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# Scope of outcomes in trials and observational studies of interventions targeting medication adherence in rheumatic conditions: a systematic review

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**Conflict of interest**

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**Running head**

Outcomes in adherence studies

**Abstract**

**Objective** Non-adherence to medications is common in rheumatic conditions and associated with increased morbidity. Heterogeneous outcome reporting by researchers compromises the synthesis of evidence of interventions targeting adherence. We aimed to assess the scope of outcomes in interventional studies of medication adherence.

**Methods** We searched electronic databases to February 2019 for published randomized controlled trials and observational studies of interventions with the primary outcome of medication adherence including adults with any rheumatic condition, written in English. We extracted and analyzed all outcome domains and adherence measures with pre-specified extraction and analysis protocols.

**Results** Overall, 53 studies reported 71 outcome domains classified into adherence (1 domain), health outcomes (38 domains) and adherence-related factors (e.g. medication knowledge) (32 domains). We subdivided adherence into three phases: initiation (n=13 studies, 25%); implementation (n=32, 60%); persistence (n=27, 51%); phase unclear (n=20, 38%). Thirty-seven different instruments reported adherence in 115 unique ways (this includes different adherence definitions and calculations, metric and method of aggregation). Forty-one studies (77%) reported health outcomes. The most frequently reported were: medication adverse events (n=24, 45%); disease activity (n=11, 21%); bone turnover markers/physical function/quality of life (each n=10, 19%). Thirty-three studies (62%) reported adherence-related factors. The most frequently reported were: medication beliefs (n=8, 15%); illness perception/medication satisfaction/satisfaction with medication information (each n=5, 9%); condition knowledge/medication knowledge/trust in doctor (each n=3, 6%).

**Conclusion** The outcome domains and adherence measures in interventional studies targeting adherence are heterogeneous. Consensus on relevant outcomes will improve the comparison of different strategies to support medication adherence in rheumatology.

## Introduction

Many rheumatic conditions require the long-term use of medications, yet adherence may be suboptimal. Adherence may be defined as *"the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider"*[1]. In rheumatoid arthritis (RA), medication adherence ranges from 14% to 80% and non-adherence can lead to poorer health outcomes such as increased disease activity, poorer quality of life and radiological progression[2, 3]. In osteoporosis (OP), less than 70% of patients start prescribed treatment and approximately 50% discontinue therapy within one year, which is associated with an increased risk of fracture[4]. Researchers are increasing efforts to develop and test strategies to improve medication adherence in rheumatology. However, differences in the design of these interventional studies, including outcome selection and reporting, hamper the comparison of these strategies.

Adherence studies to date have used heterogeneous adherence outcome measures, definitions and thresholds, and often have not assessed clinically meaningful health outcomes[5]. If researchers omit important outcome domains, or use different measures, end-users of the research are unable to judge the relative effectiveness of interventions or understand the clinical relevance of research findings. Core domain sets, which are defined as the minimum set of outcome domains that should be measured and reported in specific clinical trials, reduce inconsistent reporting, reporting bias and can help ensure the measurement of outcomes that are important to patients and decision-makers[6]. The Outcome Measures in Rheumatology (OMERACT) initiative has developed core domain sets for many rheumatic conditions[6].

The aims of this study were to describe the scope and consistency of outcome domains and adherence measures in studies (including both randomized controlled trials and observational studies) of interventions to improve medication adherence in adults with rheumatic conditions.

## Materials and Methods

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement to report this systematic review (Supplementary Table 1). We have published the original protocol and protocol amendments[7, 8].

### *Search and selection criteria*

The inclusion criteria is described with the PICOS framework (Participant/Intervention/Comparator/Outcome/Study design): 1) Participants: Adults aged 18 or older with any rheumatic condition; 2) Intervention: Any strategy to improve adherence; 3) Comparator: Management as usual (if a comparator arm was included in the study); 4) Outcomes: All outcome domains, including only studies with medication adherence as the primary outcome; 5) Study design: Randomized controlled trials (RCTs) and observational studies (non-randomized comparison studies, including pilot studies, which incorporated an intervention targeting adherence). We included both RCTs and observational studies as we anticipated a limited number of informative RCTs of adherence interventions in rheumatic conditions.

