Identifying and addressing patient-centred outcomes to improve medication adherence in rheumatology

Ayano Kelly

November 2020

A thesis submitted for the degree of Doctor of Philosophy of
The Australian National University

Declaration

I declare that the research presented in this thesis represents original work that I carried out during my candidature at the Australian National University. To the best of my knowledge, it contains no material previously published or written by another person, except where due reference is made in the text.

Word count: 77,281 words

Ayano Kelly

November 2020

Acknowledgements

To Kathie Tymms for your kindness, generosity, dedication and boundless enthusiasm. I have loved being on this PhD journey with you always by my side.

To Allison Tong for teaching me the joy and value of research. Thank you for your caring guidance during the difficult times.

To Kieran Fallon, for your constant positivity and offering me your coastal home as a place to work on my PhD. I look forward to visiting you and Sue there in the future.

To my other mentors Chandima Perera, Geraldine Hassett, Gabor Major, Lyn March and Peter Tugwell for providing me with inspiration, guidance and many opportunities that led to these research adventures.

To all my friends, family and two beautiful kittens, thank you for providing me with comfort, much needed distractions and wonderful memories. A special thanks to my research friends Karine, Valeria, Emma, and Dan, who have been by my side along the whole PhD journey. I am so grateful for your friendship, having your support has made a huge difference to me.

To Mum, Dad, Kathie, John, Penny, Ken, Julie and Irah who kindly gave me a second home while I constantly travelled back and forth between Sydney and Canberra.

To my collaborators, it has been such a pleasure working together. Especially Vicki, Maarten, Marieke, Mike and Mary for your generosity, positivity, wisdom and reassurance on the importance of this research.

To the organisations who supported this research; Arthritis Australia (including the late Beryl Stephens) and the wonderful staff at ANU.

And finally, to my loving husband Shane, who has listened to every presentation, read every paper, and celebrated all my successes. I dedicate this thesis to you and am looking forward to the next chapter in our lives!

Abstract

Many rheumatic conditions require the long-term use of medications, yet suboptimal adherence remains a major challenge. There are increasing efforts to develop and test strategies to improve medication adherence in rheumatology, however few interventions have been shown to be effective. This may be due to a number of problems. It remains uncertain whether existing interventions to improve adherence address the priorities and concerns of patients with rheumatic conditions. In addition, the outcomes reported in trials targeting adherence are heterogeneous, limiting the ability to assess the comparative effect of interventions. Core domain sets are defined as the minimum set of outcome domains that should be measured and reported in specific clinical trials. They reduce inconsistent outcome reporting and reporting bias. Furthermore, they can help ensure the use of outcomes that are important to patients and decision-makers. Through the Outcome Measures in Rheumatology (OMERACT) initiative, core domain sets have been established for multiple rheumatic conditions. This thesis aims to understand medication adherence from the perspective of patients with diverse rheumatic conditions and their caregivers; and to identify issues in outcome reporting in interventional studies targeting medication adherence in rheumatic conditions as part of OMERACT.

Chapter 2 presents a review of qualitative research principles and methodology in the context of rheumatic conditions. An overview of qualitative methods is presented and the key approaches to guide the appraisal of qualitative research are discussed.

The next part of this thesis (Chapters 3 to 5) consists of systematic reviews which provide a comprehensive evaluation of outcomes reported in interventional studies in medication adherence in rheumatic conditions and qualitative studies that describe the patients' experience in a variety of rheumatic conditions.

The second part of this thesis (Chapter 6) further explores the perspective and priorities of patients with rheumatic conditions and their caregivers using focus groups with nominal group technique. This study addresses patient and caregiver barriers and facilitators to medication adherence.

Chapters 7 is a report from a workshop convened at the 2018 OMERACT conference to discuss the challenges with developing a core set of outcomes for interventional studies targeting medication adherence. Despite the challenges of producing a core domain set

for this topic, the meeting clarified an approach of how this could be achieved using OMERACT methodology.

The thesis provides a greater understanding of outcomes and factors that are important to patients and their caregivers, and the mismatch with currently reported outcomes. It was demonstrated that consistent reporting of outcomes is needed to better inform which interventions are effective. The qualitative studies on patient and caregiver perspectives highlight the need for empathetic care that promotes trust in the doctor. Overall a patient-centred approach to supporting medication adherence is needed in both clinical care and research. This approach will help address the complexity and challenges patients with rheumatic conditions face with their medication-taking and improve outcomes that matter to them.

List of Abbreviations

ADA	Adalimumab
AS	Ankylosing spondylitis
bDMARD	Biologic disease modifying anti-rheumatic drug
CDS	Core domain set
COREQ	Consolidated criteria for reporting qualitative research
CQR	Compliance questionnaire in rheumatology
csDMARD	Conventional synthetic disease modifying anti-rheumatic drug
CZP	Certolizumab pegol
DMARD	Disease modifying anti-rheumatic drug
DXA	Dual energy X ray absorptiometry
ENTREQ	Enhancing transparency in reporting the synthesis of qualitative research
ETN	Etanercept
GOL	Golimumab
HCQ	Hydroxychloroquine
HLA-B27	Human leucocyte antigen-B27
HRT	Hormone replacement therapy
IFX	Infliximab
JIA	Juvenile idiopathic arthritis
LEF	Leflunomide
MARS	Medication adherence report scale
MASRI	Medication adherence self-report inventory
MEMS	Medication event monitoring systems
MPR	Medication possession ratio
MTX	Methotrexate
OMERACT	Outcome measures in rheumatology
OP	Osteoporosis
PDC	Proportion of days covered
PsA	Psoriatic arthritis
RA	Rheumatoid arthritis
RF	Rheumatoid factor
SEC	Secukinumab
SERM	Selective estrogen receptor modulator
SLE	Systemic lupus erythematosus
SSZ	Sulfasalazine
TNFi	Tumor Necrosis Factor inhibitor
tsDMARD	Targeted synthetic disease modifying anti-rheumatic drug
ULT	Urate lowering therapy
UST	Ustekinumab

Table of Contents

List of Tables

List of Figures

First author publications arising from this thesis

This thesis is presented as a thesis by compilation. Chapters 1-7 contain peer-reviewed journal publications. Dr Ayano Kelly is the first and corresponding author of each of these manuscripts.

Chapter 1 (Appendix)	Kelly A, Tong A, Tymms K, March L, Craig CJ, De Vera M, Evans V, Hassett G, Toupin-April K, van den Bemt B, Teixeira-Pinto A, Alten R, Bartlett SJ, Campbell W, Dawson T, Gill M, Hebing R, Meara A, Nieuwlaat R, Shaw Y, Singh JA, Suarez-Almazor M, Sumpton D, Wong P, Christensen R, Beaton D, de Wit M, Tugwell P and on behalf of the OMERACT-Adherence group. Outcome measures in rheumatology - interventions for medication adherence (OMERACT-Adherence) core domain set for trials of interventions for medication adherence in rheumatology: 5 phase study protocol. Trials. 2018; 19: 204. (Published 27/3/2018, doi: 10.1186/s13063-018-2565-z)
Chapter 2	Kelly A, Tymms K, Fallon K, Sumpton D, Tugwell P, Tunnicliffe D, Tong A. Qualitative research in rheumatology: an overview of methods and contributions to practice and policy. The Journal of Rheumatology. (Epub ahead of print 15/7/2020, doi: 10.3899/jrheum.191368)
Chapter 3	Kelly A, Crimston-Smith L, Tong A, Bartlett SJ, Bekker C, Christensen R, De Vera MA, de Wit M, Evans V, Gill M, March L, Manera K, Nieuwlaat R, Salmasi S, Scholte-Voshaar M, Singh JA, Sumpton D, Toupin-April K, Tugwell P, van den Bemt B, Verstappen S, Tymms K. Scope of outcomes in trials and observational studies of interventions targeting medication adherence in rheumatic conditions: a systematic review. The Journal of Rheumatology. 2020;47(10):1565-74. (Published 1/10/2020, doi: 10.3899/jrheum.190726)
Chapter 4	Kelly A, Tymms K, Tunnicliffe DJ, Sumpton D, Perera C, Fallon K, Craig JC, Abhayaratna W, Tong A. Patients' attitudes and experiences of disease modifying anti-rheumatic drugs in rheumatoid

arthritis and spondyloarthritis: A systematic review of qualitative studies. Arthritis Care and Research. 2018;70(4):525-32. (Published 21/7/2017, doi: 10.1002/acr.23329)

Chapter 5 Kelly A, Niddrie F, Tunnicliffe DJ, Matus Gonzalez A, Hanson C, Jiang I, Major G, Singh-Grewal D, Tymms K, Tong A. Patients' attitudes and experiences of transition from paediatric to adult healthcare in rheumatology: a qualitative systematic review. Rheumatology (Oxford). (Epub ahead of print 15/5/2020, doi: 10.1093/rheumatology/keaa168)

Chapter 6 Kelly A, Tymms K, de Wit M, Bartlett SJ, Cross M, Dawson T, De Vera M, Evans V, Gill M, Hassett G, Lim I, Manera K, Major G, March L, O'Neill S, Scholte-Voshaar M, Sinnathurai P, Sumpton D, Teixeira-Pinto A, Tugwell P, van den Bemt B, Tong A. Patient and caregiver priorities for medication adherence in gout, osteoporosis and rheumatoid arthritis: nominal group technique. Arthritis Care and Research. 2020;72(10):1410-9. (Published 10/2020, doi: 10.1002/acr.24032)

Chapter 7 Kelly A, Bartlett SJ, de Wit MP, Beaton DE, Dawson T, Evans V, Gill M, Hassett G, March L, Scholte-Voshaar M, Singh JA, Tong A, Tugwell P, Wong P, Tymms K. Addressing challenges in developing a core domain set in adherence interventions in rheumatology: a report from the OMERACT-Adherence group. The Journal of Rheumatology. 2019;46(9):1202-6. (Published 1/9/2019, doi: 10.3899/jrheum.181078)

Chapter 1: Introduction

1.1 Overview

This thesis includes a series of publications that describe the experiences, attitudes, and decision-making regarding medication-taking in patients with rheumatic conditions. Potential solutions to support adherence are discussed and current gaps in the outcomes used for interventional studies targeting medication adherence in rheumatology are identified. This first chapter provides definitions, epidemiology, and management of rheumatic conditions included in this thesis and background of the rates, reasons, and consequences of non-adherence as well as outcomes reported in research in medication adherence in rheumatology. The overall methods used in the thesis and the aims of the individual chapters are presented.

1.2 Definition and epidemiology of rheumatic conditions

The definition and epidemiology of the main rheumatic conditions that are addressed in the thesis are summarised.

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, autoimmune disease characterised by inflammatory polyarthritis preferentially affecting the small joints (1, 2). It is frequently accompanied by autoantibodies to rheumatoid factor and citrullinated proteins, although some people are negative for these autoantibodies (1, 2). RA has a prevalence of 0.5-1% in Caucasian populations. A higher prevalence of 5-6% occurs in Native American populations (3) and 2.7% of Indigenous Australian communities (4). Both genetic and environmental risk factors (e.g. smoking, microbiota, infections, obesity) contribute to the pathogenesis of RA (1). Women are two to three times more likely to develop RA than men (1).

Spondyloarthritis

While spondyloarthritis (SpA) can be considered a condition itself, it is used to describe a family of conditions including ankylosing spondylitis, psoriatic arthritis (PsA), inflammatory bowel disease-related SpA, reactive arthritis, undifferentiated SpA and juvenile-onset SpA (5, 6). These conditions have an overlap of distinguishing characteristics including inflammation of the axial joints (especially the sacroiliac joint), asymmetric oligoarthritis, enthesitis (inflammation of the tendon or ligament attachment to bone) and dactylitis (sausage digits), extra-articular features including uveitis, psoriasis, and inflammatory bowel disease, and a genetic association to the Human Leucocyte Antigen (HLA)-B27 (5, 7). Axial SpA (affecting mostly the spine and pelvic joints) or peripheral SpA (affecting the arms or legs) are categories of SpA. The presence or absence of plain radiographic changes further subdivides axial SpA into radiographic SpA (ankylosing spondylitis) or non-radiographic axial SpA (8). The prevalence of SpA worldwide ranges from 0.20% to 1.61% (6).

Osteoporosis

Osteoporosis is a disease characterised by reduced bone mineral density and disordered bone microarchitecture that results in increased bone fragility and risk of fracture (9, 10). A clinical diagnosis is based on bone mineral density (BMD) 2.5 or more standard deviations below the young adult reference mean (T score ≤ -2.5) by dual-energy x-ray absorptiometry (DXA) or fragility fracture (defined as a fracture from minimal or no trauma, less than or equal to a fall from standing height) (9, 10). The estimated prevalence of osteoporosis from 27 countries in the European Union, in those aged over 50 years is 22% in women and 7% in men (11). However, the sensitivity of DXA to predict fractures is low, and the majority of osteoporotic fractures occur in people with normal BMDs (12). The lifetime risk of any osteoporotic fracture is, therefore, higher than the prevalence of osteoporosis by BMD and is 40-50% in women and 13-22% in men (13).

Gout

Gout is a crystal deposition disease that results from chronic elevation of uric acid, leading to supersaturation in extracellular fluids and formation of monosodium urate (MSU) crystals in and around joints (14). This can lead to painful acute attacks of gouty arthritis, the formation of tophaceous MSU crystal deposits within joints and other body tissues, chronic joint damage, kidney stone formation, and kidney impairment (14). Gout is the most common form of inflammatory arthritis, the prevalence worldwide ranging from 0.1% to 10% (14). The prevalence and incidence of gout are rising in many developed countries (14). Major risk factors for gout include hyperuricaemia, genetic susceptibility, dietary factors, medications and comorbidities (14).

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) encompasses a group of different inflammatory arthritides with onset before 16 years of age and a minimum duration of 6 weeks. It is one of the most common diseases of childhood, with a prevalence of 70 per 100,000 children (15). The International League of Associations for Rheumatology (ILAR) categorises JIA into seven different subtypes depending on the number of joints involved, presence of extra-articular features and the presence of rheumatoid factor (RF) and HLA-B27 (Table 1.1) (16).

1.3 Pharmacotherapeutic management of patients with rheumatic conditions

Many conditions treated in rheumatology are chronic and require the long-term use of medications to prevent joint and organ damage, flares of disease activity or other preventable health outcomes such as a fracture. The following section summarises the medication management approach to the rheumatic conditions addressed throughout this thesis.

Rheumatoid arthritis

Without adequate treatment, RA results in cumulative joint damage which causes subsequent disability. Current management strategies aim for early diagnosis, referral and prompt therapy initiation (1, 2). A treat-to-target approach involves frequent assessments and rapid changes of treatment to attain remission or low disease activity within six months, ideally with at least 50% clinical improvement within three months (17). This approach prevents joint damage and improves physical function, quality of life, ability to work and risks of comorbidities. Disease modification is the cornerstone of treatment, which distinguishes the ability of disease modifying anti-rheumatic drugs (DMARDs) to inhibit damage to cartilage and bone from other medications used for symptom relief. DMARDs are classified as conventional synthetic (cs) DMARDs (small chemical drugs, where the mode of action is largely unknown), biologic (b) DMARDs (monoclonal antibodies or receptor constructs), and, more recently, targeted synthetic (ts) DMARDs (small chemical drugs that target specific molecules within cells). Current guidelines from the European League Against Rheumatism (EULAR) divides treatment into three phases (Figure 1.1) (17). Progression to subsequent phases occurs in cases of DMARD failure or lack of efficacy within a three to six month timeframe.

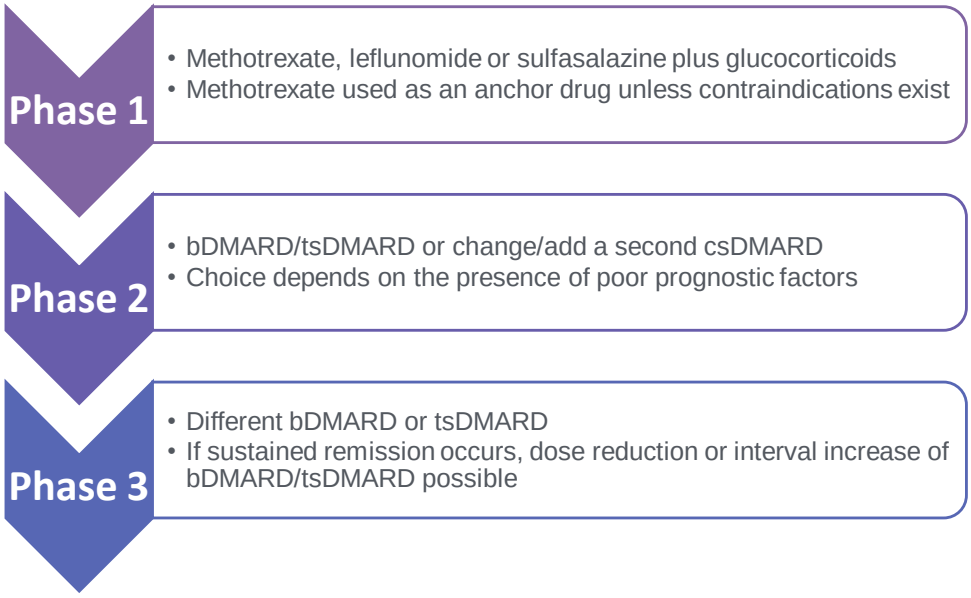


Figure 1.1. A treatment algorithm for the management of rheumatoid arthritis

bDMARD, biologic disease modifying anti-rheumatic drug; tsDMARD, targeted synthetic DMARD; csDMARD conventional synthetic DMARD.

Spondyloarthritis

The management of SpA varies depending on the subtype. This section will focus on the management of ankylosing spondylitis and PsA, two well-defined SpA subtypes that often require long-term pharmacotherapy.

In ankylosing spondylitis, pharmacotherapeutic management options include non-steroidal anti-inflammatory drugs (NSAIDs), sulfasalazine and bDMARDs (currently TNF inhibitors and IL17A inhibitors) (18, 19). NSAIDs constitute first-line therapy, in a full anti-inflammatory dose. Trial data have suggested that continuous NSAID use in patients with raised CRP reduces structural damage in the spine compared with on-demand use (20, 21). Both the 2016 Assessment of SpondyloArthritis international Society (ASAS)/EULAR and 2019 American College of Rheumatology/Spondyloarthritis Research and Treatment Network (ACR/SPARTAN) guidelines suggest continuous use only in patients whose symptoms recur after attempting to cease NSAIDs (18, 19). Sulfasalazine is only indicated in patients with peripheral arthritis, as the majority of available evidence shows a lack of efficacy in axial disease (19). For bDMARDs, which include TNF inhibitors and IL17A inhibitors, the current practice is to start with a TNF inhibitor. Phase 2 trials show promising results for the tsDMARD tofacitinib (22). Current guidelines from EULAR indicate the use of bDMARDs only when a trial of NSAIDs for four weeks has failed and there is plain radiographic evidence of sacroiliitis or high C-reactive protein (CRP) and/or inflammation of the spine and/or sacroiliac joints on MRI (18, 19). A treat-to-target approach is also recommended in ankylosing spondylitis, based on evidence that higher disease activity leads to new syndesmophyte formation (23, 24). Slow tapering of bDMARDs in those in sustained remission is possible. Unlike in RA, current DMARDs do not reduce disease progression of ankylosing spondylitis.

PsA therapy options include NSAIDs, csDMARDs (e.g. methotrexate, leflunomide, sulfasalazine), bDMARDs (TNF inhibitors, IL17A inhibitors, IL 12/23 inhibitors, T cell co-receptor inhibitor) and tsDMARDs (tofacitinib and apremilast). 2015 EULAR (25), 2015 Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) (26) and 2018 ACR guidelines (27) differ in their treatment algorithms. There is little head-to-head evidence available for different therapies with subsequent differences in approaches of the respective guideline groups (28). Each set of guidelines emphasises the use of a treat-to-target approach as well as tailoring treatment based on the disease manifestations present.

Osteoporosis

Anti-osteoporosis therapies available in Australia include bisphosphonates (alendronate, risedronate, zoledronic acid), denosumab, oestrogen replacement therapies, selective oestrogen receptor modulators (raloxifene) and teriparatide. Recommendations for thresholds for treatment in Australia are in Figure 1.2 (29). These agents all reduce the risk of vertebral fracture. Most also reduce the risk of non-vertebral fracture (11).

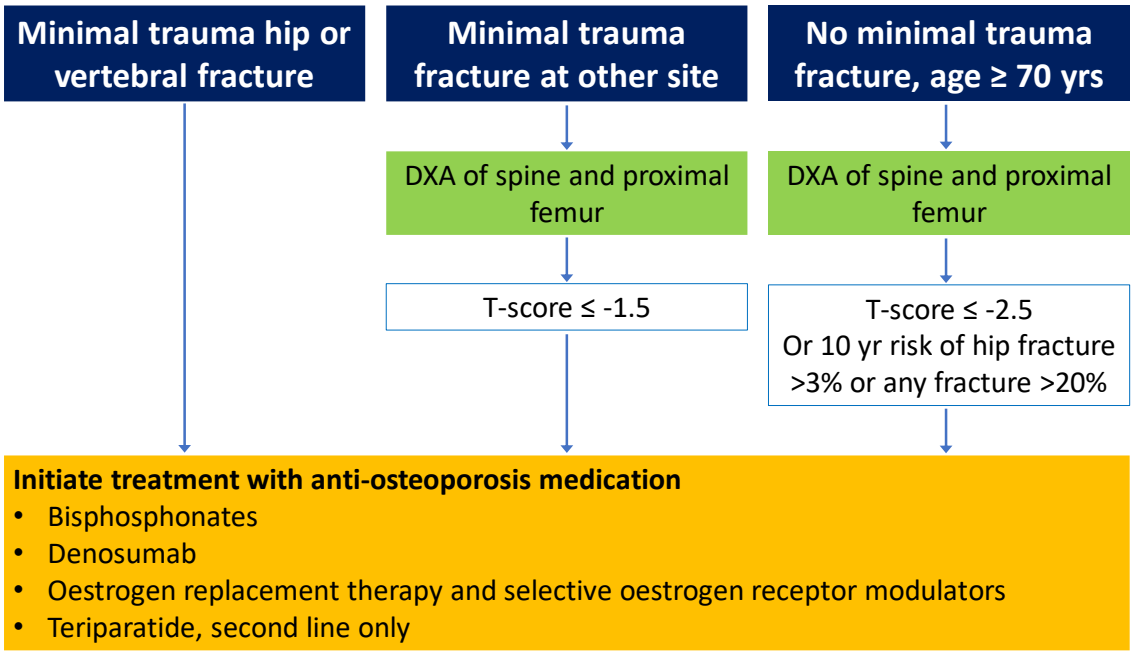


Figure 1.2. Treatment thresholds with anti-osteoporosis medications in Australia
DXA, Dual energy X ray absorptiometry; yr, year.

Gout

Acute gout flares are managed with early use of either colchicine, NSAIDs or glucocorticoids. Urate lowering therapy (ULT) is recommended in all patients with recurrent flares (≥ two/year), tophi, urate arthropathy and/or kidney stones (30). Initiation is also recommended earlier in patients presenting at a young age (<40 years), or with very elevated serum uric acid (SUA) levels (>480 µmol/L), and/or comorbidities (renal impairment, hypertension, ischaemic heart disease, heart failure) (30). Prophylaxis against flares during the first six months of ULT is recommended (e.g. low dose colchicine or NSAIDs). SUA should be monitored, and ULT titrated in order to maintain

SUA <360 µmol/L, or 300 µmol/L in severe gout (presence of tophi, chronic arthropathy, frequent attacks) (30). Options for ULT are xanthine oxidase inhibitors (allopurinol, febuxostat) and uricosuric agents (e.g. probenecid). In severe, debilitating, chronic tophaceous gout with failure or contraindication of other ULTs, pegloticase is a final option (30).

Juvenile idiopathic arthritis in adulthood

Current treatment guidelines for JIA have different treatment approaches for the following populations: the oligoarthritis population, non-systemic polyarthritis population, sacroiliitis population and enthesitis population (31, 32). These populations may overlap with different ILAR subtypes of JIA. The treatment approach that is recommended from the 2011 and 2019 ACR guidelines is summarised in Figure 1.3 (31, 32). The treatment of systemic JIA involves a complex algorithm that depends on disease activity and the presence of active systemic features (33). Treatment choices in systemic JIA include NSAIDs, glucocorticoids, csDMARDs (methotrexate or leflunomide) and bDMARDs (anakinra, tocilizumab, canakinumab, TNF inhibitors, and abatacept) (33).

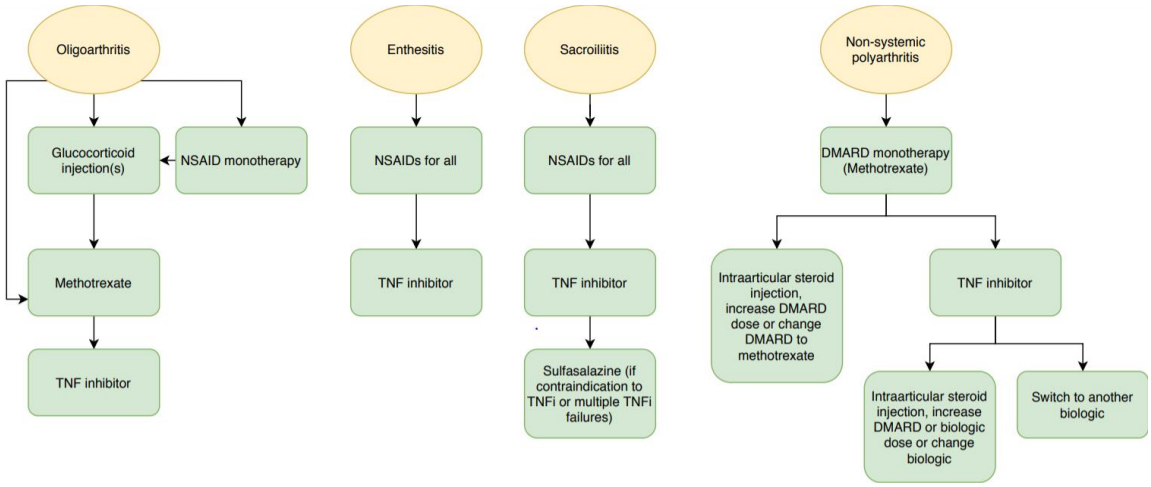


Figure 1.3. Treatment algorithms for various subtypes of juvenile idiopathic arthritis
Treatment escalation and choice dependant on ongoing disease activity and the presence of poor prognostic factors. NSAID, non steroidal anti-inflammatory drug; DMARD, disease modifying anti-rheumatic drug; TNFi, tumor necrosis factor inhibitor.

Side effects of pharmacotherapy

There is a considerable side-effect burden of the pharmacotherapies commonly used in these rheumatic conditions. These side-effects contribute to medication non-adherence and have been summarised in Table 1.2.

1.4 Medication adherence in rheumatology

Definitions and terminologies in adherence

Adherence is described by the World Health Organisation as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (34). The terminology used to describe medication-taking behaviour has evolved. Now, researchers most commonly support using “adherence” in preference to “compliance” or “concordance”(35, 36). “Compliance” portrays a paternalistic relationship between the healthcare provider and the patient (35). “Concordance” emphasises a balanced relationship between the patient and the healthcare provider (37). However, even when “concordance” is successful, patients may change or stop taking their medications (37). Therefore, the term adherence is used throughout the thesis. The ABC taxonomy of adherence (35, 38) defines adherence in three phases: a) initiation (when the patient takes the first dose of a prescribed medication); b) implementation (the extent to which a patient’s actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose); and c) discontinuation (when the patient stops taking the prescribed medication, where persistence is defined as the length of time between initiation and the last dose, which immediately precedes discontinuation). (Figure 1.4) (35)

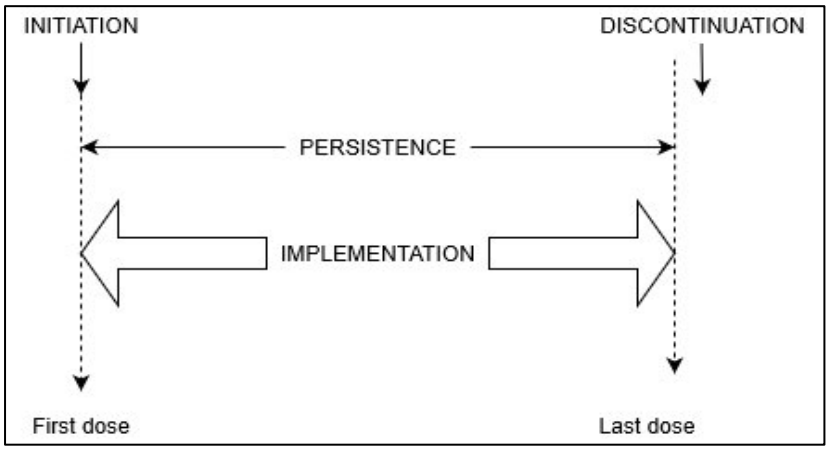


Figure 1.4. Adherence phases

Measurement of non-adherence

The measurement of adherence is challenging in both research and clinical practice (39). Many adherence measures currently exist; however there is no gold standard that is simple, valid, reliable and sensitive to change (40-42). Adherence measures may be categorised into direct (i.e. the ingestion of medication is directly measured or observed) or indirect methods, and subjective or objective methods, each with their advantages and disadvantages (Table 1.3) (40, 43).

