 1 and 2) and in accordance with the COnsensus-based Standards for the selection of health Measurement INstruments 2018 (COSMIN-2018) guideline for systematic reviews of PROMs¹⁰ (see section on assessment of methodological quality). The protocol for this systematic review is available at <https://doi.org/10.5061/dryad.8cz8w9gsq>.

Search strategy

The search strategy was aimed at retrieving articles published in the English language, on validated patient-reported outcomes, which were direct reports from patients about their medication-adherence status. Grey literature was excluded from the search criteria. The following databases were searched from January 1980 until 1 March 2022: MEDLINE (EBSCO), EMBASE (EBSCO), CINAHL (EBSCO), International Pharmaceutical Abstracts (EBSCO) and the Cochrane Library. We combined three groups of keywords: those relating to patient-reported outcomes (e.g., self-report\$, patient-report\$), those relating to conformity towards instructions pertaining to medication taking (e.g., complian\$, adheren\$, non-adheren\$, poor adherence) and those relating to psychometric measures of adherence (e.g., validity, reliability, construct, instrument). The full

strategy is available in online supplemental appendix 3. In the MEDLINE query strings, for example, we used free texts and keywords, and expanded the medical subject headings terms. The search terms included in the search strategy were agreed by two experts in the field of chronic illnesses (clinician) and COSMIN psychometric properties (biostatistician). The sensitivity search filter developed by Terwee *et al*¹¹ was adapted and used on all the databases. All selected records were uploaded and managed within EndNote X20 (Clarivate Analytics, Philadelphia, PA, USA).

Eligibility

Initially, the items for each measure were generated and content validity assessed. The research must measure what it claims to have measured, i.e., the construct of each measure must be valid for the data to be valid. Subsequently, the scale was constructed, the questions pretested, survey administered, number of items reduced and the number of factors the scale captured was studied. During the evaluation phase of the scale, the number of dimensions, reliability and validity were assessed.

We report on the types of validity measured in the quantitative studies. For example, whilst one study described the process of developing the measure's scale, other studies assessed the reliability and validity in various settings. In such cases where several studies used the same PROM, attempts were made to select the study in which the PROM was first featured or developed and validated.

Additionally, the following criteria were considered:

Inclusion criteria

1. Articles describing patient-reported and validated medication non-adherence measures development and/or validation.
2. Each item/criterion/subscale of a measure is guided by a statement or close-ended question. If the question is open-ended, the response is dichotomised.
3. At least two psychometric properties (reliability and/or validity) were assessed.
4. Included a proxy measure (employed a direct or indirect method to correlate adherence level with that evaluated by the measure).

Exclusion criteria

1. Articles where the scoring method or criteria for distinguishing the level or type of non/adherence could not be sourced.
2. Studies published only as abstracts or protocols.
3. PROMs' items consisting of open-ended questions which were without a method of rating or scoring the adherence measure. This is because without the specification for scoring (for example, an answer of 'yes' carried one mark, towards the sum score), an overall assessment of adherence, i.e., poor, moderate or good, could not be performed.
4. Translation from an original English version into a different language.

All titles and abstracts were independently screened by two reviewers, MLF and KMS. To identify relevant papers, the reference lists for articles that met the inclusion criteria were then reviewed. The reviewers were trained and a pilot with 30 papers was performed to guarantee an inter-reviewer agreement (until a kappa score of ≥ 0.75 was attained). Reasons for exclusions at the full-text screening process were recorded and discrepancies at any stage were resolved through discussions or a third reviewer consulted (KAMI) to reach a consensus.

A PRISMA flow chart summarises the process of selection (figure 1).

Data extraction and tabulation

Two reviewers (MLF and KMS) independently extracted the following data, where available, from the included articles:

- ▶ General characteristics of the study setting (year of publication, age, country).
- ▶ Characteristics of disease or condition: disease or condition studied, characteristics of the diseased respondents.
- ▶ PROMs' characteristics: methods of administration, availability of electronic administration, response scale, domains, scoring, number and type of items, proxy measures of adherence (indirect and direct methods).
- ▶ Quality assessment of the psychometric properties of the PROMs (statuses on reliability and validity of measure/instrument).

Data from each study were tabulated using a standardised and pretested Word data collection form which was used for the purpose of achieving reliable inter-rater scores (online supplemental appendix 4). The corresponding author of the included articles was contacted via email for clarification or to request for additional information on any missing or unclear data. For the purpose of reporting, all terms related to adherence, such as compliance and concordance, were standardised and reported as adherence.

Data synthesis and analyses

Eligibility criteria

- ▶ Characteristics of participants: patients with chronic diseases and/or require drug therapy, including but not limited to recipients of renal transplants.
- ▶ Characteristics of the proxy measures: used another direct (e.g., biomarkers) or indirect (e.g., pill count, electronic monitors) method in addition to administering the PROM.
- ▶ Characteristics of the criterion items: statements, open or close-ended questions that can be binary coded, for example, medium and high adherence (adherent) versus low adherence (non-adherent).
- ▶ Characteristics of the process: analyses of primary data and coded into 'behaviour', 'barrier' or 'belief'.

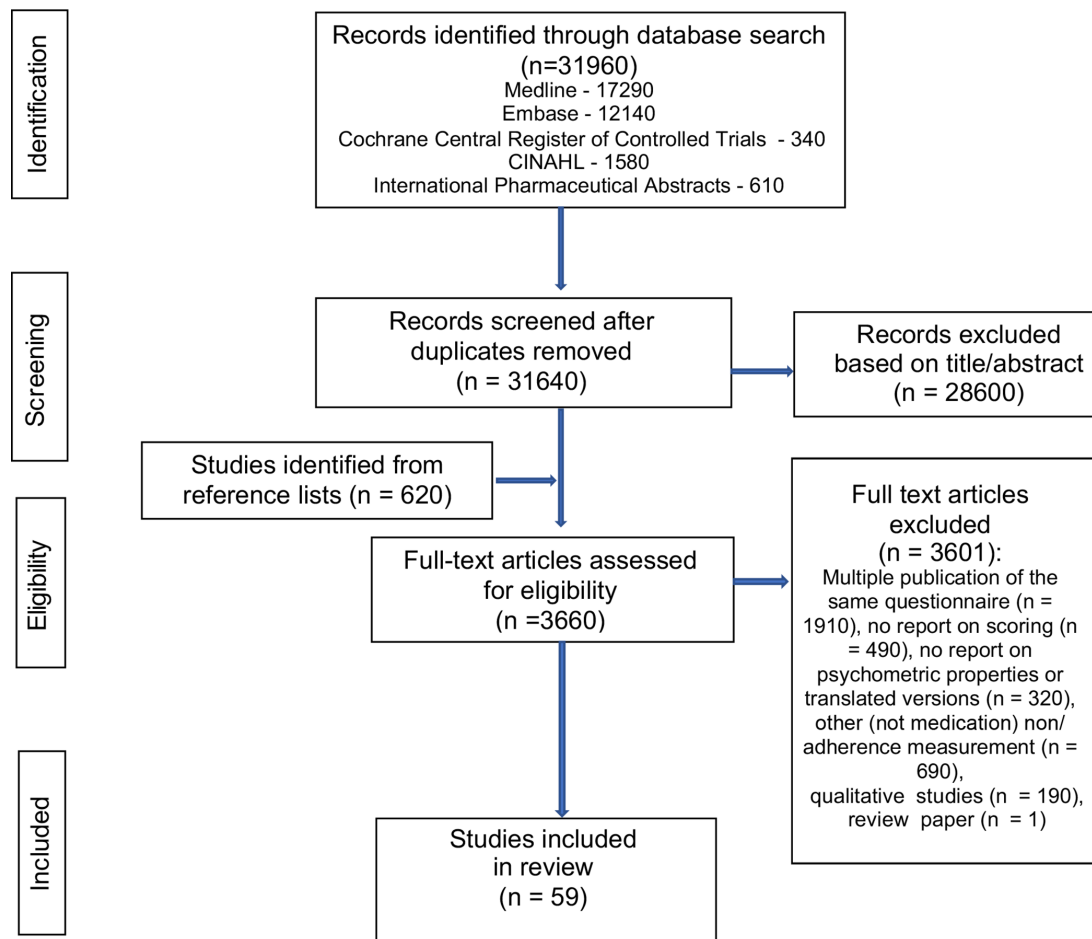


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for the systematic review. CINAHL, Cumulative Index to Nursing and Allied Health Literature.

- Characteristics of the outcome: analyses of primary data and coded into ‘intentional (I)’, ‘unintentional (UI)’ or ‘mixed (I/UI)’ non-adherence.

Item classification (binning)

Items within outcomes and process domains were classified as follows:

(1) Outcome domains: intentional, unintentional or not reported, and (2) process domains: behaviour, barrier or belief.

Guided by the Medication Adherence Model¹² and the Health Belief Model,¹³ items which were phrased to incorporate an objective reasoning or a predetermined consequence of a medication-taking decision were classified as *intentional*. An example of an item is, ‘Did you take less than the amount prescribed when you started to feel an unpleasant side effect?’

We classified items as *behaviour* when the medication-taking conduct was attributed to one’s own responsibility. Where instructions on timings, doses and frequencies are adhered to, this behaviour was habitual and reflected self-efficacy, self-management skills, motivation, social support and discipline. An example of an item is, ‘I was careful not to miss a dose’. A tangible *barrier* comprised items addressing physical or practical

aspects, for example, impaired manual dexterity, visual impairment, holidays, weekends, storage issues, prescription refills, cost and difficulty remembering, i.e., forgetting. *Belief* comprised items driving implicit judgements of the treatment or necessity beliefs—for example, perceptions, past negative experiences, knowledge on dosing, not taking when feeling better or taking only when feeling worse, trust and confidence in healthcare providers or the system. Online supplemental appendix 5 enlists the methods used to classify the PROMs’ items.

To ensure that the binning process was exhaustive, two independent reviewers (MLF and KMS) evaluated every PROM item for possible inclusion into any one of the three outcome and process domain categories depending on the nature of each criterion. The supplemental questions to the index question, for example, subquestions which explored reasons for ‘Did you forget to take your medication?’, such as ‘Did you forget to take when on holiday?’—*intentional (I)*’ were identified as an additional item, which was then assigned to a domain.

In the final data synthesis, MLF and KMS independently assigned each PROM an overall category

of either *intentional* (I), mixed of *intentional* and *unintentional* (I/UI) or *unintentional* (UI) depending on the coded items' dominant or leading domain. Items of studies which aimed at measuring adherence (vs non-adherence) were reverse worded and scored. Any discrepancies were resolved via discussions or via a third reviewer (KAMI).

Assessment of methodological quality

MLF and KMS performed the quality assessment of the psychometric properties of the PROMs independently using the COSMIN guidelines.¹⁰ Each PROM's development and its nine psychometric properties were assessed as 'doubtful', 'inadequate', 'adequate', 'good' or 'very good'. In addition, we used Terwee *et al's*¹¹ psychometric quality criteria to assess and rate each criterion as 'positive (+)', 'indeterminate (?)' or 'negative (-)'. In this review, we included PROMs which assessed and described a minimum of two psychometric properties.

Patient and public involvement

Patients or the public were not contacted nor involved in this study.

Statistical analyses

Kolmogorov-Smirnov test was used to test normality and subsequently the Spearman rank correlation was used to assess the correlation between outcome domain variables and process domains. Associations between measures' increased intentionality (dependent variable) and their increasing behaviour or barrier or belief criterion items (independent variables) were studied in regression analyses. Type of patient care (dichotomous variable—primary care vs specialised care) was included in a logistic regression model, while the number of behaviour, barrier or belief criterion items (continuous variables) was included in linear regression models. Regression models were adjusted for age. Results from the logistic and linear regression analyses are presented as an OR and standardised beta coefficients (β) with 95% CIs, respectively. The level of statistical significance was set at $p < 0.05$. The statistical analysis was performed with SPSS (version 24, SPSS Inc., Chicago, 147 IL, USA).