We searched MEDLINE, PsycINFO, Embase, CINAHL and CENTRAL from inception to 25th February 2019 to identify all studies of interventions designed to

improve medication adherence in any rheumatic condition. The search strategy included MESH terms ('Rheumatoid arthritis', 'Spondyloarthritis', 'Osteoporosis', 'Systemic lupus erythematosus', 'Systemic scleroderma', 'Vasculitis', 'Connective tissue diseases', 'Medication adherence', 'Treatment adherence and compliance', and 'Treatment refusal') (See Supplementary Table 2 for the full search strategy). We also hand searched the reference list of selected systematic reviews of adherence studies [9-11] and Google Scholar. We excluded conference reports, protocols and abstracts given the limited information provided, however we searched for the full publications of these and contacted authors if needed. We included only English language articles. Two reviewers (AK and LCS) independently screened abstracts and full texts of all identified studies. A third reviewer (KT) resolved any disagreements on included studies.

***Data extraction***

For each study, two reviewers (AK, KT) independently extracted the following study characteristics: first author, year of publication, participating countries, study design, type of intervention, sample size, study duration, and participants' mean age, sex, medication, rheumatic condition, and disease duration. In addition, the reviewers independently extracted all outcome domains, measures and the instrument, metric, method of aggregation and time points of all adherence measures

***Data synthesis and analysis***

Two reviewers (AK and LCS) grouped all outcome domains into three overarching groups: adherence, health outcomes and adherence-related factors. We calculated the number of studies reporting each outcome domain. The two reviewers discussed any

discrepancies between the extracted outcomes and outcome domain grouping until agreement was reached and consulted a third reviewer (KT) when necessary.

We subdivided adherence into phases: (1) initiation defined as when the patient takes the first dose of prescribed medication; (2) implementation defined as the extent to which a patient's actual dosing corresponds to the prescribed dosing; or (3) persistence defined as the length of time between initiation and the last dose immediately preceding discontinuation[12].

We categorized each adherence measure into subjective and objective measures. Subjective measures included all self-report questionnaire/diary/interview and clinician judgment (i.e. clinician estimate of adherence). Objective measures included: direct observation; drug concentration in body fluid; electronic monitoring (e.g. medication event monitoring systems [MEMS]); pharmacy refill record; and pill count. We also recorded the name of each instrument used to measure adherence, e.g. different self-report measures and drug levels were recorded separately. Finally, to demonstrate the heterogeneity in adherence measure reporting, we recorded a unique adherence measure which included the instrument, details on the adherence calculation/cut-off determined for adherence, metric (e.g. reporting adherence measures as change from baseline, end value or time to event) and method of aggregation (categorical, or use of means or medians when reported as a continuous measure). We recorded the time points for all adherence measures.

Health outcomes included any condition-specific outcome domain that informed the impact of the intervention on any clinical aspect of the condition including

pathophysiological manifestations (e.g. fracture, pain), life impact (e.g. quality of life), death, or resource use (e.g. utilization costs) as defined in the OMERACT handbook.[6] In order to evaluate whether studies reported important health outcome domains, we assessed whether existing studies of adherence interventions reported on medication adverse events. We also compared the health outcome domains in the included studies with existing condition-specific core domain sets via OMERACT (https://omeract.org/) and Core Outcome Measures in Effectiveness Trials websites (http://www.comet-initiative.org/), noting whether these core domain sets were available at least five years before publication of the adherence trial for feasible inclusion within the trial.

Adherence-related factors included any factors that could influence adherence behaviour using the COM-B ('capability', 'opportunity', 'motivation' and 'behaviour') framework described by Michie et al[13], reported as an outcome, e.g. medication knowledge. Supplementary Table 3 includes examples of adherence-related factors within the COM-B framework.