The choice of adherence measure depends on the purpose and context (research/ clinical), available time, resources, expertise, and the phase of adherence being measured (42, 43). As no perfect measure exists, it is generally recommended to use a combination of adherence measures (34).

The need for ongoing long-term treatment in various rheumatic conditions

Modern therapies in rheumatic diseases can control symptoms and prevent disease progression or adverse outcomes such as fractures. However, none are curative, and therefore many are required lifelong. Early discontinuation of long-term treatment, which is one form of non-adherence has been linked to adverse outcomes in multiple rheumatic conditions. For example, in RA, randomised controlled trials of discontinuation of DMARDs have resulted in a recurrence of disease in approximately 40-80% of patients

(44-48). In PsA, current evidence is predominantly based on small observational studies and indicates that discontinuing DMARDs has a substantial risk of loss of remission (49, 50). Similarly, in AS, discontinuation of bDMARDs has led to flares in the majority of patients (51-53). A study in gout showed recurrence of flares in 40% of successfully treated patients five years after the withdrawal of ULT (54). Approximately half of the patients with JIA have ongoing disease activity in adulthood (55). An observational study of 701 patients with JIA on bDMARDs followed for ten years showed that only 11.7% were in drug-free remission (56). In osteoporosis, guidelines recommend reviewing bisphosphonates after approximately five years. However, treatment should be continued in those at higher risk of fracture as stopping these therapies results in a 20-40% higher risk of new fractures, and doubling of the risk of vertebral fractures (57-60). Denosumab has a rapid offset of action and an increased risk of vertebral fractures has been observed in patients discontinuing denosumab (61, 62). Although long-term pharmacotherapy can be withdrawn successfully in some cases, many patients can experience adverse health outcomes, highlighting the need for long-term medication persistence especially with those at higher risk of disease flares and adverse outcomes such as fractures.

Rates and consequences of non-adherence in various rheumatic conditions

The heterogeneity of adherence definitions, measurement and reporting methods makes it difficult to accurately summarise the rates and consequences of adherence. Table 1.4 summarises evidence available on the rates (based on the phase of adherence) and consequences of poor adherence with health outcomes in various rheumatic conditions. Where available, rates based on existing systematic reviews and/or objective measures of adherence are presented. For discontinuation or persistence, only the evidence that indicates complete cessation of all relevant long-term preventative medications used for the condition is included in the table. Many studies report on persistence with specific medications. However, switching from one medication to another that is used for the same purpose would not constitute poor adherence from a clinical perspective (e.g. switching from one bDMARD to another).

Reasons for non-adherence in various rheumatic conditions

In rheumatic diseases, many factors have been identified to influence adherence. Factors leading to poor adherence can be categorised using the Capability, Opportunity, and Motivation – Behaviour (COM-B) system of behaviour change (Table 1.5) (38). The COM-B system is based on the idea that three factors are necessary and sufficient to generate a specific behaviour: the skills necessary to perform the behaviour, a strong intention or non-volitional mechanisms (e.g. habits) to perform the behaviour and a lack of environmental constraints to make the behaviour possible (38). Potentially modifiable factors identified in studies for various rheumatic conditions are provided in Figure 1.5 (63-74).

Figure 1.5. Factors influencing adherence in various rheumatic conditions

1.5 Outcomes reported in research in medication adherence

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.

Outcomes terminology

An outcome is any identifiable result arising from an intervention. In the case of OMERACT-Adherence, it is the result of a study testing a strategy to support adherence (e.g. extra nursing support with medications). The effect these strategies have on patients are called "outcomes".
An outcome domain is the name of a broad group of outcomes or concept to be measured (e.g. disease activity – this can include outcomes like tender joints, swollen joints and blood tests for inflammation).
Our core domain set is a group of outcome domains that, as a minimum, should be measured in every study testing an adherence strategy. Core domain sets allow us to combine and compare the results of different studies to see which strategies work best. Researchers can also use additional outcome domains.

Adherence studies to date have used a variety of adherence outcome measures, definitions, and thresholds, and often exclude clinically meaningful health outcomes (75). Omitting important outcome domains or using inconsistent measures makes it difficult to judge the relative effectiveness of interventions or understand the clinical relevance of research findings. A minimum set of outcome domains that should be measured and reported in specific clinical trials is the definition of a core domain set. Core domain sets reduce inconsistent reporting and reporting bias and can help ensure the measurement of outcomes that are important to patients and decision-makers (76) (Figure 1.6).

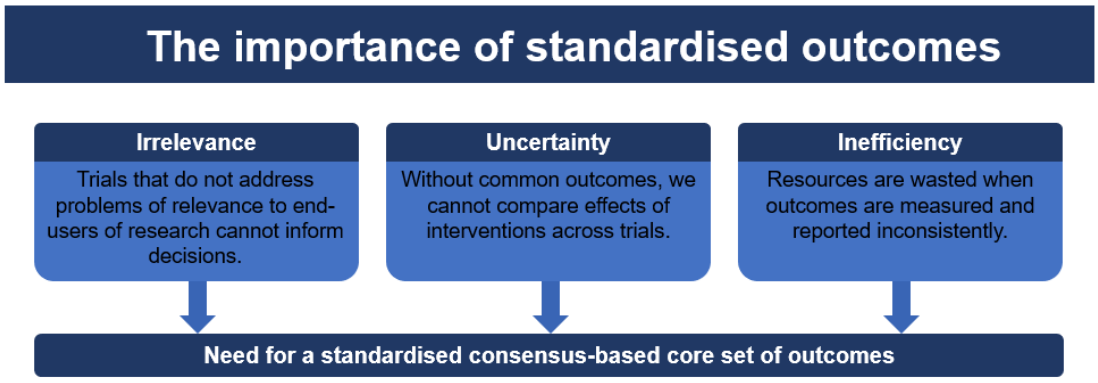


Figure 1.6 The importance of standardised outcomes

Worldwide, there are many initiatives to develop core domain sets (77, 78). The Outcome Measures in Rheumatology (OMERACT) initiative commenced in 1992 and has expanded to develop core domain sets in multiple rheumatic conditions. (76). There are several methodological groups examining core domains of interventions and measurements of outcomes that are relevant across rheumatic conditions, including health literacy, shared decision-making, and work productivity. (79-81)

The OMERACT-Adherence Group aims to establish a core domain set for clinical trials to support medication adherence in adult patients with rheumatic conditions (Figure 1.7, the published protocol for the five-phase study by OMERACT-Adherence is provided in Appendix A.1). The OMERACT-Adherence group was established in December 2016 and is comprised of over 50 members from 10 countries including Australia, Canada, Denmark, Germany, the Netherlands, Singapore, Spain, Thailand, the United Kingdom, and the United States. The members include patients, rheumatologists, nurses, pharmacists, behavioural scientists, occupational therapists, industry representatives, researchers with expertise in outcomes research and medication adherence research, and clinical trialists.

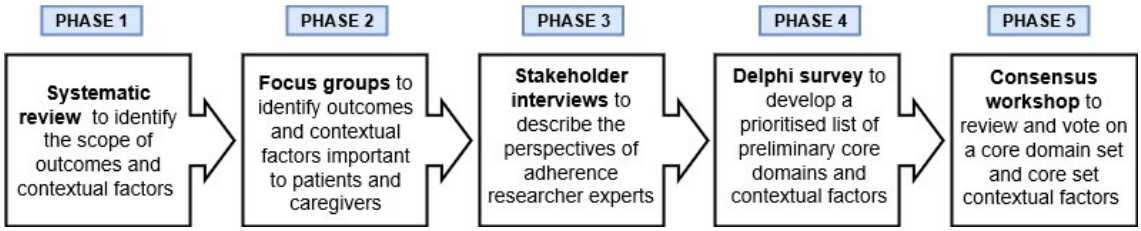


Figure 1.7. OMERACT-Adherence five-phase project

1.6 Justification for this thesis

Medication adherence and patient-centred care

Patient-centred care is a value supported by most health care systems. The concept of patient-centred care is defined as “care that is respectful of and responsive to individual needs, and values” and that ensures “that patient values guide all clinical decisions” (82). Dimensions of patient-centred care include improving health literacy through information,

communication and education; respect of patient values, preferences and needs; and involvement of the patient and their families in the care team (83-85). This definition highlights the importance of active engagement of patients and their caregivers in healthcare decisions and is particularly important in the context of medication adherence as taking long-term medications for rheumatic conditions is challenging (71, 74, 86, 87). Having a comprehensive and detailed understanding of the patients' and caregivers' values, priorities and preferences can be used to develop patient-centred interventions for medication adherence in rheumatology. Yet there is sparse literature that provides an in-depth inquiry into the specific issues surrounding adherence in various rheumatic conditions. It is unclear whether existing adherence interventions address the concerns and priorities of patients with rheumatic conditions leading to the rationale for the studies in this thesis.

Rheumatic conditions in this thesis

The conditions which are focused on in this thesis are rheumatoid arthritis, spondyloarthritis, gout, and osteoporosis. These are common rheumatic conditions, and rates of adherence are known to be suboptimal in these conditions (74, 87, 88). In addition, patients with juvenile-onset rheumatic conditions transitioning between paediatric and adult care are particularly vulnerable to discontinuity of care and medication non-adherence (89-92).

Need for outcomes research in medication adherence

Clinical trials have been conducted in people with rheumatic conditions with the aims of resolving ambivalence about the best strategies to improve medication acceptance and adherence, thereby enhancing health outcomes (93). A brief transition programme for adolescents with JIA was also conducted in order to improve medication adherence (94). Yet few interventions have demonstrated meaningful improvements in either medication adherence or clinical outcomes across medical specialties (75, 93, 94). Collating results of these trials to better identify successful interventions is difficult due to the lack of clarity of core outcomes and wide variability in adherence measures. There is a need for a

consensus-based core domain set for interventions to effectively test strategies to improve adherence in rheumatic populations.

Overall, the studies included in this thesis aimed to help improve our understanding of the challenges that patients with rheumatic conditions face with their medications and inform more patient-centred adherence research design in order to ultimately improve outcomes of importance to patients.

1.7 Methods

1.7.1 Qualitative and mixed-methods research methods

Two qualitative research methods have been used in this thesis – thematic synthesis of qualitative studies (Chapters 4 and 5) and focus groups (Chapter 6). Two systematic reviews were performed to synthesise qualitative studies conducted in different populations and settings on the perspectives of patients with RA and SpA and those undergoing transition from paediatric to adult care. The focus group study with patients with RA, gout and OP and their caregivers described the reasons for priorities related to medication adherence. The study used a mixed-methods approach which incorporated nominal group technique to quantitatively rank the priorities that were identified.

Chapter 2 provides an overview of qualitative methods including the use of focus groups. Thematic analysis, synthesising qualitative research and nominal group technique are discussed below.

1.7.1.1 Thematic analysis

The analysis of qualitative data generally seeks to develop a comprehensive understanding and description of the phenomenon being investigated. Thematic analysis yields themes (patterns of shared meaning that together give a comprehensive picture of the population of interests' experience). The processes used in thematic analysis involve data familiarisation (becoming immersed in the data and making notes), data

reduction (by assigning meaningful sections of the data to preliminary codes), data organisation (in which codes are collected and sorted) and interpretation (where data are analysed to understand meaning, and codes are categorised, compared and emerging themes are developed) (95, 96). Data analysis should be an iterative process that involves cycles of data collection, analysis and then a resumption of data collection to further explore and challenge emerging themes (97). The themes generated in the qualitative studies in this thesis are inductive, where meaning is identified from the data "bottom-up", rather than from existing concepts or theories (96).

1.7.1.2 Systematic review of qualitative research

A thematic synthesis of multiple qualitative studies can summarise and extend the results of individual qualitative studies conducted in different populations and healthcare contexts (98). Systematic reviews of qualitative studies require a structured approach including a comprehensive literature search, critical appraisal of included studies, extraction of data and synthesis of the available evidence. For the systematic review of qualitative studies included in this thesis, the Enhancing Transparency of Reporting the Synthesis of Qualitative research (ENTREQ) framework was utilised to report the findings of the systematic reviews (99). A modified version of the consolidated criteria for reporting qualitative health research framework (COREQ) (100) was used to evaluate the completeness of reporting of each interview or focus group study included in the reviews. Items specific to the research team, methods, setting, analysis and interpretations were assessed. Thematic synthesis for data analysis was conducted. This involved extracting all participant quotations and text under the "Results" and/or "Discussion/Conclusion" sections and importing them into qualitative software (HyperResearch). Preliminary concepts were identified and discussed with co-authors to ensure the codes reflected the full range and depth of data. For each article, transcripts were coded line-by-line into themes and subthemes and refined iteratively. Finally, an analytical thematic schema showing the conceptual links amongst themes was developed to present a comprehensive and new understanding of the topic based on the findings of multiple primary studies.

1.7.1.3 Nominal group technique

Nominal group technique involves structured discussion to generate a list of ideas followed by a single round of individual ranking. This takes into account each participant's opinion and encourages equal participation (101). Chapter 6 used focus groups with an embedded nominal group technique. Each group session included: 1) discussion on experiences with medications, involvement in decision making and strategies used to enhance adherence, 2) group generation of factors important for adherence, 3) individual ranking of the factors; and 4) discussion of the reasons for rankings.

1.7.2 Frameworks for establishing core domain sets for interventions

Currently, there are no existing frameworks to guide the development of a core set of outcome domains for specific interventions. The OMERACT guidelines for developing core domain sets for specific conditions were adapted for the outcome studies included in the thesis. OMERACT recommends the following steps for generating, prioritising and reaching consensus on a core domain set: 1) literature review of domains, 2) qualitative work to identify candidate domains, 3) prioritisation of candidate domains through a consensus process (e.g. Delphi survey), and finally 4) final vote by full OMERACT membership on the core domain set (76). Throughout this process, OMERACT recommends engaging patient research partners (PRPs) as integral stakeholders throughout the research process. Using these recommendations as a reference, a 5-phase protocol was developed for establishing a core domain set for use in interventional studies targeting medication adherence in rheumatic diseases (Appendix A.1) (102). PRPs are defined as "persons with a relevant disease who operate as active research team members on an equal basis with professional researchers, adding the benefit of their experiential knowledge to a research project" (103). PRPs have been involved in reviewing and contributing to the OMERACT-Adherence study protocol, design of the interview guide and co-facilitating the nominal group study (Chapter 6) and in the analysis of findings and co-authorship of manuscripts (Chapters 3, 6, 7).

1.7.2.1 Systematic reviews of outcome domains and adherence measures

A systematic review of outcome domains and adherence measures was conducted to identify existing domains and adherence measures in interventional studies targeting medication adherence in rheumatic conditions. A systematic review of existing outcome domains can identify relevant candidate core outcome domains and highlight gaps in existing outcomes being reported in the literature. For each study, two reviewers independently extracted study characteristics as well as all outcome domains, measures, and the instrument utilised. To assess reporting in detail, a unique adherence measure which included the instrument, time points, 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) was recorded.

1.8 Aims of this thesis

The overall objective of this thesis is to describe the experiences and priorities for medication adherence from the perspectives of patients with diverse rheumatic conditions and their caregivers and to identify issues in outcome reporting in interventional studies targeting medication adherence in rheumatic conditions. The specific aims of each study are:

1. To highlight recent contributions of qualitative research in rheumatology, summarise common methodologies and methods used, and outline key principles to guide appraisal of qualitative studies (Chapter 2)

2. To assess the scope of outcomes in interventional studies of medication adherence (Chapter 3)

3. To describe patients' attitudes to and experiences of DMARDs in RA and SpA (Chapter 4)

4. To describe patients' attitudes to and experiences of transition from paediatric to adult healthcare in rheumatology (Chapter 5)

5. To identify and prioritise factors important to patients and caregivers regarding medication adherence in gout, osteoporosis (OP) and rheumatoid arthritis (RA), and to describe the reasons for their decisions (Chapter 6)

6. To discuss the conceptual and methodological challenges in developing a core domain set for trials of interventions for medication adherence in rheumatology (Chapter 7)

1.9 Structure of this thesis

Chapter 1 presents background on selected rheumatic conditions and their management and a summary of the literature on medication adherence and outcomes of interventional studies targeting medication adherence in rheumatology.

Chapter 2 presents a review of qualitative research principles and methodology in the context of rheumatic conditions. An overview of qualitative methods is presented including participant selection, data collection, and analysis. The key approaches to guide the appraisal of qualitative research are discussed in terms of credibility, confirmability, dependability, and transferability.

The next part of this thesis (Chapters 3-5) consists of systematic reviews that provide a comprehensive evaluation of outcomes reported in interventional studies targeting medication adherence in rheumatic conditions and qualitative studies that describe the patients' experience in a variety of rheumatic conditions. Chapter 3 consists of a systematic review that provides an overview of the scope and consistency of outcomes in all interventional studies targeting medication adherence in adults with a rheumatic condition. In Chapter 4, a systematic review and thematic synthesis of qualitative studies were conducted to understand the experiences and attitudes of patients with RA and SpA in regard to their DMARDs. Chapter 5 examines the experiences and attitudes of patients with juvenile-onset rheumatic conditions transitioning to adult care using a systematic review and thematic synthesis of qualitative studies.

Chapter 6 ascertained the perspectives and experiences of patients with RA, gout and OP and their caregivers and their priorities for factors associated with medication adherence.

Chapters 7 is a report from a workshop convened at the OMERACT conference to discuss the challenges with developing a core set of outcomes for interventional studies targeting medication adherence.

Chapter 8 is the concluding chapter that summarises and integrates the key findings from each study. Strengths and limitations, clinical and research implications, as well as ongoing and future plans to continue this research are discussed.

Table 1.1. Subtypes of juvenile idiopathic arthritis

JIA subtype	Description
Oligoarthritis	Arthritis affecting one to four joints in the first six months of disease
Systemic arthritis	Arthritis in one or more joints, with or preceded by fever, lasting at least two weeks that is daily for at least three days and at least one of: • Non-fixed erythematous rash • Generalised lymph node enlargement • Hepatomegaly or splenomegaly • Serositis
Polyarthritis (RF positive)	Arthritis affecting five or more joints during the first six months; two or more tests for RF at least three months apart during the first six months of the disease are positive
Polyarthritis (RF negative)	Arthritis affecting five or more joints during the first six months; a test for RF is negative
Enthesitis-related arthritis	Arthritis or enthesitis with at least two of: • Presence or history of sacroiliac joint tenderness or inflammatory lumbosacral pain • HLA-B27 positive • The onset of arthritis in a male > 6 years of age • Acute (symptomatic) anterior uveitis • First-degree relative with a history of ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with inflammatory bowel disease, reactive arthritis or acute anterior uveitis
Psoriatic arthritis	Arthritis and psoriasis, or arthritis and at least two of: • Dactylitis • Nail pitting or onycholysis • First-degree relative with psoriasis
Undifferentiated arthritis	Arthritis that does not fulfil the criteria in any category, or meets criteria in two or more of the above categories

JIA, Juvenile idiopathic arthritis; HLA-B27, Human Leucocyte Antigen-B27, RF; rheumatoid factor

Table 1.2. Side effects of medications used for selected rheumatic conditions

Medication	**Common (>1%)**	**Infrequent (0.1-1%)**	**Rare (<0.1%)**
Bisphosphonates	Nausea, vomiting, diarrhoea, headache, hypocalcaemia, musculoskeletal pain IV: fever, flu-like symptoms, injection site reaction, increased creatinine, hypophosphatemia, myalgia, bone pain, hypertension	Oesophagitis, oesophageal erosions and ulcers, gastritis, duodenitis, glossitis, rash IV: Hypotension, hypomagnesaemia, hypokalaemia	Heart failure, renal impairment, ocular inflammation, osteonecrosis, atypical femoral fractures, allergic reactions, severe skin reactions IV: Anaphylactic shock
Denosumab	Eczema, hypercholesterolemia, musculoskeletal pain		Hypocalcaemia, osteonecrosis, hypersensitivity, vasculitis, lichen planus, atypical femoral fractures
Raloxifene	Hot flushes, sweating, leg cramps, peripheral oedema, sleep disorders		Venous thromboemboli
Teriparatide	Nausea, headache, dizziness, muscle cramp, arthralgia, hyperuricaemia, injection site reactions	Hypercalcaemia, myalgia, increased ALP	Allergic reactions
Xanthine oxidase inhibitors	Flare of acute gout, raised liver enzymes, oedema, rash	Arthralgia, dizziness, drowsiness, taste disturbance, abdominal pain	Hypersensitivity, anaphylaxis, hepatotoxicity, nephrolithiasis blood dyscrasias
Probenecid	Rash, nausea, vomiting	Headache, dizziness, flushing, sore gums, alopecia, urinary frequency, uric acid kidney stones	Nephrotic syndrome, aplastic anaemia, leukopenia, thrombocytopenia, hepatic necrosis, allergic reactions
Colchicine	Diarrhoea, nausea, abdominal discomfort, vomiting, pharyngolaryngeal pain	Gastrointestinal haemorrhage, rash	Peripheral neuropathy, myopathy, myalgia, rhabdomyolysis, alopecia, hepatitis, myelosuppression, agranulocytosis, thrombocytopenia, leukopenia, aplastic anaemia, arrhythmia, respiratory failure, hypersensitivity, angioedema

Medication	**Common (>1%)**	**Infrequent (0.1-1%)**	**Rare (<0.1%)**
Non Steroidal Anti-Inflammatory Drugs	Nausea, dyspepsia, gastrointestinal ulceration or bleeding, raised liver enzymes, diarrhoea, headache, dizziness, salt and fluid retention, hypertension	Oesophageal ulceration, heart failure, hyperkalaemia, renal impairment, confusion, bronchospasm, rash	Blood dyscrasias, interstitial nephritis, cystitis, nephrotic syndrome, acute renal failure, myocardial infarction, stroke, photosensitivity, hypersensitivity, hepatitis, aseptic meningitis, blurred vision, tinnitus, severe skin reactions
Prednisone	Adrenal suppression, infection, sodium and water retention, oedema, hypertension, hypokalaemia, hyperglycaemia, diabetes, dyslipidaemia, osteoporosis, fractures, increased appetite, dyspepsia, delayed wound healing, skin atrophy, bruising, acne, facial flushing, hirsutism, growth retardation in children, myopathy, muscle weakness and wasting, fat redistribution, weight gain, menstrual irregularity, amenorrhoea, psychiatric effects, cataracts	Osteonecrosis, ocular hypertension, glaucoma	Peptic ulceration, hypersensitivity reaction, tendon rupture, central serous chorioretinopathy, fat deposition around spinal cord
Methotrexate	Nausea and vomiting, oral mucositis, myelosuppression, increased aminotransferases, rash, itch, urticaria, photosensitivity, nephrotoxicity, alopecia, neurotoxicity	Malaise, chills, fever, headache, dizziness, tinnitus, blurred vision, ocular irritation, oligospermia	Anaphylaxis, severe skin reactions, radiation recall, osteoporosis, skin and bone necrosis, pneumonitis, pulmonary fibrosis, serious hepatotoxicity
Leflunomide	Abdominal pain, diarrhoea, nausea, vomiting, cholelithiasis, raised liver enzymes, hair loss, mild allergic reactions, itch, eczema, weight loss, weakness, synovitis, tenosynovitis, headache, dizziness, paraesthesia, peripheral neuropathy, bronchitis, pharyngitis, dyspnoea, pneumonia, hypertension	Constipation, oral thrush, stomatitis, taste disturbance, thrombocytopenia, urticaria	Anaphylaxis, angioedema, anaemia, agranulocytosis, eosinophilia, leukopenia, pancytopenia, vasculitis, serious skin reactions, multi-organ hypersensitivity syndrome, cutaneous lupus erythematosus, severe infection, interstitial lung disease, hepatic cirrhosis, liver failure
Sulfasalazine	Vomiting, reversible male infertility, haemolysis	Yellow-orange discolouration of body fluids or skin	Fibrosing alveolitis, meningitis, arthralgia
Hydroxychloroquine	Ocular effects (blurred vision common, reversible corneal changes infrequent, retinopathy dependent of dose and duration of treatment), nausea, vomiting, diarrhoea, anorexia, abdominal cramps, rash, itch, alopecia, headache	Hyperpigmentation, bleaching of hair, dizziness, vertigo, ototoxicity, nervousness, absent deep tendon reflexes, muscle weakness, neuromyopathy	Agranulocytosis, aplastic anaemia, thrombocytopenia, seizures, cardiac toxicity, severe hypoglycaemia, hepatitis, psoriasis, severe skin reactions, photosensitivity, allergy

Medication	**Common (>1%)**	**Infrequent (0.1-1%)**	**Rare (<0.1%)**
TNF inhibitors	Infections, rash, itch, headache, autoantibodies	Psoriasis, eczema, lupus-like syndrome, blood dyscrasias, malignancies (skin cancers)	Demyelination, interstitial lung disease, vasculitis, heart failure or worsening of existing disease
Ustekinumab	Infections, dizziness, headache, fatigue, diarrhoea, itch, arthralgia, myalgia pain, injection site reactions	Malignancies, psoriasis, hypersensitivity reactions	Exfoliative dermatitis, eosinophilic pneumonia, interstitial pneumonia
Abatacept	Infections, autoimmune disorders, headache, dizziness, paraesthesia, hypertension, increased liver enzymes, leukopenia, infusion-related reactions, injections site reactions, alopecia, rash, nausea, diarrhoea, dyspepsia, mouth ulcers, weakness	Malignancies, depression, anxiety, vertigo, thrombocytopenia, arrhythmias, hypersensitivity, amenorrhoea	Anaphylaxis
Secukinumab	Menstrual disorders, diarrhoea, infections	Hypersensitivity reactions, neutropenia	Inflammatory bowel disease
Tocilizumab	Infections, neutropenia, hypofibrinogenemia, increased liver enzymes, gastritis, mouth ulcers, increased lipids, hypertension, infusion-related reactions, injection site reactions, rash, itch, headache, dizziness	Gastrointestinal perforation, thrombocytopenia, hypersensitivity reactions	Serious hepatotoxicity
Anakinra	Injection site reactions, headache, serious infections, neutropenia, thrombocytopenia, hypercholesterolemia		Allergy
Tofacitinib	Infections, increased liver enzymes, increased creatinine, diarrhoea, nausea, rash, headache	Dyslipidaemia, neutropenia, lymphopenia, anaemia, hypertension, skin cancer, paraesthesia, gastrointestinal perforation, hypersensitivity reactions	

Table 1.3. Adherence measures

Measure	Direct/Indirect Objective/Subjective	Advantages	Disadvantages
Drug or metabolite levels in biological fluids / biomarkers	Direct Objective	Physical evidence of ingestion	Limited to recent ingestion Only available for some medications Variation in drug metabolism Expensive/Invasive
Directly observed therapy	Direct Objective	Physical evidence of ingestion	Intrusive Expensive Time-consuming Impractical for frequent medications
Ingestible event marker (Ingestible microsensor fixed to a tablet and recorded from a skin patch)	Direct Objective	Physical evidence of ingestion	Expensive Invasive
Pill counts	Indirect Objective	Inexpensive Simple	Unable to identify medication-taking patterns The patient can discard unused pills
Pharmacy refill records	Indirect Objective	Non-invasive Can assess large populations and long-term data Can assess multi-drug adherence	Limited to the completeness of the dataset (e.g. if refills occur outside of the system or the prescriber verbally discontinues or alters the medication dose) The patient may not take prescriptions
Electronic monitoring (Medication packages containing electronic microchips that can detect opening or activation of a device)	Indirect Objective	Identifies medication-taking patterns and sensitive to change in medication adherence	Expensive Technical support needed Patients can open the device without actual ingestion of medication Maybe inconvenient to carry/refill device
Clinical outcomes	Indirect Objective or subjective	Adherence is a surrogate marker of clinical outcomes	Many other factors other than adherence can influence clinical outcomes
Self-report, proxy-report or physician estimate	Indirect Subjective	Inexpensive Easy to administer Can identify medication-related beliefs and barriers to adherence	Decreased sensitivity in detecting poor adherence Influenced by memory recall and can be distorted by the desire to appear adherent Influenced by questions asked and interviewer skill