RESULTS

Search results and study characteristics

In total, 31,960 articles were retrieved from the five databases (figure 1). After removing duplicates, a further 28,600 articles were excluded based on the titles and abstracts (online supplemental appendix 6). Six hundred twenty relevant articles were identified from the reference lists. Hence, 3660 articles remained for full-text review. These articles were scrutinised against the paper's inclusion and exclusion criteria. At this stage, 3601 articles were eliminated. In the span of four decades, i.e., from January 1980

through to March 2022, a total of 59 PROMs relevant to adherence were extracted—one from each of the remaining articles ($n=59$).

In instances where a number of studies utilised the same PROM, subsequent reporting for that PROM was based on the initial study in which the measure first appeared. As for methodological quality, the studies fulfilled the inclusion criteria of adequate description of at least two psychometric properties, for example, its content, construct, structural validity and/or reliability. Criterion validity was achieved by all included studies. This is because studies on PROMs that were juxtaposed against another standard or proxy measure were included, which meant that the studies included presented a correlate, i.e., a corresponding indirect or direct method employed in parallel with the PROMs to assess adherence. For instance, the pill count method, using an additional PROM, or data mining from medication possession ratio or from a medication events monitoring system, or direct measurements of biomarker plasma levels were undertaken.

The studies were conducted across regions of North and South America, Europe, Australasia, and in 16 countries, i.e., the USA (24), the United Kingdom (8), Canada (4), France (3), the Netherlands (3), Spain (3), Malaysia (2), Australia (2), China (1), Brazil (2), Hungary (1), Switzerland (2), Belgium (1), Germany (1), Romania (1) and Turkey (1). The respondents' ages ranged from 18 to 88 years. The respondents included organ transplant recipients or patients receiving specified treatments for chronic conditions such as retroviral or cardiovascular diseases, kidney and endocrine disorders, ophthalmic conditions, gout, psychiatric illnesses or oncology. They were attending doctor appointments either at their general practice, or within secondary or tertiary care settings, or visiting primary healthcare facilities (community pharmacies, optometry services). Additionally, several patients were admitted from the emergency departments or hospitalised after surgery.

Evidence synthesis

Many of the PROMs were predominantly intentional followed by mixed intentionality and unintentional. These 59 PROMs yielded a total of 740 items/criteria that were related to adherence. Of those items, 572 were intentional in nature, 90 were unintentional and 78 did not report. Tables 1–3 depict the process and outcome domains assigned to individual criterion items, as well as the overall categorisation of each measure.

Outcome measures

Each measure or instrument was grouped into one of the three PROMs of non-adherence categories: table 1—*intentional*, I ($n=44$ of 59 instruments)^{5 6 14–55}; or table 2—*mixed*, I/UI ($n=13$ of 59 instruments)^{55–67}; or

Table 1 PROMs of intentional (I) non-adherence – n=44 of 59 measures, 593 items^{5,6} 14–55

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years):SD or IQR, correlates
1	Hogan <i>et al.</i> , 1983, Canada ¹⁴	Drug Attitude Inventory (DAI)	I=30	Belief (30-stop taking when feeling better or worse, etc)	<ul style="list-style-type: none"> 30-item questionnaire E.g., feeling like a zombie after taking medication, take only when sick, unnatural to take medications, do not need medications once feel better, medication makes no difference and will do no harm if not taken 	Habitual to occasional refusers of medications	Dichotomised scale high–low; yes=+2; no=+1	<ul style="list-style-type: none"> Good discriminant validity and reliability Test–retest reliability=0.82 Internal consistency, Cronbach's alpha=0.93 	<ul style="list-style-type: none"> Patients diagnosed with schizophrenia at a mental institution Mean age male: 40.0±12.8 Mean age female: 42.1±10.8 Juxtaposed against a 10-item (Van Puitten & May) scale and clinical change over 3 weeks, as measured by the Brief Psychiatric Rating Scale
2	Morisky <i>et al.</i> , 1986, USA ⁵	Morisky, Green and Levine (MGL) Scale or MAQ	I=3, not reported=1	Barrier (1- forgetting), Behaviour (1-careless), Belief (2-stopping medications when feeling better/worse)	<ul style="list-style-type: none"> 4-item questionnaire Forgetting, careless and stopping medications when feeling better or worse 	High, medium, low adherence	Dichotomised scale high–low; yes=0; no=1	<ul style="list-style-type: none"> Good concurrent & predictive validity Internal consistency, Cronbach's alpha=0.61 	<ul style="list-style-type: none"> Patients with hypertension in 2 outpatient clinics of a large teaching hospital Median age (IQR): 54 (46–62) Juxtaposed against blood pressure measurements
3	Shea <i>et al.</i> , 1992, USA ¹⁵	Modified MGL Scale or MAQ	I=2, not reported=3	Barrier (1-forgetting), Behaviour (2-careless, self-management 'Do you ever miss your medication for any reason?'), Belief (2-stopping medications when feeling better/worse)	<ul style="list-style-type: none"> 5-item questionnaire derived from the 4 items developed by Morisky <i>et al.</i> Minor modifications made to the wording of the original 4th question Added the 5th question: 'Do you ever miss taking your high blood pressure medication for any reason?' 	More adherent (n=87) or less adherent (n=115)	Dichotomised scale high–low; yes=0; no=1	<ul style="list-style-type: none"> Good concurrent & predictive validity Internal consistency, Cronbach's alpha=0.71 	<ul style="list-style-type: none"> Patients with incidence of hypertensive urgency and emergency Mean age: 54.7±11.5 in less adherent group; mean age: 59.8±11.8 in more adherent group Juxtaposed against blood pressure measurements and emergency admissions
4	Barber <i>et al.</i> , 1997, USA ¹⁶	The Comparison of Ophthalmic Medications for Tolerability (COMTOL) Questionnaire	I=3, not reported=1	4 questions on adherence: Barrier (1- forgetting), Behaviour (1-careless), Belief (2- stopped when feeling better, satisfaction)	<ul style="list-style-type: none"> 4 of 12 items assessed adherence Measured side effects and limitations in ADL /HRQoL, medication compliance and patient satisfaction with the medication 	Higher scores (4 and 5)=higher adherence	5-point Likert scale (where 5=I did not miss any dose, 4=rarely, 3=a few times, 2=fairly often and 1=usually, almost always and always)	<ul style="list-style-type: none"> Good-to-excellent internal consistency Cronbach's alpha=0.73–0.98 	<ul style="list-style-type: none"> Patients with open-angle glaucoma or ocular hypertension Mean age: 53.4 (range 33–82) Juxtaposed against drugs' known side effects and impact on ADL such as reading, driving or walking several blocks

Continued

Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years), SSD or IQR, correlates
5	Home and Weirman, 1999, UK ¹⁷	Beliefs about Medicine Questionnaire (BMQ)	I=18	Belief (18); specific items (10); general items (8)	<p>▲ 18-item cognitive representation of medication</p> <p>▲ 2 subscales: BMQ-specific scale, i.e., specific-necessity; specific-concerns; BMQ-General scale, i.e., general overuse and general harm</p>	Higher scores in BMQ-General scale meant an overall negative perception of medication; High scores in the Specific-Concerns scale represented the notion that adverse reactions were potentially harmful when taking medication on a regular basis; High scores in the Specific-Necessity scale represented patient's need to adhere to medication to maintain health.	5-point Likert scale with scores ranging from 4 to 20	<p>▲ Good discriminant validity; the diabetic group had higher specific-necessity psychiatric samples had higher specific-concerns score; patients attending the complementary clinic had higher scores for both general harm and overuse scales</p> <p>▲ Patients with asthma, diabetes and psychiatric conditions from hospital clinics and cardiac, general medical and renal (haemodialysis recipients) inpatients of hospitals</p> <p>▲ A matched group of patients seeking care from allopathic (community pharmacy) and complementary sources (homeopathy herbal clinic)</p> <p>▲ Age range: 45, 5–63.6</p> <p>▲ Juxtaposed against IPQ, RAM and the Sensitive Soma Scale</p>	
6	Svarstad et al, 1999, USA ⁶	Brief Medication Questionnaire	I=7, UI=2	Behaviour (7), Belief (2)	<p>▲ 9-item questionnaire to screen adherence and barriers to adherence</p> <p>▲ 5-item Regimen Screen that asks patients how they took each medication in the past week (How many times did you miss taking a pill?)</p> <p>▲ 2-item Belief Screen that asks about drug effects and bothersome features (How much it bothers you?)</p> <p>▲ 2-item Recall Screen about potential difficulties remembering (I stop or interrupt therapy, decrease the prescribed amount, take extra doses than prescribed)</p>	Positive score ≥ 1 indicated positive screen for potential non-adherence or recall barriers; Belief barriers—Type of non-adherence in past week according to MEMS electronic prescribing: repeat=took at least 20% over or under the prescribed amount; sporadic=took 1%–19% over or under the prescribed amount	4-point Likert scale (range=0–2)	<p>▲ Concurrent and predictive validity</p> <p>▲ Discriminant validity: Regimen and Belief Screens had 80%–100% sensitivity for 'repeat' non-adherence</p> <p>▲ Recall screen had 90% sensitivity for 'sporadic' non-adherence</p>	<p>▲ Recruited in 3 pharmacies if non-institutionalised</p> <p>▲ Mean age=52.6</p> <p>▲ Juxtaposed against pill count</p>
7	Thompson et al, 2000, Australia ⁸	Medication Adherence Rating Scale (MARS)	I=8, UI=2	Barrier (1-forgetting), Behaviour (1-careless), Belief (8-stopping medications when feeling better/worse)	<p>▲ 10-item questionnaire</p> <p>▲ E.g., thoughts are clearer, prevent getting sick, take when sick, and stop when feeling worse, feel unnatural/weird/ tired/sluggish</p>	Adherent or non-adherent	Dichotomised scale: yes=0, no=1	<p>▲ Good concurrent and predictive validity, good discriminant and content validity</p> <p>▲ Internal consistency, Cronbach's alpha=0.75</p>	<p>▲ Majority with schizophrenia, others with psychosis-like symptoms</p> <p>▲ Mean: 32.9+11.1</p> <p>▲ Juxtaposed against lithium levels and carer ratings of compliance</p>