## Results

### *Study characteristics*

We included 53 studies (41 RCTs, 77%) with a total of 26,361 participants (Fig 1). Interventional studies in adherence in rheumatology have exponentially increased over the last two decades (Supplemental Fig 1). Table 1 provides the characteristics of included studies. Supplementary Table 4 includes a descriptive summary of all studies. The review included studies conducted in 33 countries (four studies in

multiple countries) with participants with nine rheumatic conditions (OP, RA, gout, systemic lupus erythematosus, psoriatic arthritis, 'systemic rheumatic diseases', 'early inflammatory arthritis', 'inflammatory polyarthritis', 'degenerative joint disease'). Studies had a mean follow-up duration of 13 months (range four weeks to two years for RCTs, ten days to five years for observational studies) and mean sample size of 497 participants (range 18 – 2,382 for RCTs, 18 – 5,413 for observational studies).

***Adherence as an outcome domain and its measurement***

The phases of adherence measured included initiation (n=13 studies, 25%), implementation (n=32, 60%) and persistence (n=27, 51%). The phase of adherence was unclear in 20 studies (38%). Self-report questionnaires which assessed more than one phase of adherence were used in most of the studies with an unclear phase of adherence.

We categorized all adherence measures into subjective and objective measures. Studies used objective measures more often overall (n=28, 53%). This included pharmacy refill records, pill count, MEMS and drug concentration in body fluid. Subjective measures included all self-report questionnaires/interviews/diaries (n=25 studies, 47%). Five studies combined subjective and objective measures to report a single value for adherence (e.g. combining pharmacy refill record and self-report, n=5, 9%). RCTs used more objective measures (n=20, 49% of RCTs) compared with observational studies (n=5, 42% of observational studies). OP studies used more objective measures (n=20, 61% of OP studies) compared with RA studies (n= 4, 33 % of RA studies).

In total, studies used 37 different instruments to measure adherence (mean 1.5 instruments per study, range 1-5). The five most frequently reported instruments were pharmacy refill record (n=20 studies, 38%), pill count (n=7, 13%), 4-item Morisky (n=6, 11%), Compliance Questionnaire in Rheumatology (CQR) (n=4, 8%) and MEMS (n=4, 8%). Six studies (11%) did not specify the instrument used to measure adherence. Twenty-nine instruments appeared in one study only. These were predominantly self-report questionnaires or interviews created specifically for the study. Figure 2 depicts the range of all adherence instruments and their time points.

When combining the instrument, definition/calculation for adherence, metric and method of aggregation, studies reported adherence in 115 unique ways (Fig 3). The most frequent were: pharmacy refill record, adherence defined as filling an initial prescription, reported as an end value, categorical method of aggregation (n=8 studies, 15%); pharmacy refill record, adherence defined as no discontinuation of therapy, reported as an end value, categorical method of aggregation (n=5 studies, 9%); pill count, adherence calculated as the percentage of tablets taken, reported as an end value, continuous method of aggregation (mean) (n=4, 8%). Ninety-four (82%) appeared in one study only. Supplementary Table 4 includes the unique adherence measurement approaches for each study.

***Health outcomes***

Forty-one studies (77%) reported 38 health outcomes. Twenty-four studies (45%) reported on medication adverse events. We reviewed the compatibility of the reported health outcomes in the included adherence studies against the existing condition-specific core domain sets. We excluded five studies from this analysis as they

included conditions for which no core domain set currently exists or existed at least five years prior to the date of the publication of the respective study. Of the remaining 48 studies, only one study reported all outcome domains in the existing condition-specific core domain set, 32 studies (67%) reported at least one domain and 16 studies (33%) did not use any outcome domains from the existing condition-specific core domain set (Table 2).

Thirty-three studies (including 28 RCTs) with participants with osteoporosis-related conditions assessed the impact of the adherence intervention on a total of 10 health outcomes. The five most frequently reported health outcomes were: adverse events (n=17 studies, 52%), bone turnover markers (n=10, 30%), bone mineral density (n=5, 15%), fractures (n=5, 15%), quality of life (n=4, 12%). None of the studies reported on pain or height, which are outcome domains in the existing core domain set for osteoporosis[67].