Table 1.4. Adherence rates and health outcome associations

Condition	Rate of adherence	Associations of adherence with health outcomes
RA	**Implementation:** - 66% (Multiple DMARDs), MEMS /prescription claims/interview, categorical (using cut points for adherence in included studies)* (66) - 53.8% (SSZ), 69.3% (MTX), MEMS, 21% (Multiple csDMARDs), categorical variable (percentage of patients, with mean adherence >80%†) (63, 104) - 55% (SSZ), 80-81% (MTX), 64-80% (Multiple csDMARDs), MEMS, mean adherence, continuous variable† (63, 104-106) - 16-73% (ETN), 21-70% (ADA), 38-43% (IFX), 81% (GOL), pharmacy refill data, categorical variable (percentage of patients with PDC or MPR ≥ 80%)‡ (107) **Discontinuation/persistence:** - 54% of newly used csDMARDs and bDMARDs were discontinued, claims database§ (108) - 688 (ETN), 232 (MTX), 231 (IFX), 228 (LEF), 211 (ADA),182 days (HCQ), 61 (SSZ), medication claims data, median persistence in days§ (108)	Disease activity (63, 104, 109) Disability (110) Radiological progression (63) Health care costs (111)
PsA	**Implementation:** - 15% (CZP), 37% (ETN), 39% (GOL), 43% (ADA), 53% (SEC), claims database, categorical (percentage of patients with PDC ≥ 80%)‡ (112) **Discontinuation/Persistence:** - 10-15% (ADA), 7-11% (IFX), 6-10% (ETN), of new and experienced bDMARD users discontinued, claims database‖ (113) - 30% (UST), 28% (ETN), 27% (ADA), 24% (CZP), IFX (23%), 20% (GOL) of new bDMARD users discontinued, claims database¶ (114) - 5.3% (csDMARDs and bDMARDs) of new csDMARD and bDMARD users discontinued, claims database**	Disease activity (104) Health care costs (111, 115)
AS	**Implementation:** - 81% (NSAIDs), MEMS, continuous variable†† (116) **Discontinuation/Persistence:** - 13-16% (ADA), 5-16% (ETN), 5-13% (ETN), of new and experienced bDMARD users discontinued, claims database‖ (113)	No correlation of adherence to NSAIDs with pain or morning stiffness (116) Non-DMARD health care resource utilisation costs (115)

Condition	Rate of adherence	Associations of adherence with health outcomes
OP	**Implementation:** - 43-53% (Bisphosphonates, HRT, SERMs), claims data, categorical variable (percentage of patients with MPR ≥ 66-80%)* (88) - 26% (Risedronate), 31% (Alendronate), 38% (Raloxifene), 52% (Teriparatide), 71% (Denosumab), claims data, categorical variable (percentage of patients with MPR ≥ 80%) (117) **Discontinuation/Persistence:** - 50-52% (Bisphosphonates, HRT, SERMs) discontinued therapy within 12 months, claims data*‡‡ (88)	Risk of fracture (88, 118) Hospitalisation (119) Mortality (119)
Gout	**Implementation:** - 42% (various ULTs), claims/prescription data, categorical variable (percentage of patients with MPR or PDC ≥ 80%)* (120) - 44% (Colchicine), 74% (Allopurinol, benzbromarone), MEMS, mean adherence, continuous variable† (105) - 17-83.5% (various ULTs), claims/prescription data, categorical variable (percentage of patients with MPR or PDC ≥ 80%) (121-125) **Discontinuation/Persistence:** - 57.3% (Allopurinol, febuxostat, benzbromarone) discontinued therapy within 12 months, prescription database§§ (124) - 248 days (Allopurinol, febuxostat, benzbromarone), prescription database mean persistence§§ (124)	Serum uric acid level (123)
JIA	**Implementation:** - 93% (NSAIDs), MEMS, continuous variable†† (126) - 52% (NSAIDs), MEMS, categorical (percentage of patients, with mean adherence ≥80%, including correct timing +/- 2hours) (126) - 33% (All non-biologic DMARDs), 47% (All bDMARDs), claims data, categorical variable percentage of patients with MPR ≥ 80%) (127) - 70% (GOL), 85% (CZP), 89% (ETN), 90% (ADA), IFX (93%), claims data, continuous variable (Mean PDC) ‖(128)	Disease activity (129) Absence from school (130)

RA, Rheumatoid arthritis; PsA, Psoriatic arthritis; AS, Ankylosing spondylitis; OP, Osteoporosis; JIA,, Juvenile idiopathic arthritis; MTX Methotrexate; SSZ, Sulfasalazine; HCQ, Hydroxychloroquine; LEF, Leflunomide; ADA, Adalimumab; ETN, Etanercept; IFX, Infliximab; GO,,L Golimumab; CZP Certolizumab Pegol; UST, Ustekinumab; SEC, Secukinumab; MEMS, Medication Event Monitoring Systems; PDC, Proportion of Days Covered (ratio of the number of days the patient is covered by the medication to the number of days the patient is eligible to have the medication); MPR, Medication Possession Ratio (calculated as the ratio of the amount of days a patient has the medication on hand to the number of days a patient is eligible to have the medication); csDMARD, conventional systemic Disease Modifying Anti-Rheumatic Drug; bDMARD, biologic DMARD; HRT, Hormone replacement therapy; SERM, Selective estrogen receptor modulator; ULT, Urate lowering therapy.

*systematic review
† Adherence calculations performed using the percentage of days (or weeks for methotrexate) on which the patient took the correct dose of the prescribed medication
‡ Adherence defined as MPR or PDC ≥ 80%
§ Discontinuation occurred on the date when the last DMARD refill was expected to be exhausted and was not followed with refills of any other DMARD within 90 days
| Discontinuation occurred on the date when the last bDMARD refill was expected to be exhausted and was not followed with claims of any bDMARD within 45 days, and the same bDMARD was not restarted ≥45 days after discontinuation
¶ Discontinuation occurred on the date when the last bDMARD refill was expected to be exhausted and was not followed with claims of any bDMARD within 90 days
** Discontinuation occurred on the date when the last cs DMARD or bDMARD refill was expected to be exhausted and was not followed with claims of any DMARD within 180 days
†† Adherence calculations performed using the percentage of days on which the patient took NSAIDs (any dose)
‡‡ Discontinuation data from the subgroup of information derived from claims data presented (calculated as 1-“persistence” rate at different time points), definition of discontinuation based on gaps in refill varied in included studies, duration of follow up varied from 1month to >24 months, subgroup of data from first 12 months presented.
§§ Discontinuation occurred on the date when the last ULT refill was expected to be exhausted and was not followed with refills of any other ULT within 30 days
|| This cohort included young adults (≤ 24 years and children) with JIA and RA

Table 1.5. COM-B system description and subtypes

Sources of behaviour	Description	Subtypes
Capability	The individual's psychological or physical capacity to engage in the behaviour	Psychological capability Physical capability
Opportunity	Factors that lie outside the individual that prompts a behaviour or makes it possible	Physical opportunity Social opportunity
Motivation	All the brain processes that energise and direct behaviour	Reflective motivation Automatic motivation

Chapter 8: Discussion and conclusions

8.1 Summary and synthesis of findings

The overall aim of this thesis is to describe patient and caregiver experiences and perspectives with their medications and care, and to identify issues in outcome reporting in interventional studies targeting medication adherence in a variety of rheumatic conditions.

In detail, this thesis addressed the following aims:

1. To highlight recent contributions of qualitative research in rheumatology, summarise common methodologies and methods used, and outline key principles to guide appraisal of qualitative studies (Chapter 2)

2. To assess the scope of outcomes in interventional studies of medication adherence (Chapter 3)

3. To describe patients' attitudes to and experiences of DMARDs in RA and SpA (Chapter 4)

4. To describe patients' attitudes to and experiences of transition from paediatric to adult healthcare in rheumatology (Chapter 5)

5. To identify and prioritise factors important to patients and caregivers regarding medication adherence in gout, OP and RA, and to describe the reasons for their decisions (Chapter 6)

6. To discuss the conceptual and methodological challenges in developing a core domain set for interventional studies targeting medication adherence in rheumatology (Chapter 7)

Qualitative, quantitative and mixed methods approaches are used to address these aims. A background on the contributions, methodologies, methods and appraisal of qualitative research is provided in Chapter 2. The systematic review of outcomes in

interventional studies targeting medication adherence in rheumatic conditions (Chapter 3) found a wide range of outcome domains reported. These included adherence, health outcomes and adherence-related factors. There was also heterogeneity in adherence measures. The qualitative systematic reviews (Chapters 4 and 5) showed the impact of DMARDs in RA and SpA patients, and experiences of patients transitioning from paediatric to adult rheumatology care. The focus group using nominal group technique (Chapter 6) elicited priorities in medication adherence in patients with gout, OP and RA and their caregivers. Finally, I chaired a special interest group session for the OMERACT-Adherence group at the OMERACT 2018 conference (Chapter 7), which provided ideas on how to develop an intervention-based core domain set that would complement OMERACT methodology. The following section contains a summary and integration of the findings of each chapter.

Chapters 4-6: The experiences and perspectives of patients with rheumatic conditions and their caregivers regarding their medications and care

The systematic review and thematic synthesis in Chapter 4 demonstrated the impact DMARDs have in patients' lives, and the many factors that interact to serve as barriers and facilitators to adherence. Dependence on DMARDs exacerbated an unwanted "disease identity" in patients with RA and SpA. They feared side effects, felt uneasy with the uncertainty of treatment efficacy, which was made worse with conflicting medical advice. Concerns were reduced through trustworthy and supportive healthcare environments and positive attitudes of family and friends. Some were motivated to take DMARDs because of the noticeable dramatic and immediate effects whereas others felt disappointed and hopeless after experiencing an inadequate response from multiple DMARDs. The high cost of and limited access to bDMARDs caused patients to perceive that these medications were valuable.

Chapter 5 focused on transition from paediatric to adult care as the transition period is a vulnerable time in young peoples' lives and is associated with discontinuity of care and medication non-adherence. Adolescents felt abandoned, disconnected, vulnerable, and were shocked to meet adults with visible arthritic damage or disability in waiting rooms in the adult healthcare setting. Some felt symptoms of pain and fatigue which were perceived to be dismissed by their new adult rheumatologist. A gradual and supportive approach to transition including explanations of differences in treatment options such as

joint injection procedures, having continuity of care, and access to a transition co-ordinator helped patients prepare for the major changes they faced. Patients were dealing with uncertain prognoses and treatment burdens and needed stability, connection and belonging within and outside of their health care setting. Therefore, healthcare during transition needed to be minimally disruptive, age-appropriate and address issues relevant to their daily lives. Patients could feel tension between wanting autonomy and the changing relationships with their parents and clinicians.

The focus groups, using nominal group technique, with patients with gout, OP and RA and their caregivers (Chapter 6) identified factors that were perceived to help or hamper medication adherence. Factors related to their doctor (trust and knowledge), medication properties (effectiveness, side effects) and patient capabilities (routine) were important regarding adherence. Patients and caregivers valued supportive and trustworthy doctors, and the ability to achieve a balance between medication benefits and harms in order to live well overall. They wanted to be involved and in control of medication management, though some barriers limited access to medications and were unnecessarily difficult.

There were similarities and differences in the themes that emerged from RA, SpA, gout and OP patients. Trust in the prescribing doctor and a supportive health care environment where different health professionals communicated and provided consistent information and advice was valued by all patients. All patient groups wanted to feel in control of their disease and their lifestyles by making informed medication decisions, and choosing to take, adjust or stop their medications in order to maintain important social roles. Although side effects, polypharmacy and the potential of drug interactions were a major concern for all, patients with RA/SpA were particularly alarmed about the potential toxicity of DMARDs including immune suppression, increased risk of cancer and mortality. In contrast, patients with gout had a lower ranking of side-effects in their nominal group ranking of barriers and facilitators to medication taking. All patients expressed uncertainty about the efficacy of their medications and the need for long-term medications, however there were differences in the timing and reason for this. Patients with RA/SpA and severe gout were motivated to start taking their medications to reduce perceptible symptoms of pain, but would doubt the need for long-term medications when they were in remission. Patients with infrequent gout flares and those who were asymptomatic with OP were not convinced of the need for long-term pharmacotherapy from the beginning. Monitoring in the form of blood tests in RA/SpA and gout, and bone density scans in OP, helped reassure patients of the benefit and safety of their

medications. However, patients with gout and OP who had infrequent blood test monitoring and bone density scans could feel frustrated from the lack of positive feedback and validation compared with patients with RA/SpA.

The findings from these chapters highlight the unmet care needs of patients with rheumatic conditions requiring long-term pharmacotherapy. A core theme that was present throughout all the qualitative studies was the importance of having a supportive healthcare environment.

Chapters 3,6,7: The development of a core domain set for interventions targeting adherence

The report from the OMERACT-Adherence special interest group meeting at the OMERACT 2018 conference (Chapter 7) highlighted the difficulties in developing a core domain set for interventions that address medication adherence across rheumatic conditions. Participants suggested adding adherence to the inner circle of a condition-specific CDS (as being mandatory in an adherence trial) as a potential solution. Though some adherence-related factors may be candidate outcome domains, they may be better classified as targets of interventions whose improvement may lead to better adherence (i.e. a time-dependent contextual factor). A separate line of investigation would be required to investigate adherence in the setting of drug trials (e.g. trials comparing different treatment options), and future work should aim towards consensus on standardised adherence measures. Following on from the special interest group session, we adjusted and completed the first two phases of the five-phase project to develop a core domain set for interventional studies targeting adherence in rheumatic conditions.

The first phase, a systematic review of existing outcomes (Chapter 3) included 53 studies. An increasing number of studies, especially RCTs, are conducted to test strategies to improve adherence in rheumatic conditions. The included studies reported a broad range of outcome domains and adherence measures. In one-third of the studies the phase of adherence was unclear. Thirty-seven different instruments measured and reported adherence in 115 unique ways. Adherence was linked to health outcomes in 77% of the studies. However, studies rarely used existing disease-specific core domain sets and only half of the studies reported medication adverse events. Studies evaluated multiple adherence-related factors. The most frequently reported were medication

beliefs, illness perception, medication satisfaction, satisfaction with medication information, condition knowledge, medication knowledge, and trust in the doctor. However, no specific factor was reported in more than 15% of studies.

The second phase, a focus group study using nominal group technique (Chapter 6) included patients with OP, gout and RA and their caregivers. The 49 factors that helped or hampered medication adherence could be considered contextual factors that can impact the outcome of adherence. The top five factors based on the ranking of all participants were trust in the doctor (importance score 0.46), medication effectiveness (0.31), doctor's knowledge (0.25), side effects (0.23), medication taking routine (0.13).

These chapters together highlight the deficiencies in the reporting of adherence, health outcomes and adherence-related factors. In order to address this; firstly, adherence as a domain could include specification of the phase of adherence. Secondly, health outcomes could use the core domain set for the condition (if available), including reporting of adverse events. Thirdly, adherence-related factors could be considered as being relevant in the core domain set as contextual factors of adherence trials. The focus group study demonstrated that some factors are of greater importance than others. Finally, after finalisation of the core domain set, consensus on the measurement of adherence is needed.

Based on the studies to date, a potential core domain set may include adherence (with the phase of adherence specified) and health outcomes (including medication adverse events and the use of the condition-specific core domain set). A set of core contextual factors may also be developed alongside the core domain set.

8.2 Strengths and limitations

The strengths and limitations of each study are discussed in detail in each chapter. In this section I will discuss the strengths and limitations of the overall thesis.

All studies were reported using established reporting criteria: Preferred reporting items for systematic reviews and meta-analyses (PRISMA) (372) statement (Chapter 3), enhancing transparency in reporting the synthesis of qualitative research (ENTREQ) (99) (Chapters 4 and 5), and consolidated criteria for reporting qualitative research (COREQ) (100) (Chapter 6). The ESPACOMP Medication Adherence Reporting Guidelines

(EMERGE) guides the reporting of medication adherence research and was published in 2018 (369). The EMERGE guidelines aim to enhance the quality of reporting of relevant aspects of medication adherence research in a standard manner and used the ABC taxonomy of medication adherence as a conceptual basis including the phases of adherence (initiation, implementation and discontinuation/persistence) (35). Aspects of the guidelines that can be applied to qualitative studies include stating the phase of medication adherence studied, the definition of the phase of medication adherence, and describing the results of the analysis appropriate to each phase of medication adherence. Primary qualitative studies describing patients' perspectives of their medications could provide an in-depth enquiry into a specific phase of medication adherence. A limitation of the studies included in the thesis is that the EMERGE guidelines have not been explicitly used. However, some chapters were published prior to the EMERGE guideline publication and Chapters 3 and 7 refer to the ABC taxonomy of adherence.

A comprehensive and sensitive search strategy was used for all three systematic reviews. Each search strategy was reviewed by a medical librarian or information specialist. Searches aimed for high sensitivity including both free-text and Medical Subject Headings (MeSH). The search strategy for interventional studies targeting adherence was based on the published search strategy of the Cochrane review of interventions for enhancing medication adherence (75).

All of the qualitative studies were guided by the Lincoln and Guba framework for rigor: credibility, confirmability, dependability and transferability (210). For example, for credibility, purposive sampling, continuing data collection until data saturation, and researcher triangulation were used. For confirmability, a table of quotations was presented and preliminary results of the focus group study were sent back to participants for participant checking. For dependability, audio recordings were transcribed verbatim, and qualitative software was used to conduct data analyses such that coding choices could be audited. For transferability, a detailed description of the characteristics of the participants in the focus group study and characteristics of included studies in the systematic reviews of qualitative studies were provided.

All studies were conducted in English only. However, the systematic reviews included studies conducted in 33 countries (Chapter 3), 13 countries (Chapter 4), 11 countries (Chapter 5) and the focus group study included participants born in 16 countries. There were a limited number of rheumatic conditions represented in the various studies.

Patients with immune mediated multisystem diseases such as SLE and vasculitis are likely to have different experiences and perspectives of their medications. Therefore, the transferability of the qualitative studies and generalisability of the results of the outcomes systematic review to other settings and populations that were not included is uncertain.

A major limitation in systematic reviews can be the quality of the included studies. The thesis included two qualitative systematic reviews and one systematic review of outcomes used in interventional studies. For the qualitative systematic reviews, as highlighted in section 2.5, rigor in qualitative research can be judged using the framework by Lincoln and Guba based on the criteria of credibility, confirmability, dependability and transferability. The qualitative systematic reviews we conducted included studies with variable levels of reporting of important aspects in qualitative research such as data saturation, use of researcher triangulation, and a detailed description of the sample and setting of data collection, which limits the reader's ability to judge the rigor of the individual qualitative studies. For the systematic review of outcomes, we did not include an analysis of the risk of bias of included studies, as highlighted in the PRISMA checklist in Appendix C.1, as the review aimed to assess the reporting of outcomes, rather than summarizing and combining the results of the included studies. A risk of bias assessment may have allowed a comparison of the outcomes of studies with a higher risk of bias to those with a lower risk of bias.

8.3 Comparison with other studies

In this thesis, new insights into medication adherence specific to patients and caregivers with RA, SpA, gout and OP were identified, including a prioritised list of perceived barriers and facilitators to adherence. Also provided was a comprehensive description of the experiences of patients with juvenile-onset rheumatic conditions transitioning from paediatric to adult care and relevant perspectives of medications. The thesis includes the first two phases of a novel project to develop a core domain set for interventional studies targeting adherence. Unique findings from the studies included in this thesis and comparison to other studies are discussed below.

Experiences and priorities of patients with RA, SpA, gout and OP and their caregivers (Chapters 4 and 6)

Multiple systematic reviews have been conducted on the topic of barriers and facilitators to medication adherence in RA, SpA (in particular AS and PsA), gout and OP (65, 69, 74, 276). It has been shown that many factors have conflicting evidence for an association with adherence. However, beliefs about the necessity of medication (65, 66, 69) and the patient-physician relationship (65, 69) are two factors that have been consistently identified in these reviews to be associated with adherence. The qualitative studies in this thesis provide some insight into these factors. For a medication to be deemed necessary, patients emphasised that overall, the benefits should outweigh harms and help them live well, restore function and have minimal lifestyle intrusions. Medications needed to be effective, interact safely and not impact other conditions. The concept of necessity could be challenged when DMARDs and urate lowering therapy took a long time to lead to any benefit, or in the case of OP, when the medications were treating a largely asymptomatic disease. It could also be influenced by experiences and opinions relayed by others, the perceived value of the medications (biologics), and the level of benefit compared with patients' expectations. To build trust with their doctor, patients explained that doctors needed to demonstrate genuine interest and concern, impart knowledge around medication benefits, harms, and options, and foster understanding and agreement with other health care professionals. Importantly these two factors interrelated with each other, in that supportive care promoted beliefs about medication necessity by helping patients to feel safe and confident in taking their medications.

A review of 51 systematic reviews of determinants of medication adherence in multiple conditions identified 771 individual factors across multiple conditions (86). Our qualitative studies also demonstrated a range of different factors, and their complex interactions. Ranking or rating exercises can help to assess the relative importance of factors. A study conducted in the US used focus groups and nominal group technique with patients with gout. 17 people participated in three nominal groups addressing challenges to taking gout treatments (373). The scores from all patients within each nominal group were combined into an overall score and priority ranking. For one group, their top three factors were; recognising a gout attack had started and start taking medicine, side effects of colchicine, and balance between managing gout and other conditions. For the second group the top factors were; eating the right food and taking enough fluids, concern about medication side effects, and trouble taking gout medication due to kidney problems. For the third group these were; knowing when and what to take during a gout attack, concern about interaction with other medications, and allergic reactions or side effects to gout medications. The focus group with nominal group technique in Chapter 6 was able to

prioritise all factors generated by participants by combining the results across all 14 focus groups, and using statistical analysis that accounted for both the importance given to the factor by the rank position and the consistency of being nominated by participants.

Perspectives of patients with juvenile-onset rheumatic conditions transitioning to adult care (Chapter 5)

Transition of patients with juvenile-onset rheumatic conditions was chosen for this thesis as these patients are at increased risk of discontinuity of care and medication non-adherence (89-92). An international and interdisciplinary Delphi survey and the EULAR/PreS guidelines for transitional care in rheumatology identified medication adherence as one of ten outcomes that determine the success of a process of health care transition (307, 374). Despite this, a brief transition program for adolescents with JIA found no impact on medication adherence (94). The transition program comprised of eight components: a transition co-ordinator; providing information and education about JIA and medication management, health behaviour, dealing with fatigue, school, friends and any problems with medication adherence; availability by phone; information about and contact with the adult rheumatology service; parental guidance; meeting with peers; a transfer plan; and actual transfer to the adult rheumatology service. These components were implemented in 5 steps over 1.5 years, that comprised of two outpatient appointments with the transition co-ordinator, information day for adolescents and their parents, individualised transfer plan and the actual transfer. (375). However this brief transition program may not have had an impact on adherence as young people develop self-management skills over many years (329-331), and many continue to develop these skills after the age of 18 (332). In a cross-sectional survey of 52 adolescents (aged 13-20) with juvenile-onset rheumatic diseases, medication adherence (self-reported adherence in the last week) did not increase with age. Some medication related self-management skills and knowledge improved with age (filling prescriptions), and others did not (knowing medication names, purposes and side effects).

The systematic review of qualitative studies identified several areas of need during transition that are not currently addressed in transitional care guidelines in rheumatology. The review showed that some young people avoided taking medications in front of friends and reduced medication intake when well to maintain a sense of normality. Some continued to rely on their parents' reminders to take medications in adult care and may

be more comfortable discussing non-adherence with clinicians without parental presence. They wanted to be more informed and involved in treatment decision-making and be presented with information about medications face-to-face from the transition co-ordinator. Though medication adherence is an issue that many adults with rheumatic conditions face, it is clear that patients undergoing transition face a unique set of challenges. A developmentally appropriate approach to support medication adherence is needed that can be embedded into transition services.

Core outcome domains and contextual factors for interventional studies targeting medication adherence (Chapter 3, 6 and 7)

Difficulties with comparing the effectiveness of interventions across trials testing different adherence strategies is evident in multiple systematic reviews. The 2014 Cochrane review of 182 RCTs of interventions to improve medication adherence (75) included studies measuring both medication adherence and clinical outcomes in many medical conditions. The large number of adherence measurements and clinical outcomes precluded the synthesis of findings with a meta-analysis. In addition, they noted that many outcomes reported were surrogate outcomes (e.g. hypertension) rather than patient important outcomes (e.g. heart attack). A systematic review and meta-analysis included 79 RCTs targeting medication adherence, using Medication Event Monitoring Systems (MEMS) as the instrument to measure adherence (376). Fifty seven studies (72%) measured clinical outcomes. In addition, even with the one instrument to measure adherence (MEMS), the definition used to calculate adherence varied across studies. Patient-centred outcomes were assessed in another systematic review and meta-analysis of 141 studies testing strategies to improve adherence (220). This was conducted as an increasing number of studies are assessing the impact of outcomes that are of importance to patients such quality of life, physical function, symptoms (depression, pain, energy/vitality, cardiovascular and respiratory) and medication knowledge. The study distinguished these ‘patient-centred outcomes’ from adherence (i.e. medication-taking behaviour) and clinical outcomes. They found statistically significant standardised mean differences in all evaluated patient-centred outcomes except for anxiety.

The systematic review of outcomes included in this thesis also demonstrated heterogeneity in the reporting of medication adherence and clinical outcomes (Chapter

3). In addition, many studies did not specify the phase of the medication adherence outcome and did not use existing core domain sets for specific rheumatic conditions. Using OMERACT definitions, quality of life, physical function and symptoms would all fit under the core areas that constitute the core domain set for the condition. The condition-specific core domain set were termed ‘health outcomes’ in this thesis. Although the authors of the systematic review of patient-centred outcomes in adherence studies (220) identified medication knowledge in addition to health outcomes, many more adherence-related factors that are of relevance to patients were identified in this thesis. The focus group study using nominal group technique (Chapter 6) has provided preliminary data on the relative importance of some of these factors. Considering these contextual factors of adherence trials presents a novel way of integrating patient-important factors into the evaluation of studies testing adherence strategies.

8.4 Future research

Following on from the studies in this thesis, I am continuing with the subsequent phases of the five-phase project in collaboration with other members of the OMERACT-Adherence group. This includes international focus groups with patients with inflammatory arthritis, an interview study with adherence research experts, a Delphi survey and consensus voting (102).

International focus group study with patients with inflammatory arthritis

The focus group study with nominal group technique (Chapter 6) focused on adherence-related factors and was conducted in Australia. Another focus group study was designed to gain patients’ perspectives on outcome domains and will be conducted three countries. I have conducted three focus groups with patients with inflammatory arthritis (RA, PsA, ankylosing spondylitis, and undifferentiated inflammatory arthritis) prescribed DMARDs in Australia. Two focus groups have also been conducted in the Netherlands, and one focus group is planned in Canada. The findings will ensure that an international patient perspective is incorporated into the proposed core domain set.

Adherence researcher interview study

Developing a core domain set for interventions targeting medication adherence has been a challenge. Accordingly, an additional study to garner input from experts in adherence research has been designed. Adherence researchers have the practical experience of using outcomes in adherence interventions and are key stakeholders that represent end-users of the core domain set. I am a co-investigator on an interview study that includes adherence research experts who have conducted an interventional study targeting medication adherence in any condition. Thirteen researchers, from seven countries, have been interviewed to describe their experiences in conducting their research, and perspectives in establishing and implementing a core domain set for interventional studies targeting medication adherence. This study will help inform the core domain set from the perspectives of researchers and will also allow us to identify potential barriers to implementation.

Delphi study

I will be leading an international Delphi survey to generate a consensus-based prioritised list of core outcome domains and core contextual factors for studies testing adherence strategies in rheumatology. The three round Delphi survey will involve patients with diverse rheumatic conditions, caregivers, health professionals, researchers and other stakeholders. Preliminary items for inclusion in the Delphi survey to OMERACT will be presented to delegates at the OMERACT conference in April 2020.