Continued

Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years):SD or IQR, correlates
8	Duong et al, 2001, France ¹⁹	Patient Medication Adherence Questionnaire	I=42, UI=13, not reported=6	Barrier (13- ADL/ routine affected, sociodemographic), Behaviour (12- self-confidence, support, motivation), Belief (36- adverse effect, comorbidities, knowledge, attitude, perception)	<ul style="list-style-type: none"> 61-item questionnaire E.g., frequency of non-adherence, adverse effects, social support, psychological status, knowledge, attitudes, perception, alcohol and illicit drug use, socioeconomic status 	Adherent or non-adherent	4-point or 6-point Likert scale (ranging from strongly agree to strongly disagree)	Moderate predictive validity for half of the items (author suggested for future, PMAQ to focus on the variables identified as strong predictors of non-adherence)	<ul style="list-style-type: none"> Patients enrolled in Dijon Hospital AIDS day-care Mean age: 40 (range: 21-79) Juxtaposed against viral RNA level and plasma PI concentration
9	Horne and Weimann, 2002, UK ²⁰	Medication Adherence Report Scale (MARS-9)	I=6, UI=1, not reported=2	Barrier (1- forgetting), Behaviour (2- self-management), Belief (6- avoid if can, keep reserve medication, use when needed, alter dose, decide to miss, decide to take less)	<ul style="list-style-type: none"> 9-item questionnaire forgetting, alter dose, stop taking, use when breathless, decide to miss, take less, avoid, as reserve, use regularly 	Higher scores=higher adherence	5-point Likert scale (where 5=never, 4=rarely, 3=sometimes, 2=often and 1=very often)	<ul style="list-style-type: none"> Good construct and predictive validity Internal consistency Cronbach's alpha=0.85 	<ul style="list-style-type: none"> Community-based asthma clinics Mean age: 49.3±8.1; age range: 16-84 years Juxtaposed against IPQ and BMQ
10	Walsh et al, 2002, UK ²¹	Medication Adherence Self-Report Inventory (MASRI)	Not reported=12	Behaviour (12-self-management, commitment, motivation)	<ul style="list-style-type: none"> 12 items with 2 themes First part: 5 questions on missing doses and 1 question on VAS: Second part: 4 questions on timing of doses and 2 on VAS 	Adherent or non-adherent	Dichotomised scale: (yes=0; no=1) <ul style="list-style-type: none"> Two response formats: 5-point Likert scale and a VAS (ratio scale) First part related to the doses actually taken; VASDOSE=VAS for the proportion of doses taken in the preceding month 	<ul style="list-style-type: none"> Moderate predictive validity (1 item), good discriminant and content validity (VASDOSE) 	<ul style="list-style-type: none"> HIV-infected adults from public specialist clinics Age range: 18-65 Juxtaposed against MEMS, pill count and viral RNA level
11	De Klerk et al, 2003, Netherlands ²²	Compliance Questionnaire Rheumatology (CQR -19)	I=15, UI=4	Barrier (4-organiser used and stored strategically for ease of consumption, travelling/careless over weekends), Belief (15-trust in provider, stopping/alter medications when feeling better/worse/due to adverse effect/lack of efficacy)	<ul style="list-style-type: none"> 19-item questionnaire E.g., trust (and fear) in healthcare provider, fewer problems after taking medications, no alternatives, access to medication (practicalities and when on vacation) 	Unsatisfactory or good adherence	4-point Likert scale where 1=don't agree at all; 2=don't agree; 3=agree; 4=agree very much	<ul style="list-style-type: none"> Good discriminant and content validity, good reliability Internal consistency Cronbach's alpha=0.71 	<ul style="list-style-type: none"> Outpatients at the rheumatology wards of 3 hospitals Age range: 56-72 Juxtaposed against pill count using MEMS

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
12	Godin <i>et al.</i> , 2003, Canada ²³	Self-Reported Questionnaire Assessing Adherence to Antiretroviral Medication	I=1, not reported=5	<ul style="list-style-type: none"> Barrier (6- stop taking temporarily one or more antiretroviral medication during the last month) ▲ Pills missed the preceding day ▲ Pills missed the penultimate day ▲ Pills missed during the preceding 7 days ▲ Taking the initiative to take fewer pills of one or more of antiretroviral medications during the last month ▲ Had missed taking one or more antiretroviral pills during the last month 	<ul style="list-style-type: none"> ▲ 6-item questionnaire ▲ Patients reported antiretroviral pills (n) missed on the preceding and penultimate days ▲ 3 questions used as aided-recall tools for situations that might have hampered the regular adherence to medication during the preceding 7 days ▲ 2 questions were used to assess non-adherence during the preceding 7 days ▲ Last question referred to the preceding 30 days as a time frame 	Adherent or non-adherent (non-adherent if, for at least one measurement time, they reported having missed taking more than 5% of their pills on the preceding day)	5-point Likert scale (ranging from strongly disagree to strongly agree)	<ul style="list-style-type: none"> ▲ Adequate predictive validity with only one item ▲ Low sensitivity to detect increased viral load ▲ Internal consistency, Cronbach's alpha=0.76⁸⁶ 	<ul style="list-style-type: none"> ▲ HIV-infected patients from four clinics participated in a prospective longitudinal study ▲ Mean age: 43±8.39 ▲ Juxtaposed against change in viral load
13	Ogedegbe <i>et al.</i> , 2003, USA ²⁴	Medication Adherence Self-Efficacy Scale (MASES)	I=26	<ul style="list-style-type: none"> Barrier (20- ADL/routine/lifestyle access to medication), Behaviour (4- self-management refill, motivation, self-efficacy), Belief (2- adverse effect, take when feeling better) 	<ul style="list-style-type: none"> ▲ 26-item questionnaire measuring self-efficacy as a predictor of health behaviour ▲ E.g., how confident patients can take blood pressure medications on different occasions like when busy at home, when at work, when there is no one to remind, when worry about taking them for the rest of life, when they cause some side effects, when they cost a lot of money, when back home late from work, when do not have symptoms, when with family members, in public place, afraid of becoming dependent on them, afraid of affecting sexual performance, etc. and how confident patients can carry out tasks such as filling prescription on time whatever the cost, etc 	Adherent or non-adherent	3-point Likert scale (where 1=not at all sure, 2=somewhat sure, 3=very sure and 4=does not apply)	<ul style="list-style-type: none"> ▲ Good predictive and content validity ▲ Very good reliability Cronbach's alpha=0.95 	<ul style="list-style-type: none"> ▲ Ambulatory African-American patients with hypertension in 2 sequential phases in urban primary care ▲ Mean age: 55.7±12.8; 58.9±12.6 ▲ Juxtaposed against mean clinic blood pressure measurements

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years),SD or IQR, correlates
14	Atkinson <i>et al.</i> , 2004, USA ²⁵	Treatment Satisfaction Questionnaire for Medication (TSQM)	I=14	Barrier (3- ADL, convenience), Behaviour (4- confidence, motivation), Belief (7- adverse effect, knowledge)	<p>▲ 14 items</p> <p>▲ E.g., satisfaction regarding medication taking, experience with side effects, e.g., interfering with physical health and ability to function and mental function, convenience and confidence in medication taking</p>	Adherent or non-adherent	5-point or 7-point Likert scale or a VAS (ratio scale)	<p>Good reliability and construct validity</p> <p>▲ Internal consistency, Cronbach's alpha=0.85</p> <p>▲ Mean age: 50.5±13</p> <p>▲ Age range: 18–88</p>	<p>▲ 8 patient groups (arthritis, asthma, major depression, type I diabetes, high cholesterol, hypertension, migraine and psoriasis)</p> <p>▲ Mean age: 50.5±13</p> <p>▲ Age range: 18–88</p>
15	Dolder <i>et al.</i> , 2004, USA ²⁶	Brief Evaluation of Medication Influences and Beliefs (BEMIB)	I=7, UI=1	Barrier (1- forgetting), Behaviour (4-confidence, motivation), Belief (3- adverse effect, knowledge)	<p>▲ 8 items</p> <p>▲ E.g., feel better, prevent from hospitalisation, having a system that helps remember to take medications, forgetting, no problem getting medications from the hospital/ pharmacy and having a psychotic disorder that antipsychotics can improve</p>	Adherent or non-adherent	5-point Likert scale ranging from 1=completely disagree to 5=completely agree	<p>Acceptable construct validity, acceptable reliability</p> <p>▲ Internal consistency, Cronbach's alpha=0.63</p> <p>▲ Middle-aged and older outpatients at psychiatry clinics</p> <p>▲ Mean age: 57±12.1</p> <p>▲ Juxtaposed against DAI</p>	<p>▲ Middle-aged and older outpatients at psychiatry clinics</p> <p>▲ Mean age: 57±12.1</p> <p>▲ Juxtaposed against DAI</p>
16	Chisholm <i>et al.</i> , 2005, USA ²⁷	Immunosuppressant Therapy Barrier Scale (ITBS)	I=13	Barrier (2- ADL, socioeconomic), Belief (11- adverse effect, frequency, and doses)	<p>▲ 13-item questionnaire and frequency per day, cannot tell if immunosuppressants are helping, skipping doses when out of town/feel good/when think there may be side effects, missing doses when depressed, confused/ don't understand about how/when to take medications, skip when short of money</p>	Adherent or non-adherent	5-point Likert scale ranging from 1=strongly disagree to 5=strongly agree	<p>Moderate construct and concurrent validity</p> <p>▲ Internal consistency, Cronbach's alpha=0.91</p> <p>▲ Patients who underwent transplant and on immunosuppressant therapy</p> <p>▲ Mean age: 52.2±14.1; 54.79±14.3</p> <p>▲ Juxtaposed against graft rejection</p>	<p>▲ Patients who underwent transplant and on immunosuppressant therapy</p> <p>▲ Mean age: 52.2±14.1; 54.79±14.3</p> <p>▲ Juxtaposed against graft rejection</p>

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years):±SD or IQR, correlates
17	Liu <i>et al</i> , 2006, USA ²⁸	Adherence to antiretroviral therapy	I=9, not reported=3	Barrier (3- forgetting), Behaviour (4- self-efficacy, support for taking antiretroviral), Belief (5- values placed on antiretroviral, healthcare providers, knowledge on resistance to antiretroviral)	<p>▲ 12 items on adherence</p> <p>▲ E.g., forgetting within 3 or 7 days, 'over the past 3/7 days, how many times did you miss a dose of (this medication)?' 3 domains: (1) medication regimen descriptions (e.g., "How many pills has your provider asked you to take each time?"), (2) medication regimen timing (e.g., "How long have you been on antiretroviral medication?") and (3) attitudinal factors (e.g., "Taking HIV medication is too much trouble for what you get out of it.")</p>	Adherent or non-adherent — Fraction of the doses of medications taken divided by the doses of medication prescribed. Adherence was expressed as a percentage and capped at 100%	3-point Likert scale ranging from 1=none of the time, 2=sometimes, 3=all the time	Good criterion and construct validity	<p>▲ 2 prospective longitudinal clinical investigations conducted at 5 HIV clinics</p> <p>▲ Mean age: 38.76±8.1</p> <p>▲ Juxtaposed against pill count, self-report, serum antiretroviral levels, MEMS and medication diaries</p>
18	George <i>et al</i> , 2006, Australia ²⁹	Beliefs and Behaviour Questionnaire (BBQ)	I=23, UI=2	Barrier (8- forgetting, confusion, lifestyle changes/storage/routine, refill prescriptions), Behaviour (1- follow strictly), Belief (16- satisfaction with healthcare provider, stop taking depending on mood)	<p>▲ 25 items on adherence</p> <p>▲ E.g., experience/beliefs, physical barriers, confusion on medications, make changes to suit lifestyle and mood</p>	Adherent or non-adherent	5-point Likert scale where 1=not at all and 5=extremely	Good validity and reliability	<p>▲ Ambulatory patients with chronic lung diseases</p> <p>▲ Mean age: 71.1±8.7</p> <p>▲ years</p> <p>▲ Juxtaposed against MARS</p>
19	Weitzels <i>et al</i> , 2006, Netherlands ³⁰	Maastricht Utrecht Adherence in Hypertension Questionnaire (MUAH)	I=17, UI=2	Barrier (3- forgetting, busy lifestyle), Behaviour (3- careless, lack of support, and discipline, unsure), Belief (13- stop taking when feeling better or worse, would take alternative, knowledge, aversion towards medication)	<p>▲ 19 items on medication adherence</p> <p>▲ E.g., positive attitude towards healthcare and medication, lack of discipline and aversion towards medication (MUAH)</p>	Adherent or non-adherent	7-point Likert scale where 1=totally disagree to 7=totally agree	Good convergent validity	<p>▲ Patients on medication for hypertension and part of a randomised clinical trial from 2 regions in the Netherlands</p> <p>▲ Age range: 55–75</p> <p>▲ Juxtaposed against the BMO, pharmacy refill records and MEMS</p>
20	Glass <i>et al</i> , 2006, Switzerland ⁴⁶	Swiss HIV Cohort Study Adherence Questions (SHCS-AQ)	Not reported=2	Behaviour (2- self-management)	<p>▲ 2 items on adherence</p> <p>▲ Part 1: (1) How often did you miss a dose in the last 4 weeks? and (2) Did you have a period of no drug intake for >24 hours in the last 4 weeks? Yes/ No</p> <p>▲ Part 2: VAS</p>	Adherence defined in terms of missed doses (0, 1, 2 or >2) in the previous 28 days	Timing: daily, more than once a week, once a week, once every second week, once a month, never	Good concurrent and predictive validity	<p>▲ Outpatients from clinics of participating HIV centres, associated hospitals or specialised private practices</p> <p>▲ Mean age: 41.4±8.3</p> <p>▲ Juxtaposed against HIV viral load</p>