Studies including participants with RA (12 studies in total, including 8 RCTs), reported 26 health outcomes. The five most commonly reported health outcomes were: disease activity (n=7 studies, 58%), physical function (n=7, 58%), pain (n=5, 42%), quality of life (n=4, 35%), adverse events (n=3, 25%), erythrocyte sedimentation rate or C-reactive protein (n=3, 25%). In RA, only one study reported on all outcome domains from the existing RA core domain set[47].

***Adherence-related factors***

Thirty-three studies (62%) reported 32 adherence-related factors. Table 3 outlines the proportion of studies reporting each factor. The most frequently reported factor was

reasons for adherence/non-adherence (n=12 studies, 23%), where studies would list a variety of reasons elicited from participants. The next four most commonly reported factors were: medication beliefs (including necessity, concerns, harms, overuse) (n=8, 15%); illness perception, medication satisfaction, and satisfaction with medication information (each in n=5, 9%).

**Discussion**

This systematic review of 53 studies shows that researchers are conducting an increasing number of studies, especially RCTs to evaluate strategies to improve adherence in rheumatic conditions. There is considerable heterogeneity in the outcome domains and adherence measures that assess the impact of these interventions. A third of studies had an unclear phase of adherence and the review identified 37 different instruments that measured and reported adherence in 115 unique ways. Although adherence was linked to health outcomes in 77% of studies, the 38 reported health outcome domains were varied. Studies rarely used the existing disease-specific core domain sets and only half of studies reported medication adverse events. Studies evaluated multiple adherence-related factors. However, the review did not find any specific factor in more than 15% of studies.

Studies included in this systematic review assessed medication initiation least frequently compared to other phases of medication adherence. This may be due to difficulty in patient recruitment, as patients who are not intending to start treatment are unlikely to agree to participate in an adherence trial. In previously published studies, medication adherence dramatically drops in the first year after initiation[68].

The step prior to this – the actual rate of initiation of prescribed medications is still poorly characterised in rheumatology studies.

Adherence measures varied at many levels: instrument, definitions for the calculation of adherence, metric and method of aggregation. There are many adherence measures available, with no gold standard of adherence measurement. Measures may differ for different phases of adherence and require differing amounts of time, expertise and costs associated with their use. Variability in medication dosing, route and polypharmacy further complicates how adherence is measured and reported in rheumatic conditions.

Health outcomes are dependent on both the efficacy of the medication and adherence. Patients and health professionals may perceive health outcomes to be important outcome domains of medication adherence studies. Despite this, 23% of studies in this review did not report on any health outcomes. Furthermore, the condition-specific core domain set includes outcome domains that are mandatory in all clinical trials[6] and represent the minimum set of outcome domains of highest importance to multiple stakeholders. However, only one adherence study in this review used the entire condition-specific core domain set to assess health outcomes. There may be some explanations for this including considerations of study power and duration of follow-up, or the added participant burden and study costs when researchers incorporate health outcomes into their studies. Qualitative studies indicate that concerns about medication adverse effects and experience of side effects influences adherence behaviour[69]. Conversely, adherence can also affect the occurrence of side effects. However, only half of studies reported on this.

This review identified many adherence-related factors. Members of the OMERACT-Adherence group found it difficult to delineate which factors should be considered candidate domains for a core domain set to be used for interventional studies targeting adherence. These factors may be better classified as intervention targets or explanatory variables for adherence (i.e., in the causal pathway to adherence) and not true outcome domains.[8] Some of the same factors could be considered to be potential contextual factors (a covariate that could be measured at baseline that could serve as an effect modifier of the outcome, e.g. trust in the doctor). No specific adherence-related factor was reported frequently, this may be because factors influencing adherence are complex and numerous and some factors are tied directly to theories of adherence used to design the intervention (e.g. medication beliefs). Therefore, any single factor may not have relevance across all potential adherence interventions in different rheumatic conditions and is unlikely to be in the core domain set for adherence interventions.