Consensus voting

The final phase in the OMERACT-Adherence project will be an online discussion and voting session. OMERACT members and other invited members including patients, health care professionals, researchers and representatives from the pharmaceutical industry and policy makers will review, vote and reach consensus on the proposed OMERACT-Adherence core domain set and core contextual factors.

8.5 Implications for clinical practice, research and policy

The studies in this thesis have demonstrated a gap in the care needs of patients with various rheumatic conditions and in outcome reporting in interventional studies to support medication adherence. The findings can help to establish and evaluate outcomes of importance to patients and caregivers to support medication adherence in clinical practice, research, and for policy.

Clinical practice

The World Health Organisation and GRADE (Grading of Recommendations, Assessment, Development and Evaluations – a framework for grading the quality of evidence for use in clinical practice guidelines) recommend incorporating systematic reviews of qualitative studies into guideline recommendations (133, 327, 328). However, current guidelines used in rheumatology do not incorporate qualitative research findings (17, 26-32, 276). The World Health Organization's handbook for guideline development provides guidance on how qualitative evidence can be used to help define the scope of a guideline, assess the acceptability of interventions to key stakeholders, feasibility of interventions, identify contextual factors to consider when implementing guideline recommendations, and explore the effects of different interventions on equity (377). Practically, the guideline steering groups needs to explore how qualitative research could improve the quality and usability of the guideline, search for existing qualitative systematic reviews or if needed prepare their own. Steps involved in preparing a systematic review for guideline development include formulating the research question, retrieving evidence with the guidance of a written protocol and thorough search strategy, synthesizing the evidence, assessing the rigor of the included studies, and presenting this evidence alongside the quantitative evidence of the intervention's benefits and harms, resource implications and implications for equity and human rights (133, 327, 328).

The thesis has highlighted the critical role of health professionals, particularly the doctor, in the patient's acceptance of their medications. Closer collaboration and consistency among health professionals, creating opportunities for patients to discuss side effects between clinic appointments, checking for drug interactions, providing feedback with drug monitoring and addressing the patients' goals of living well and improving function are potential patient-centred strategies to support optimal use of medications. By

remaining optimistic, validating patients' fears and understanding their practical needs, physicians can foster a trusting and more successful therapeutic relationship with their patients. Communicating potential benefits and harms of medications by using examples of other patients' experiences may improve patients' understanding. Referring to reliable online resources may help patients feel more confident in treatment recommendations.

The findings of this thesis can be translated into strategies for multiple health professionals. These varying ideas could be incorporated into a medication adherence model of care within a hospital-based rheumatology service. Clinicians within the rheumatology department could: 1) receive medication adherence education including learning about patients' perspectives and experiences of their medications; 2) receive training in using shared-decision making tools to aid discussions about efficacy and safety of medications and to illicit patients' values and goals; 3) be supported by multi-disciplinary meetings of complex patients on multiple medications, including liaison with hospital pharmacists and comprehensive medication reviews; 4) incorporate medication adherence monitoring and feedback within the service which would require further evaluation of feasible and acceptable measures of medication adherence monitoring in a clinical setting; and 5) provide webinars/workshops to promote patient empowerment through medication and condition education, teaching medication-related self-management skills and habit formation.

Research

Our systematic review of interventional studies targeting medication adherence in rheumatic conditions showed that only a minority of studies focused on the initiation phase of medication adherence. In RA and SpA, international guidelines recommend the use of DMARDs early post-diagnosis. Further studies focused on initiation adherence in these rheumatic conditions is particularly pertinent.

Caregivers were included in the study using focus groups with nominal group technique (Chapter 6). The findings from the caregivers were analysed in combination with patients as well as separately in both the quantitative and qualitative analysis. Our patient research partners argued for the importance of including caregivers in this study as they can offer important insights into the patient's health status and have an important role in supporting patients with the management of their rheumatic condition. There is a positive

association between family support and medication adherence in the literature, including practical support (e.g. assistance, reminders, organization of medications), emotional support and having a cohesive family unit (e.g. warmth, closeness and acceptance) (378). Little is known about caregivers' perspectives of medications, and their role in supporting medication adherence in rheumatology. Our focus group study showed that caregivers had a different ordering of factors important for medication adherence compared with patients. However, only 15 caregivers were included in this study. For a more in-depth inquiry into the perspective and role of caregivers in this topic, future studies could continue to recruit caregivers until data saturation within this subgroup, or conduct a dedicated qualitative study with caregivers.

The qualitative studies included in this thesis have identified gaps in the care needs of patients with rheumatic conditions and in transitional care. An interventional study could confirm whether provider-related factors identified to be important in these studies can be improved with consequent impact upon adherence. A medication adherence model of care intervention such as one described above could be further developed and designed for the rheumatology service with input from patients, caregivers, healthcare professionals and healthcare managers. The intervention could be evaluated by monitoring outcomes using a consensus-based core domain set (once finalised). These outcomes may include medication adherence, condition-specific clinical outcomes (using a core domain set for the condition if available), and monitoring for adverse events. The literature supports provider-focused medication adherence interventions. For example, a meta-analysis of 21 studies involving training physicians in communication skills found that all studied interventions improved adherence (289). The use of decision aids may also improve knowledge, reduce decisional conflict and increase participation in decision making (290).

Use of a consensus-based core domain set can reduce inconsistent reporting, reporting bias, and promote measurement of outcomes that matter to patients (10). The core domain set will help to evaluate and compare different adherence interventions. Subsequently it will help to compare and identify effective adherence strategies to inform decisions on how to support medication adherence.

Policy

Medication non-adherence accounts for approximately 4% of hospitalisations globally (379), and the annual cost of medication non-adherence ranges from $100-300 billion in the US (380, 381) and $125 billion Euro in Europe (382). A world health organisation report stated that improving adherence to existing treatments could lead to more health benefits worldwide than developing new medical treatments (34). The importance of medication adherence is recognised by multiple policy initiatives worldwide focused on improving adherence (383-385).

Methods used to prioritise and ascertain barriers and facilitators to medication adherence included in this thesis can generate evidence to be included within policy documents targeting medication adherence. Standardised outcome reporting can help determine the best strategies to support medication taking that can be scaled and supported to improve medication adherence at a population level.

8.6 Conclusions

In conclusion, this thesis provides a comprehensive understanding of the perspectives and experiences of patients with various rheumatic conditions and their caregivers. and preliminary findings to inform a consensus-based core domain set that reflects the shared priorities of patients, caregivers and clinicians. The studies highlight the need for patient-centred strategies to support medication adherence in rheumatology and standardised outcomes to assess their effectiveness. Adherence (including all phases), health outcomes (using existing core domain sets of the condition and including medication related adverse events), and a core set of contextual factors (i.e. adherence-related factors that influence the outcome of adherence) are elements of the OMERACT-Adherence core domain set that will be further explored and developed in subsequent phases. A core domain set and core set of contextual factors developed from patient derived priorities would improve the relevance and consistency of outcomes reported in interventional studies aiming to support adherence.

Appendix B: Supporting data for Chapter 2

B.1 Qualitative research published in the top ten rheumatology journals

Journal	2015	2016	2017	2018	2019	Total per journal
Annals of the Rheumatic Diseases	1 (0.4%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	2 (0.2%)
Arthritis & Rheumatology	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)
Rheumatology (Oxford)	7 (2.9%)	3 (1.3%)	1 (0.5%)	3 (1.4%)	1 (0.5%)	15 (1.4%)
Seminars in arthritis and rheumatism	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.8%)	1 (0.2%)
Therapeutic advances in musculoskeletal disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Osteoarthritis and Cartilage	1 (0.5%)	0 (0%)	1 (0.4%)	1 (0.6%)	2 (1.1%)	5 (0.5%)
Arthritis Care & Research	9 (4.5%)	11 (5.1%)	7 (3.2%)	17 (7.7%)	10 (5.9%)	54 (5.3%)
Arthritis Research & Therapy	0 (0%)	1 (0.4%)	2 (0.8%)	2 (0.8%)	1 (0.4%)	6 (0.4%)
Current Rheumatology Reports	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Journal of Rheumatology	3 (1.1%)	3 (1.3%)	2 (1.1%)	1 (0.6%)	1 (0.7%)	10 (1.0)
Total qualitative studies per year (% of all original research articles)	22 (1.1%)	18 (1.0%)	14 (0.8%)	24 (1.5%)	16 (1.1%)	94 (1.1%)

N.B. Both qualitative and mixed methods studies were included. All journals were hand-searched online. Articles were screened by title and if necessary, by abstract or full text. Nature Reviews Rheumatology and Current Opinion in Rheumatology were excluded from this analysis as they do not publish original research articles.

Appendix C: Supporting data for Chapter 3

C.1 PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	7. (PROSPERO does not accept systematic reviews looking at the reporting of and/or use of outcomes in research)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	8
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	9 (Under Methods, Search and selection criteria)
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	9
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	9

Section/topic	#	Checklist item	Reported on page #
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	9
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp.Table 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA (the review aimed to assess the reporting of outcomes, rather than summarising and combining results of studies)
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	NA
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Fig. 1

Section/topic	#	Checklist item	Reported on page #
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1, Supp. Table 3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA for risk of bias. Outcome level assessment 12-15
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	4

C.2 Search strategy

Database: Ovid MEDLINE <1946 to 25/2/2019>

1. exp Arthritis, Rheumatoid/ OR Rheumatoid arthritis.mp. OR exp Arthritis, Psoriatic/ OR Psoriatic arthritis.mp. OR exp Spondylitis, Ankylosing/ OR Ankylosing spondylitis.mp. OR exp Spondylarthritis/ OR Spondyloarthritis.mp. OR exp Spondylarthropathies/ OR Spondyloarthropathies.mp. OR Polyarthritis.mp. OR exp Arthritis, Juvenile/ OR Juvenile rheumatoid arthritis.mp. OR Chronic arthritis.mp. OR Oligoarthritis.mp. OR Juvenile idiopathic arthritis.mp. OR Systemic onset arthritis.mp. OR exp GOUT/ OR Gout.mp. OR exp OSTEOPOROSIS/ OR Osteoporosis.mp. OR exp Lupus Erythematosus, Systemic/ OR Systemic lupus erythematosus.mp. OR Lupus.mp. OR exp Scleroderma, Systemic/ OR Scleroderma.mp. OR Systemic sclerosis.mp. OR Limited scleroderma.mp. OR Diffuse scleroderma.mp. OR exp Systemic Vasculitis/ OR vasculitis.mp. OR exp Mixed Connective Tissue Disease/ OR mixed connective tissue disease.mp. OR *Rheumatic Diseases/ OR exp Sjogren's Syndrome/ OR Sjogren's syndrome.mp. OR Inflammatory arthritis.mp. OR Connective tissue disease.mp.
2. exp Medication Adherence/ OR exp Patient Compliance/ OR Adherence.mp. OR Compliance.mp. OR Persistence.mp. OR exp COMPLIANCE/ OR exp "TREATMENT ADHERENCE AND COMPLIANCE"/ OR exp Treatment Refusal/
3. (clinical trial or random:).mp. not ((mice or rat or rats).tw. or editorial.pt. or letter.pt. or comment.pt.) not (animals not humans).sh. OR exp Clinical Trial/ not ((mice or rat or rats).tw. or editorial.pt. or letter.pt. or comment.pt.) not (animals not humans).sh.
4. 1 and 2 and 3

Database: Embase <1980 to 2019 Week 08>

1. exp rheumatoid arthritis/ OR rheumatoid arthritis.mp. OR exp psoriatic arthritis/ OR psoriatic arthritis.mp. OR exp ankylosing spondylitis/ OR ankylosing spondylitis.mp. OR exp spondylarthritis/ OR Spondyloarthritis.mp. OR exp spondyloarthropathy/ OR spondyloarthropath$.mp. OR exp polyarthritis/ OR polyarthritis.mp. OR exp juvenile rheumatoid arthritis/ OR exp chronic arthritis/ OR Oligoarthritis.mp. OR juvenile idiopathic arthritis.mp. OR systemic onset arthritis.mp. OR exp gout/ OR gout.mp. OR exp osteoporosis/ OR osteoporosis.mp. OR exp systemic lupus erythematosus/ OR Systemic lupus erythematosus.mp. OR lupus.mp. OR exp systemic sclerosis/ OR systemic sclerosis.mp. OR scleroderma.mp. OR exp systemic vasculitis/ OR vasculitis.mp. OR exp mixed connective tissue disease/ OR connective tissue disease.mp. OR *Rheumatic diseases/ OR exp Sjoegren syndrome/ OR Sjoegren syndrome.mp. OR Inflammatory arthritis.mp.
2. exp medication compliance/ OR exp patient compliance/ OR adherence.mp. OR compliance.mp. OR persistence.mp. OR exp treatment refusal/
3. (clinical trial or controlled study or randomized controlled trial).mp. AND (intervention:or outcome: or treatment outcome).mp.
4. 1 and 2 and 3

Database: PsycINFO <1806 to February Week 3 2019>

1. exp Rheumatoid Arthritis/ OR rheumatoid arthritis.mp. OR psoriatic arthritis.mp. OR ankylosing spondylitis.mp. OR spondyl#arthr$.mp. OR Polyarthritis.mp. OR Juvenile arthritis.mp. OR chronic arthritis.mp. OR oligoarthritis.mp. OR juvenile idiopathic arthritis.mp. OR gout.mp. OR exp OSTEOPOROSIS/ OR osteoporosis.mp. OR exp

Lupus/ OR lupus.mp. OR systemic
sclerosis.mp. OR scleroderma.mp. OR vasculitis.mp. OR connective tissue
disease.mp. OR dermatomyositis.mp. OR Sjogren's syndrome.mp.
2. exp Treatment Compliance/ OR exp Treatment
Refusal/ OR adherence.mp. OR compliance.mp. OR persistence.mp.
3. (random$ or clinical or control or trial).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] OR (intervention or outcomes or treatment outcomes).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
4. 1 and 2 and 3

Database: CINAHL <1979 to 25/2/2019>

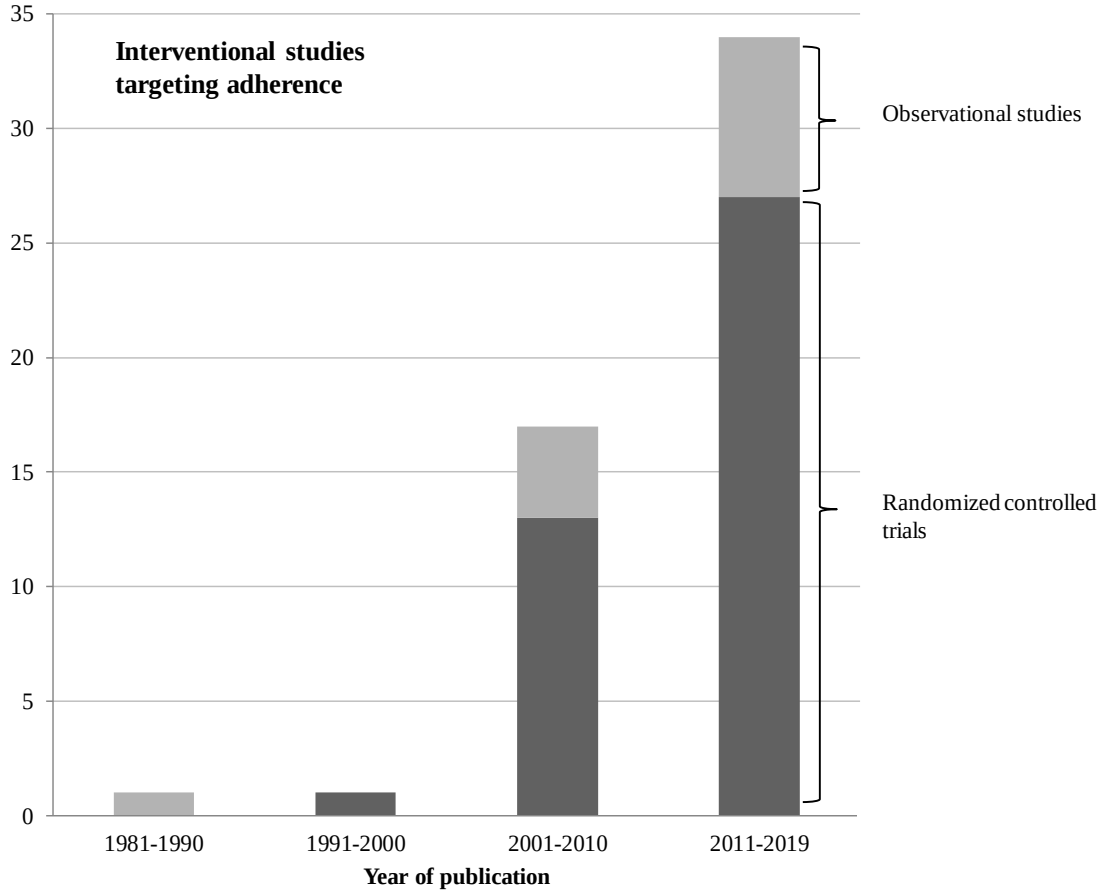
1. (MH "Arthritis, Rheumatoid+") OR (MM "Arthritis, Psoriatic") OR (MM "Spondylitis, Ankylosing") OR (MH "Spondylarthritis+") OR "polyarthritis" OR (MM "Arthritis, Juvenile Rheumatoid") OR (MM "Dermatomyositis") OR (MM "Gout") OR (MH "Osteoporosis+") OR (MH "Lupus Erythematosus, Systemic+") OR (MH "Scleroderma, Systemic+") OR (MH "Vasculitis+") OR (MH "Connective Tissue Diseases+") OR (MM "Sjogren's Syndrome") OR (MH "Rheumatic Diseases+")
2. MM "Medication Compliance") OR (MH "Patient Compliance+") OR (MM "Noncompliance of Therapeutic Regimen (Saba CCC)") OR (MM "Noncompliance of Medication Regimen (Saba CCC)") OR (MM "Treatment Refusal")
3. (MH "Patient Education+") OR TX((random* OR control*)) AND TX((medicat* or drug therapy)) OR (MH "Psychotherapy+") NOT ((Pt editorial or Pt letter or TI qualitative or AB qualitative or TI mice or AB mice or TI rat or AB rat or TI rats or AB rats))
4. 1 and 2 and 3

Database: CENTRAL <to 25/2/2019>

1. rheumatoid or psoriatic or spondyloarth* or lupus or gout or osteoporosis or vasculitis or scleroderma or arthritis or sjogren* or myositis or connective tissue disease or ankylosing spondylitis:ti,ab,kw
2. medicat* or treatment* or drug* or therap*:ti,ab,kw
3. complian* or adheren* or persistence or concordance:ti,ab,kw
4. random* or intervention* or trial*:ti,ab,kw not systematic or cochrane or letter or editorial or comment or rat or mice or rats:ti
5. 1 and 2 and 3 and 4 (Word variations have been searched)

C.3 Description of adherence-related factors using the COM-B framework

Sources of behaviour	Description	Examples
Capability	The individual's psychological or physical capacity to engage in the behaviour	Psychological capability (e.g. medication knowledge) Physical capability (e.g. medication taking skill)
Opportunity	Factors that lie outside the individual that prompts a behaviour or makes it possible	Physical opportunity (e.g. cost of medication) Social opportunity (e.g. societal acceptance of medication taking)
Motivation	All the brain processes that energise and direct behaviour	Reflective motivation (e.g. analytical decision making) Automatic motivation (e.g. immediate emotional response to medication taking)



C.4 Interventional studies targeting adherence

C.5 Descriptive summary of included studies

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Abhishek(265) (2017) [United Kingdom]	Single arm interventional prospective cohort study (N=75) [Gout/urate lowering therapy]	1. 62 ± 10 2. 88%	Full clinical assessment from a rheumatologist including aspiration, patient education and individualised management plan involving patient in decision making, with nurse-led follow-up and titration of treatment for 1 year.	(Persistence) Self-report (Questionnaire - Created), Persistent if no discontinuation of therapy, End point, Categorical (Implementation) Self-report (Questionnaire - Created), Average days taking ULT/week, End value, Categorical	Unmet treatment needs (Gout impact questionnaire)	Pain, Activities limitation, General health, Fatigue, Mental health, Quality of life (SF36) Gout concerns, adverse events, gout flare (Gout impact questionnaire)
Akarirmak(239) (2016) [Turkey]	RCT (N=979) [OP/bisphosphonates]	1. 63 ± 7 2. 0%	*Intervention group* Training booklets on OP, exercise, nutrition, patient rights, telephone calls and individual face-to-face educational meetings on OP, fractures prevention and treatments, and reminders to read booklets. *Control group* Patient education as per routine clinical practice by physicians.	(Persistence) Pharmacy refill record, Persistent if ≤30 days between refills, End value and Time to event, Categorical (Implementation) Pharmacy refill record, PDC, End value, Categorical (0-50%, 50%, 75%, 100%)		Adverse events

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Alhefny(254) (2016) [Egypt]	Single arm interventional prospective cohort study (N=100) [RA/Prednisolone, Hydroxychloroquine, Methotrexate, Leflunomide, Sulphasalazine, NSAIDs]	1. 35 ± 9 2. 20%	*Intervention group* Analysis of reasons for non-adherence and management of these reasons, e.g. decreasing cost, improving doctor patient relationship and communication, patient and family education, reducing number of medications, monthly monitoring of adherence.	(Phase unclear) Self-report (Questionnaire - Existing), CQR, adherent if CQR ≥80%, End value, Categorical	Medication cost	ESR, CRP, tender joint count, swollen joint count, pain (using VAS), physical function (HAQ), morning stiffness and disease activity (DAS 28) Joint inflammation and damage (ultrasound) Adverse events (Hb, platelets, total leucocyte counts)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Bianchi(243) (2015) [Italy]	RCT (N=334) [OP/Bisphosphonates, Selective Estrogen Receptor Modifiers, Strontium ranelate]	1. NS 2. 0%	*Intervention group 1* Booklets on OP and importance of adherence, instructions to use medication reminders plus phone calls to take medications and invitations to patient meetings. *Intervention group 2* Same as group 1 minus phone calls and invitations to patient meetings. *Control group* Managed according to standard care.	(Initiation) Combination: Clinician judgement, Self-report, Pill count, Bone turnover markers, End value, Categorical (Implementation) Same instruments as above. Taking treatment 10 out of 12 months, >50% doses taken, no break >2 weeks, End value, Categorical (“Full persistence”) Same instruments as above, Persistent if no discontinuation of therapy, End value, Categorical (Implementation and Persistence) Combination of above	Medication beliefs Health and medication information source	

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Bond(271) (1984) [United States]	Interventional prospective cohort study (N=214) [Multiple including RA, degenerative joint disease/ Gold, Penicillamine, Prednisone, Azathioprine, Cyclophosphamide]	1. NS 2. NS	*Intervention group 1* Pharmacist and nurse support at clinic including medication education, monitoring side effects, drug interactions, duplicate prescriptions, medication documentation, refilling of medications with protocols for monitoring and adjusting and refilling medications, also provided in-service programs. *Intervention group 2* Earlier time-point with only pharmacist support in outpatient clinic, no protocols in place. *Comparison group* Prior to pharmacist allocation to clinic.	(Implementation) Pharmacy refill record, Refilled a prescription ± 7 days of expected day, End value, Categorical	Drug interactions, prescription documentation, duplication of prescriptions, duplication of therapeutic class (Medical and prescription records)	
Briot(240) (2009) [France]	Interventional prospective cohort study (N=5413) [OP/Teriparatide]	1. 72 ± 15 2. 0%	*Intervention group* Phone calls to check on injection ability, sending nurses to help with injection, checking for adverse events. General information on OP sent to patient. *Comparison group* Data on health reimbursements for Teriparatide from French Health Insurance System.	(Persistence) Self-report (Interview - Created), Persistent if no discontinuation of therapy, End value, Categorical For comparator group: Pharmacy refill record, Persistent if ≤60 days between refills, End value, Categorical		Adverse events

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Brus(256) (1998) [Netherlands]	RCT (N=60) [RA/Sulphasalazine]	1. 59 ± 12 2. 20%	*Intervention group* Patient education meetings (information on RA and treatments, discussed beliefs, potential problems with medications, training on physical exercises, planning treatment regimens). *Control group* Brochures on medications, physical and occupational therapy.	(Implementation) Pill count, % tablets taken, End value, Continuous (Mean) (Persistence) Pill count, Persistent if no discontinuation of therapy, End value, Categorical		Disease activity (DAS), ESR, CRP, swollen joint count, physical function (M-HAQ), physical function/mental health/pain/social activities (Dutch-AIMS questionnaire) Joint range of motion (goniometer)
Cizmic(244) (2015) [United States	RCT (N=245) [OP or osteopenia/Bisphosphonate]	1. 72 ± 11 2. 7%	*Intervention group* Automated interactive voice response phone call to patients not purchasing a new oral bisphosphonate. Phone script contains information about OP, benefits and risks of bisphosphonates and can be transferred to the pharmacy to fill their prescription. If the medication was still not purchased a letter with benefits and risks was sent. *Control group* No phone call or letter.	(Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical (Implementation) Pharmacy refill record, MPR, End value, Continuous (Mean) (Implementation) Pharmacy refill record, MPR, Adherent if MPR ≥80%, End value, Categorical		

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Clifford(264) (2006) [United Kingdom]	RCT (N=500) [RA (n=37), stroke, cardiovascular disease, asthma or diabetes]	1. 67 2. 48%	*Intervention group* Phone call from trained pharmacist asking about medication related problems, adherence and information needs and provision of information, advice or reassurance. *Control group* No phone call.	(Implementation) Self-report (Interview - Created), Doses missed in last seven days, Adherent if no doses missed, End value, Categorical	Medication beliefs (BMQ) Medication problems (Interview) Intervention satisfaction (Interview) Safety of pharmacist's recommendation and helpfulness of pharmacist's recommendation (Judgement of expert panel)	General health (SF 36)
Clowes(221) (2004) [United Kingdom]	RCT (N=75) [Osteopenia/Raloxifene]	1. 62 ± 1 2. 0%	*Nurse-monitored group* Visits with nurse, who asked about well-being, problems with medications and adverse events. *Marker monitored group* In addition to nurse follow up, bone turnover marker results presented on a graph. *Control group* Collected medications at week 24, no medical contact.	(Implementation) MEMS, Adherent if >75% tablets taken, End value, Categorical (Implementation) MEMS, % tablets taken, End value, Continuous (Mean) (Persistence) MEMS, Persistent if tablets taken for >7/14 days immediately before 1 year visit, End value, Categorical		Adverse events (Collected during nurse follow up) Bone turnover marker (Urinary N-telopeptide) Bone density (DEXA)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Delmas(222) (2007) [21 countries including Australia, North and South America, Europe and Africa]	RCT (N=2382) [OP/Risedronate]	1. 71 ± 4 2. 0%	*Intervention group* Reinforcement based on bone turnover markers. *Control group* No reinforcement.	(Persistence) MEMS, Persistent if no discontinuation of therapy, End value, Categorical (Implementation and Persistence) MEMS, Average daily % of people who were both persistent (continued treatment) and compliant (took drug properly on that day), End value, Categorical	Medication satisfaction (Patient satisfaction questionnaire)	Fractures (Lateral thoracic and lumbar x rays, non-vertebral fractures from self-report) Adverse events (Case report forms) Bone turnover marker (Urinary N-telopeptide)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Ducoulombier(245) (2015) [France]	RCT (N=164) [OP/Oral anti-osteoporosis therapy]	1. 70 2. 0%	*Intervention group* Phone calls from trained medical secretaries to motivate patient to adhere, detect difficulties in adherence. Encouragement to contact primary care physician if poor adherence detected. *Control group* No phone call.	(Implementation) Self-report (Questionnaire and Interview) Morisky and physician interview, Adherent if taking medications in last 2 months and MPR ≥80%, End value, Categorical (Persistence) Self-report (Questionnaire and Interview) Morisky and physician interview, Persistent if taking medications in 2 months preceding evaluation, End value, Categorical	Reasons for adherence/non-adherence	