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
21	Mannheimer <i>et al.</i> , 2006, USA ³¹	Center for Adherence Support Evaluation (CASE) Adherence Index	I=1, not reported=2	Barrier (1- difficult), Behaviour (2- self-management)	<p>▲ 3-item questionnaire E.d., a composite (sum) of 3 measures of antiretroviral therapy, difficulty taking on time, average number of days per week at least 1 dose missed, last time missed at least one dose</p> <p>▲ E.d., a composite (sum) of 3 measures of antiretroviral therapy, difficulty taking on time, average number of days per week at least 1 dose missed, last time missed at least one dose</p>	Adherence level categorised as 100%, 80%–99% and <80%	Timing: all, most, about half, very few, none in the past 7 days	<p>▲ Participants in a longitudinal, prospective cross-site evaluation of 12 adherence programmes throughout the USA</p> <p>▲ Mean age: 40.1±8.6</p> <p>▲ Juxtaposed against HIV RNA level</p>	
22	Risser <i>et al.</i> , 2007, USA ³²	The Self-Efficacy for Appropriate Medication Use Scale (SEAMS)	I=13	Barrier (4- fill Rx, keep to appointment, inconvenience, routine), Behaviour (2- no social support, discipline), Belief (7- stop taking or worse, alternative, knowledge, adverse effect towards medication)	<p>▲ 13 items from 21 on adherence, e.g., self-efficacy in adhering to prescribed medications</p>	Adherent or non-adherent	3-point Likert scale (where 1=not confident, 2=somewhat confident, and 3=very confident)	<p>▲ Good construct validity</p> <p>▲ Internal consistency, Cronbach's alpha=0.89</p>	<p>▲ Patients with coronary heart disease (CHD) and other comorbid conditions</p> <p>▲ Mean age: 63.8±10.4</p> <p>▲ Juxtaposed against Morisky scale</p>
23	Gehl <i>et al.</i> , 2007, USA ³³	Single-item measure of self-reported adherence	I=1	Behaviour (1- discipline)	<p>▲ Single item</p> <p>▲ Strictly following the prescribed frequency</p>	Adherent or non-adherent, Non-adherence=taking medications as prescribed 75% of the time or less	5-point Likert scale (where 1=all of the time and 5=less than half the time)	<p>▲ Good predictive validity</p>	<p>▲ Outpatients with stable CHD</p> <p>▲ Mean age: 64±11</p> <p>▲ Juxtaposed against cardiovascular events (CHD death, MI or stroke)</p>
24	Prado <i>et al.</i> , 2007, Brazil ³⁴	Self-report on adherence	I=1	Behaviour (1- discipline)	<p>▲ Single item</p> <p>▲ Strictly following the prescribed frequency, if not, justify with reason</p>	Adherent or non-adherent	Dichotomised scale: yes=0, no=1	<p>▲ Moderate predictive validity</p>	<p>▲ Primary care hypertensives</p> <p>▲ 54% aged >60</p> <p>▲ Juxtaposed against pill count</p>
25	Byerly <i>et al.</i> , 2008, USA ³⁵	Brief Adherence Rating Scale (BARS)	Not reported=4	Behaviour (4- self-management, commitment, motivation)	<p>▲ 4 items</p> <p>▲ 3 items (number of doses missed in a day, in a month, and reduced dose, if any)</p> <p>▲ 1-item VAS to assess the proportion of doses taken in the past month (0%–100%)</p>	Adherent or non-adherent	Nominal scale: number of days patient did not take or took less over past 1 month and the proportion of doses taken by the patient in the past month (0%–100%)	<p>▲ Good concurrent and predictive validity, excellent reliability</p> <p>▲ Internal consistency, Cronbach's alpha=0.92</p>	<p>▲ Outpatients with schizophrenia and schizoaffective disorder from public mental health clinics</p> <p>▲ Mean age: 44.3±9.1; age range: 21–59</p> <p>▲ Juxtaposed against MEMS</p>
26	Kerr <i>et al.</i> , 2008, Canada ³⁶	Self-reported HAART adherence	Not reported=1	Behaviour (1- self-management)	<p>▲ Single item</p> <p>▲ Frequency of taking medication in the last 6 months</p>	Adherent or non-adherent	5-point Likert scale (where 1=occasionally (<25%) and 5=always (100%))	<p>▲ Moderate predictive validity</p>	<p>▲ HIV-infected patients enrolled in the Vancouver Injection Drug Users Study</p> <p>▲ Mean age: 40±6.8</p> <p>▲ Juxtaposed against pharmacy refill data</p>

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years), SD or IQR, correlates
27	Deschamps <i>et al</i> , 2008, Belgium ³⁷	European HIV Treatment Questionnaire (EHTQ)	Not reported=2	Behaviour (2- self-management)	<p>▲ 2-item questionnaire on frequency and doses</p>	Non-adherence was defined as (1) adherence: the percentage of doses taken compared with the total doses prescribed and (2) drug holidays: no medication intake for 24 hours+50% of the dosing interval of the medication	Nominal scale: either less than 100% or 1 or more days per 30 days	Poor concurrent validity	<p>▲ HIV-positive adults on antiretroviral therapy followed up at a university hospital</p> <p>▲ Mean age: not presented</p> <p>▲ Juxtaposed against SHCS-AQ and MEMS</p>
28	Lu <i>et al</i> , 2008, USA ³⁸	Self-reported antiretroviral adherence questionnaire	I=1, not reported=4	Behaviour (5- self management, commitment)	<p>▲ 5-item questionnaire</p> <p>▲ 2 items (past 3 days and 7 days: number of doses missed)</p> <p>▲ 3 items (past 1 month: frequency: 'Did you take all your medications all the time?'; percentage: 'What percentage of the time were you able to take your medications exactly as your doctor prescribed them?'; and ability: 'Rate your ability to take all your medications as prescribed'</p>	Adherent or non-adherent	Both nominal scale and rated on 6-point Likert scale where for (1) frequency: 1=none of the time to 6=all the time; (2) percentage of the time, were able to take medications exactly as prescribed (0%–100%); (3) ability to take all medications as prescribed (very poor–excellent)	Good convergent and predictive validity	<p>▲ Patients on antiretrovirals from academic medical centres, a community health centre, a general practice based in an academic medical centre and a private infectious diseases practice</p> <p>▲ Mean age: 42 (SD not available)</p> <p>▲ Juxtaposed against MEMS</p>
29	Kripalani <i>et al</i> , 2009, USA ³⁹	Adherence to Refills and Medications Scale (ARMS)	I=11, UI=1	<p>Barrier (7- fill Rx, keep to appointment, inconvenience, cost),</p> <p>Behaviour (3- carelessness, discipline, ability to follow instruction),</p> <p>Belief (2- stop taking when feeling better or worse)</p>	<p>▲ 12-item scale</p> <p>▲ 2 subscales: (a) adherence to the filling or refilling of prescriptions on schedule; (b) adherence to taking medications</p>	Adherent or non-adherent	4-point Likert scale where 1=none to 4=all	<p>Good criterion and predictive validity</p> <p>▲ Internal consistency, Cronbach's alpha=0.81</p>	<p>▲ Patients with CHD attending a primary care clinic</p> <p>▲ Mean age: 63.7±10.3</p> <p>▲ Juxtaposed against Morisky scale, medication refill adherence and blood pressure measurements</p>
30	Duggan <i>et al</i> , 2009, USA ⁴⁰	Adherence to antiretroviral therapy	I=30	<p>Barrier (7- storage, physical difficulty, routine),</p> <p>Behaviour (7- support, motivation, self-management),</p> <p>Belief (16- values placed on antiretrovirals, healthcare providers, knowledge on antiretrovirals, stigma)</p>	<p>▲ 30 items</p> <p>▲ 3 categories of questions: (a) acceptance/avoidance; (b) completely tethered and (c) motivation</p> <p>Have you ever thought having HIV was a 'punishment'? Do you feel that your medicines are hard to take? Do you believe the medicines for HIV that you take are working for you?</p>	Adherent or non-adherent	Positive/negative–add 1 mark for positive and minus 1 for negative	<p>Good criterion and predictive validity</p>	<p>▲ Patients seeking treatment for HIV infection</p> <p>▲ Age range: 18–51</p> <p>▲ Juxtaposed against change in viral load</p>

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age, (years)±SD or IQR, correlates
31	Gabriel and Violato, 2010, Canada ⁴¹	Antidepressant Adherence Scale (AAS)	I=3, not reported=1	Barrier (1- forgetting), Behaviour (1- careless), Belief (2- stopping medications when feeling better/worse)	<ul style="list-style-type: none"> ▲ 4-item questionnaire Forgetting, careless and stopping medications when feeling better or worse ▲ Measure the frequency of any or all these omissions during the 4 weeks 	High, medium, low adherence	Nominal scale: high-low	Moderate concurrent & predictive validity (adherence level correlated with physicians knowledge and attitude scores); acceptable reliability <ul style="list-style-type: none"> ▲ Internal consistency, Cronbach's alpha=0.66 	<ul style="list-style-type: none"> ▲ Patients treated as outpatients at university hospital following referrals by their family physicians ▲ Mean age 52±11.6 ▲ Juxtaposed against depression literacy (knowledge and attitudes towards depression and its treatments); 2 instruments completed: MCC knowledge test of depression and its treatment, and a Likert self-report questionnaire to measure attitudes toward depression and its treatments
32	Umri <i>et al.</i> , 2014, USA ⁴²	Medication Adherence Reasons Scale (MARS)	I=15	Barrier (8- access, challenges in physical dexterity, routine), Behaviour (2- self-management, support), Belief (5- attitude, side effects, number of concurrent medications, healthcare provider trust, treatment efficacy)	<ul style="list-style-type: none"> ▲ 15 items related to medication adherence E.g., management, belief, multiple medications, availability, forgetfulness 	Adherent or non-adherent	5-point Likert scale where 1=none of the time to 5=all of the time	Moderate concurrent & predictive validity; acceptable reliability <ul style="list-style-type: none"> ▲ Internal consistency, Cronbach's alpha=0.8-0.9 	<ul style="list-style-type: none"> ▲ Internet users taking cholesterol-lowering medications or asthma maintenance medications or both ▲ Mean age: asthma: 48.7; hypercholesterolaemia: 59.4 ▲ Juxtaposed against Morisky scale
33	Muller <i>et al.</i> , 2015, Germany ⁴³	Adherence Barrier Questionnaire (ABQ)	I=14	Barrier (3- forgetting, challenges, cost), Behaviour (4- careless), Belief (7- stopping medications when feeling better/worse, knowledge)	<ul style="list-style-type: none"> ▲ 14 items Intentional adherence barriers (3) Medication-related barriers (4) Unintentional adherence barriers (4) Healthcare system-related barriers (3) 	Adherent or non-adherent	4-point Likert scale where 1=strongly disagree and 4=strongly agree	Good construct validity and reliability <ul style="list-style-type: none"> ▲ Internal consistency, Cronbach's alpha=0.82 	<ul style="list-style-type: none"> ▲ Patients with atrial fibrillation from several general practices - mean age: 72.7±9.3 ▲ Juxtaposed against anticoagulation quality achieved by patients treated with oral anticoagulants
34	Kleppe <i>et al.</i> , 2015, Netherlands ⁴⁴	The Probabilistic Medication Adherence Scale (ProMAS)	I=7, UI=4, not reported=7	Barrier (2- away from home, Rx refill), Behaviour (11- self-management), Belief (5- trust in doctor)	<ul style="list-style-type: none"> ▲ 18 items E.g., forgetting, take at a later moment, stopped, did not take, have taken all that should, take exactly the same time every day, never changed frequency of use 	Adherent or non-adherent	Dichotomised scale high-low; yes=0; no=1	Good discriminant validity and reliability	<ul style="list-style-type: none"> ▲ Elderly receiving medications for chronic conditions recruited by a Dutch agency ▲ Mean age: 68±7.1 ▲ Juxtaposed against MARS