Many systematic reviews in rheumatic conditions and a broader range of chronic conditions have noted the difficulty of combining adherence results because of the inconsistency in adherence measurement[5, 9]. This review adds an in-depth analysis of different points at which heterogeneity exists at the level of instrument, definition/calculation of adherence, metric and method of aggregation. A previous systematic review and meta-analysis of medication adherence interventions across multiple health conditions showed a positive impact of adherence interventions on some patient-centred outcome domains including quality of life, physical function and symptoms[70]. However, it remains unclear which outcome domains are of most

importance to patients in trials targeting adherence in rheumatic conditions, which is needed to inform the design of patient-centred adherence interventions.

This review provides a detailed analysis of the scope and consistency of outcome domains, including adherence measures across a large number of adherence interventions in rheumatic conditions from 33 countries. However, there are some limitations. We included studies published in English and did not include studies published in other languages. The majority of studies in this systematic review focused on osteoporosis. The findings are likely to differ in other rheumatic conditions and may therefore not be generalizable.

This review provides a broad understanding of the outcomes reported in interventional studies across multiple rheumatic conditions. The evidence from this review informs the next phases in the OMERACT-Adherence five-phase project which includes qualitative research with patients and researchers, a Delphi survey and consensus voting[7]. The OMERACT-Adherence group aims to develop a core domain set that includes outcome domains that are important to patients and health professionals and also feasible for researchers. A core domain set for adherence interventions can enhance the quality of adherence research conducted in rheumatology and ensure studies lead to improvements for patients in outcomes that are important and relevant to them.

This systematic review also demonstrates the need for clear guidance of the method for measuring and reporting adherence in interventional studies targeting adherence in rheumatic conditions. A consensus-based recommendation for adherence measures in

adherence trials should be specific for the phase of adherence, applicable to the different frequencies, modes of administration and combinations of medications used in rheumatology and consider the time, resources and expertise needed for their use.

In summary, studies of adherence interventions in adults with rheumatic conditions measure and report a broad range of adherence outcomes, health outcomes and adherence-related factors. Adherence measures are highly heterogeneous and there is no consistency in which health outcomes are reported. A significant portion of outcome domains were not true outcomes and are better classified as determinants of adherence whose improvement may lead to better adherence (i.e. a time-dependent contextual factor). A core domain set will enhance the ability to compare results across adherence studies on outcomes of significance to patients and other stakeholders.

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## Tables and figures



NS, Not specified; CQR, Compliance Questionnaire in Rheumatology; MEMS, Medication Event Monitoring System; MARS, Medication Adherence Report Scale; MASRI, Medication Adherence Self-Report Inventory; MTB-Thai, Medication Taking Behaviour measure for Thai patients



## Appendix and Data Supplements

**Table 1.** Characteristics of included studies

| Study Characteristic | No. of Studies | (%) |
|---|---|---|
| **Type of study** | | |
| Randomized controlled trial | 41 | (77%) |
| Observational studies | 12 | (23%) |
| **Year of publication** | | |
| 1981-2000 | 2 | (4%) |
| 2001-2010 | 17 | (32%) |
| 2011-2019 | 34 | (64%) |
| **Country** | | |
| United States | 16 | (30%) |
| United Kingdom | 6 | (11%) |
| Other* | 27 | (51%) |
| Multinational studies | 4 | (8%) |
| **Sample size** | | |
| 1-100 | 14 | (26%) |
| 101-300 | 19 | (36%) |
| >300 | 20 | (38%) |
| **Duration of study** | | |
| ≤6 months | 14 | (26%) |
| >6-12 months | 29 | (55%) |
| >12 months | 10 | (19%) |
| **Condition** | | |
| Osteoporosis/osteopenia/fracture/at risk of osteoporosis | 33 | (62%) |
| Rheumatoid arthritis | 12 | (23%) |
| Gout | 2 | (4%) |
| Systemic lupus erythematosus | 1 | (2%) |
| Systemic rheumatic diseases | 1 | (2%) |
| Early inflammatory arthritis | 1 | (2%) |
| Multiple † | 3 | (6%) |

