INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Psychometric evaluations of patient reported outcome measures of intentional and unintentional medication non-adherence: a systematic review

Fahrni, ML[1]; Saman, KM[2]; Isa, KAM[3].

Review question / Objective: **How does the psychometric evaluations of patient reported outcomes measures (PROM) of medication nonadherence compare for intentional versus unintentional?**
Condition being studied: **The PICO statement was as follows: P, human subjects/ patients with chronic disease(s) which require drug therapy; I, not applicable (the review assessed PROM of adherence in patients with chronic illnesses); C, not applicable (no comparator group); O, adherent or non (for a validated PROM which contained close-ended items or dichotomised response to open-ended items and, which reported at least two psychometric properties).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 September 2021 and was last updated on 07 September 2021 (registration number INPLASY202190021).

INTRODUCTION

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METHODS

Search strategy: MEDLINE; EMBASE; CINAHL; International Pharmaceutical Abstracts; Cochrane Library. Search dates from 01.01.1980 up to 31.12.2021. Example: Search filter – MEDLINE (January 1980 – 28 December 2020) #1 (Instrumentation[sh] OR methods[sh] OR "Validation Studies"[pt] OR "Comparative Study"[pt] OR "psychometrics"[MeSH] OR psychometr*[tiab] OR clinimetr*[tw] OR clinometr*[tw] OR "outcome assessment (health care)"[MeSH] OR "outcome assessment"[tiab] OR "outcome measure*"[tw] OR "observer variation"[MeSH] OR "observer variation"[tiab] OR "Health Status Indicators"[Mesh] OR "reproducibility of results"[MeSH] OR reproducib*[tiab] OR "discriminant analysis"[MeSH] OR reliab*[tiab] OR unreliab*[tiab] OR valid*[tiab] OR "coefficient of variation"[tiab] OR coefficient[tiab] OR homogeneity[tiab] OR homogeneous[tiab] OR "internal consistency"[tiab] OR (cronbach*[tiab] AND (alpha[tiab] OR alphas[tiab])) OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab])) OR agreement[tw] OR precision[tw] OR imprecision[tw] OR "precise values"[tw] OR test-retest[tiab] OR (test[tiab] AND retest[tiab]) OR (reliab*[tiab] AND (test[tiab] OR retest[tiab])) OR stability[tiab] OR interrater[tiab] OR inter-rater[tiab] OR intrarater[tiab] OR intra-rater[tiab] OR intertester[tiab] OR inter-tester[tiab] OR intratester[tiab] OR intra- tester[tiab] OR interobserver[tiab] OR inter-observer[tiab] OR intraobserver[tiab] OR intra-observer[tiab] OR intertechnician[tiab] OR inter-technician[tiab] OR intratechnician[tiab] OR intra-technician[tiab] OR interexaminer[tiab] OR inter-examiner[tiab] OR intraexaminer[tiab] OR intra-examiner[tiab] OR interassay[tiab] OR inter-assay[tiab] OR intraassay[tiab] OR intra-assay[tiab] OR interindividual[tiab] OR inter- individual[tiab] OR intraindividual[tiab] OR intra-individual[tiab] OR interparticipant[tiab] OR inter-participant[tiab] OR intraparticipant[tiab] OR intra-participant[tiab] OR kappa[tiab] OR kappa's[tiab] OR kappas[tiab] OR repeatab*[tw] OR ((replicab*[tw] OR repeated[tw]) AND (measure[tw] OR measures[tw] OR findings[tw] OR result[tw] OR results[tw] OR test[tw] OR tests[tw])) OR generaliza*[tiab] OR generalisa*[tiab] OR concordance[tiab] OR (intraclass[tiab] AND correlation*[tiab]) OR discriminative[tiab] OR "known group"[tiab] OR "factor analysis"[tiab] OR "factor analyses"[tiab] OR "factor structure"[tiab] OR "factor structures"[tiab] OR dimension*[tiab] OR subscale*[tiab] OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab])) OR "item discriminant"[tiab] OR "interscale correlation*"[tiab] OR error[tiab] OR errors[tiab] OR "individual variability"[tiab] OR "interval variability"[tiab] OR "rate variability"[tiab] OR (variability[tiab] AND (analysis[tiab] OR values[tiab])) OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab])) OR "standard error of measurement"[tiab] OR sensitiv*[tiab] OR responsive*[tiab] OR (limit[tiab] AND detection[tiab]) OR "minimal detectable concentration"[tiab] OR interpretab*[tiab] OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND (important[tiab] OR significant[tiab] OR detectable[tiab]) AND (change[tiab] OR difference[tiab])) OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR difference[tiab])) OR "meaningful change"[tiab] OR "ceiling effect"[tiab] OR "floor effect"[tiab] OR "Item response model"[tiab] OR IRT[tiab] OR Rasch[tiab] OR "Differential item functioning"[tiab] OR DIF[tiab] OR "computer adaptive testing"[tiab] OR "item bank"[tiab] OR "cross-cultural equivalence"[tiab]). #2 (Surveys and Questionnaires[MeSH Terms]) OR ("Surveys and Questionnaires"[Title/Abstract])) OR (Survey Methods[MeSH Terms])) OR ("Survey Methods"[Title/Abstract])) OR (Questionnaires and Surveys[MeSH Terms])) OR ("Questionnaires and Surveys"[Title/