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Feldman(269) (2018) [United States]	Single arm interventional prospective cohort study (N=107) [Systemic rheumatic diseases/oral DMARD]	1. 55 ± 16 2. 7%	*Intervention group* Patient navigator (non-health professional), trained in motivational interviewing, care co-ordination, advocacy, basic pharmacology and rheumatic disease management assessed specific needs and barriers to DMARD use and designed tailored strategies to assist each patient.	(Phase unclear) Self-report (Questionnaire - Existing), 8-item Morisky, Poor (MMAS <6), Borderline (MMAS 6 to <8), High (MMAS =8), End value, Categorical (Poor, borderline, high) (Phase unclear) Self-report (Questionnaire - Existing) 8-item Morisky, End value, Continuous (Mean)	Medication beliefs (BMQ) Illness perception (Brief Illness Perception Questionnaire)	Disease activity (Rheumatoid Arthritis Disease Activity Index and Systemic Lupus Questionnaire) Mental health (Mental Health Inventory)
Ferguson(257) (2015) [United Kingdom]	Pilot RCT (N=18) [RA/NS]	1. 50 ± 15 2. 0%	*Intervention group* Sessions with psychologist, drawing on cognitive behavioural therapy and motivational interviewing, focusing on practical and perceptual factors impacting adherence, ambivalence towards medications, pros and cons of taking medications, challenging and modifying unhelpful treatment and illness beliefs. *Control group* Standard care.	(Phase unclear) Self-report (Questionnaire - Existing), 5-item MARS, End value and change from baseline, Continuous (Mean) (Phase unclear) Self-report (Questionnaire - Existing) 4-item Morisky, End value and change from baseline, Continuous (Mean)	Illness perception (Illness Perception Questionnaire) Medication beliefs (BMQ)	Quality of life (EQ-5D) Anxiety (General Anxiety Disorder Questionnaire) Depression (Patient Health Questionnaire) Disease activity (DAS 28) Physical function (HAQ)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Ganda(227) (2014) [Australia]	RCT (N=102) [Osteoporotic fracture/Oral bisphosphonate]	1. 67 ± 11 2. 16%	*Intervention group* After initiation of bisphosphonate at a secondary fracture prevention (SFP) clinic in hospital, follow up with the SFP at baseline, 3, 6, 12, 18 and 24 months. *Control group* Follow up at SFP at 3 months, then managed by primary care physician until 24 months.	(Implementation) Pharmacy refill record, MPR, End value, Continuous (Median) (Implementation) Pharmacy refill record, MPR, Adherent if MPR ≥80%, End value, Categorical (Persistence) Pharmacy refill record, Persistent if ≤90 days between refills, End value and Time to event, Categorical (Implementation) Self-report (Questionnaire - Created), How often medication missed, End value, Categorical (never missing, one in 10 times, five in 10 times, often missing)		Bone mineral density (DEXA) Bone turnover marker (Urinary deoxypyridinoline)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Gonnelli(228) (2016) [Italy]	RCT (N=816) [OP/Oral anti-osteoporosis treatment]	1. 65-66 (Median) 2. 0%	*Intervention group* Patients starting OP therapy for the first time received information about individual fracture risk and a leaflet with 10 year absolute risk of major osteoporotic fracture. *Control group* Drug prescription with usual explanation and recommendation from physician.	(Phase unclear) Self-report (Questionnaire - Existing), 4-item Morisky, High (MMAS score 0), moderate (MMAS score 1), low (MMAS score 2-4), End value, Categorical (High, moderate, low) (Persistence) Self-report (Interview - Created), Dose, administration and schedule of medication in last 12 months, high persistence >75%, low persistence <30%, End value, Categorical		Adverse events (Case report forms) Fractures (Case report forms)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Gorai(223) (2010) [Japan]	RCT (N=137) [OP or osteopenia/Raloxifene, Alfacalcidol]	1. 65 ± 7 2. 0%	*Drug regimen Group 1* Alfacalcidol. *Group 2* Raloxifene. *Group 3* Alfacalcidol and Raloxifene.	(Implementation) Pharmacy refill record, MPR, End value, Continuous (Mean) (Implementation) Pharmacy refill record, Medication Possession Ratio (MPR), Adherent if MPR >80%, End value, Categorical (Persistence) Pill count and Self-report (Questionnaire - Created), Persistent if tablets taken for >7/14 days immediately before 1 year visit, End value and Time to event, Categorical (Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical	Reasons for adherence/non-adherence (Questionnaire)	Bone mineral density (DEXA) Bone turnover marker (Serum bone alkaline phosphatase, Urinary N-telopeptide and C-telopeptide) Adverse events (Patient report at each visit)
Guillera(229) (2006) [Spain]	RCT (N=745) [OP/Raloxifene]	1. 62 2. 0%	*Intervention group* Educational leaflet on menopause, diet and lifestyle measures and importance of therapeutic adherence provided, attending physician spent 15 minutes reviewing the leaflet with each participant. *Control group* No leaflet.	(Phase unclear) Self-report (Questionnaire - Existing), 4-item Morisky, High (MMAS score 0), moderate (MMAS score 1-2), low (MMAS score 3-4), End value, Categorical (High, moderate, low)		Health related quality of life (EQ-5D) Adverse events

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Hill(258) (2001) [United Kingdom]	RCT (N=100) [RA/D-penicillamine]	1. 62-63 (Median) 2. 27%	*Intervention group* Individual sessions of patient education (condition, medication, exercise, joint protection, pain control, coping) with a rheumatology nurse practitioner. *Control group* Standard management including sessions with nurse practitioner, provided with drug information leaflet, no individual patient education.	(Implementation) Drug concentration in body fluid (Phenobarbitone), Adherent if level correlated to ≥85% ingestion, End value, Categorical		Systemic inflammation (plasma viscosity and CRP) Tender and swollen joints (Articular index) Morning stiffness Pain (Pain score) Adverse events (Self-report interview)
Homer(268) (2009) [United Kingdom]	RCT (N=62) [RA, PsA/Methotrexate, Sulfaslazine, Leflunomide]	1. 54 2. 40%	*Intervention group (Individual session*) 30 minute counselling with nurse practitioner about condition, medication and provided contact details for nurse in case of difficulty. *Intervention group (Group session)* 45 minutes session in groups of 3-6 of counselling, with same information as individual counselling, slides presented.	(Implementation) Pill count, Non-adherent if any three pill counts were not as expected, End value, Categorical (Implementation) Self-report (Diary), Adherent if diary matching pill count, End value, Categorical (Persistence) Pharmacy refill record, Persistent if no discontinuation of therapy, End value, Categorical	Satisfaction with information about medication (Satisfaction with Information about Medicines Questionnaire)	Adverse events (From hospital records)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Joplin(260) (2016) [Australia]	Single arm interventional study (N=18) [RA/Immunosuppression]	1. 57 ± 15 2. 28%	*Intervention group* 20 min ultrasound session, ultrasound was shown and explained to patient during the session.	(Phase unclear) Self-report (Questionnaire - Existing), CQR, End value, Continuous (Mean)	Medication beliefs (BMQ) Patient activation (Patient Activation Measure)	Disease activity (RAPID3 in MDHAQ)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Kendler(224) (2011) [United States, Canada]	RCT (N=250) [RA and OP/Denosumab, Alendronate]	1. 65 ± 8 2. 0%	*Drug regimens Group 1* Subcutaneous Denosumab every 6 months. *Group 2* Oral Alendronate weekly, with crossover after 12 months.	(Implementation) MEMS, Adherent if ≥80% tablets taken, End value, Categorical (Implementation) MEMS, % tablets taken, End value, Continuous (Mean) (Implementation) Pill count, % tablets taken, End value, Continuous (Mean) (Implementation) Adherence measure unspecified, Adherent if all injections given within 1 month of due date, End value, Categorical (Persistence) MEMS, Persistent if ≥2 tablets taken in last month and returned for month 12 visit, End value, Categorical (Persistence) Adherence measure unspecified, Persistent if all injections given and returned for 12 month visit, End value, Categorical (Implementation and Persistence – Phase unclear) Combinations of the above.	Medication beliefs and medication preferences (BMQ) Medication satisfaction and bother (Patient Satisfaction Questionnaire)	Bone mineral density (DEXA) Bone turnover markers (Serum C-telopeptide and urinary N-telopeptide) Adverse events (Patient report at each study visit)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Kung(230) (2009) [Hong Kong, Indonesia, Philippines, Taiwan, Thailand]	RCT (N=596) [OP/Ibandronate]	1. 66 ± 7 2. 0%	*Intervention group* Bone turn over marker feedback provided. *Control group* No bone turn over marker feedback.	(Implementation) Adherence measure unspecified, 5/6 or 10/12 monthly doses taken within -1 to +21 day dose window, End value, Categorical	Medication satisfaction (Osteoporosis Patient Satisfaction Questionnaire and Osteoporosis Patient Perception Survey Questionnaire)	Bone turnover marker (Serum C-telopeptide) Adverse events (Collected at each visit and if needed with phone calls)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Lai(231) (2011) [Malaysia]	RCT (N=198) [OP/Alendronate, Risedronate]	1. 66 ± 9 2. 0%	*Intervention group* Verbal counselling package - Pharmacist educating patients on OP, lifestyle and medication management, importance of medication adherence. Phone calls with pharmacist. Bone turnover marker feedback. *Control group* No verbal counselling or bone turnover marker feedback.	(Implementation) Self-report (Interview - Created) How many doses missed since last visit, End value, Continuous (Mean and Median) (Implementation) Pill count, % tablets taken, End value, Continuous (Mean and Median) (Implementation) Self-report (Diary), End value, Continuous (Mean and Median (Implementation) Self-report (Diary), Absolute adherence defined as taking medications on the same day each week, End value, Categorical (Absolute adherence) (Implementation) Self-report (Diary), Taking less than prescribed, End value, Categorical (Non-adherent) (Persistence) Pharmacy refill record, Persistent if no discontinuation of therapy, End value, Categorical	Reasons for adherence/non-adherence (self-report	Bone turnover marker (Serum C-telopeptide and serum osteocalcin) Adverse events (self-report

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
LeBlanc(236) (2015) [United States]	RCT (N=79) [OP or osteopenia/Bisphosphonate]	1. 67 ± 9 2. 0%	*Intervention group (Decision aid arm)* Use of a decision aid which showed individualised 10-year risk of having a fracture with and without bisphosphonate and potential harms of using a bisphosphonate. The physician and patient review the decision aid and make a decision together. *Intervention group (FRAX arm)* Clinicians provided with a copy of patient's individualised 10 year risk of having a fracture using FRAX prior to clinical encounter. *Control group* Usual care.	(Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical (Implementation) Pharmacy refill record, PDC, End value, Continuous (Median) (Implementation) Pharmacy refill record, PDC, Adherent if PDC >80%, End value, Categorical	Medication and condition knowledge (Questionnaire) Decisional conflict (Decisional Conflict Scale) Involvement in decision making (OPTION scale) Fracture risk (Patient's estimate) Satisfaction with medication information Medication initiation decision (survey after clinical encounter)	Quality of life (EQ-5D)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Majmunder(242) (2007) [Canada]	Non-randomised controlled trial (N=102) [Patients with wrist fracture/OP prescription medication]	1. 66 (Median) 2. 22%	*Intervention group* Physician reminders, local opinion leader endorsed treatment guidelines, and patient education. *Control group* Received intervention 6 months later.	(Persistence) Pharmacy refill record, Persistent if no discontinuation of therapy, End value, Categorical (Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical (Implementation) Self-report (Questionnaire - Created), Taking ≥75% of medications as prescribed, End value, Categorical		Resource use (Markov decision-analytic model)
McAlister(225) (2019) [Canada]	RCT (N=361) [Patients with upper extremity fracture/Oral bisphosphonate]	1. 65 ± 9 2. 5%	*Intervention group 1* Patient education on OP, encouragement to follow up with primary care physician, fax to patient's primary care physician including their patient's recent fracture and OP treatment guidelines. *Intervention group 2* Registered nurse met with patients face to face or called patients, education about OP, BMD tests, medications, organised BMD and lab tests, discussed results, initiated treatments if appropriate, communicated test results and treatment plans to family physician.	(Initiation) Pharmacy refill record and Self-report (Details unspecified), Initiated treatment, End value, Categorical (Initiation) Pharmacy refill record and Self-report (Details unspecified), Refused treatment, End value, Categorical (Primary non-adherence) (Implementation) Pharmacy refill record and Self-report (Details unspecified), Adherent if >80% of tablets taken, End value, Categorical	Reasons for adherence/non-adherence (Self-report)	Quality of life (SF-12 and Osteoporosis Quality of Life Index) Functional ability (Disability of Arm, Shoulder and Hand Index) Adverse events (Self-report)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Miedany(255) (2012) [Egypt]	RCT (N= 147) [RA/DMARDs]	1. 53 ± 10 2. 27%	*Intervention group* Participants encouraged to set goals, review PROMS, and took part in the joint fitness program (aimed at patients - education, self-management, coping, monitoring arthritis outcomes, impact on personal life, physical exercises and aimed at physician - about value and use of PROMS and patient education). *Control group* Standard care including discussion of disease activity, PROMS and medications verbally.	(Phase unclear) Adherence measure unspecified, End value, Categorical	Reasons for adherence/non-adherence Medication knowledge (Questionnaire) Trust in doctor (Questionnaire)	Pain, patient global assessment, functional disability, quality of life, helplessness (Multidimensional PROM) Disease activity (DAS 28) Adverse events Arthritis flare (No. of clinic visits for follow up)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Miedany(267) (2012) [Egypt]	RCT (N=111) [Early inflammatory arthritis/DMARDs]	1. 51 ± 11 2. 25%	*Intervention group* Visualisation of computer charts showing the progression of disease activity parameters plus standard management. *Control group* Standard management including verbally discussing changes in disease activity, PROMS, medications, falls, cardiovascular risk and viewing previously completed forms.	(Phase unclear) Adherence measure unspecified, End value, Categorical	Reasons for adherence/non-adherence Medication knowledge (Questionnaire) Trust in doctor (Questionnaire)	Pain, patient global assessment, functional disability, quality of life, helplessness (Multidimensional PROM) Disease activity (DAS 28) Adverse events Arthritis flare (No. of clinic visits for follow up)
Mikuls(266) (2018) [United States]	RCT (N=1463) [Gout/Allopurinol]	1. 58 ± 14 2. 82%	*Intervention group* Interactive voice response system to assess whether medications were continued, alert patients on pending orders or prescriptions and provide encouragement. Pharmacist called patient if allopurinol was not refilled, or patient did not undergo lab monitoring or respond to automated messaging. *Control group* Usual care and automated reminders to perform a serum urate.	(Implementation) Pharmacy refill record, PDC, Adherent if PDC ≥80%, End value, Categorical (Implementation) Pharmacy refill record, PDC, End value, Continuous (Mean)		Serum urate Gout flares (Medical or pharmaceutical claims) Adverse events (Electronic health records)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Montori(246) (2011) [United States]	RCT (N=100) [OP or osteopenia/Oral bisphosphonate]	1. 67 (Median) 2. 0%	*Intervention group* Decision aid showing pictographic 10-year fracture risk estimate, absolute risk reduction with bisphosphonates, side effects, out of pocket costs. *Control group* Usual care plus standard brochure.	(Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical (Implementation) Pharmacy refill record, PDC, End value, Continuous (Median) (Implementation) Pharmacy refill record, PDC, Adherent if PDC >80%, End value, Categorical (Implementation) Self-report (Interview - Existing), Haynes' single item adherence question, "Have you missed any of your pills in the last week?", End value, Categorical (Persistence) Pharmacy refill record, No. of days covered, End value, Continuous (Median)	Medication and condition knowledge (Questionnaire) Fracture risk (Patient's estimate) Decisional conflict (Decisional conflict scale) Involvement in decision making (OPTION scale) Trust in doctor (Trust in Physician Scale) Satisfaction with medication information Medication initiation decision (Survey) Reasons for adherence/non-adherence	

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Muratore(232) (2013) [Italy]	Randomised multi-arm trial (N=87) [RA and osteopenia/Neridronate, Alendronate, Risedronate]	1. 62 ± 9 2. 0%	*Drug regimens Group 1* Intramuscular Neridronate monthly. *Group 2* Oral Alendronate weekly. *Group 3* Oral Risedronate weekly.	(Phase unclear) Self-report (Questionnaire - Existing), 4-item Morisky, Adherent if MMAS ≥3, End value, Categorical (Phase unclear) Self-report (Questionnaire - Existing), 4-item Morisky, End value, Continuous (Mean)		Bone mineral density (DEXA) Disease activity (DAS 28) Adverse events
Naranjo(247) (2015) [Spain]	Single arm interventional prospective cohort study (N=759) [OP/Anti-resorptive agent]	1. 72 ± 9 2. 22%	*Intervention group* Secondary fracture prevention clinic which incorporates capture, assessment, patient education, communication and a co-ordinator. Nurse co-ordinator also stresses the importance of adherence and checks adherence with phone calls and offers help to address concerns.	(Initiation) Pharmacy refill record and Self-report (Interview - Created) "Are you taking the medications prescribed for OP?", Initiated treatment, End value, Categorical (Persistence) Pharmacy refill record and Self-report (Interview - Created) "Are you taking the medications prescribed for OP?", Persistent if prescription disposal confirmed and affirmative answer to self-report question, End value, Categorical	Reasons for adherence/non-adherence	

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Nielson(241) (2010) [Denmark]	RCT (N=300) [OP/"Specific pharmacological therapy"]	1. 64 (Median) 2. 11%	*Intervention group* Multidisciplinary group-based patient education program about OP, investigations, diet, exercise, medication, and computerised support program and brush up course. *Control group* Asked to take OP therapy as prescribed and offered control visits at GP or clinic as appropriate.	(Implementation) Self-report (Questionnaire - Created), How, when and how often the patient took their medication, Adherent if patients took medicine correctly at the appropriate time, End value, Categorical	Medication and condition knowledge (Questionnaire) Satisfaction with medication information (Questionnaire)	Adverse events (Questionnaire)
Oral(233) (2015) [Turkey, Poland]	RCT (N= 448) [OP/Risedronate]	1. NS 2. 0%	*Intervention group* Initial randomisation to fixed timing to take risedronate, followed by patients either choosing a fixed time or flexible time to take risedronate.	(Implementation) Pill count, % tablets taken, Adherent if >50%, End value, Categorical (Persistence) Pill count, Persistent if no discontinuation of therapy, End value, Categorical (Implementation and Persistence – Phase unclear) Pill count, Response defined as a combination of the above, End value, Categorical (Responder)	Medication satisfaction (Subject's Preference Questionnaire)	Bone turnover marker (Urinary N-telopeptide) Adverse events

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Ravindran(259) (2013) [India]	RCT (N=122) [RA/Triple therapy]	1. 54 ± 10 2. 25%	*Intervention group* 10-minute education regarding RA at first consultation with "reinforcement" at first 4 week follow up. *Control group* Standard information.	(Phase unclear) Self-report (Questionnaire - Existing), 4-item Morisky, Method of scoring unspecified, End value, Categorical (High, partial, poor)	Reasons for adherence/non-adherence (4-item Morisky and additional questions)	Disease activity (DAS 28)
Robbins(248) (2004) [United States]	Interventional prospective cohort study (N=109) [Women enrolled in OP trial/Low dose estrogen or placebo]	1. 74 ± 5 2. 0%	*Intervention group* Participants divided into three racial groups, all groups received standardised condition and medication education, monthly telephone calls to encourage adherence, 3 monthly pill counts. All participants used pill boxes. For the last 6 months, participants in the minority groups used electronic monitoring bottles with data shown to them at 9 and 12 months, and suggestions to improve adherence.	(Implementation) Pill count, % of tablets taken, if value > 100% (overdosing), the value over 100% was taken away from 100%, End value, Continuous (Mean or Median) (Implementation) MEMS, % of tablets taken, if value > 100% (overdosing), the value over 100% was taken away from 100%, End value, Continuous (Mean or Median)		

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Roh(234) (2018) [Korea]	RCT (N=432) [OP/Bisphosphonate]	1. 62 ± 8 2. 0%	*Drug regimen Group 1* Intravenous Ibandronate every 3 months. *Group 2* Oral Alendronate weekly.	(Implementation) Pill count and Self-report (Details unspecified), Adherent if ≥80% tablets taken, End value, Categorical (Implementation) Adherence measure unspecified, Adherent if all injections given within 1 month of due date, End value, Categorical (Persistence) Pill count and Self-report (Details unspecified), Persistent if ≥2 tablets taken in last month and returned for 12 month visit, End value, Categorical (Persistence) Adherence measure unspecified, Persistent if all injections given and returned for 12 month visit, End value, Categorical		Adverse events (Patient report at each study visit) Fractures (Patient report at each study visit)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Roux(235) (2012) [France]	RCT (N=596) [OP/Ibandronate]	1. 69 ± 8 2. 0%	*Intervention group* Bone turnover marker feedback. *Control group* No feedback, standard care	(Persistence) Adherence measure unspecified, Persistent if 10/12 monthly doses taken and still treated at last visit, End value, Categorical (Implementation) Adherence measure unspecified, Adherent if 10/12 monthly doses taken, End value, Categorical		Bone turnover marker (Serum C-telopeptide) Adverse events
Rudd(270) (2009) [United States]	RCT (N=127) [RA, PsA, Inflammatory polyarthritis/Medications unspecified]	1. 59 ± 14 2. 21%	*Intervention group* Plain language educational materials, some patients had two visits with a rheumatology educator who reviewed the plain language material, the process of using a medication calendar, communication with caregivers and challenges in navigating the health care system, and was available for other appointments and phone calls between visits. *Control group* received pamphlets from the Arthritis Foundation.	(Phase unclear) Self-report (Questionnaire - Existing), 4-item Morisky, End value and Change from baseline, Continuous (Mean)	Satisfaction with medical care (Medical Interview Satisfaction Scale) Self-efficacy (Lorig's self-efficacy scale)	Mental health (SF36 mental subscale) Physical function (HAQ)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Schousboe(249) (2005) [United States]	RCT (N=310) [OP or osteopenia/Anti-resorptive therapy	1. 72 ± 8 2. 0%	*Intervention group* Nurse educator provided one-to-one education on OP (BMD results, risk of fracture, other risk factors, consequences of fracture, calcium, vitamin D, lifestyle measures and anti-resorptive medication use if appropriate), telephone follow up and brochures on OP. *Control group* Brochures regarding OP. Both groups received BMD and personalised report of recommendations to primary care physician.	(Persistence) Self-report (Interview - Created), Persistent if no discontinuation of therapy, End value, Categorical (Initiation) Self-report (Interview - Created), Participants asked if physician had prescribed medication, End value, Categorical		

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Shu(250) (2009) [United States]	RCT (N=1867) [Patients at risk of OP/Alendronate, Calcitonin, Estrogen, Raloxifene, Risedronate, Teriparatide]	1. NS 2. 2%	*Intervention group* Pharmacist educators who had training and learnt teaching techniques, provided primary care providers with list of patients at risk for OP, summary of OP epidemiology, diagnosis and treatment, checklist with boxes for fall prevention, calcium and vitamin D use, BMD testing and treatment. The study paid physicians to apply for CME credit. Patients received a letter on OP, diagnosis and treatment, and an automated phone call inviting them to do BMD. *Control group* No education	(Implementation) Pharmacy refill record, MPR, End value, Continuous (Median) (Persistence) Pharmacy refill record, Persistent if <30 days between refills, Time to event, Continuous (Median) (Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical		
Silverman(237) (2012) [United States]	RCT (N=239) [OP or osteopenia/Alendronate]	1. 67 2. 0%	*Intervention group 1* Bone turnover marker feedback. *Intervention group 2* Education materials monthly and membership in the National OP Foundation. *Combination of intervention 1 and 2* Both bone turnover marker feedback and educational materials. *Control group* Usual Care	(Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical (Persistence) Pharmacy refill record, Persistent if no discontinuation of therapy, End value, Categorical	Reasons for adherence/non-adherence and Intervention's influence on adherence (Interviews at end of study)	Bone turnover marker (Urinary N-telopeptide)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Solomon(238) (2012) [United States]	RCT (N=2087) [OP/Prescription OP medication]	1. 78 2. 6%	*Intervention group* Telephone-based counselling sessions using a motivational interviewing framework and mailed educational materials. *Control group* Mailed educational materials	(Implementation) Pharmacy refill record, MPR, End value, Continuous (Median) (Implementation) Pharmacy refill record, MPR, End value, Categorical (MPR <20%) (Implementation) Pharmacy refill record, MPR, Adherent if MPR >80%, End value, Categorical (Persistence) Pharmacy refill record, Persistent if ≤60 days between refills, End value, Categorical		Fractures, falls, general health (Self-report) Mortality Resource use (Per patent intervention cost)
Stephens(251) (2016) [New Zealand]	RCT (N=58) [OP/Bisphosphonate]	1. 73 2. 9%	*Intervention group* 3D bone models used to educate patients about the difference between healthy and osteoporotic bone plus standard medical interview. *Control group* Standard medical interview only.	(Initiation) Pharmacy refill record and Self-report (Details unspecified), Initiated treatment, End value, Categorical	Illness perception (Illness Perception Questionnaire) Medication beliefs (BMQ) Intervention's influence on adherence, condition knowledge and anxiety about OP (Questionnaire)	

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Stockl(261) (2010) [United States]	Interventional prospective cohort study (N=828) [RA/bDMARD]	1. 62 ± 12 2. 17%	*Intervention group* RA disease therapy management program. Phone calls from pharmacist or nurse providing condition and medication (including adherence) education/training. Personalised care plan and monthly educational materials sent. Attended specialty pharmacy. *Specialty pharmacy* Refill reminder calls, patient educational materials, mail service delivery, 24-hour access to pharmacist. *Community pharmacy* Medications not filled through specialty pharmacy.	(Implementation) Pharmacy refill record, PDC, End value, Continuous (Mean) (Persistence) Pharmacy refill record, Persistent if <30 days between refills, End value, Categorical		Quality of life (SF 12) Worker productivity (Worker Productivity Activity Impairment) Physical function (HAQ-DI) Resource use (Pharmacy ingredients cost)
Stuurman-Bieze(252) (2014) [Netherlands]	Interventional prospective cohort study (N=937) [OP/OP medication]	1. 67 ± 15 2. 22%	*Intervention group* Continuous monitoring of medication adherence and tailored counselling by community pharmacists. *Internal reference group* Usual pharmacy care.	(Implementation) Pharmacy refill record, PDC, Adherent if PDC ≥80%, End value, Categorical (Persistence) Pharmacy refill record, Persistent if no discontinuation of therapy, End value, Categorical (Implementation or Persistence – Phase unclear) Either one of the above	Intervention satisfaction (Questionnaire) Reasons for adherence/non-adherence (Patient's medical history or patient/provider interview)	