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years):SD or IQR, correlates
35	Sidorikiewicz <i>et al.</i> , 2016, France ⁴⁵	Sidorikiewicz adherence tool	I=2, not reported=3	Barrier (2- holiday/weekends, forgetting), Behaviour (3- self-management, timing careless)	<ul style="list-style-type: none"> ▲ 5 items ▲ (a) Early discontinuation of the drug; (b) systematic omission of a daily dose (e.g., at noon); (c) drug holidays; (d) skipping doses and (e) schedule errors 	High, good, moderate, poor, very poor adherence	Nominal scale assisted by pictogram; Never to sometimes (6-7 days or more)	Good construct validity and test-retest reliability	<ul style="list-style-type: none"> ▲ Consecutive patients in 6 general practices and 6 care units of university hospitals ▲ Median age (IQR): 59.1 (42.5-70.6) ▲ Juxtaposed against (1) Liu instrument⁴⁶; (2) the Adherence Estimator; (3) Physician's rating of patient's adherence; (4) Morris scale and (5) Treatment Burden Questionnaire
36	Weinman <i>et al.</i> , 2018, UK ⁴⁷	Intentional Non-Adherence Scale (INAS)	I=22	Barrier (3- inconvenience, schedule, cost) Behaviour (1- self-management) Belief (18- knowledge, treatment efficacy, perception, trust in healthcare provider, attitude)	<ul style="list-style-type: none"> ▲ 22 items on adherence ▲ E.g., 'To see if I really need it', 'Because I don't like chemicals in my body', 'Because my body is sensitive to the effects of the medicine', 'Because I think the drug might become less effective over time' and 'Because it reminds me that I have an illness' 	Adherent or non-adherent	5-point Likert scale where 1=strongly disagree, 2=disagree, 3=neutral, 4=agree, 5=strongly agree	<ul style="list-style-type: none"> ▲ Good construct and moderate predictive validity ▲ Internal consistency, Cronbach's alpha=0.93 	<ul style="list-style-type: none"> ▲ Patients from 3 different outpatient clinics (hypertension, oncology and gout) ▲ Mean age: hypertension, 56.2; oncology, 62.2; gout, 61.6 ▲ Juxtaposed against a biomarker measure and with self-reported adherence (BMQ, PAM, BIPQ)
37	Tan <i>et al.</i> , 2019, China ⁴⁸	A Chinese and Western medication adherence scale	I=29, UI=2	Barrier (1- forgotten) Behaviour (4- self-management, careless) Belief (26- knowledge, side effects, dose, stopped taking when feeling better/worse)	<ul style="list-style-type: none"> ▲ 31 items ▲ Measures knowledge, belief and behaviour 	Higher scores, better the patients' medication adherence.	Nominal scale: MCQ options A-E	<ul style="list-style-type: none"> ▲ Good content and construct validity; excellent internal consistency and test-retest reliability ▲ Internal consistency Cronbach's alpha=0.92 	<ul style="list-style-type: none"> ▲ Patients with CKD who kept long-term follow-up visits to the chronic disease department of a hospital ▲ Age range age: 18-80 ▲ Juxtaposed against MGL Scale
38	Sustersic <i>et al.</i> , 2019, France ⁴⁹	The Global Adherence Scale for Acute Conditions (GASAC) Questionnaire	I=21, not reported=3	Barrier (2- forgetting, Rx refill), Behaviour (3- self-management), Belief (19- felt better/worse, confidence in healthcare providers, system)	<ul style="list-style-type: none"> ▲ 24 items about adherence <ul style="list-style-type: none"> - 3 index questions - 21 additional questions on reasons for non-adherence (self, healthcare provider and healthcare system reasons) ▲ E.g., forgetting, did not refill Rx, issues with treatment regimen, did more harm than good, felt better or worse, confidence in healthcare providers and system 	Low, highly adherent	Ordinal scale where 1=no; 2=rather not; 3=rather yes; 4=yes -final score was expressed as the ratio between 0 and 1	<ul style="list-style-type: none"> ▲ Good content and construct validity ▲ Internal consistency Cronbach's alpha=0.78 	<ul style="list-style-type: none"> ▲ Patients consulting a hospital emergency department ▲ Age range: 21-71 ▲ Juxtaposed against Girerd questionnaire

Continued

Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years):±SD or IQR, correlates
39	Hatah <i>et al.</i> , 2020, Malaysia ³⁰	Malaysia Medication Adherence Assessment Tool (MYMAAT)	I=9, not reported=3	Barrier (2- Rx refill), Behaviour (6- self-management, social support), Belief (4- did not take when felt better, did not see the significance, fear of side effects, lack of dosing knowledge)	<ul style="list-style-type: none"> 12 items 5 constructs: <ul style="list-style-type: none"> Medication-taking behaviour Perceived utility of medications i.e., benefits, costs and efficacy Perceived barriers Perceived self-efficacy and social support Perceived severity and susceptibility of diabetes 	Higher scores indicated better adherence	5-point Likert scale where 5=strongly disagree to 1=strongly agree	Good content and construct validity, good-excellent reliability Internal consistency, Cronbach's alpha=0.91	<ul style="list-style-type: none"> Patients with diabetes who presented to primary and secondary care (public hospitals and clinics) Mean age: 57.2±10.8 Juxtaposed against SEAMS and MPR
40	Khatib <i>et al.</i> , 2020, UK ⁵¹	My experience of taking medicine (Mymeds) questionnaire	I=13, UI=1	Barrier (7- refill Rx, forgetting, physical dexterity), Belief (7- did not take when felt better, lack knowledge on dosing and side effects)	<ul style="list-style-type: none"> 14 items 6 sections: <ul style="list-style-type: none"> current medicines, understanding and satisfaction with medicines, concerns about medicines, practical barriers, fitting medicines into daily routine and adherence to secondary prevention medicine over the past month 	Adherent or non-adherent	<ul style="list-style-type: none"> 5-point Likert scale for how often each medicine was taken as prescribed in the past month (all of the time; nearly all of the time; most of the time; about half the time; less than half the time) 4-point Likert scale from 1=strongly agree to 4=strongly disagree for other items 	Good face validity	<ul style="list-style-type: none"> Patients prescribed with medicine for secondary prevention of CHD events at clinics Mean age 70.5±10.9 Juxtaposed against MMAS-8
41	Goh <i>et al.</i> , 2020, Malaysia ³⁴	Patient-Medication Adherence Instrument (P-MAI) and a Healthcare Professional-Medication Adherence Instrument (H-MAI)	I=24, not reported=2	Barrier (13- routine, forgetting, Rx refill, cost, other coexisting conditions, missed appointments, lack of privacy, confused about instructions), Behaviour (3- take less/more as directed), Belief (10- knowledge, relationship with healthcare provider, dosing, stopped taking when feeling better/worse, efficacy)	<ul style="list-style-type: none"> 26 items on patient-reported adherence (P-MAI-9) Adherence=2 items; Adherence/ belief=7 items and reason(s) for not taking medications as directed for the past 2 weeks=17 items 	Higher score indicates better adherence	5-point Likert scale where 1=strongly disagree to 5=strongly agree	Good content and construct validity Internal consistency, Cronbach's alpha=0.72	<ul style="list-style-type: none"> Patients diagnosed with DM, taking at least one oral hypoglycaemic agent and enrolled in tertiary-based primary care clinics Median age (IQR): 63 (57-69) P-MAI juxtaposed against H-MAI

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Table 1 Continued

No	Author, year, country	PROM/scale/rating/criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain; barriers (practical), behaviour (habit) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
42	Heaq <i>et al.</i> 2021, Switzerland ⁶³	Barriers to Oral short-Term antibiotic Adherence (BIOTICA)	I=15	Barrier (4- difficulty to swallow, forgetting, difficult to incorporate in daily life, no support from caregiver), Behaviour (3- no intention to take/intend to miss a dose), Belief (8- side effect/interactions, knowledge, unnecessary, unfamiliar with consequence, no trust in prescriber, information could not be understood / insufficient)	<ul style="list-style-type: none"> 15 items Barrier-items were in 10 of 11 theoretical domain framework and included environmental context and resources, knowledge, social influence, emotions, capabilities Intentions, memory, skills, beliefs about consequences and social, professional role and identity 	Higher scores indicated higher degree of non-adherence	5-point Likert scale where 1=strongly disagree to 5=strongly agree	<ul style="list-style-type: none"> Good content and construct validity Internal consistency Cronbach's alpha=0.72 Item correlation >0.2 (acceptable) 	<ul style="list-style-type: none"> Patients assessed before antibiotic initiation in the outpatient setting (pharmacies and surgeries) Mean age 51.53±16.7 (range: 19-85 years) Juxtaposed against pill count by MEMS REDCap
43	De Las Cuevas <i>et al.</i> 2021, Spain ⁶⁴	Patient Health Beliefs Questionnaire on Psychiatric Treatment	I=8	Belief (8- side effect/interactions, knowledge, unnecessary, unfamiliar with consequence, no trust in prescriber, information could not be understood / insufficient)	<ul style="list-style-type: none"> 17-item self-reported health beliefs scale, 2 subscales (8 items) were related to medications: <ul style="list-style-type: none"> Negative aspects of medication (pharmacophobia) Positive aspects of medication (pharmacophilia) 	Higher scores on each subscale indicate a stronger belief towards psychotropic treatment	6-point Likert scale where 1=totally disagree, 6=totally agree	<ul style="list-style-type: none"> Good construct validity and reliability 	<ul style="list-style-type: none"> Outpatients with schizophrenia and other psychiatric conditions Mean age 41.2±12 (n=212 for schizophrenia) and 44.5±14 (n=1160 for other mental disorders) Juxtaposed against Sidorkiewicz Adherence Tool
44	Seyma and Baysal, 2022, Turkey ⁶⁵	Scale for Compliance to the Treatment in Type II Diabetes Mellitus	I=7	Behaviour (3- anxious when time for insulin, schedules, medication intake, take regularly), Belief (4- knowledge on DM, consequence of condition, trust in healthcare, diet over medication)	<ul style="list-style-type: none"> 30-item self-reported adherence to type 2 DM treatment 	Good, moderate, poor adherence	5-point Likert scale where 1=strongly agree, 5=strongly disagree	<ul style="list-style-type: none"> Good content and construct validity Internal consistency, Cronbach's alpha=0.7 	<ul style="list-style-type: none"> Patients with DM presenting to the Internal Diseases and Endocrinology clinics of a hospital Mean age 54.6±9.5 Juxtaposed against Diabetes Health Literacy Scale

Number of measures, n=44 of 58; *Intentional*, I items=35; *Not reported*=67 items.