* 1-3 studies: Australia, Canada, Denmark, Egypt, France, India, Italy, Japan, Korea, Malaysia, Netherlands, New Zealand, Spain, Thailand, Turkey

† Rheumatoid arthritis (RA) and degenerative joint disease; RA and psoriatic arthritis (PsA); RA, PsA and inflammatory polyarthritis

**Table 2.** Reporting of health outcomes, core domain set and medication-related adverse events

| Osteoporosis/osteopenia/fracture/at risk for osteoporosis | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| No. CDS items | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Adverse events | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | × | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | × | × |

| Osteoporosis/osteopenia/fracture/at risk for osteoporosis | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | × | × | × | × | × | × | × | × | × | × | × |
| No. CDS items | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Adverse events | × | ✓ | ✓ | ✓ | × | × | × | × | × | × | × | × | × | × | × | × |

| Rheumatoid arthritis | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | 57 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| No. CDS items | 7 | 6 | 6 | 5 | 5 | 4 | 4 | 3 | 1 | 1 | 1 | 0 |
| Adverse events | × | ✓ | ✓ | × | × | ✓ | × | × | × | × | × | ✓ |

| Gout | | SLE | Other or multiple conditions | | | | |
|---|---|---|---|---|---|---|---|
| Study | 58 | 59 | 60 | 61 | 62 | 63 | 64 | 65 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| No. CDS items | 5 | 2 | 2 | NA | NA | NA | NA | NA |
| Adverse events | ✓ | ✓ | × | ✓ | ✓ | × | × | × |

✓ (blue) – reported; × (orange) – not reported; CDS – Core domain set (Number of items in the core domain set that was reported in each study; blue – full core domain set reported, orange – full core domain set not reported); NA - not applicable (No core domain set existing or did not exist at least 5 years prior to date of publication)

**Table 3.** Adherence-related factors

| Adherence related factor | No of studies | (%) |
|---|---|---|
| Reasons for adherence/non-adherence | 12 | (23%) |
| Medication beliefs (Necessity/Concerns/Overuse/Harms) | 8 | (15%) |
| Illness perception | 5 | (9%) |
| Medication satisfaction | 5 | (9%) |
| Satisfaction with medication information | 5 | (9%) |
| Condition knowledge | 3 | (6%) |
| Medication and condition knowledge | 3 | (6%) |
| Trust in doctor | 3 | (6%) |
| Decisional conflict | 2 | (4%) |
| Illness risk | 2 | (4%) |
| Intervention satisfaction | 2 | (4%) |
| Intervention's influence on adherence | 2 | (4%) |
| Involvement in decision making | 2 | (4%) |
| Medication initiation decision | 2 | (4%) |
| Medication knowledge | 2 | (4%) |
| Satisfaction with medical care | 2 | (4%) |
| Anxiety | 1 | (2%) |
| Drug interactions | 1 | (2%) |
| Duplication of prescriptions | 1 | (2%) |
| Duplication of therapeutic class | 1 | (2%) |
| Health and medication information source | 1 | (2%) |
| Helpfulness of pharmacist's recommendation | 1 | (2%) |
| Intention to adhere | 1 | (2%) |
| Medication bother | 1 | (2%) |
| Medication cost | 1 | (2%) |
| Medication preference | 1 | (2%) |
| Medication problems | 1 | (2%) |
| Patient activation (engagement with therapy) | 1 | (2%) |
| Prescription documentation | 1 | (2%) |
| Safety of pharmacist's recommendations | 1 | (2%) |
| Self-efficacy | 1 | (2%) |
| Unmet treatment needs | 1 | (2%) |