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Taibanguay(219) (2019) [Thailand]	RCT (N=120) [RA/DMARDs]	1. 57 ± 12 2. 16%	*Intervention group* 30-minute directed counselling and disease information pamphlet. *Control group* Disease information pamphlet only.	(Implementation) Pill count, % tablets taken, End value and Change from baseline, Continuous (Mean) (Implementation) Pill count, % tablets taken, Adherent if >80%, End value, Categorical (Phase unclear) Self-report (Questionnaire - Existing), MTB-Thai, End value and Change from baseline, Continuous (Mean) (Phase unclear) Self-report (Questionnaire - Existing), MTB-Thai, Adherent if ≥22, End value, Categorical	Illness perception (Brief Illness Perception Questionnaire)	Patient global assessment, physician global assessment Pain (pain score) Quality of life (EQ-5D) Anxiety and Depression (HADS) Cognitive impairment (Montreal Cognitive Assessment and Thai Mental State Examination) Disease activity (DAS 28)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Ting(91) (2012) [United States]	RCT (N=41) [Childhood onset SLE/Hydroxychloroquine]	1. 19 ± 3 2. 7%	*Intervention group* Cellular text messaging reminders to take each scheduled medication dose. *Control group* Standard of care education.	(Implementation) Pharmacy refill record, MPR, End value, Continuous (Mean) (Implementation) Pharmacy refill record, MPR, Adherent if MPR >80%, End value, Categorical (Implementation) Drug concentration in body fluid (HCQ level), End value, Continuous (Mean) (Implementation) Drug concentration in body fluid (HCQ level), Adequate exposure defined as HCQ level ≥900ng/ml, End value, Categorical (Implementation) Drug concentration in body fluid (HCQ level), End value, Categorical (Undetectable HCQ level) (Implementation) Self-report (Questionnaire - Existing), MASRI, End value, Continuous (Mean)		Disease activity (SLE Disease Activity Index) Disease damage (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index) Physician global assessment Emergency department visits and hospitalisation (Administrative database)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Tüzün(226) (2013) [Turkey]	RCT (N=448) [OP/Alendronate, Risedronate]	1. 62 ± 8 2. 0%	*Intervention group* Active training (Phone calls and interactive social/training meetings on OP, exercise, nutrition and patient rights). *Control group* Passive training (Medication usage guide and OP training booklet)	(Implementation) Self-report (Details unspecified), 'Patients who received bisphosphonate treatment at the exact day', End value, Categorical (Implementation) Self-report (Details unspecified), 'Patients who did not receive bisphosphonate treatment at the exact day', End value, Categorical (Implementation) Self-report (Details unspecified), 'Always used their drugs regularly on recommended days and dosages', End value, Categorical (Phase unclear) Self-report (Details unspecified), 'Patients who received bisphosphonate treatment', End value, Categorical (Phase unclear) Self-report (Details unspecified), 'Patients who did not complete bisphosphonate dose', End value, Categorical	Reasons for non-adherence, medication satisfaction, intention to adhere Condition knowledge (OP awareness test)	Fracture (Patient or investigator report) Quality of life (Quality of Life European Foundation for Osteoporosis) Adverse events (Patient or investigator report)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Unk(262) (2014) [United States]	RCT (N=108) [RA/NS]	1. 50 ± 12 2. 20%	*Intervention group* 15-minute multimedia educational program (Power point presentation containing information about RA, treatment options, and self-care). *Control group* Educational literature with similar information.	(Implementation) Self-report (Questionnaire - Existing), Medication Self-report Questionnaire, Six items with Likert scale 1-5, End value, Continuous (Mean) (Implementation) 'Adherence rate' also reported but definition/calculation unspecified.	Illness perception (Brief Illness Perception Questionnaire)	Physical function (HAQ)
Van den Bemt(263) (2011) [Netherlands]	Single arm interventional prospective cohort study (N=50) [RA/DMARDs]	1. 55 ± 12 2. 30%	*Intervention group* Written report of patient's drug use and adherence rate was provided to the patient's Rheumatologist.	(Phase unclear) Self-report (Questionnaire - Existing), CQR, End value, Continuous (Mean) (Phase unclear) Self-report (Questionnaire - Existing), CQR, Adherent if CQR ≥80%, End value, Categorical	Medication beliefs (BMQ) Satisfaction with medication information (Satisfaction with Information about Medicines Questionnaire)	Physical function (HAQ-DI)

First author (Year published) [Country]	Study type (total participants) [Condition /Medication targeted]	Participant 1. Age (Mean ± SD) 2. % Males	Brief description of intervention	Adherence outcome (phase) Unique adherence measure: Instrument, Definitions used for adherence calculation, Metric, Method of aggregation	Adherence-related factors (Measure/ instrument)	Health outcomes (Measure/ instrument)
Waalen(253) (2009) [United States]	RCT (N=235) [OP/OP medication]	1. 71 ± 10 2. 0%	*Intervention group* Phone based OP clinic - patients prescribed Vitamin D/Calcium/OP medication, received medication education, training on adherence strategies, addressed medication concerns, checked medication initiation and reasons for non-adherence. Monthly phone calls until medication initiated and patient had no problems with the medication. *Control group* Referral to their usual primary care physician.	(Persistence) Pharmacy refill record, Persistent if ≤130 days between refills, End value, Categorical (Initiation) Pharmacy refill record, Filled initial prescription, End value, Categorical	Condition knowledge (Questionnaire) Satisfaction with medical care (Questionnaire)	

*NA – Not applicable if no core domain set, or if core domain set did not exist at time of publication

Abbreviations: SD, standard deviation; ULT, urate lowering therapy; SF, short form survey; RCT, randomised controlled trial; OP, osteoporosis; PDC, proportion of days covered; RA, rheumatoid arthritis; NSAID, non-steroidal anti-inflammatory drug; CQR, compliance questionnaire in rheumatology; ESR, erythrocyte sedimentation rate; CRP, c reactive protein; VAS, visual analogue scale; HAQ, health assessment questionnaire; DAS, disease activity score; Hb, haemoglobin; NS, not specified; M-HAQ, modified health assessment questionnaire; AIMS, arthritis impact measurement scales; MPR, medication possession ratio; BMQ, beliefs about medicines questionnaire; MEMS, medication event monitoring systems; DEXA, dual-energy x-ray absorptiometry; DMARD, disease-modifying anti-rheumatic drug; MMAS, Morisky medication adherence scale; MARS, medication adherence report scale; EQ-5D, EuroQol-5 Dimension; PsA, psoriatic arthritis; RAPID 3, routine assessment of patient index data 3; MDHAQ, multidimensional health assessment questionnaire; FRAX, fracture risk assessment tool; BMD, bone mineral density; PROM, patient reported outcome measure; OPTION scale, observing patient involvement in decision making; CME, continuing medical education; bDMARD, biologic disease-modifying anti-rheumatic drug; MTB-Thai, medication taking behaviour measure for Thai patients; SLE, systemic lupus erythematosus; HCQ, hydroxychloroquine; MASRI; medication adherence self-report inventory; HAQ-D, health assessment questionnaire disability index.

Appendix D: Supporting data for Chapter 4

D.1 Search strategy

Database (search range)	Search terms
Ovid MEDLINE (1946 to 12/01/2016)	{exp Arthritis, Rheumatoid OR exp Arthritis, Psoriatic OR exp Spondylitis, Ankylosing OR exp Arthritis, Reactive OR [exp Arthritis AND exp inflammatory bowel disease] OR Inflammatory arthritis.tw. OR exp Spondylarthritis} AND {exp qualitative research OR qualitative.tw. OR interview$.tw. OR focus group$.tw. OR [thematic$ or theme$].tw. OR grounded theory.tw. OR phenomenol$.tw. OR content analysis.tw. OR ethnograph$.tw. OR exp decision making OR exp Illness Behavior OR exp Knowledge/ or Health Knowledge, Attitudes, Practice OR exp Medication Adherence/ or exp Patient Medication Knowledge OR exp Compliance/ or exp Patient Compliance OR Persistence.tw.} AND { exp Antirheumatic Agents/tu [Therapeutic Use] OR DMARD$.tw. OR medicine$.tw.}
Embase (1974 to 12/01/2016)	{exp Arthritis, Rheumatoid OR exp Arthritis, Psoriatic OR exp Spondylitis, Ankylosing OR exp Arthritis, Reactive OR [exp Arthritis AND exp inflammatory bowel disease] OR Inflammatory arthritis.tw. OR exp Spondylarthritis} AND {exp qualitative research OR qualitative.tw. OR interview$.tw. OR focus group$.tw. OR [thematic$ or theme$].tw. OR grounded theory.tw. OR phenomenol$.tw. OR content analysis.tw. OR ethnograph$.tw. OR exp decision making OR exp Illness Behavior OR exp Knowledge/ or Health Knowledge, Attitudes, Practice OR exp Medication Adherence/ or exp Patient Medication Knowledge OR exp Compliance/ or exp Patient Compliance} AND { exp Antirheumatic Agents/tu [Therapeutic Use] OR DMARD$.tw. OR medicine$.tw.}
PsycINFO (1806 to 12/01/2016)	{exp Arthritis, Rheumatoid OR Arthritis, Psoriatic.tw. OR ankylosing spondylitis.tw. OR Reactive arthritis.tw. OR [exp Arthritis AND (exp Ulcerative Colitis OR Inflammatory bowel disease.tw. OR Crohn$ Disease.tw.)] OR Inflammatory arthritis.tw. OR Spondyl#arthr$.tw.} AND {exp qualitative research OR qualitative.tw. OR interview$.tw. OR focus group$.tw. OR [thematic$ or theme$].tw. OR grounded theory.tw. OR phenomenol$.tw. OR content analysis.tw. OR ethnograph$.tw. OR exp decision making OR exp Illness Behavior OR exp Compliance/ or exp Patient Compliance}
CINAHL (to 12/01/2016)	(MM "Arthritis, Rheumatoid+") OR (MM "Arthritis, Psoriatic") OR (MM "Spondylarthritis+") OR (MM "Reiter Disease") OR (MM "Spondylarthropathies+") OR (MM "Arthritis+") Limiters - Clinical Queries: Qualitative - Best Balance

D.2 Characteristics of included studies

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
Ahlmem (2005)(283)	Sweden	25	Median 55 (range 31-77)	9:16	Median 14 (range 3-44)	25		NS	NS	Qualitative study	Focus groups	Unclear	Perspectives on treatment outcomes
Arkell (2013)(409)	UK	10	Median 64 (range 47-85)	5:5	Median 18 (range 5-26)	10			10	Colaizzi's procedural steps	Focus groups	Content analysis combined with Colaizzi's procedural steps	RA patients experiences of starting anti-TNF therapy
Backman (2007)(410)	Canada	9	Range 24 - 53	0:9	Range 3 - 40	6	3	NS	NS	Grounded theory	Interviews	Grounded theory	Experience of mothers
Bath (1999)(411)	UK	15	Mean 59 (range 28-75)	6:9	Mean 5.4 (range 1 mth- 17 yrs)	15		NS	NS	Qualitative study	Interviews	Grounded theory	Psychological needs of patients with RA
Boonen (2009)(412)	The Netherlands	19	Mean 54 (SD 11.5, range 31-69)	14:5	Mean 18.7 (SD 10, range 4-36)		19		12	Qualitative study	Focus groups	Meaning condensation	Functioning for patients with AS
Chilton (2008)(413) (interview)	UK	7	Median 52 (Range 37-80)	2:5	NS	7			7	Qualitative study	Semi-structured interviews	Thematic analysis	Decision making regarding anti-TNF therapy
Chilton (2008)(413) (questionnaire)	UK	24	NS	NS	NS	24		NS	NS	NA	Survey with open-text response	NS	Decision making regarding anti-TNF therapy
Cinar (2014)(414)	Turkey	101	Mean 36.6	95:6	Mean 12.4 (SD 6.42)		101		101	NS	Survey with open-text response	NS	Perspective of anti TNF medications

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
			(SD 7.45)										
Donovan (1992)(415)	UK	39	NS	NS	NS	NS	NS	NS	NS	Anthropology interpretative sociology	Semi-structured interviews, and observations of clinical consultations	Thematic analysis	Reactions to advice and medication prescribed by rheumatologists
Edwards (2004)(416)	UK	7	Mean 52 (SD 7.8, range 43-61)	1:6	Mean 6.9 (SD 4.9, range 3-16)	7			7	Phenomenology	Semi-structured interviews	Colaizzi's phenomenological data analysis	Experiences on anti-TNF therapy
Flurey (2014)(417)	UK	30	Mean 54.6 (SD 11.8)	8:22	Mean 15.2 (SD 11.3)	30		16	13	Q-methodology†	Participants ranked pre-determined statements, with some open ended comments	Q-methodology†	Experiences of daily life on current treatment and help-seeking behaviour for RA flares
Flurey (2014)(418)	UK	15	Mean 51.1 (SD 11.8)	3:12	Mean 14.8 (SD 8.6)	15		13	5	Qualitative study	Semi-structured interviews	Thematic analysis	Experiences and self-management with modern medications
Fraenkel (2015)(282)	USA	88	Mean 55 (SD 13, range 20-83)	23:65	Mean 12	88			18	Grounded theory	Conjoint analysis task with 'think aloud process'	Grounded theory	Patients approach to escalating treatment
Garcia Popa-Liseanu (2005)(419)	USA	18	Mean 49	2:16	Mean 5.7 (3 months – 14 yrs)	18		NS	NS	Health Beliefs Model	Focus groups	Grounded theory analysis	Determinants of treatment/ appointment adherence

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
Goodacre (2004)(280)	UK	29	Mean 54 (range 28 -71)	7:22	Mean 4.9 (range 0.5 – 16)	29		NS	NS	Grounded theory	In-depth interviews, activity diaries and focus groups	Grounded theory analysis	Beliefs about DMARDs
Gronning (2011)(420)	Norway	24	Range 18-80	4:20	Range 2-23	18	6	NS	NS	Qualitative study	Semi-structured interviews	Systematic text condensation – modified Giorgi's method	Coping with chronic inflammatory arthritis
Hart (2015)(421)	UK	10	NS	NS	NS	1	9	NS	10	Qualitative study	Interviews, recorded patient/professional interactions and focus groups	Open and focused coding mapping and memoing techniques	The influence of trusted others on treatment decisions made by young people
Headland (2006)(422)	UK	NS	NS	NS	NS	NS	NS	NS	NS	Qualitative study	Written accounts on a website, audio recordings	Thematic analysis	Patient's experiences of living with arthritis
Hirsh (2009)(423)	Australia	27	Mean 52 (rang 23-77)	5:22	Mean 13 (range 1-36)	27		23 MTX, 19, SSZ	4	Qualitative study	Face-to-face interviews, focus groups and self-administered questionnaires	Thematic analysis	Patient assessment of medication leaflets
Hofmann (2015) (424)	UK	17	Median 57 (range 34-71)	4:13	Median 11 (range 3-44)	17			8	Qualitative study/feasibility study	Focus groups and questionnaires	Thematic content analysis	Expectations of new RA treatment
Kett (2010)(425)	UK	21	Median 56 (range 23-72)	7:14	Median 4 (range 0.5-12)	21		NS	NS	Grounded theory	Semi-structured face-to-face interviews	Grounded theory	Self-management in flares of RA.
Kristiansen (2012)(426)	Denmark	11	Mean 62	4:7	Median 3.3	11		NS	NS	Phenomenology	Focus groups	Qualitative content analysis	Every-day life, support needs and experience

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
			(range 48-81)		(range 2-4)								with health care providers in early remission
Kumar (2011)(295)	UK	18	NS	NS	NS	18		NS	NS	Qualitative study	Focus groups	Thematic analysis	Factors that influence beliefs about medication
Larsson (2009)(427)	Sweden	20	Mean 49 (range 21-82)	10:10	Mean 14 (range 0.5-53)	NS	NS		20	Phenomenography	Face-to-face interviews	As described by Dahlgren and Fallsberg, 1991; Sjöström and Dahlgren, 2002.	Patients' conception of their dependence on a nurse for intravenous anti-TNF therapy
Lempp (2006)(428)	UK	26	Mean 56	4:22	Mean 10 (range 1-29)	26		NS	NS	Qualitative study	Semi-structured face-to-face interviews	Content analysis	Impact of RA on patients' identity
Lempp (2012)(429)	UK	18	Mean 49 (range 21-70)	4:14	NS	18		18	5	Qualitative study	Face-to-face or telephone interviews	Content analysis	Expectations, concerns and the impact of combination therapy
Li (2014)(430)	Canada	11	Mean 53.9 (SD 11.4, range 31-67)	3:8	Median 0.5 (IQR‡ 0.05-3.5)	11		11		Mixed-methods	Semi-structured telephone interviews	Thematic analysis	Experiences with a web-based methotrexate decision aid
Lindbald (2002)(431)	Sweden	22	Mean 60 (range 30-82)	7:15	Mean 14 (range 1-40)	22			5	Phenomenography	Semi-structured face-to-face interviews	Phenomenology	Priority setting in anti-TNF therapy

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
Linden (2010)(432)	Sweden	15	Mean 48.8 (range 25-70)	4:11	NS	15			15	Phenomenology	Unstructured in-depth face-to-face interviews	Malterud's modified model from Giorgi's phenomenological analysis	Experiences of everyday life with anti-TNF therapy
Lorish (1990)(433)	USA	140	Median 48 (SD 26)	59:81	Median 10.5 (SD 6.8)	140		NS	NS	Ajzen and Fishbein's theory of reasoned action	Interview survey with open and closed questions	Holsti's content categorisation	Medication taking behaviour and beliefs about arthritis medications
Markusse (2014)(434)	The Netherlands	20	Median 71 (IQR‡ 52-74)	7:13	Median 15 (IQR‡ 4-25)	20		NS	NS	Qualitative study	Structured interview	Phenomenological analysis	Perspectives on therapy tapering and discontinuation
Marshall (2004)(435)	UK	19	Median 52 (Range 32-69)	1:18	Median 11 (Range 3-31)	19			19	Qualitative study	Focus group	Thematic analysis	Perspectives of anti-TNF therapy
McArthur (2015)(436)	UK	27	Range 21-78	11:16	Range 2-30	19	8		27	Interpretive phenomenological analysis and within case and across-case analytical framework	In depth interview	Interpretive phenomenological analysis and within case and across-case analysis	Occupational gain in patients receiving anti-TNF therapy
Meade (2013)(437)	Australia	14	Mean 37 (Range 25-51)	0:14	Mean 15 (Range 11 months-32 years)	14		NS	NS	Qualitative study	Written accounts	Thematic analysis	Motherhood decisions in RA
Meyfroidt (2015)(438)	Belgium	26	Median 55	8:18	NS	40		40		Phenomenology	Semi-structured face-to-face	Qualitative Analysis Guide of	Experience with intensive combination

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
											interviews and focus groups	Leuvan (QUAGOL)	treatment strategies with glucocorticoids in early RA
Minnock (2016)(439)	Ireland	10	Mean 59	4:6	Range 6-36	10			10	Qualitative study	Semi-structured face-to-face interviews	Content analysis	Perceptions of fatigue in patients with RA on anti-TNF therapy
Nota (2015)(149)	The Netherlands	32	Mean 54	6:26	Mean 7.8	28	4	16	16	Qualitative study	In depth, semi-structured face-to-face interview	Thematic analysis	Patients' decision making process when initiating DMARDs
O'Hare (2000)(440)	UK	18	NS	NS	NS	18		NS	NS	Nominal group methodology	Semi-structured individual interviews and focus groups	Thematic analysis	Pharmaceutical care issues in RA
Pasma (2015)(153)	The Netherlands	33	Median 51	4:29	Range <1 - >5 years	23	10	NS	NS	Qualitative study	Face-to-face individual interviews and focus groups	Thematic analysis	Adherence in initiation of DMARDs in patients with inflammatory arthritis
Rose (2006)(183)	UK	5	Range 38-61	0:5	Range 4-15	5		NS	NS	Phenomenology, naturalistic research	Unstructured face-to-face interviews	Thematic analysis	Motivations for use of complementary therapies in RA
Salt (2011)(154)	USA	30	Range 29-86	0:30	Range 2-49	30		NS	NS	Grounded theory	Semi-structured interviews	Constant comparative, grounded theory analysis	Decision making when participating in evidence-based

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
													treatment regimens in RA
Salt (2012)(150)	USA	15	Mean 57	5:10	Mean 12	15		NS	NS	Qualitative study	Semi-structured face-to-face individual interviews and quasi-focus groups	Constant comparative, grounded theory analysis	Perception of quality of patient-healthcare provider communication
Sanderson (2009)(284)	UK	17	Range 35-74	4:13	Range 4-40	17			17	Grounded theory	Face-to-face, semi-structured informal interviews	Grounded theory	Explore RA patients' experience of access to and switching of anti-TNF therapy
Sanderson (2010)(441)	UK	23	Range 27-79	5:18	Range 3-40	23		6	17	Grounded theory	In-depth interviews	Grounded theory using the 'Framework' analytical tool	Understand RA patient priorities in treatment outcomes for pharmacologic interventions
Sanderson (2010)(442)	UK	23	Range 27-79	5:18	Range 3-40	23		6	17	Grounded theory	In-depth interviews	Grounded theory using the 'Framework' analytical tool	Explore the meaning of 'feeling well' for people with RA
Sanderson (2011)(286)	UK	23	Range 27-79	5:18	Range 3-40	23		6	17	Qualitative study	Interviews	Grounded theory using the 'Framework' analytical tool	Understand concepts of biographical disruption and normalisation in RA
Sanderson (2012)(443)	UK	26	Range 29-79	5:21	Range 2-36	26			13	Qualitative study	Nominal group technique with	Grounded theory	Understand patient priority treatment

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
											face-to-face group discussions		outcomes in RA
Sandhu (2013)(444)	Canada	18	Range 18-70	2:16	NS	18		NS	NS	Qualitative study	Face-to-face interviews and diary entries	Constant comparative thematic analysis	Peer support mentoring in early inflammatory arthritis
Schildmann (2008)(445)	Germany	22	Mean 57	3:19	NS	22		NS	NS	Qualitative study	Semi-structured face-to-face interviews	Grounded theory	Understand perception of participation in treatment decision making in RA patients
Stamm (2010)(285)	Austria	15	Mean 52	4:11	Range 2-29	15		NS	NS	Narrative biographical study	Narrative biographic interviews	Thematic analysis	How contextual factors affect lives of RA patients
Stockdale (2009)(446)	UK	8	Range 34-56	8:0	Range 5-37		10		8	Phenomenology	Semi-structured face-to-face interviews	Thematic analysis	Impact of anti-TNF treatments on quality of life in AS
Stockdale (2014)(447)	UK	20	Range 26-74	18:2	Range 3-36		20		20	Phenomenology	Semi-structured face-to-face interviews	Thematic network analysis	Effects of anti-TNF treatment on exercise behaviour in AS
Townsend (2013)(281)	Canada	38	Range 30-70s	1:37	<1 - 12 months	38		NS	NS	Qualitative study	Face-to-face semi-structured interviews, follow up phone and email interviews	Iterative, thematic, constant comparative analysis.	Experiences of medication use in early RA.
Van der elst (2015)(448)	Belgium	26	Median 55	8:18	NS	26		NS	NS	Qualitative study	Face to face semi-structured	Qualitative Analysis Guide of	Patient preferred

Study ID	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis		DMARD		Conceptual methodological framework	Data collection	Analysis	Main topic
						RA	SpA*	cDMARD	bDMARD				
											interviews and focus groups	Leuven (QUAGOL) with constant comparative analysis	health and treatment outcomes in early RA
Van Tuyl(2008)(151)	Netherlands	12	NS	3:9	Mean 22	11	1	12		Qualitative study	Focus groups and semi-structured in-depth telephone interviews	Interpretative phenomenological analysis	Views on combination therapy in early RA
Van Tuyl (2015)(148)	Netherlands Austria, UK	47	Mean 56	16:31	Mean 8	47		NS	NS	Qualitative study	Focus groups	Inductive thematic analysis	Patient perspective on remission in RA
Zhang (2002)(449)	Canada	NS	NS	NS	NS	NS		NS	NS	Grounded theory	In depth, open-ended face-to-face interviews	Grounded theory	Arthritis management amongst Chinese immigrants

US, United States' UK, United Kingdom; NS, not stated; RA, Rheumatoid arthritis; SpA, Spondyloarthritis; AS, Ankylosing spondylitis; IBD, Inflammatory bowel disease related arthritis; cDMARD, conventional disease modifying anti-rheumatic drug; bDMARD, biologic DMARD.
* Included all patients with psoriatic arthritis, ankylosing spondylitis and inflammatory bowel disease related arthritis
† Q methodology uses qualitative and quantitative methods to sort people according to subjective experience, ‡ Interquartile range

D.3 Comprehensiveness of reporting of included studies

Item	Studies reporting each item	No.
Personal Characteristics		
Interviewer / facilitator identified	(148-151, 153, 280, 281, 284, 286, 295, 409-413, 416-418, 420, 421, 423, 425-427, 429, 431, 432, 435, 438, 439, 442, 443, 445-448)	36
Occupation of the interview of facilitator	(282, 410-413, 416, 418, 424, 425, 432, 435, 439)	16
Experience or training in qualitative research	(148, 281)	2
Relationship with participants		
Relationship established prior to study commencement	(148, 151, 153, 286, 411, 413, 418, 420, 421, 425, 432, 434, 435, 438, 439)	15
Participant Selection		
Selection strategy (e.g. snowball, purposive, convenience, comprehensive)	(148-150, 183, 280-282, 284-286, 409-413, 415-418, 420, 421, 423-429, 431-436, 438-443, 445-449)	45
Method of approach or recruitment	(148-151, 153, 154, 183, 280-284, 286, 295, 409, 411, 413, 416, 417, 419-421, 423, 427, 431, 432, 434-436, 438, 439, 442-449)	39
Sample size	(148-151, 153, 154, 183, 280-286, 295, 409-413, 415-421, 423-436, 438-449)	53
Number and/or reasons for non-participation	(148, 149, 151, 153, 183, 281, 295, 409, 413, 417-420, 423-426, 428-435, 438, 439, 443-446, 448, 449)	33
Setting		
Venue of data collection	(149, 150, 153, 280, 281, 286, 295, 409, 410, 415-418, 420, 424-429, 431, 432, 438, 439, 445-449)	29
Presence of non-participants (e.g. clinical staff)	(281, 426)	2
Description of the sample	(148-151, 153, 154, 280-286, 295, 409-413, 416-421, 423-436, 438, 439, 441, 443-449)	49
Data Collection		
Questions, prompts or topic guide	(148-151, 153, 154, 281-284, 286, 409, 412, 415-420, 423-432, 434-436, 438, 439, 441, 442, 445-449)	41
Repeat interviews / observations	(150, 280, 285, 415, 421, 423, 424, 438-440, 444, 448)	12
Audio / visual recording	(148-151, 153, 154, 183, 280-286, 295, 409, 410, 412, 413, 415, 416, 418-421, 423-428, 430-436, 438-449)	50
Field notes	(153, 281, 285, 409, 410, 419, 421, 423, 426, 436, 438, 444, 448, 449)	14
Duration of data collection	(148-150, 153, 154, 280-282, 285, 286, 295, 409, 410, 413, 416-421, 423-429, 432, 436, 438, 439, 442-444, 446-449)	39
Translation and interpretation	(148, 149, 295, 419, 420, 425, 434, 449)	8
Protocol for data preparation and transcription	(148-150, 153, 154, 281-286, 295, 409-413, 415-421, 424-427, 429-436, 438-443, 445-449)	47
Data (or theoretical) saturation	(148-151, 183, 284, 295, 410, 412, 416, 418, 423, 425, 428-430, 432, 434, 438, 439, 441, 442, 445, 449)	24
Data Analysis		

Researcher/expert triangulation (multiple researchers involved in coding and analysis)	(148, 149, 151, 153, 154, 183, 281-286, 295, 409-412, 416, 418-421, 423-425, 427-429, 431-436, 438, 439, 441-443, 445-449)	44
Translation (language in which analysis was done)	(148, 149, 295, 420, 434, 449)	6
Derivation of themes or findings (e.g. inductive, constant comparison)	(148-151, 153, 154, 183, 280-286, 409-412, 416-418, 420, 421, 424-427, 429-436, 438, 439, 441-449)	46
Use of software (e.g. NVivo)	(149, 151, 153, 183, 280, 281, 284, 286, 417-420, 424, 426, 428, 429, 431, 438, 439, 441-443, 448)	23
Participant feedback on findings	(148, 283, 285, 286, 409, 410, 416-418, 421, 425, 432, 436, 438, 439, 441-443, 447-449)	21
Reporting		
Participant quotations or raw data provided (e.g. picture, diary entries)	(148-151, 153, 154, 183, 280-286, 295, 409-411, 413, 415-421, 423-432, 434-436, 438, 439, 441-447, 449)	49
Range and depth of insight into participant perspectives of DMARDs (thick description)	(149-151, 153, 154, 280-284, 286, 295, 409, 413, 416, 419, 421, 427, 429, 430, 432, 434-436, 438, 441-443, 445-449)	33

N.B. COREQ is designed to evaluate interviews and focus groups. Open ended surveys and written accounts are not presented in this table.