For a measure to be classified as *Intentional*, >30% of its items are to be *Intentional* and the remainder *Unintentional* and/or *Not reported* (if any).

*Some values were reported as median, range or not reported.

†All terms related to adherence, e.g., compliance is standardised and reported as adherence; Belief=326, Barrier=135, Behaviour=132 items.

ADL, activities of daily living; BIPQ, Brief Illness Perception Questionnaire; CKD, chronic kidney disease; DM, diabetes mellitus; HAART, Highly Active Antiretroviral Therapy; HRQL, health-related quality of life; IPO, Illness Perception Questionnaire; MAQ, Medication Adherence Questionnaire; MCC, multiple choice questions; MEMS, medication events monitoring system; Mi, myocardial infarction; MIMAS, Morisky Medication Adherence Scale; MPR, medication possession ratio; PAM, Patient Activation Measure; Ph, protease inhibitor; PMAQ, Patient Medication Adherence Questionnaire; PROMs, patient-reported outcome measures; RAM, Reported Adherence to Medication Scale; VAS, Visual Analogue Scale.



Table 2 PROMs of mixed *intentional/unintentional* (I/U) non-adherence — n=13 of 59 measures, 138 items ⁵⁵⁻⁶⁷

No	Author, year, country	PROM/scale/instrument criteria/instrument	Outcome measure, number of intentional or unintentional items (I, U), (not reported)	Process measure, item domain: barriers (physical/practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
1	Brooks <i>et al</i> , 1994, USA ⁵⁶	Brooks Medication Adherence Scale (BMAS)	I=8, UI=4	Barrier (1- forgetting), Behaviour (1- careless), Belief (10- stopping/alter medications when feeling better/worse/due to adverse effect/lack of efficacy)	<ul style="list-style-type: none"> ▲ 12-item questionnaire ▲ Forgetting, careless and stopping medications when feeling better and worse, stopping/alter due to adverse effects or apparent lack of efficacy 	High, medium, low adherence — whether patients took their medicine or used their inhaler at the prescribed times and in the prescribed amount	Dichotomised scale high–low yes=0; no=1	<ul style="list-style-type: none"> ▲ Good discriminant validity and reliability ▲ Internal consistency, Cronbach's alpha=0.93 	<ul style="list-style-type: none"> ▲ Pulmonary disease clinics ▲ 47% aged 50 or older ▲ Juxtaposed against physician rating of asthma severity
2	Kim <i>et al</i> , 2000, USA ⁵⁷	Hill-Bone Compliance to High Blood Pressure Therapy Scale	I=4, UI=2	Barrier (4- Rx refill, forgetting, miss appointments), Behaviour (1- careless), Belief (1- stopping when feeling better or worse)	<ul style="list-style-type: none"> ▲ 6 items related to medication-taking conduct as part of 14 items in 3 subscales ▲ E.g., forgetting, decide not to take, missing appointments to get prescription filled, run out of pills, skip medicine, stopping medications when feeling better or worse 	Adherent or non-adherent	4-point Likert scale (where 4=all the time, 3=most of the time, 2=some of the time and 1=never) Total scores=14–56	<ul style="list-style-type: none"> ▲ Good content, construct and predictive reliability ▲ Internal consistency, Cronbach's alpha=0.74 	<ul style="list-style-type: none"> ▲ Adults with hypertension enrolled in 2 separate clinical trials ▲ Mean age (trial 1)=41.3±5.3 ▲ Mean age (trial 2)=59.2±13.1

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Table 2 Continued

No	Author, year, country	PROM/scale/ rating/ criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (physical/practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
3	Lewis and Abell, 2000, USA ⁵⁸	Adherence Attitude Inventory (AAI)	I=16, UI=12	Barrier (12), Behaviour (8), Belief (8)	<ul style="list-style-type: none"> ▲ 28-item questionnaire ▲ E.g., forgetting to take, to refill prescriptions, forget to inform doctor about adverse effect, involvement of healthcare provider to assist adherence, fear of keeping to schedule, self-doubt, self-management, commitment - In the afternoon, I have a hard time remembering if I took my early dose of medication. - Even though I want to take my medication, I just forget to take it. - My medical provider wants me to participate in making decisions about my medicine. - Things get in the way of my taking my medication as prescribed. - I am committed to taking my medication even if it tastes bad or is hard to swallow 	Adherent or non-adherent	7-point Likert scale (ranging from none of the time to all of the time)	<ul style="list-style-type: none"> Good content and construct validity, good to acceptable reliability ▲ Internal consistency, Cronbach's alpha between 0.85 and 0.95 	<ul style="list-style-type: none"> ▲ Clients of AIDS service organisations and/or medical centres ▲ Mean age: 41±8.8 ▲ Juxtaposed against Multidimensional Quality of Life for Persons with HIV/AIDS and the General Perceived Self-Efficacy Scale

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Table 2 Continued

No	Author, year, country	PROM/scale/ rating/ criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (physical/practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
4	Ziegelmann <i>et al</i> , 2002, UK ⁵⁹	Transplant Effects Questionnaire (TxEQ)	I=2, UI=2, not reported=1	Barrier (3), Behaviour (1), Belief (1)	<ul style="list-style-type: none"> 5 items related to medication-taking conduct as part of 24 items E.g., do not take, sometimes forget to take, forget to take when busy, sometimes think do not need, find it difficult to adjust to taking, anti-rejection medicines 	Adherent or non-adherent	5-point Likert scale (ranging from strongly disagree to strongly agree)	<ul style="list-style-type: none"> Content validity established, acceptable reliability Internal consistency, Cronbach's alpha=0.79 	<ul style="list-style-type: none"> Patients registered at a teaching hospital Mean age: 45.2±14.5 Juxtaposed against self-efficacy
5	Knobel <i>et al</i> , 2002, Spain ⁶⁰	Simplified Medication Adherence Questionnaire (SMAQ)	I=2, UI=2, not reported=2	Barrier (4), Behaviour (1), Belief (1)	<ul style="list-style-type: none"> 6-item questionnaire E.g., forget, careless, stop taking if feel worse, did not take over the past weekend, how many days did not take any medicine at all over the past 3 months 	Adherent or non-adherent	Dichotomised scale: yes=0; no=1	<ul style="list-style-type: none"> Content, concurrent and predictive validity established, good reliability Internal consistency, Cronbach's alpha=0.75 	<ul style="list-style-type: none"> HIV-infected patients from 69 multicentres or hospitals Mean age: 35.8±7.9 Juxtaposed against MEMS
6	Greaves <i>et al</i> , 2005, UK ⁶¹	Patterns of Asthma Medication Use Questionnaire	I=3, UI=2, not reported=1	Barrier (2- forgetting, ADL/routine), Behaviour (2- careless, self-efficacy), Belief (2- lesser dose, stopped when feeling better)	<ul style="list-style-type: none"> 6-item questionnaire E.g., forgetting frequency and main reason for not taking, take regularly but less than recommended, decide each day whether to use it, depending on how I feel, stop taking when feeling better 	Adherent or non-adherent	Response coded into 4 categories: (1) regular=patients who take their medication regularly; (2) forgetting=those who forgot on two or more occasions per week, (3) low dosing=those who took medication regularly but at a reduced amount, (4) symptom directed=those who varied their strategy in response to symptom levels, in some cases stopping completely	<ul style="list-style-type: none"> Good criterion and construct validity 	<ul style="list-style-type: none"> Unscheduled asthma care visits and quality of life for adherent and non-adherent patient groups from a semirural GP practice Mean age: 42.1±10.6 Age range: 21–61 Juxtaposed against pharmacy records and clinical outcome (asthma)

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Table 2 Continued

No	Author, year, country	PROM/scale/ rating/ criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (physical/practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
7	Schroeder <i>et al.</i> , 2006, UK ⁶²	Adherence Self-Report Questionnaire (ASRQ)	I=2 (I always take at the same time)† I/UI=3 (knowingly/unknowingly), not reported=1 (I hardly take any medication)	Behaviour (6- self-management) ▲ I miss knowingly/unknowingly	▲ 6 items on adherence ▲ E.g., miss taking at specific times, knowingly or unknowingly	Adherent or non-adherent	6-point Likert scale where 1=perfect and 6=low	▲ Good content validity, moderate predictive validity ▲ Patients with uncontrolled hypertension from GP practices enrolled in an RCT ▲ Mean age: 67.9±10.3 ▲ Juxtaposed against MEMS	
8	Muñoz-Moreno <i>et al.</i> , 2007, Spain ⁶³	Self-Report Adherence Questionnaire (SERAD)	I=1, UI=1	Behaviour (1-discipline) ▲ Not having the medication on time ▲ for the reason for non-adherence, choose, either - Barrier ▲ Simply forget, routine, holidays/weekend, clash with other medications, presence of others not within CoC, refill Rx OR - Belief (1)‡ ▲ Attitude, adverse events, not willing, misunderstanding with prescription/prescriber	▲ 2 items ▲ 2 types of indexes: - number of times the patient failed to take the medication (adherence percentage) - the patient failed to observe the intake conditions (intake conditions observed percentage), specifies any of the 13 reasons for non-adherence	Adherent or non-adherent	Nominal scale 1. Adherence with regard to the doses missed during the last week, last month and last 3 months, % 2. Reasons for non-adherence during the last week, last month and last 3 months, % 3. Adherence with regard to the times that intake conditions were not observed during the last week, % 4. Reasons for intake conditions not observed during the last week, last month and last 3 months	▲ HIV-infected outpatients ▲ Mean age: 38±10 ▲ Juxtaposed against pill count, plasma level, MEMS	
9	Chesney <i>et al.</i> , 2000, USA ⁶⁴	Adult AIDS Clinical Trials Group (AACTG) Adherence Instrument	I=6, UI=6, not reported=5	Barrier (6- ADL/routine affected), Behaviour (7- self-management, motivation), Belief (4- stopping medications when feeling better/worse)	▲ 17-item questionnaire ▲ 2 sets: 'Adherence to Anti-Retroviral Medications' and 'Baseline Correlates of Adherence' - 5 items on recent and distal adherence (missed doses) - 12 items on reasons for missed dose	Adherent or non-adherent	Rated on 4-point Likert scale (where 4=never, 3=rarely, 2=sometimes and 1=often)	Excellent reliability, good content, convergent and predictive (construct) validity ▲ Internal consistency, Cronbach's alpha ≥0.8 ▲ Patients enrolled in 10 AIDS Clinical Trials Units in the USA ▲ Mean age: 39 (range: 20-72) ▲ Juxtaposed against pill count using MEMs and viral load	