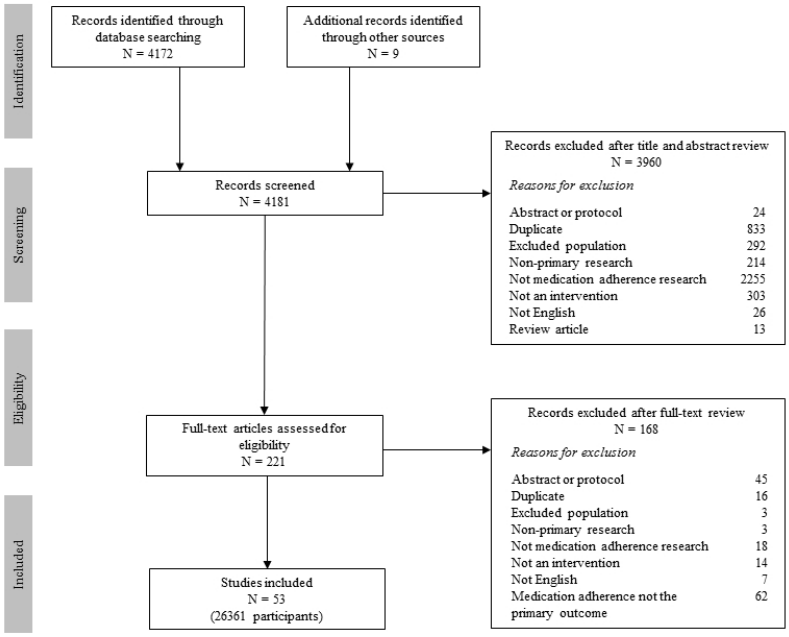


Figure 1. Search results

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**Figure 2.** Frequency and time points of instruments measuring adherence

| 115 unique ways of measuring and reporting adherence | | | | | |
|---|---|---|---|---|---|
| Top 6 | | | | Studies | (%) |
| Pharmacy refill record | Filled initial prescription | End value | Categorical | 6 | (11) |
| Pharmacy refill record | Persistent if no discontinuation of therapy | End value | Categorical | 5 | (9) |
| Pill count | Percentage of tablets taken | End value | Continuous (Mean) | 4 | (8) |
| Pharmacy refill record | Medication Possession Ratio >80% | End value | Categorical | 3 | (6) |
| Pharmacy refill record | Medication Possession Ratio | End value | Continuous (Mean) | 3 | (6) |
| Pharmacy refill record | Medication Possession Ratio | End value | Continuous (Median) | 3 | (6) |
| Instrument | Adherence definition and calculation | Metric | Method of aggregation | | |

Figure 3. Unique ways of measuring and reporting adherence

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## Correction

Scope of Outcomes in Trials and Observational Studies of Interventions Targeting Medication Adherence in Rheumatic Conditions: A Systematic Review

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In Table 2, the column heads indicating the studies used showed references 13–65. The correct studies should be references 14–66. A corrected Table 2 from the article follows below.

This correction only applies to the August 15 First Release. The correct table appears online and in the October print edition.

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*Table 2.* Reporting of health outcomes, core domain set, and medication-related adverse events.

| | Osteoporosis/osteopenia/fracture/at risk for osteoporosis | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study (ref.) | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| No. CDS items | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Adverse events | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✗ |

| | Osteoporosis/osteopenia/fracture/at risk for osteoporosis | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study (ref.) | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ |
| No. CDS items | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Adverse events | ✗ | ✓ | ✓ | ✓ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ | ✗ |

| | Rheumatoid Arthritis | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study (ref.) | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | 57 | 58 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| No. CDS items | 7 | 6 | 6 | 5 | 5 | 4 | 4 | 3 | 1 | 1 | 1 | 0 |
| Adverse events | ✗ | ✓ | ✓ | ✗ | ✗ | ✓ | ✗ | ✗ | ✗ | ✗ | ✗ | ✓ |

| | Gout | | SLE | Other or Multiple Conditions | | | | |
|---|---|---|---|---|---|---|---|---|
| Study (ref.) | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 |
| Health outcome | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| No. CDS items | 5 | 2 | 2 | NA | NA | NA | NA | NA |
| Adverse events | ✓ | ✓ | ✗ | ✓ | ✓ | ✗ | ✗ | ✗ |

✓ Reported. ✗ Not reported. CDS: core domain set (no. items in the core domain set that was reported in each study; ✓: full core domain set reported; ✗: full core domain set not reported); NA: not applicable (no core domain set existing or did not exist at least 5 yrs prior to date of publication).