Abstract])) OR (Methods, Survey[MeSH Terms])) OR ("Methods, Survey"[Title/Abstract])) OR (Survey Method[MeSH Terms])) OR ("Survey Method"[Title/Abstract])) OR (Methodology, Survey[MeSH Terms])) OR ("Methodology, Survey"[Title/Abstract])) OR (Survey Methodology[MeSH Terms])) OR ("Survey Methodology"[Title/Abstract])) OR (Community Surveys[MeSH Terms])) OR ("Community Surveys"[Title/Abstract])) OR (Community Survey[MeSH Terms])) OR ("Community Survey"[Title/Abstract])) OR (Survey, Community[MeSH Terms])) OR ("Survey, Community"[Title/Abstract])) OR (Surveys, Community[MeSH Terms])) OR ("Surveys, Community"[Title/Abstract])) OR (Repeated Rounds of Survey[MeSH Terms])) OR ("Repeated Rounds of Survey"[Title/Abstract])) OR (Surveys[MeSH Terms])) OR (Surveys[Title/Abstract])) OR (Survey[MeSH Terms])) OR (Survey[Title/Abstract])) OR (Questionnaire Design[MeSH Terms])) OR ("Questionnaire Design"[Title/Abstract])) OR (Design, Questionnaire[MeSH Terms])) OR ("Design, Questionnaire"[Title/Abstract])) OR (Designs, Questionnaire[MeSH Terms])) OR ("Designs, Questionnaire"[Title/Abstract])) OR (Questionnaire Designs[MeSH Terms])) OR ("Questionnaire Designs"[Title/Abstract])) OR (Baseline Survey[MeSH Terms])) OR ("Baseline Survey"[Title/Abstract])) OR (Baseline Surveys[MeSH Terms])) OR ("Baseline Surveys"[Title/Abstract])) OR (Survey, Baseline[MeSH Terms])) OR ("Survey, Baseline"[Title/Abstract])) OR (Surveys, Baseline[MeSH Terms])) #3 (Medication Adherence[MeSH Terms]) OR "Medication Adherence"[Title/Abstract]) OR Adherence, Medication[MeSH Terms]) OR "Adherence, Medication"[Title/Abstract]) OR Medication Nonadherence[MeSH Terms]) OR "Medication Nonadherence"[Title/Abstract]) OR Nonadherence, Medication[MeSH Terms]) OR "Nonadherence, Medication"[Title/Abstract]) OR Medication Noncompliance[MeSH Terms]) OR "Medication Noncompliance"[Title/Abstract]) OR Noncompliance, Medication[MeSH Terms]) OR "Noncompliance, Medication"[Title/Abstract]) OR Medication Non-Adherence[MeSH Terms]) OR "Medication Non- Adherence"[Title/Abstract]) OR Medication Non Adherence[MeSH Terms]) OR "Medication Non Adherence"[Title/Abstract]) OR Non-Adherence, Medication[MeSH Terms]) OR "Non-Adherence, Medication"[Title/Abstract]) OR Medication Persistence[MeSH Terms]) OR "Medication Persistence"[Title/Abstract]) OR Persistence, Medication[MeSH Terms]) OR "Persistence, Medication"[Title/Abstract]) OR Medication Compliance[MeSH Terms]) OR "Medication Compliance"[Title/Abstract]) OR Compliance, Medication[MeSH Terms]) OR "Compliance, Medication"[Title/Abstract]) OR Medication Non-Compliance[MeSH Terms]) OR "Medication Non-Compliance"[Title/Abstract]) OR Medication Non Compliance[MeSH Terms]) OR "Medication Non Compliance"[Title/Abstract]) OR Non-Compliance, Medication[MeSH Terms]) OR "Non-Compliance, Medication"[Title/Abstract]) OR ((Patient Compliance[MeSH Terms]) OR "Patient Compliance"[Title/Abstract]) OR Compliance, Patient[MeSH Terms]) OR "Compliance, Patient"[Title/Abstract]) OR Patient Adherence[MeSH Terms]) OR "Patient Adherence"[Title/Abstract]) OR Adherence, Patient[MeSH Terms]) OR "Adherence, Patient"[Title/Abstract]) OR Patient Cooperation[MeSH Terms]) OR "Patient Cooperation"[Title/Abstract]) OR Cooperation, Patient[MeSH Terms]) OR "Cooperation, Patient"[Title/Abstract]) OR Patient Non-Compliance[MeSH Terms]) OR "Patient Non- Compliance"[Title/Abstract]) OR Non-Compliance, Patient[MeSH Terms]) OR "Non-Compliance, Patient"[Title/Abstract]) OR Patient Non Compliance[MeSH Terms]) OR "Patient Non Compliance"[Title/Abstract]) OR Patient Nonadherence[MeSH Terms]) OR "Patient Nonadherence"[Title/Abstract]) OR Nonadherence, Patient[MeSH Terms]) OR "Nonadherence, Patient"[Title/Abstract]) OR Patient Noncompliance[MeSH Terms]) OR "Patient Noncompliance"[Title/Abstract]) OR Noncompliance, Patient[MeSH Terms]) OR "Noncompliance, Patient"[Title/Abstract]) OR Patient Non-Adherence[MeSH Terms]) OR "Patient Non-