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Table 2 Continued

No	Author, year, country	PROM/scale/ rating/ criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (physical/practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
10	Fernandez <i>et al.</i> , 2008, USA ⁶⁵	Medication Adherence Self-Efficacy Scale-Revision (MASES-R)	I=8, UI=6	Barrier (8- challenging situations, e.g., busy, when travelling, holiday), Behaviour (1- self-management), Belief (4- stop taking when feeling better)	<ul style="list-style-type: none"> ▲ 13-item questionnaire ▲ E.g., confidence to adhere to prescribed anti-hypertensive medications under a variety of situations: busy, when travelling, stop taking when feeling better and self-management 	Adherent or non-adherent	4-point Likert scale where 1=not at all sure to 4=extremely sure	<ul style="list-style-type: none"> ▲ Good predictive validity ▲ Internal consistency, Cronbach's alpha=0.95 	<ul style="list-style-type: none"> ▲ Hypertensives attending primary care practices ▲ Mean age: 54±12.4 ▲ Juxtaposed against MEMS
11	Hahn <i>et al.</i> , 2008, USA ⁶⁶	Adherence Starts with Knowledge-20 (ASK-20)	I=12, UI=8	Barrier (8- refill Rx, forgetting, challenges like hard to swallow, dosing, cost), Behaviour (1- lack of support), Belief (11- dosing, trust in healthcare provider, medicine didn't work)	<ul style="list-style-type: none"> ▲ 20-item questionnaire ▲ E.g., just forgot, ran out of medicine, use of alcohol gets in the way, taking more than once a day is inconvenient, have to take too many medicines a day, hard to swallow, taken less than prescribed, skipped or stopped because didn't think it was working and cost 	Adherent or non-adherent	5-point Likert scale ranging from 'strongly disagree' or from 'in the last week' to 'never'	<ul style="list-style-type: none"> ▲ Good concurrent validity ▲ Internal consistency, Cronbach's alpha=0.85 	<ul style="list-style-type: none"> ▲ Patients on medications for asthma, depression and diabetes ▲ Mean age: 52.5±13.8 ▲ Juxtaposed against self-reported adherence
12	Turcu-Stiolicia <i>et al.</i> , 2021, Romania ⁶⁷	Adherence to Direct-Acting Agents for Hepatitis C Virus (HCV-AD)	I=7, UI=3	Barrier (1- no stock), Behaviour (3- skipped, forgot, not daily), Belief (6- side effects, not sure works, too many, fear of addiction, feeling better/worse, not a miracle)	<ul style="list-style-type: none"> ▲ 10-item questionnaire ▲ E.g., forgot, ran out of medicine, skipped, worried about quantity, side effects, addiction, stopped when feeling better or sick 	Adherent or non-adherent	5-point Likert scale ranging from 'strongly disagree' or from 'never' to 'very often'	<ul style="list-style-type: none"> ▲ Good concurrent validity and content validity ▲ Internal consistency, Cronbach's alpha=0.867, item-total correlations (0.17–0.79) 	<ul style="list-style-type: none"> ▲ Patients at a hospital's gastroenterology department taking direct-acting antivirals for HCV infection ▲ Mean age: 60.8±12.1 ▲ Juxtaposed against VAS and MPR

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Table 2 Continued

No	Author, year, country	PROM/scale/ rating/ criteria/instrument	Outcome measure, number of intentional or unintentional items (I, UI, not reported)	Process measure, item domain: barriers (physical/practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age* (years)±SD or IQR, correlates
13	Silveira et al, 2021, Brazil ⁸⁷	Treatment Adherence Measure of Immunomodulators for Patients with Multiple Myeloma	I=5, UI=2	Behaviour (2- forgot, careless), Belief (5- feeling better/worse, interrupted treatment)	<ul style="list-style-type: none"> ▲ 7-item questionnaire ▲ E.g., careless, forgot, feeling better/sick 	Adherent or non-adherent	5-point Likert scale ranging from 'always' to 'never'	<ul style="list-style-type: none"> Construct and convergent validity established ▲ Internal consistency, Cronbach's alpha=0.41 (authors acknowledged the low value that alpha values around 0.5 are acceptable for scales with few items) 	<ul style="list-style-type: none"> ▲ Patients at outpatient clinics, diagnosed with myeloma and treated with an immunomodulator for at least 1 month ▲ Median age (IQR): 62.7 years (14.4) ▲ Juxtaposed against Quality of Life Questionnaire Core and the Quality of Life Questionnaire Multiple Myeloma module

Number of measures, n=13 of 59; *Intentional*, I=79, *Unintentional*, UI=60, *Not reported*=9 items; for a measure to be classified as mixed, a balanced of I and UI items are to be present i.e., >30% items I; >30% items UI.

*Some values were reported as median, range or not reported.

†When item specifies both I and UI (e.g., 'knowingly or unknowingly'), the item is categorised as *belief* (a domain which can have targeted intervention by healthcare professionals); *Barrier*=56, *Belief*=54, *Behaviour*=28 items.

‡When a patient is expected to choose one answer from *barrier* OR *belief*, the item is categorised as *belief* (a domain which can have targeted intervention by healthcare professionals); *Barrier*=56, *Belief*=54, *Behaviour*=28 items.

ADL, activities of daily living; CoC, Circle of Confidentiality; GP, general practitioner; MEMS, medication event monitoring system; MPR, medication possession ratio; PROMs, patient-reported outcome measures; RCT, randomised controlled trial; Rx, Prescription; SD, standard deviation; VAS, Visual Analogue Scale.

Table 3 PROMs of unintentional (UI) non-adherence—n=2 of 59 measures, 9 items^{68 69}

No	Author, year, country	PROM/scale/ rating/ criteria/instrument	Outcome measure, number of UI, intentional (I), not reported items	Process measure, item domain: barriers (physical/ practical), behaviour (act) or belief (perception)	Item construct	Classification of non-adherence*	Method of scoring	Psychometric properties, (reliability and/or validity)	Setting, age (years)±SD, correlates
1	Fodor et al, 2005, Hungary ⁶⁸	Adherence Questionnaire	UI=3, I=1	Behaviour (3 self-management, careless), Belief (1)	<ul style="list-style-type: none"> ▲ 8th of 9 items; 8th item has 4 subquestions ▲ E.g., patient's self-efficacy, self-management (occasionally forget, sometimes forget, frequently forget, or decide not to take for short or extended period) 	<ul style="list-style-type: none"> Adherent or non-adherent ▲ Patients who claimed to be taking medications every day were classified as adherent 	Dichotomised scale: yes=0; no=1	Good determinant validity, no report on reliability	<ul style="list-style-type: none"> ▲ Hypertensives among blue collar employees in 3 central European countries: Austria, Hungary and Slovakia during work site screening for hypertension ▲ Mean age: 48.9±7.4 in the adherent group and 46.7±8.9 in the non-adherent group ▲ Juxtaposed against blood pressure control
2	Chisholm et al, 2005, USA ⁶⁹	Immunosuppressive Therapy Adherence Instrument (ITAS)	UI=2, I=1, not reported=2	Barrier (1-forget), Behaviour (2-careless, self-management), Belief (2-stop when feeling better or worse)	<ul style="list-style-type: none"> ▲ 5-item questionnaire ▲ E.g., how often: 'forgot to take, careless about taking, stop because you felt worse and miss ... for any reason' 	<ul style="list-style-type: none"> Adherent or non-adherent ▲ Non adherence defined as not taking their ciclosporin or tacrolimus as advised/ prescribed over a 3-month time period given a particular circumstance 	A=0% of the time (none), B=1%–20% of the time, C=21%–50% of the time and D=>50% of the time	<ul style="list-style-type: none"> Moderate concurrent validity, good reliability ▲ Internal consistency, Cronbach's alpha=0.81 	<ul style="list-style-type: none"> ▲ Organ transplant recipients ▲ Mean age: 52.2±14.1 ▲ Juxtaposed against refill record, adherence rates, serum immunosuppressant concentrations, graft rejection and increased serum creatinine levels

Number of measures, n=2 of 59; Unintentional, UI items=5, Intentional, I items=2, Not reported=2 items; for a measure to be classified as Unintentional, >30% of its items are to be Unintentional and the remainder Intentional and/or Not reported (if any).

*All terms related to adherence, E.g., compliance is standardised and reported as adherence; Behaviour=5, Belief=3, Barrier=1 item(s). BP, blood pressure; NA, not applicable; PROMs, patient-reported outcome measures; SD, standard deviation.

Table 4 Associations between PROMs increasing propensity to detect an intentional non-adherence outcome and type of patient care, and the process domains

	Type of patient care—primary care (general practice, community pharmacy and optometry versus specialised care)			Belief criterion items		Barrier criterion items		Behaviour criterion items	
	OR	95% CI	P value	Standardised beta	P value	Standardised beta	P value	Standardised beta	P value
Increase in the detection of intentional non-adherence	*1.9	1.01 to 2.66	0.044	*0.79	<0.001	*0.34	<0.001	0.087	0.62

*p≤0.05.
PROMs, patient-reported outcome measures.

table 3—*unintentional*, UI (n=2 of 59 instruments).^{68 69}

Of the total 572 intentional criterion items, I=491, I=79, and I=2 were split into the *intentional*, mixed *intentional/unintentional*, and in the *unintentional* categories, respectively. Of the total 90 unintentional criterion items, UI=35, UI=50, and UI=5 were split into the *intentional*, mixed *intentional/unintentional*, and in the *unintentional* categories, respectively. Finally, additional n=67, 9 and 2 items were *not reported* within each category.

Process measures

The process domains which affected non-adherence were belief (383 items), barrier (192 items) and behaviour (165 items).

Correlation and regression analyses

There was a strong positive correlation between the outcome domain, intentional (I) and the process domains, belief (Spearman's $\rho=0.88$, $p<0.001$) and barrier (Spearman's $\rho=0.59$, $p<0.001$), i.e., the numbers of *belief* and *barrier* criterion items increased, along with the numbers of *intentional* criterion items.

The results of the regression analyses are displayed in table 4. Regression models were adjusted for respondents' age. There was a positive and significant association between increased PROMs' propensity to detect *intentional* non-adherence and primary care (vs specialised care) that patients received (OR=1.9; 95% CI=1.01 to 2.66), i.e., a measure was 1.9 times more likely to have detected an *intentional* non-adherence event among patients who attended primary care as compared to those attending secondary and tertiary care appointments, or who were hospitalised at these facilities. Similar findings were obtained for negative beliefs and barriers encountered. For every belief or barrier criterion item included, the PROMs' aptitude for detecting intentional non-adherence increased by $\beta=0.79$ and $\beta=0.34$ units, respectively. Model $R^2=0.94$, i.e., 94% of variance in the outcome variable *intentional* non-adherence can be explained by the predictor variables *belief* and *barrier*.

PROM characteristics

Psychometric properties

All studies included had a minimum of two psychometric properties assessed and described (online supplemental appendices 6–8). With reference to validity, hypotheses testing for content (including face) validity and/or construct validity were evaluated in a majority of the studies.^{6 18 20–22 24–27 31 39 42 43 46–50 52 57 58 60 64 66} With reference to reliability, the parameter internal consistency, was evaluated in 38 studies, respectively. Measurement error or cross-cultural validity/measurement invariance was not evaluated in any of the studies. In addition, many of the studies assessed PROMs' development, but they were not necessarily of good methodological quality (for example, limited information on data validity as described in the eligibility section) and were hence excluded.

Defining and scoring adherence

There was heterogeneity in the term 'adherence' used in the studies. First, this was evidenced in the cut-off points used for determining level of non-adherence, for example, 'habitual to occasional refusers of medications',¹⁴ 'high, medium or low adherence',^{5 41 56} and 'adherent' or 'non-adherent'.^{19 21 23–30 32–40 42–44 47 51 52 57–66 68–70}

All PROMs that had a component of unintentional had binomial categories of 'adherent' versus 'non-adherent'. While a handful of studies specified the score which determined 'high' score¹⁶ and hence 'highly' adherent, others reported that a higher score indicated better adherence.^{17 48 50} A majority of the measures (n=47 of 59 instruments) were worded as closed-ended questions and provided responses in the form of nominal or Likert scales; seven measures were open-ended and provided dichotomised Yes/No scale (which ultimately yielded a positive or negative overall score which determined level of adherence).^{5 14 15 18 21 34 44} Several measures incorporated an addition of Visual Analogue Scales (VAS).^{21 35 46}

The measures for assessing adherence were patient or interviewer-administered and conducted via face-to-face interviews (real-time or virtual), telephone interviews, questionnaires, diaries or internet surveys.

Extent of non-adherence

Seven measures specified a time period for non-adherence, for example, 'Did you miss a tablet-yesterday? last week? last month? or in the last 3 months?' Fifteen adherence measures specified a frequency for skipping or missing doses, for example, 'How many days over the past month did you take less than prescribed?' The time frame specified ranged from 1 day to 12 months. Most of the items were interpreted from measures that state the number/amount of doses taken compared with those prescribed for that time period. Haag *et al*⁵³ went on to stratify their analysis according to level of adherence for daily, two times per day and three times a day regimen.