Adherence"[Title/Abstract]) OR Non-Adherence, Patient[MeSH Terms]) OR "Non-Adherence, Patient"[Title/Abstract]) OR Patient Non Adherence[MeSH Terms]) OR "Patient Non Adherence"[Title/Abstract]) OR Treatment Compliance[MeSH Terms]) OR "Treatment Compliance"[Title/Abstract]) OR Compliance, Treatment[MeSH Terms]) OR "Compliance, Treatment"[Title/Abstract]) OR Treatment Compliances[MeSH Terms]) OR "Treatment Compliances"[Title/Abstract]) OR Therapeutic Compliance[MeSH Terms]) OR "Therapeutic Compliance"[Title/Abstract]) OR Compliance, Therapeutic[MeSH Terms]) OR "Compliance, Therapeutic"[Title/Abstract]) OR Compliances, Therapeutic[MeSH Terms]) OR "Compliances, Therapeutic"[Title/Abstract]) OR Therapeutic Compliances[MeSH Terms]) OR "Therapeutic Compliances"[Title/Abstract])) OR ("drug adherence")) OR ("drug compliance")) OR ("taking medication")) OR ("medication initiation")) OR ("medication implementation") #4 ("Regime" [Title/ Abstract] OR "Number OR Tablet*" [Title/Abstract]) OR "Medication*" [Title/Abstract] OR "Medicaments"[Title/Abstract] OR "Prescription*"[Title/Abstract] OR "Pills"[Title/Abstract] OR "Drugs"[Title/Abstract])) OR "Dose*"[Title/Abstract] OR "Mealtime*[Title/Abstract] OR "Meal" [MeSH Terms]) OR "Meal"[Title/Abstract] OR "Intake Frequency"[Title/Abstract] OR "Polypharmacy"[Title/Abstract] OR Polypharmacy[MeSH] OR "Pill Burden" [Title/Abstract] OR ("Different"[Title/Abstract] OR "Various"[Title/Abstract] OR "Several"[Title/Abstract] AND ("Tablets" [Title/Abstract] OR "Tablets"[MeSH Terms] OR "Medications"[Title/Abstract] OR "Pills" [Title/Abstract])) OR ("Duration"[Title/Abstract] OR "Length"[Title/Abstract] AND ("Therapy"[Title/Abstract] OR "Treatment" [Title/Abstract] OR "Diseases"[Title/Abstract] "Illness"[Title/Abstract])) #5 #1 AND #2 AND #3 AND #4.

Participant or population: Human subjects/ patients with chronic disease(s) which require drug therapy.

Intervention: Not applicable.

Comparator: Not applicable.

Study designs to be included: Randomised and non-randomised controlled trial.

Eligibility criteria: The following eligibility criteria were considered: Inclusion criteria(i) randomized or non-randomized controlled studies; (ii) patient-reported and validated medication adherence measures (iii) closed-ended or if open-ended items, their responses dichotomized; iv) at least two psychometric properties evaluatedExclusion criteria(i) Articles where we could not source the scoring method or criteria for distinguishing the level or type of adherence/non. ii) Studies published only as abstracts or protocols. iii) Open-ended PROM items which were without a method of rating or scoring the adherence/non measure (eg, "Did you forget to take your medication?") This is because without the specification for scoring, for example, an answer of "yes" carried a mark, towards the sum score, an overall assessment of adherence ie, poor, moderate or good, could not be performed).

Information sources: Electronic databases searched from January 1980-Dec 2020: MEDLINE; EMBASE; CINAHL; International Pharmaceutical Abstracts; Cochrane Library.

Main outcome(s): • General characteristics of the study setting, disease and population: age, and country. • Characteristics of disease or condition: disease studied, duration of illness, or treatment. • PROM characteristics: methods of administration, availability of electronic administration, language, response scale, domains, and number of items.

Quality assessment / Risk of bias analysis: Quality assessment of the psychometric properties of the PROM will be done using the Consensus-based Standards for the selection of health Measurement Instruments(COSMIN) guidelines (Mokkink et al., 2018). Articles which assessed and described a PROM with at least 2

psychometric properties/ statuses of reliability and validity will be included.

Strategy of data synthesis: We will extract the PROM data and depending on the nature of its criterion, code every PROM item of nonadherence into both an outcome domain: intentional, unintentional, or unclassified, and, a process domain: behaviour (e.g. self-efficacy), barrier (e.g. practicality, impaired visual, difficulty remembering), or belief (e.g. perceptions, experiences, knowledge, trust). In the final data synthesis, each PROM will be assigned an overall category of either intentional(I), mixed of unintentional and intentional(UI/I) or unintentional(UI) depending on the coded items' leading domain.

Subgroup analysis: None applicable.

Sensitivity analysis: Eligibility criteria: Characteristics of participants: patients with chronic diseases and/ or require drug therapy - including but not limited to patients who undergo renal transplant. Characteristics of the proxy measures: both direct (biomarkers) and indirect (pill count, electronic monitors) Characteristics of the outcome: open ended questions that can be binary-coded eg. medium and high adherence (adherent) vs low adherence (non-adherent) Characteristics of the outcome: Analyses of primary data to code into Intentional and Unintentional/ Mixed Non-adherence

Language: English.

Country(ies) involved: Malaysia.

Keywords: adherence, scale, questionnaire, reliability, validity, patient-reported outcome measure, critical appraisal, belief, perception, knowledge, attitude, behavior.

Contributions of each author:

Author 1 - Mathumalar L Fahrni - planning, supervision, search strategy, data extraction, data synthesis and analysis, drafting the manuscript.
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