Disease-specific measures

Some of these adherence scales are disease-specific and thus explored common predictors that may influence adherence in those diseased populations. Examples of diseases or statuses explored were asthma,⁶¹ diabetes, AIDS,⁵⁸ hypertension,^{57 68} chronic diseases, acute osteoporosis, eye-related conditions,¹⁶ cardiovascular, and organ transplant recipients.^{27 59}

DISCUSSION

Quantification of adherence and non-adherence

Medication adherence has been defined as 'the extent to which patients take medications as prescribed by their healthcare providers',⁷¹ while its measurement is the process of systematically assigning numbers or words to tangible and intangible characteristics so that they can be defined, quantified and differentiated. In our review of 59 PROMs, these self-reported measures aimed at quantifying medication adherence based on the responses from a nominal or Likert-point scale and assigning categories to the total scores. A small number of adherence measures had taken a different approach to assigning the 'adherent' category. The Medication Adherence Questionnaire (MAQ), Morisky Medication Adherence Scale (MMAS), Brief Medication Questionnaire, Adherence Self-Report Questionnaire (ASRQ) and VAS categorised patients into levels of adherence. For example, the MAQ and MMAS categorised the population into high, medium and low levels of adherence whilst several others collectively grouped respondents with medium and low adherence scores into a broader 'non-adherent' class. For the Brief Medication Questionnaire, the study population was grouped into repeat, sporadic and no non-adherence. The ASRQ and VAS classified non-adherence into six and seven levels, respectively, based on the researchers' expertise. Where reported, the most common cut-off point for non-adherence is the score below the corresponding point of another objective or self-reported measure. For instance, the cut-off was the point where it was revealed that the patients took 80% of their medication. The MMAS cut-off points, for instance, were selected based on the correlation with blood pressure control. Other adherence measures, such as the

Drug Attitude Inventory, Adherence Attitude Inventory and Medication Adherence Self-Efficacy Scale-Revision first segregated the population into adherent and non-adherent based on responses to questions about whether medications were taken or not, and then compared the mean scores of the two adherence measures to determine the cut-off.

Psychometric properties

Since the publication of the inaugural study on adherence in 1968,⁷² many studies aimed at understanding factors related to poor adherence, yet they lacked crucial perspectives on the measurement tools used to evaluate non-adherence. The approach for combining adherence and its measurement is complex given that adherence impacts health-related clinical outcomes.⁷³ The analyses of PROMs' psychometric properties were hence essential, given the vast and multidimensional outcomes they evaluated. To ensure construct validity, several studies used exploratory factor analysis to ascertain that the smallest number of factors that best represented the items was retained.^{27 42 50} Reliability was evaluated using Cronbach's alpha tests for internal consistency to assess how closely related a set of items were as a group and this was frequently reported and often yielded values of more than 0.7, indicating a relatively acceptable level of internal consistency and correlation between PROM items. In addition, the reliability of a measurement tool in consistently reproducing the same result across several measurements, denoted using a test/retest reliability score, were also not regularly reported.

It is crucial to evaluate PROM in the context of evaluating medication-taking conduct, i.e., its construct and structure need to be sensitive and adequately detect aspects of medication-taking behaviour. Medication-taking behaviours were often detected when using a direct, indirect or a combined method. The most precise approaches were postulated to have been direct methods, such as directly observed therapy, biological methods, and measurement of the level of medicine or metabolite, for example, blood or urine drug concentrations. Numerous indirect methods were equally proposed, such as the use of clinician reports, data from rates of prescription refills, pill counts, electronic medication monitors, patient diaries and patient self-report measures as well as healthcare provider-reported measures. When reporting on aspects of PROMs' construct, many of the studies evaluated its criterion and/or discriminant validity. However, there is also a school of thought that described criterion validity as being inaccessible for evaluation as it requires a component of comparison with an established 'gold' standard. The authors synthesised the studies and deemed proxy measures as either direct, indirect or a combination of both, as standards against which the PROMs were validated.

In summary, the review identified 59 unique PROMs of medication adherence. The selected 59 PROMs demonstrated ease of administration primarily in community

dwellers seeking services at primary healthcare facilities. Patients who visited secondary or tertiary care outpatient clinics, blue collar workers undergoing health screening and patients hospitalised following emergency department visits were end-users of the PROMs. These measures were tested primarily on adherence to pharmacotherapy for psychiatric disorders, and for retroviral and cardiovascular diseases. This was an indication that the PROMs had good usability and credibility, and were meaningful to be used for their targeted populations. Eight of these outcome measures had *adequate*, evidence-based psychometric properties, and had the aptitude to identify those who intentionally failed to adhere to good medication-taking conduct. They were the Compliance Questionnaire Rheumatology,²² Immunosuppressant Therapy Barrier Scale,²⁷ Medication Adherence Rating Scale,²⁰ Treatment Satisfaction Questionnaire for Medication,²⁵ Self-Efficacy for Appropriate Medication Use Scale,³² Medication Adherence Assessment Tool,⁵⁰ Patient-Medication Adherence Instrument and Healthcare Professional-Medication Adherence Instrument⁵² and Barriers to Oral short-Term antibiotic Adherence⁵³ questionnaires. Two measures with *adequate*, evidence-based psychometric properties had the aptitude to identify those who intentionally and unintentionally failed to adhere to good medication-taking conduct. They were the Adherence Starts with Knowledge-20⁶⁶ and Hill-Bone Scale⁵⁷ questionnaires.

Intentionality (intentional and/or unintentional)

While the advantages of those psychometric properties were recognised, authors seldom weighed in on the inherent ability of self-reports to assess intentionality. A patient's belief, past experiences and cognition level may equally come into play, influencing medication-taking conduct. Decisions by patients may be well-informed or ill-informed driven by concerns over the benefits and risks of their medication.⁷⁴ Using theories of Planned Behaviour and the Common Sense Self-regulatory Model of Illness, several attempts were made to explain variation in adherence to medication.¹⁷ A social cognition model that aims to explain one's intentional non-adherent conduct was developed in 1999 by Horne¹⁷ and was founded on the Health Belief Model⁷⁵ and the Illness Perceptions Model.⁷⁶ According to Horne, adherence to medication is based on patients' deeply-rooted belief concerning perceived severity of illnesses, i.e., perceptions and their understandings, and hence, knowledge of the nature of the illness, and treatability.¹⁷ In the context of adherence, belief is usually associated with intentional non-adherence because the belief can strongly lead to an active decision either to follow or not to follow instructions by healthcare professionals.

Self-efficacy, on the contrary, is key for habitual non-adherence and is a term that encompasses self-management skills, discipline and the state of being self-sufficient.^{77 78} In our review, we observed more of such terms in the later versions of the health beliefs model to increase the explanatory power of the theory, placing

emphasis on patient accountability.^{79 80} In recent times, during the COVID-19 pandemic, the health promotion model is also referenced to as it emphasises self-efficacy and purports that judgement about one's ability to successfully perform challenging tasks is based on four types of criteria: (a) behavioural engagement and evaluating performance, (b) observation of how others perform, (c) verbal persuasion by others about one's ability, and (d) anxiety, fear, calm, tranquillity, or other physiological states associated with self-judgement of competencies.^{81 82}

When used effectively, measurement tools such as self-reports essentially screen for these predictors (be it one's belief system—perceptions, experiences, knowledge and trust towards healthcare professionals or one's behaviours—self-efficacy and habits). These perspectives are important for better understanding of the underlying reasons contributing to non-adherence. As this review demonstrates, distinguishing intentional from unintentional non-adherence is pertinent. Only then can appropriate and targeted interventions be provided to the patient.^{73 83}

Limitations

Although we successfully classified each item of every measure or instrument based on intentionality for non-adherence, future research using a similar approach may reveal varied findings. This is because the process of classification was largely dependent to a certain extent, on one's interpretation of the criterion items' construct and thereby the consequences of treatment default. Our findings also cannot be used to ascertain the phase of medication taking, whether 'initial, i.e., starting a recommended medication regimen', or 'implementation, i.e., executing the prescribed dosage schedule' or 'persistence, i.e., length of time on regimen before discontinuation'.⁸⁴ In addition, while there is a body of evidence to suggest that past negative experiences with the healthcare systems were attributed to the intention to default treatment, the key role of healthcare professionals in advocating positive habits for medication adherence remains vital. In other words, past negative experiences could become positive and the new experience should equally influence medication-taking conduct.

Recommendations for best practice

Many of the studies identified PROMs of adherence towards antiretroviral and post-organ transplant therapies. End-users of these measures can easily be subjected to stigmatisation, and as such, undergoing a series of validity tests including cross-cultural validity, can prove beneficial for the development of individual measure items. This is also true for measures where the appeal, social desirability and sensitivity are of concern, and yet the assessment needs to be conducted without compromising the method in which the latent trait of the measure is being measured across cultures and populations. For instance, as proposed by Stirratt *et al*,⁸⁴ respondents with cognitive impairment may require other approaches such as daily

texts, interactive voice response surveys, or computer-assisted measures.

In addition, the testing for criterion and construct validity was often conducted using proxy measures as opposed to direct measures. Although our review demonstrated the link between intentional non-adherence and one's belief system, and in theory, responses to sociocognitive domains can be used as proxy measures, we recommend further statistical analyses, for example sensitivity and positive predictive value calculations, to assess the concordance of direct and proxy measures of individual measure items. Despite having the advantage of producing quick results, a PROM needs to be reliable, its results reproducible, and have an ability to capture a single underlying aspect of behaviour, barrier, or belief, and map that construct onto a valid measurement scale.

Our findings demonstrated that existing measures had sufficient evidence-base and psychometric properties, and therefore, should first be used, as opposed to developing a new measure, unless the study subjects do not correspond with the tested population.⁸⁵ Consensus of a panel of experts is necessary for determining criteria for scoring and cut-off for adherence versus non-adherence. They need to consider frequency and dose (and the allowable deviation in the amount prescribed whenever the patient decides to lower or increase dose), as well as determine habitual versus occasional refusers. Additionally, developing response items that differentiate adherence in ordinal terms (e.g., anchored Likert rating scale), nominal or VAS (e.g., estimated level of doses taken) may help decrease ceiling effects. To curb recall bias, phrases like 'during the last weekend' and 'in the past 7 days (to include one weekend)' were preferred. A 30-day recall period, as opposed to brief intervals, can also be considered in view of its advantageous impact on ceiling effect reduction.

Finally, future research could underscore the adjudication of measurement errors and their sources of variability, as there is a paucity of information in these areas. Elucidating responsiveness of PROMs and their ability to detect changes in clinical conditions of patients are also potential areas for psychometric characteristic evaluation.

CONCLUSION

The data spanning four decades revealed that PROMs were developed to assess medication non-adherence, which had increasingly become more intentional. Of the 59 studies, ten PROMs had *adequate*, evidence-based psychometric properties. Of the ten, eight and two PROMs were able to detect total and partial intentionality to medication default, respectively. Measures with matching intentionality properties will better detect non-adherence, thereby relieving clinicians from having to contemplate on ineffective medications

or therapeutic failure due to drug resistance. Finally, recommendations for patients to simply use daily reminders to consume medication should be brought to a halt as it seems counterintuitive to tackle the premeditated intentional non-adherence. Instead, because our data demonstrated a link between intentional non-adherence and one's belief, empowering patients with the appropriate knowledge, helping them to better manage their illnesses, and strengthening their trust in medications and healthcare providers could be more reliable impetuses to drive positive attitudes and perceptions. However, these need to commence at the primary care level.

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