D.4 Illustrative quotations

Theme	Quotations	Contributing studies
Intensifying disease identity		
Severity of sudden pharmacotherapy	No. Because then you feel like you really are sick, as it were. That you actually have something. And I didn't want to start, and I … I keep repeating to myself: 'I don't have arthritis, I don't have arthritis. I'm too young.' (153) I was also thinking, if this is the drug they start with [methotrexate], what will be the side effects of the next drug? (149)	(149, 153, 295, 414, 415, 430)
Signifying deteriorating health	The more medication you take. . .the more ill you feel. Maybe even more than you really are. (149) When I look at my medicines in the morning I wish they would disappear from me. I want my list to be reduced. Why, why, I am taking so many medicines. If these are working then why my list is so big? (295)	(149, 151, 281, 415, 420, 426, 432, 434, 441, 442, 448)
Daunting lifelong therapy	When I try to stop them I cannot get on with things. It's like your body cannot do without them. I don't like that. (295) And in one sense that's quite upsetting…to know that there's no cure for your, for rheumatoid arthritis, if you think that you're going to be on drugs for the rest of your life. (286)	(148, 149, 154, 280, 286, 295, 411, 414, 415, 426-429, 432, 434, 448)
Distressing uncertainties and consequences		
Poisoning the body	... the issue I decided to take the drug on was quality of life,' cause all these drugs shorten your life end of story, so the question is do you want to be old and crippled or do you want to die younger. (280) I was worried when I learned that the drugs increased the risk of tuberculosis and cancer (414) You know sometimes I sit there and think – I take so many and all these chemicals in our body, I will blow up like a toxic bomb one day. What are they doing inside you? (295)	(148, 149, 151, 153, 154, 183, 280-282, 284, 295, 409, 413-415, 419, 420, 424, 425, 429, 430, 432, 433, 435, 449)
Doubting efficacy	This is actually the hard part ... if you have to start with a new drug that takes three months before you know whether it helps or not. (283) It's meant to stop things getting worse isn't it. I don't suppose it's meant to make things better and I don't feel like it does do, I mean it might be, I might be worse without, I don't know now whether it is working or it's just that I'm not getting worse. (280)	(148, 149, 280-283, 286, 295, 411, 414, 430)
Conflicting and confusing advice	The rheumatology nurse, the substitute rheumatologist, and my own rheumatologist all gave contradictory information. That wasn't easy. (149) My orthopaedist said: ''arthritis patients actually have 2 diseases, that is arthritis and methotrexate''; I have always remembered that. (151)	(149, 151, 154, 280, 282, 283, 411, 414, 423, 441)
Prognostic uncertainty with changing	You're so frightened when you come off them because you feel so well and then you know when you come off that within a few weeks ... you'll be back to square one and you won't be able to do anything and it is it's frightening. (280)	(148, 149, 280, 284, 286, 295, 409,

Theme	Quotations	Contributing studies
treatment regimens		416, 424, 429, 434, 435, 446)
	Powerful social influences	
Swayed by others' experiences	My grandmother also had RA, but her fingers got deformed, so I thought the faster I could start treatment, the better. (448) Methotrexate . . . my mother took it and she started having some hemorrhaging of the stomach and they took her off right away and it quit but it never really, it seemed like it kept coming back with the bleeding, internal bleeding from somewhere. Now whether the methotrexate started it. I don't know but she died with that. Dr. wanted me to take methotrexate but I was afraid of it because of the experience that my mother had. (150)	(149-151, 153, 154, 414, 421, 435, 443, 448)
Partnering with physicians	And she [the rheumatologist] knew how frightened I was, but she just accepted it. And that was really important to me. She didn't say like: 'Yeah, well, what nonsense. If you don't take this then that's your lookout, your loss.' No, she accepted it and dealt with it. And that's what persuaded me quite quickly, from that point on really, to just start taking the pills. (153) I feel I have a good doctor and I feel that he was doing what was best for me personally. If it wasn't for the trust I have in my doctor, then no, I wouldn't have took it [the medication]. (154)	(149-151, 153, 154, 183, 281-283, 409, 413, 415, 417, 430, 449)
Maintaining roles	For me, it is important that daily activities function, that I can look after my home, my children and manage to work. (283) So, I don't have any other choice. I'll put it like that, other than that to take my medicine; other than go to the doctor's when I am supposed to. I just love my grandchildren and I want to be there for them just in case they need Granny. (154)	(149, 151, 154, 280, 282, 283, 410, 414, 416, 417, 428, 429, 432, 435, 441, 443, 448)
Confidence in comprehensive and ongoing care	The nurses know their job and they interpret my tests, thus I feel secure coming. If there is something wrong with my values, it will be taken care of immediately (427) I felt that the backup was absolutely super, you knew you were not on your own and that you knew you could phone for anything, which was super. (435)	(149, 151, 154, 284, 409, 414, 427, 435, 446)
Valuing peer support	I enjoyed being all together, just talking amongst ourselves while we were having the treatment. We all have the same illness. (416)	(283, 413, 416, 421, 427, 444)
	Privilege and right of access to bioogics	
Expensive medications must be better	My family were absolutely delighted because there was also all this going on in the press about how it's really expensive. When you read stories in the press […] we only ever see the good ones. (284) You sit there and try and get every single drop out of, and then you make sure that the syringe, you really press it and try to squeeze the bit down to make sure you've got every drop. But it does I mean it is precious because it's expensive. (284)	(149, 284, 435)
Right to receive a biologic	I was angry at the time because I knew that this treatment was available but I wasn't eligible for it. I was frustrated and wrote to the Department of Health and my MP. I thought: There's a treatment that could potentially really help and could stop further joint damage and allow me to keep working, but I can't get it. (284) I think of all the people in the very early stage and I think to myself, surely they'll benefit more before it gets to the point where you knuckles and joints, you know and I feel guilty that I'm on it and yet there's other people who perhaps could end up with a much more viable life not getting it. (435)	(149, 284, 422, 431, 435, 441)

Theme	Quotations	Contributing studies
Fearing dispossession	This is a thing that worries me you know, you know that you might reach the stage where you say right, you've got to come off it now.' (435) I don't know whether feeling rotten was due to arthritis or waiting for the decision." (284)	(284, 409, 435)
	Maintaining control	
Complete ownership of decision	They want to write a script, and then I am like, no I don't think so. You know, give me something. Show me statistics. Show me where this many people started feeling good. Because medicine changes all the time and half the time they do not tell you the side effects so you know that if the joints hurt you or whatever, you can get and take aspirins but if you are spending money on a drug that is not going to do anything and all but kill you, you know, it is another no brainer. (282) Let me have the choice that I want to be treated aggressively... Don't take that away from me. (150)	(149, 150, 154, 282, 283, 413, 427)
Taking extreme risks	And he [the physician] said: "Please take cortisone, and no MTX any more." I said: "I have never felt so well. Over the past 10 years, I have not been this well, and now you want to take my elixir of life [the MTX] away?" He said: "No alternative, Maria, cortisone!" '. . . I still took it, but I had my regular blood tests done of course (285) I think I'd kill for it now. If it has this sort of effect on you. I don't like to say anything to the nurse in case she says this is your last. (284)	(149, 280, 282, 284, 285, 409, 414, 446)
Minimising lifestyle intrusion	I like drinking a glass of red wine at night, but you can't have that for 3 days, can you? Well, I took just a small glass. But on the day before, the day of the treatment, and the day after, you absolutely shouldn't. You really have to consider that. I'd like to have known before. (149) Taking methotrexate [which is administered once a week] makes me very nauseous. Then we adjusted the scheme and considered the best time for taking it. I deliberately did not choose to take it before the weekend starts, because suppose you keep being troubled by the side effects?. . . I would have liked assistance with that sooner. (149)	(149, 151, 154, 183, 281-284, 410, 413, 424, 427-429, 435, 441, 443, 446)
	Negotiating treatment expectations	
Miraculous recovery	I didn't know that the colours were so bright, the music so beautiful, I have lived inside a bubble of glass. (283) I woke up at 3 o'clock in the night and was able to lift the quilt and turn around in bed without any trouble. I became so happy that I went down to the kitchen and had some tea and sat for two hours solving a crossword at the kitchen table, and thought: is it true? Is it true? (432)	(151, 283, 284, 286, 409, 414, 416, 429, 432, 435, 441, 446, 447)
Mediocre benefit	I am a bit disappointed now, the pain is sort of coming back more strongly now; and I had my jab [steroid injection] today. . .I find it difficult to walk, and my ankles get weak and in my fingers I don't have the strength. (429) The combination therapy has helped, but not as much as I hoped it would. I think I was hoping for a miraculous change [pain, mobility] and it did not happen (429)	(148, 284, 286, 416, 422, 429, 432, 435)
Reaching the end of the line	I think when you've got to a stage where you've tried everything, you'll literally go for anything that's available. Whatever relief you can get for it. (435) I mean I was, you know, really hoping against hope that it would work, having been on, sort of, most of the other conventional drugs and thinking well 'If this doesn't work, then what?'… (286)	(149, 154, 280, 282, 284, 286, 414, 429, 435)

Appendix E: Supporting data for Chapter 5

E.1 Search strategy

Database	Search terms
Ovid MEDLINE (1946 to 30/08/2019)	[{exp juvenile rheumatoid arthritis OR Juvenile rheumatoid arthritis.mp. OR chronic arthritis.mp. OR oligoarthritis.mp. OR juvenile idiopathic arthritis.mp. OR systemic onset arthritis.mp. OR polyarticular arthritis.mp. OR exp polyarthritis/ OR polyarthritis.mp. OR exp psoriatic arthritis/ OR psoriatic arthritis.mp. OR juvenile arthritis.mp. OR rheumatoid arthritis.mp. OR exp ankylosing spondylitis/ OR ankylosing spondylitis.mp. OR exp juvenile dermatomyositis/ OR exp dermatomyositis/ or Dermatomyositis.mp. OR Lupus Erythematosus, Systemic.mp. or exp systemic lupus erythematosus/ OR lupus.mp. OR Scleroderma, Systemic.mp. or exp systemic sclerosis/ OR exp scleroderma/ OR exp localized scleroderma/ OR systemic sclerosis.mp. OR limited scleroderma.mp. OR diffuse scleroderma.mp. OR exp systemic vasculitis/ OR vasculitis.mp. OR Mixed Connective Tissue Disease.mp. or exp mixed connective tissue disease/ OR *musculoskeletal disease/ OR *rheumatic disease/ OR systemic juvenile idiopathic arthritis.mp. OR undifferentiated juvenile arthritis.mp. OR exp spondylarthritis/ OR spondyl*arth*.mp} AND {exp transition to adult care/ OR Adolescent Health Services.mp. OR exp adaptive behavior/ OR exp social support/ OR exp patient preference/ OR exp patient participation/ OR exp qualitative research OR exp interview/. Personal Narratives.mp. OR Focus Groups.mp.} AND {limit to adolescent <13 to 17 years>.}]
Embase (1974 to 30/08/2019)	[{exp juvenile rheumatoid arthritis OR Juvenile rheumatoid arthritis.mp. OR chronic arthritis.mp. OR oligoarthritis.mp. OR juvenile idiopathic arthritis.mp. OR systemic onset arthritis.mp. OR polyarticular arthritis.mp. OR exp polyarthritis/ OR polyarthritis.mp. OR exp psoriatic arthritis/ OR psoriatic arthritis.mp. OR juvenile arthritis.mp. OR rheumatoid arthritis.mp. OR exp ankylosing spondylitis/ OR ankylosing spondylitis.mp. OR exp juvenile dermatomyositis/ OR exp dermatomyositis/ or Dermatomyositis.mp. OR Lupus Erythematosus, Systemic.mp. or exp systemic lupus erythematosus/ OR lupus.mp. OR Scleroderma, Systemic.mp. or exp systemic sclerosis/ OR exp scleroderma/ OR exp localized scleroderma/ OR systemic sclerosis.mp. OR limited scleroderma.mp. OR diffuse scleroderma.mp. OR exp systemic vasculitis/ OR vasculitis.mp. OR Mixed Connective Tissue Disease.mp. or exp mixed connective tissue disease/ OR *musculoskeletal disease/ OR *rheumatic disease/ OR systemic juvenile idiopathic arthritis.mp. OR undifferentiated juvenile arthritis.mp. OR exp spondylarthritis/ OR spondyl*arth*.mp} AND {exp transition to adult care/ OR Adolescent Health Services.mp. OR exp adaptive behavior/ OR exp social support/ OR exp patient preference/ OR exp patient participation/ OR exp qualitative research OR exp interview/. Personal Narratives.mp. OR Focus Groups.mp.} AND {limit to adolescent <13 to 17 years>.}]
PsycINFO (1806 to 30/08/2019)	[{exp Arthritis/ OR Juvenile rheumatoid arthritis.mp. OR chronic arthritis.mp. OR oligoarthritis.mp. OR juvenile idiopathic arthritis.mp. OR polyarticular arthritis.mp. OR polyarthritis.mp. OR psoriatic arthritis.mp. OR juvenile arthritis.mp. OR rheumatoid arthritis.mp. OR OR ankylosing spondylitis.mp. OR exp myopathy/ OR Dermatomyositis.mp. OR exp Lupus/ OR Scleroderma.mp. or systemic sclerosis.mp. OR limited scleroderma.mp. OR diffuse scleroderma.mp. OR systemic vasculitis.mp. OR vasculitis.mp. OR Mixed Connective Tissue Disease.mp. or Rheumatic Diseases OR systemic juvenile idiopathic arthritis.mp. OR spondyl*arth*.mp} AND {exp Adolescent Attitudes/ OR exp “Continuum of Care”/ OR transition$.mp. OR Adolescent Health Services.mp. OR exp Health Care Delivery/ OR exp Client Attitudes/ OR exp Preferences/ OR exp Client Participation/ OR exp qualitative research OR exp interviews/. OR exp Narratives/OR exp Life Experiences/ OR exp Storytelling/ OR exp Group Discussion/ OR Focus Groups.mp. OR exp Content Analysis OR exp Ethnography/} AND {limit to adolescence or young adulthood}]
CINAHL (to 30/08/2019)	[{"Juvenile arthritis” OR MH “Arthritis, Juvenile Rheumatoid” OR “Chronic arthritis” OR “oligoarthritis” OR “juvenile idiopathic arthritis” OR “systemic onset arthritis” OR “polyarticular arthritis” OR “polyarthritis” OR MH "Arthritis, Psoriatic" OR MH “Arthritis, Rheumatoid” OR MH “Spondylitis, Ankylosing” OR MH “Dermatomyositis” OR MH “Lupus Erythematosus, Systemic” OR “lupus” OR MH “Scleroderma, Systemic” OR “scleroderma” OR “systemic sclerosis” OR MH “Vasculitis” OR “mixed connective tissue disease” OR MH “Rheumatic Diseases” OR “spondyloarthritis” OR “spondyloarthropathies”} AND {“Transition to Adult Care OR MH “Transitional Care” OR MH “Adolescent Health Services” OR “Health Services Research” OR MH “Self-Care” OR MH “Patient Preference” OR MH “Consumer Participation” OR “patient participation” OR MH “Qualitative Studies” OR “qualitative research” OR MH “Interviews” OR “interviews” OR “Personal narratives” OR MH “Narratives” OR MH “Focus Groups” OR MH “Content Analysis” OR MH “Ethnographic Research” OR “ethnography”} AND Limiters – Age Groups: Adolescent: 13-18 years]

E.2 Characteristics of included studies

	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis					Conceptual methodological framework	Data collection	Analysis	Main topic
						JIA	SLE	DM	MCTD	Other				
Applebaum (2013)(319)	US	20	NS	NS	NS	NS*	NS*	NS*		NS*	NS	Focus groups	NS	Transition readiness and preferences for technology in transition programs
Cai (2019)(336)	UK	87	Median 19 (range 12-24)	21:66	Median 9	64	15	14			NS	Focus groups, semi-structured individual interviews and cognitive interviews	Content analysis	Developing a benchmarking toolkit to enable comparative evaluation of young people rheumatology services
Cruikshank (2016)(333)	UK	8	Median 15 (range 12-17)	NS	NS	8					NS	Semi-structured focus groups and individual interviews	NS	Impact of clinical networks on provision of transitional care
Dickinson (2013)(318)	New Zealand	8	Range 16-21	4:4	NS	8						Semi-structured focus group		Experiences of young people transferring from paediatric to adult care
Felsenstein (2015)(303)	US	41	Mean 24 (SD 4.2)	4:37	Mean 11.5 (SD 3.8)		41				NS	Structured telephone interviews and a questionnaire with open and closed questions	NS	Experience with the transition and referral process

	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis					Conceptual methodological framework	Data collection	Analysis	Main topic
						JIA	SLE	DM	MCTD	Other				
Grande (2019)(339)	Sweden	15	Mean 12.3 (range 5-15	8:7	Mean 3.8 (range 1-14)	15					NS	Semi-structured interviews	Content analysis	How mobile or wireless technology to support health influences self-management and communication
Hanghoj (2018)(337)	Denmark	14	Range 12-20	3:11	NS	14					NS	Focus groups and telephone interviews	Thematic analysis	The advantages and disadvantages of participating in a transition intervention and reasons for no-shows
Harry (2019)(340)	US	22	Mean 18.3 (range 12-24)	1:21	Mean 3.6		22				NS	Focus groups		Factors influencing self-management and quality of life and barriers and facilitators of treatment adherence
Hilderson (2013)(160)	Belgium	11	Range 18-30	3:8	NS	11					NS	Semi-structured, in-depth interviews	Content analysis	Experiences of transfer into adult care
Hilderson (2016)(94)	Belgium	12	Mean 17 (range 16-18)	1:11	NS	12					NS	In-depth interviews with open-ended questions	Content analysis	Experiences with participation in the transition programme

	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis					Conceptual methodological framework	Data collection	Analysis	Main topic
						JIA	SLE	DM	MCTD	Other				
Howland (2015)(156)	UK	6	Range 16-18	NS	NS	6					NS	Individual interviews, repeat interviews with five patients with parent/carer present	Interpretive phenomenological analysis	Needs when transitioning to adult care
Knight (2016)(322)	US	16	Mean 17 (SD 3.6, range 11-22)	3:13	Mean 3.8 (SD 1.8)		11		5		NS	Open-ended semi-structured interview	Constant comparative method	The psychosocial and physical impact of living with SLE/MCTD
Knudsen (2018)(338)	Denmark	3	Mean 20.3 (range 19-21)	1:2	Range 10-21	3					NS	Semi-structured interviews		Experiences and needs during transition
Östlie (2007)(158)	Norway	13	Range 15-27	1:12	Range 5-24	13					NS	Focus groups	Transcript based analysis	Experience of patients and health professionals in transition
O'Sullivan (2018)(343)	Republic of Ireland	16	Mean 14.2 (range 12-18)	6:10	Mean 3.6 (SD 3.3, range 0.6-13.8)	16						Focus groups and interviews		Self-management needs and the acceptability of an adapted version of a self-management programme

	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis					Conceptual methodological framework	Data collection	Analysis	Main topic
						JIA	SLE	DM	MCTD	Other				
Reiss (2005)(341)	US	NS	NS	NS	NS	NS†	NS†			NS†	NS	Focus groups and interviews	Content and narrative analysis	Health care transition experience of young adults, their family members and health care providers
Secor-Turner (2011)(344)	US	10	Mean 20.8 (range 14-28)	3:7	NS	10					NS	Focus groups	Descriptive content analysis	Challenges of living with JIA
Shaw (2004)(161)	UK	30	Range 13-30	11:19	Range 1-26	30					NS	Focus groups	Interpretive phenomenological analysis	Transitional care needs
Shaw (2006)(334)	UK	8	Median 15.7 (range 14-16)	4:4	Median 5 (range 2.3-13)	8					Framework recommended by Krueger (1994)	Focus groups	Steps recommended by Krueger (2004) and interpretive phenomenological analysis	Prevocational and early employment needs
Stinson (2008)(317)	Canada	36	Mean 15.1 (SD 2.1)	12:24	Mean 7.2 (SD 2.6)	36					Descriptive exploratory qualitative design as described by Sandelowski	Semi-structured focus groups and individual interviews	Thematic analysis	Self-management needs of adolescents with arthritis

	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis					Conceptual methodological framework	Data collection	Analysis	Main topic
						JIA	SLE	DM	MCTD	Other				
Stinson (2010)(342)	Canada	19	Mean 15.7 (SD 1.5)	5:14	Mean 7 (SD 5, range 0.3-15.2)	19					NS	Semi-structured interviews	Content analysis	Usability of the self-management program for youth with JIA and their parents to refine a prototype health portal
Tong (2013)(335)	Australia	13	14-15 n=7, 16-17 n=3, 18-19 n=1, >19 n=2	4:9	<5 years n=19, 5-10 years n=11, > 10 years n=7	13					NS	Focus groups and semi-structured face-to-face or telephone interviews	Thematic analysis	Consumer perspectives on paediatric rheumatology care and service delivery
Tuchman (2008)(316)	US	2	NS	NS	NS	2					Exploratory model	Open-ended interview	Editing organising style	Experiences and expectations of adolescents with chronic illness in transition to adult care
Tunnicliffe (2016)(162)	Australia	26	Mean 18 (range 14-26)	2:24	Median 6 (SD 3.7)		26				NS	Focus group or face-to-face semi-structured interview	Grounded theory and thematic analysis	The experiences, perspectives and health care needs of adolescents and young adults with SLE

	Country	n	Age (years)	Sex (M:F)	Disease duration (years)	Type of arthritis					Conceptual methodological framework	Data collection	Analysis	Main topic
						JIA	SLE	DM	MCTD	Other				
Van Staa (2011)(321)	The Netherlands	3	NS	NS	NS	3					NS	Semi-structured interviews	Thematic analysis	Expectations and experiences of transfer and perceived quality of care in paediatric and adult services
Wells (2015)(159)	US	12	Mean 31 (range 26-35)	0:12	Mean 23.5 (range 8-33)	11	1				Narrative research model	Semi-structured face-to-face interviews	Thematic analysis using the narrative research model and principle of Vital Involvement	Experience of growing up with rheumatic diseases, current health status and coping mechanisms

JIA, juvenile idiopathic arthritis ; SLE, systemic lupus erythematosus ; DM, dermatomyositis ; MCTD, mixed connective tissue disease ; US, United States ; UK, United Kingdom; NS, not stated; SD, standard deviation.
* Patients with JIA, SLE, DM and scleroderma included in surveys, the demographics of patients included in focus groups was unspecified.
† Patients with JIA, SLE and “rheumatic diseases” included in the study

Appendix F: Supporting data for Chapter 6

F.1 Focus group guide

Time	Details
Phase 1 – Focus group discussion (40 mins)	
40 mins	**Focus Group** To begin with, we will talk about your general experiences of medications for (gout/osteoporosis/RA). 1) How do (gout/osteoporosis/RA) medications impact your life? What is most challenging about taking medication, why – how do you cope with it? 2) To what extent do you feel involved and informed in making decisions about your medication? 3) Have you ever struggled to take your medications? Why? 4) What things do you do, what supports, or programs might you use to help you take medications? What was helpful about these things?
Phase 2 – Nominal group technique (35 mins)	
35 mins	**Nominal Group Technique (Part 1)** Now we are going to have a more focused discussion and an activity to find out what factors matter to you most and why. I am going to read you a question. After I have read, I would ask that you take a couple of minutes to write down **three** ideas (by yourself) on the paper provided to the question shown on the flip chart/board. This is the question: "What helps and what hampers you taking your medication as prescribed? Please write down your 2-3 ideas related to medication taking/adherence that you think are important, then we will share them with each other and generate a group list on the board/flipchart. I am going to go around the table and ask each of you to give me one or two ideas from your worksheet, summarised in a few words. After the entire list is on the board, we will discuss and clarify the ideas. Please do not repeat an idea already listed on the board. You can offer a different idea, or you can pass. We will now briefly discuss each idea, to clarify the meaning of each item on the board/flipchart as I write them up. You should feel free to express different points of view as people will have different experiences and perspectives. Does anyone have any other outcomes they would like to add before I start adding outcomes other patients have told us in the past.
25 mins	**Nominal Group Technique (Part 2)** Now we are going to look at all the ideas raised by the group and I will ask you to rank them in order of most important to least important to you from 1 being most important. If you find it difficult to rank the whole list, please try to rank the top 20. Now we will have a discussion to discuss any similarities and differences in ranking. What did everyone put as: number 1, number 2, number 3, least important? Would anyone like to explain why they ranked [outcome] or how they made their decisions about ranking? Why do you think most people ranked [outcome] high/low? Why do you think there are differences in ranking of [outcome]?

F.2 COREQ checklist

No	Item	Comment
	Personal Characteristics	
1	Interviewer/facilitator	AK
2	Credentials	MBBS BSc (Med) BA FRACP
3	Occupation	Rheumatologist, PhD candidate
4	Gender	Female
5	Experience and training	AK has conducted and published qualitative research and received training in qualitative methods from AT
	Relationship with participants	
6	Relationship established	2 participants with prior clinical relationship with facilitator/co-facilitator were aware and consented to participating in the focus groups
7	Participant knowledge of the interviewer	Participants were aware of the primary investigator AK's occupation
8	Interviewer characteristics	AK is a rheumatologist and co-chair of the Outcome Measures in Rheumatology-Adherence Special Interest Group
	Theoretical framework	
9	Methodology/Theory	Qualitative study (using techniques from grounded theory)
	Participant selection	
10	Sampling	Purposive sampling
11	Method of approach	Rheumatologists, nurses and research assistants recruited patients face-to-face from their clinics or provided lists of eligible patients to study staff. Study staff called all potential participants.
12	Sample size	82
13	Non-participation	59 did not participate, reasons for non-participation included feeling unwell, being overseas, work or child care commitments, disinterested in the topic, difficulty with transport or poor mobility.
	Setting	
14	Setting of data collection	Research office meeting rooms, library meeting rooms, all separated from participants' usual rheumatology clinical setting
15	Presence of non-participants	None
16	Description of the sample	Table 1
	Data Collection	
17	Interview guide	Supplementary Table 1
18	Repeat interviews	All participants participated in single interviews only
19	Audio / visual recording	All focus groups audio recorded
20	Field notes	Yes, made by facilitator and co-facilitators
21	Duration	Approximately two hours per group
22	Data saturation	Yes
23	Transcripts returned	Offered to all participants
	Data Analysis	
24	Number of data coders	Single data coder
25	Description of the coding tree	See themes
26	Derivation of themes	Inductively derived from data
27	Software	HyperRESEARCH
28	Participant checking	Yes
	Reporting	
29	Quotations presented	Under results, and Table 2
30	Data and findings consistent	Description and quotations provided to illustrate each theme
31	Clarity of major themes	Yes – Described under each theme in results
32	Clarity of minor themes	N/A

F.3 Nominal group ranking and importance score calculation

We calculated an importance score (IS) which is a summary measure of the importance of each factor. This was calculated using the probability of each rank for each factor and incorporated 1) the importance given to the factor by the rank position and 2) the consistency of being nominated by participants. The probability of the factor F_j being assigned the rank i is written mathematically as $P\ F⁡j⁡\ in\ rank\ i⁡$. Using the total law of probabilities, these probabilities can be explained as:

$$P\ F⁡j⁡\ in\ rank\ i⁡ == P\ F⁡j⁡\ in\ rank\ i\ ⁡\ F⁡j⁡\ is\ nominated) \times$$
$$P\ F⁡j⁡\ is\ nominated⁡ + P\ F⁡j⁡\ in\ rank\ i\ ⁡\ F⁡j⁡\ not\ nominated) \times$$
$$P(\ F⁡j⁡\ not\ nominated)$$

"Nominated" means the participant considered and ranked the factor. $P\ F⁡j⁡\ in\ rank\ i\ ⁡\ F⁡j⁡\ not\ nominated)$ equals 0 because the probability of any rank is 0 if the participant did not mention or rank the factor $F⁡j⁡$. Therefore, the above simplifies to:

$$P\ F⁡j⁡\ in\ rank\ i⁡ = P\ F⁡j⁡\ in\ rank\ i\ ⁡\ F⁡j⁡\ is\ nominated) \times P\ F⁡j⁡\ is\ nominated⁡$$

The IS is the weighted sum of the reciprocal ranking $1⁡i⁡⁡$:

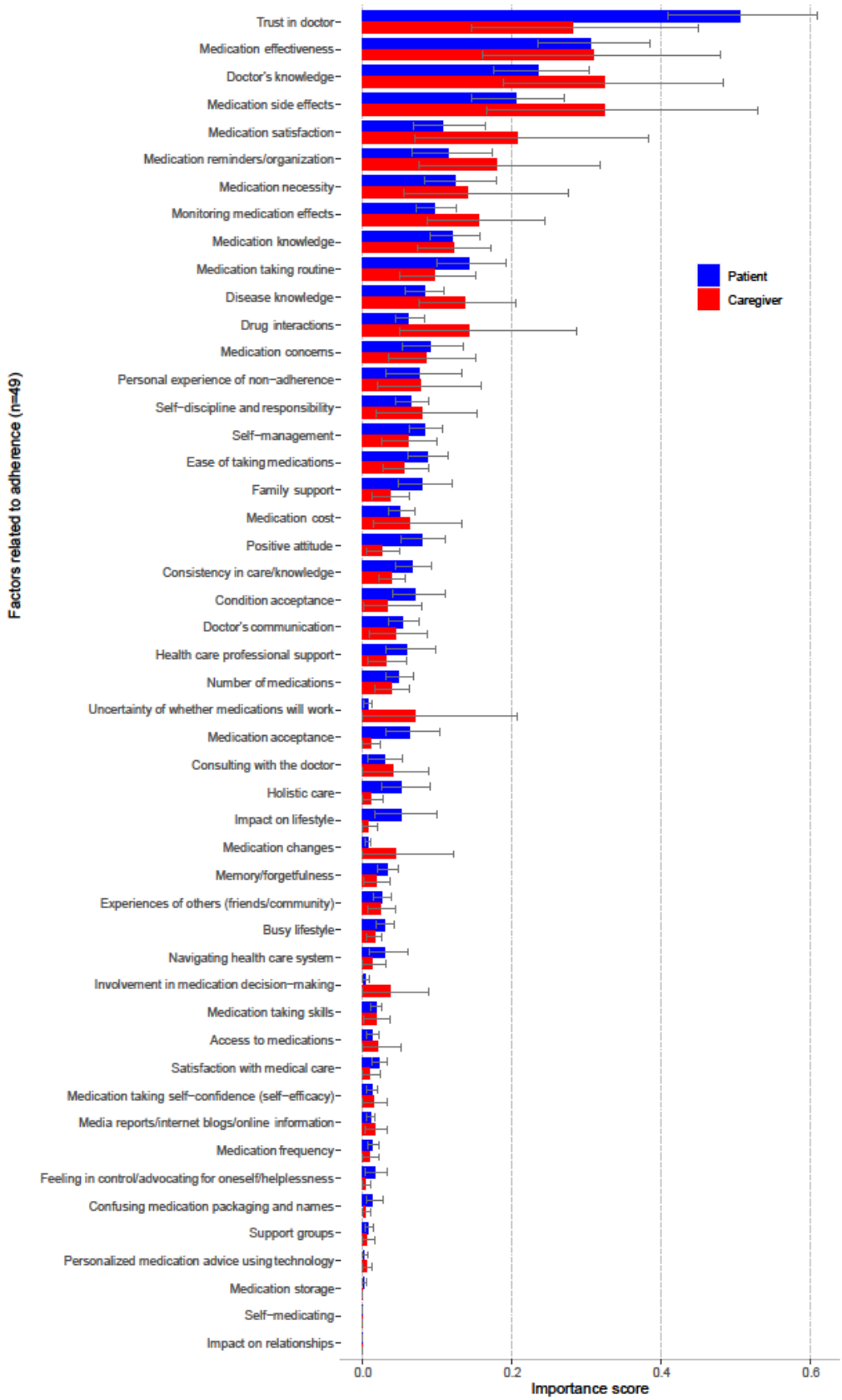
$$IS = \ i = 1⁡\ nr\ of\ ⁡factors⁡⁡P\ F⁡j⁡\ in\ rank\ i⁡⁡ \times\ 1⁡i⁡$$

The ranking is inverted to give greater weight to higher ranks. For example, if "side effects" was ranked 1st by one participant, 3rd by another the reciprocal rankings would be 1, 1/3 respectively. If the outcome "side effects" was not ranked by another participant, their reciprocal ranking would be 0. The average of the three reciprocal rankings (1, 1/3 and 0) is 0.44, the IS for this factor. The IS ranges from 0 to 1. Higher scores reflect factors that are more valued by participants. The standard error was obtained through bootstrapping (randomly re-sampling the data 1000 times). The IS was calculated separately for patients and caregivers, males and females and each condition. The analysis was conducted using statistical software R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

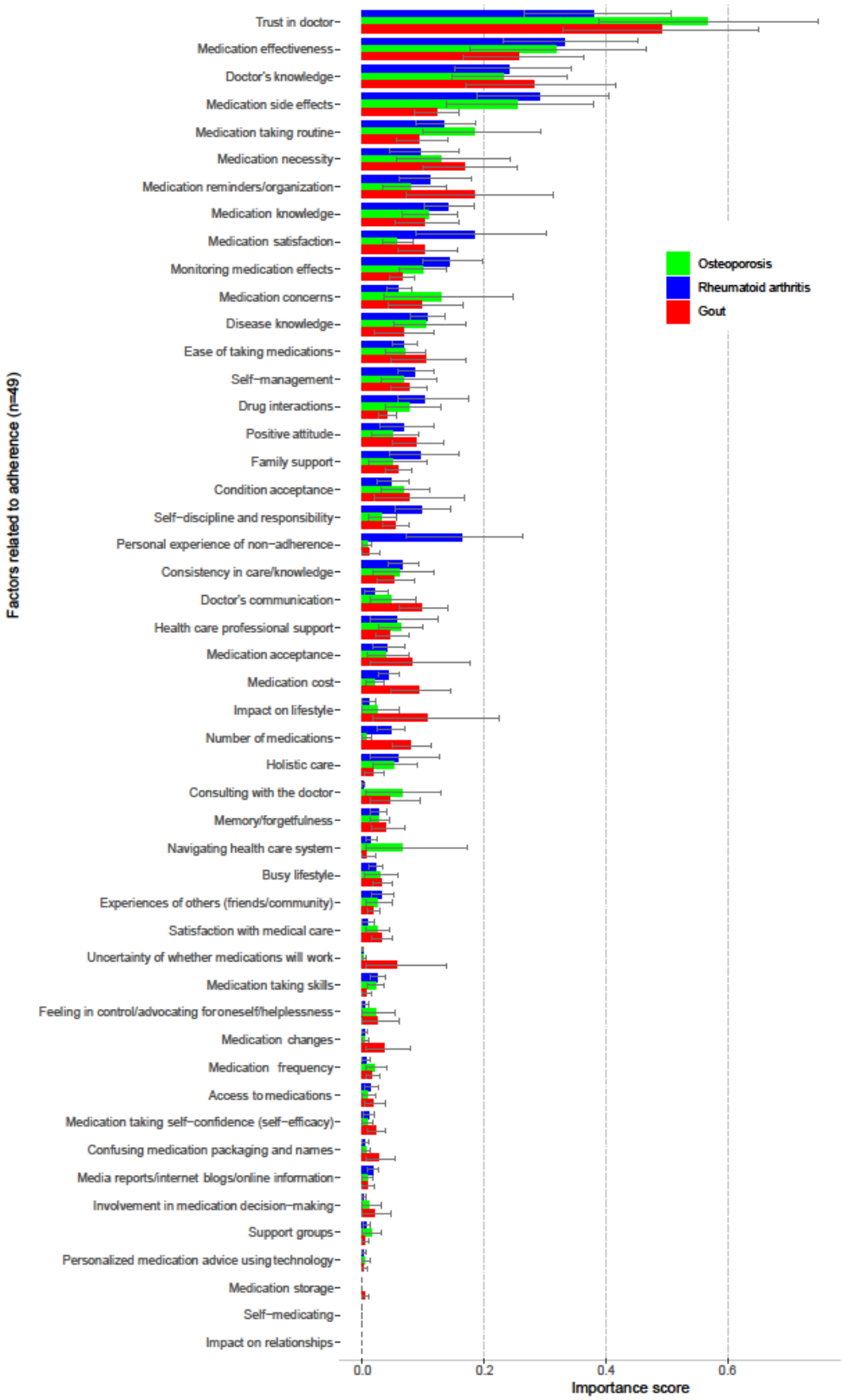
F.4 Ranking and description of all factors influencing medication adherence

Rank	Factor	Description	Importance score	Standard error
1	Trust in doctor	Whether the participant trusted the doctor/prescriber	0.46	0.05
2	Medication effectiveness	How effective the medication was	0.31	0.03
3	Doctor's knowledge	Participant's perception of the doctor's knowledge	0.25	0.03
4	Medication side effects	Side effects from medications	0.23	0.03
5	Medication taking routine	Having a routine to take medications	0.13	0.02
6	Medication necessity	General feeling of necessity of the medication	0.13	0.02
7	Medication satisfaction	General satisfaction with the medication	0.13	0.03
8	Medication reminders/organisation	Use of reminders or organisers to take medications	0.13	0.03
9	Medication knowledge	Participant's knowledge of medications	0.12	0.01
10	Monitoring medication effects	Using blood tests or bone density scans to monitor the effectiveness of and/or side effects	0.11	0.01
11	Disease knowledge	Participant's knowledge of their condition	0.09	0.01
12	Medication concerns	General concerns with medications	0.09	0.02
13	Ease of taking medications	Ease of taking medications, e.g. being able to swallow pills, open pill bottles	0.08	0.01
14	Self-management	Ability to get prescriptions, fill them out, organise and take medications	0.08	0.01
15	Drug interactions	Potential interactions between different medications	0.08	0.01
16	Personal experience of non-adherence	Motivation to continue taking medications after trying to stop in the past	0.08	0.02
17	Family support	Emotional support and/or family reminders/organisation/administration of medication	0.07	0.01
18	Positive attitude	Participant's positive attitude about their condition and medications	0.07	0.01
19	Self-discipline and responsibility	Being self-disciplined and responsible about taking medications	0.07	0.01
20	Condition acceptance	Acceptance of having the condition	0.06	0.01
21	Consistency in care/knowledge	Consistency in care and advice from different health care professionals	0.06	0.01
22	Health care professional support	Support from other health care professionals including pharmacists and nurses	0.05	0.01
23	Medication acceptance	Acceptance of needing to take the medication	0.05	0.01
24	Medication cost	Monetary cost of the medication	0.05	0.01
25	Doctor's communication	Participant's perception of the doctor's communication ability	0.05	0.01
26	Number of medications	Total number of medications being taken	0.05	0.01
27	Impact on lifestyle	Impact of the medication on the participant's lifestyle (e.g. ability to drink alcohol)	0.04	0.02
28	Holistic care	That the doctor considers other health conditions and non-pharmacological care (e.g. diet and exercise)	0.04	0.01

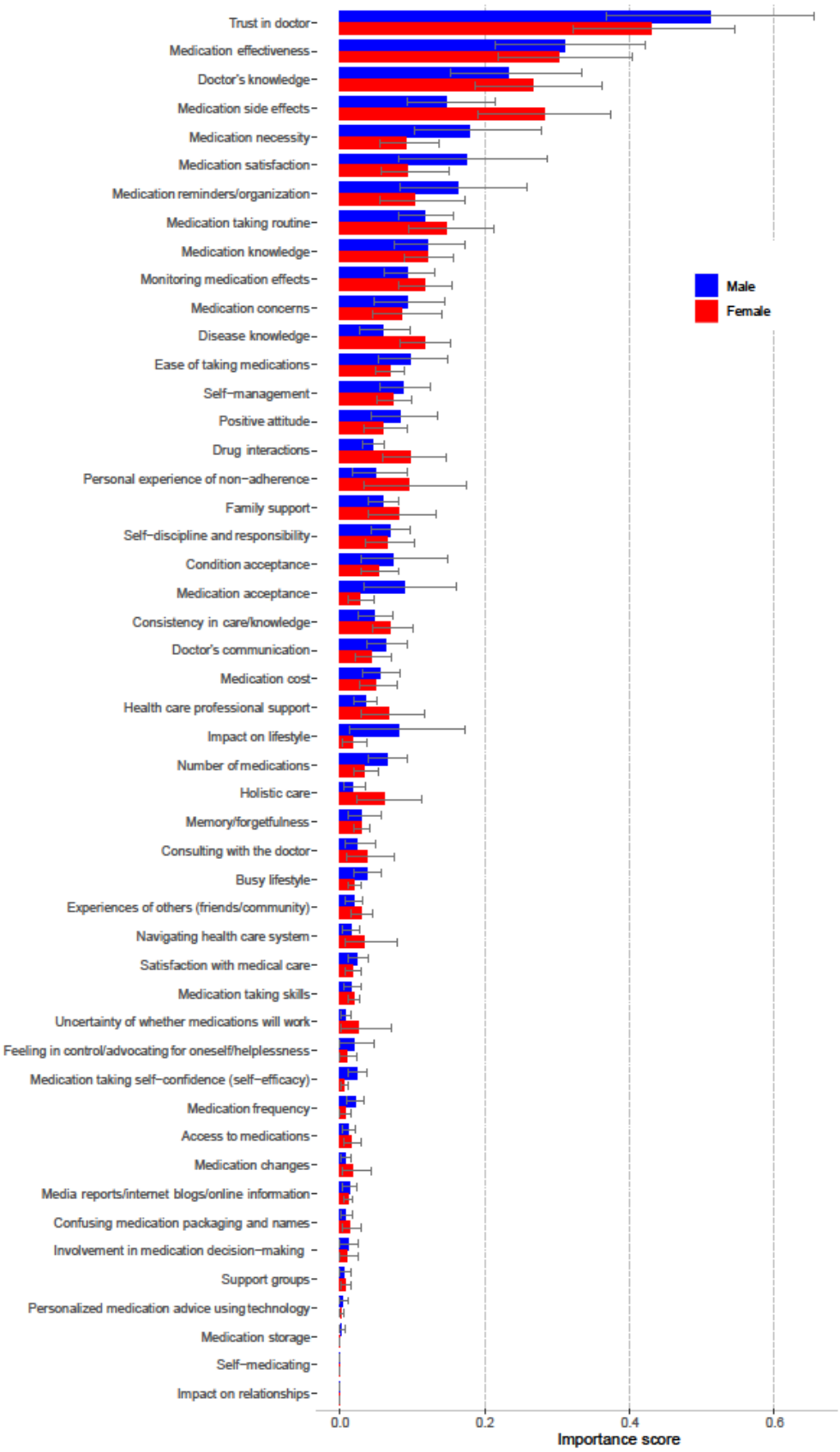
Rank	Factor	Description	Importance score	Standard error
29	Consulting with the doctor	Consulting with the doctor about problems with medications before making changes	0.03	0.01
30	Memory/forgetfulness	Ability to remember to take medications including conditions causing problems with memory (dementia)	0.03	0.01
31	Busy lifestyle	Having a busy work or personal lifestyle	0.03	0.01
32	Navigating health care system	Ability to make appointments, see the doctor and have access to prescriptions	0.02	0.01
33	Experiences of others (friends/community)	The advice and experiences of friends or colleagues in the community	0.02	0.01
34	Satisfaction with medical care	Overall satisfaction with medical care	0.02	0.00
35	Uncertainty of whether medications will work	Feeling uncertain of the effectiveness of medications, the sense of doctor's experimenting with the medications	0.02	0.01
36	Medication taking skills	Skills in taking medications (e.g. ability to swallow pills or self-inject)	0.02	0.00
37	Feeling in control/advocating for oneself/helplessness	Overall feeling of being in control of decision making	0.01	0.01
38	Medication changes	Confusion that arises when medication doses are changed at appointments	0.01	0.01
39	Access to medications	Restrictions in access due to specific prescribing requirements (e.g. biologic medications, vitamin D injections)	0.01	0.00
40	Medication taking self-confidence (self-efficacy)	The confidence in one's ability to take their medications	0.01	0.00
41	Medication frequency	Difficulty remembering infrequent medications (e.g. weekly)	0.01	0.00
42	Media reports/internet blogs/online information	Information from the media, internet blogs or online	0.01	0.00
43	Confusing medication packaging and names	Confusion with generic medications due to difference in packaging, names, size and shape	0.01	0.00
44	Involvement in medication decision-making	Feeling involved in medication decision making	0.01	0.01
45	Support groups	Organised support groups for people with specific conditions	0.01	0.00
46	Personalised medication advice using technology	Technology that could personalise which medications would work and cause least harm for an individual	0.00	0.00
47	Medication storage	Pill bottles which are hard to open, having to keep injections in fridges when travelling	0.00	0.00
48.5	Self-medicating	Making decisions to change doses, take medications or stop medications outside of medical advice	0.00	0.00
48.5	Impact on relationships	The impact not taking medication would have on relationships (e.g. spouse getting upset)	0.00	0.00



F.5 Ranking of factors for patients versus caregivers



F.6 Ranking of factors by condition



F.7 Ranking of factors by gender

Bibliography

1. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. Nature reviews Disease primers. 2018;4:18001.
2. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016;388(10055):2023-38.
3. Peschken CA, Esdaile JM. Rheumatic diseases in North America's indigenous peoples. Seminars in arthritis and rheumatism. 1999;28(6):368-91.
4. McDougall C, Hurd K, Barnabe C. Systematic review of rheumatic disease epidemiology in the indigenous populations of Canada, the United States, Australia, and New Zealand. Seminars in arthritis and rheumatism. 2017;46(5):675-86.
5. Dougados M, Baeten D. Spondyloarthritis. Lancet. 2011;377(9783):2127-37.
6. Stolwijk C, van Onna M, Boonen A, van Tubergen A. Global Prevalence of Spondyloarthritis: A Systematic Review and Meta-Regression Analysis. Arthritis Care Res. 2016;68(9):1320-31.
7. Bakland G, Nossent HC. Epidemiology of spondyloarthritis: a review. Current rheumatology reports. 2013;15(9):351.
8. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis. 2009;68(6):777-83.
9. Siris ES, Adler R, Bilezikian J, Bolognese M, Dawson-Hughes B, Favus MJ, et al. The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2014;25(5):1439-43.
10. Morin SN, Lix LM, Leslie WD. The importance of previous fracture site on osteoporosis diagnosis and incident fractures in women. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2014;29(7):1675-80.
11. Kanis JA, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2019;30(1):3-44.
12. Kanis JA, Johnell O, Oden A, Dawson A, De Laet C, Jonsson B. Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2001;12(12):989-95.
13. Johnell O, Kanis J. Epidemiology of osteoporotic fractures. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2005;16 Suppl 2:S3-7.
14. Kuo CF, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nature reviews Rheumatology. 2015;11(11):649-62.
15. Thierry S, Fautrel B, Lemelle I, Guillemin F. Prevalence and incidence of juvenile idiopathic arthritis: a systematic review. Joint Bone Spine. 2014;81(2):112-7.

16. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390-2.
17. Smolen JS, Landewe R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017;76(6):960-77.
18. van der Heijde D, Ramiro S, Landewe R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017;76(6):978-91.
19. Ward MM, Deodhar A, Gensler LS, Dubreuil M, Yu D, Khan MA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheum. 2019;71(10):1599-613.
20. Wanders A, Heijde D, Landewe R, Behier JM, Calin A, Olivieri I, et al. Nonsteroidal antiinflammatory drugs reduce radiographic progression in patients with ankylosing spondylitis: a randomized clinical trial. Arthritis Rheum. 2005;52(6):1756-65.
21. Kroon F, Landewe R, Dougados M, van der Heijde D. Continuous NSAID use reverts the effects of inflammation on radiographic progression in patients with ankylosing spondylitis. Ann Rheum Dis. 2012;71(10):1623-9.
22. van der Heijde D, Deodhar A, Wei JC, Drescher E, Fleishaker D, Hendrikx T, et al. Tofacitinib in patients with ankylosing spondylitis: a phase II, 16-week, randomised, placebo-controlled, dose-ranging study. Ann Rheum Dis. 2017;76(8):1340-7.
23. Ramiro S, van der Heijde D, van Tubergen A, Stolwijk C, Dougados M, van den Bosch F, et al. Higher disease activity leads to more structural damage in the spine in ankylosing spondylitis: 12-year longitudinal data from the OASIS cohort. Ann Rheum Dis. 2014;73(8):1455-61.
24. Poddubnyy D, Protopopov M, Haibel H, Braun J, Rudwaleit M, Sieper J. High disease activity according to the Ankylosing Spondylitis Disease Activity Score is associated with accelerated radiographic spinal progression in patients with early axial spondyloarthritis: results from the GErman SPondyloarthritis Inception Cohort. Ann Rheum Dis. 2016;75(12):2114-8.
25. Gossec L, Smolen JS, Ramiro S, de Wit M, Cutolo M, Dougados M, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis. 2016;75(3):499-510.
26. Coates LC, Kavanaugh A, Mease PJ, Soriano ER, Laura Acosta-Felquer M, Armstrong AW, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 Treatment Recommendations for Psoriatic Arthritis. Arthritis Rheum. 2016;68(5):1060-71.
27. Singh JA, Guyatt G, Ogdie A, Gladman DD, Deal C, Deodhar A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheum. 2019;71(1):5-32.
28. Gossec L, Coates LC, de Wit M, Kavanaugh A, Ramiro S, Mease PJ, et al. Management of psoriatic arthritis in 2016: a comparison of EULAR and GRAPPA recommendations. Nature reviews Rheumatology. 2016;12(12):743-50.
29. The Royal Australian College of General Practitioners and Osteoporosis Australia.
Osteoporosis prevention, diagnosis and management in postmenopausal women and men over 50 years of age. 2nd ed. East Melbourne, Vic: RACGP; 2017.
30. Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castaneda-Sanabria J, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017;76(1):29-42.

31. Beukelman T, Patkar NM, Saag KG, Tolleson-Rinehart S, Cron RQ, DeWitt EM, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011;63(4):465-82.
32. Ringold S, Angeles-Han ST, Beukelman T, Lovell D, Cuello CA, Becker ML, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Care Res. 2019;71(6):717-34.
33. Ringold S, Weiss PF, Beukelman T, DeWitt EM, Ilowite NT, Kimura Y, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013;65(10):2499-512.
34. Sabaté E. Adherence to long-term therapies: evidence for action: World Health Organization; 2003.
35. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691-705.
36. Helmy R, Zullig L, Dunbar-Jacob J, Hughes D, Vrijens B, Wilson I, et al. ESPACOMP Medication Adherence Reporting Guidelines (EMERGE): a reactive-Delphi study protocol. BMJ Open. 2017;7(2):e013496.
37. Dickinson D, Wilkie P, Harris M. Taking medicines: concordance is not compliance. BMJ. 1999;319(7212):787.
38. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implement Sci. 2011;6(1):42.
39. Meddings J, Kerr EA, Heisler M, Hofer TP. Physician assessments of medication adherence and decisions to intensify medications for patients with uncontrolled blood pressure: still no better than a coin toss. BMC health services research. 2012;12:270.
40. Lehmann A, Aslani P, Ahmed R, Celio J, Gauchet A, Bedouch P, et al. Assessing medication adherence: options to consider. International journal of clinical pharmacy. 2014;36(1):55-69.
41. Lam WY, Fresco P. Medication Adherence Measures: An Overview. BMC health services research. 2015;2015:217047.
42. Zullig LL, Mendys P, Bosworth HB. Medication adherence: A practical measurement selection guide using case studies. Patient education and counseling. 2017;100(7):1410-4.
43. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. Clinical therapeutics. 1999;21(6):1074-90.
44. Schett G, Emery P, Tanaka Y, Burmester G, Pisetsky DS, Naredo E, et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. Ann Rheum Dis. 2016;75(8):1428-37.
45. Haschka J, Englbrecht M, Hueber AJ, Manger B, Kleyer A, Reiser M, et al. Relapse rates in patients with rheumatoid arthritis in stable remission tapering or stopping antirheumatic therapy: interim results from the prospective randomised controlled RETRO study. Ann Rheum Dis. 2016;75(1):45-51.
46. ten Wolde S, Breedveld FC, Hermans J, Vandenbroucke JP, van de Laar MA, Markusse HM, et al. Randomised placebo-controlled study of stopping second-line drugs in rheumatoid arthritis. Lancet. 1996;347(8998):347-52.
47. Emery P, Hammoudeh M, FitzGerald O, Combe B, Martin-Mola E, Buch MH, et al. Sustained remission with etanercept tapering in early rheumatoid arthritis. The New England journal of medicine. 2014;371(19):1781-92.

48. Fautrel B, Pham T, Alfaiate T, Gandjbakhch F, Foltz V, Morel J, et al. Step-down strategy of spacing TNF-blocker injections for established rheumatoid arthritis in remission: results of the multicentre non-inferiority randomised open-label controlled trial (STRASS: Spacing of TNF-blocker injections in Rheumatoid ArthritiS Study). Ann Rheum Dis. 2016;75(1):59-67.
49. Araujo EG, Finzel S, Englbrecht M, Schreiber DA, Faustini F, Hueber A, et al. High incidence of disease recurrence after discontinuation of disease-modifying antirheumatic drug treatment in patients with psoriatic arthritis in remission. Ann Rheum Dis. 2015;74(4):655-60.
50. Ye W, Tucker LJ, Coates LC. Tapering and Discontinuation of Biologics in Patients with Psoriatic Arthritis with Low Disease Activity. Drugs. 2018;78(16):1705-15.
51. Song IH, Althoff CE, Haibel H, Hermann KG, Poddubnyy D, Listing J, et al. Frequency and duration of drug-free remission after 1 year of treatment with etanercept versus sulfasalazine in early axial spondyloarthritis: 2 year data of the ESTHER trial. Ann Rheum Dis. 2012;71(7):1212-5.
52. Moreno M, Gratacos J, Torrente-Segarra V, Sanmarti R, Morla R, Pontes C, et al. Withdrawal of infliximab therapy in ankylosing spondylitis in persistent clinical remission, results from the REMINEA study. Arthritis Res Ther. 2019;21(1):88.
53. Song IH, Haibel H, Poddubnyy D, Braun J, Sieper J. Withdrawal of biologic therapy in axial spondyloarthritis: the experience in early disease. Clinical and experimental rheumatology. 2013;31(4 Suppl 78):S37-42.
54. Perez-Ruiz F, Herrero-Beites AM, Carmona L. A two-stage approach to the treatment of hyperuricemia in gout: the "dirty dish" hypothesis. Arthritis Rheum. 2011;63(12):4002-6.
55. Minden K. Adult outcomes of patients with juvenile idiopathic arthritis. Hormone research. 2009;72 Suppl 1:20-5.
56. Minden K, Horneff G, Niewerth M, Seipelt E, Aringer M, Aries P, et al. Time of Disease-Modifying Antirheumatic Drug Start in Juvenile Idiopathic Arthritis and the Likelihood of a Drug-Free Remission in Young Adulthood. Arthritis Care Res. 2019;71(4):471-81.
57. Black DM, Reid IR, Boonen S, Bucci-Rechtweg C, Cauley JA, Cosman F, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2012;27(2):243-54.
58. Curtis JR, Westfall AO, Cheng H, Delzell E, Saag KG. Risk of hip fracture after bisphosphonate discontinuation: implications for a drug holiday. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2008;19(11):1613-20.
59. Mignot MA, Taisne N, Legroux I, Cortet B, Paccou J. Bisphosphonate drug holidays in postmenopausal osteoporosis: effect on clinical fracture risk. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2017;28(12):3431-8.
60. Ensrud KE, Barrett-Connor EL, Schwartz A, Santora AC, Bauer DC, Suryawanshi S, et al. Randomized trial of effect of alendronate continuation versus discontinuation in women with low BMD: results from the Fracture Intervention Trial long-term extension. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2004;19(8):1259-69.
61. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. The New England journal of medicine. 2009;361(8):756-65.

62. Bone HG, Wagman RB, Brandi ML, Brown JP, Chapurlat R, Cummings SR, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. The lancet Diabetes & endocrinology. 2017;5(7):513-23.
63. Waimann CA, Marengo MF, de Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD, et al. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: consequences of low adherence. Arthritis Rheum. 2013;65(6):1421-9.
64. van den Bemt BJ, van den Hoogen FH, Benraad B, Hekster YA, van Riel PL, van Lankveld W. Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs. J Rheumatol. 2009;36(10):2164-70.
65. Pasma A, van't Spijker A, Hazes JM, Busschbach JJ, Luime JJ. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. Seminars in arthritis and rheumatism. 2013;43(1):18-28.
66. Scheiman-Elazary A, Duan L, Shourt C, Agrawal H, Ellashof D, Cameron-Hay M, et al. The Rate of Adherence to Antiarthritis Medications and Associated Factors among Patients with Rheumatoid Arthritis: A Systematic Literature Review and Metaanalysis. J Rheumatol. 2016;43(3):512-23.
67. Salt E, Frazier S. Adherence to Disease Modifying Anti-Rheumatic Drugs in Rheumatoid Arthritis Patients: A Narrative Review of the Literature. Orthop Nurs. 2010;29(4):260-75.
68. Viller F, Guillemin F, Briancon S, Moum T, Suurmeijer T, van den Heuvel W. Compliance to drug treatment of patients with rheumatoid arthritis: a 3 year longitudinal study. J Rheumatol. 1999;26(10):2114-22.
69. Vangeli E, Bakhshi S, Baker A, Fisher A, Bucknor D, Mrowietz U, et al. A Systematic Review of Factors Associated with Non-Adherence to Treatment for Immune-Mediated Inflammatory Diseases. Adv Ther. 2015;32(11):983-1028.
70. Maniadakis N, Toth E, Schiff M, Wang X, Nassim M, Szegvari B, et al. A Targeted Literature Review Examining Biologic Therapy Compliance and Persistence in Chronic Inflammatory Diseases to Identify the Associated Unmet Needs, Driving Factors, and Consequences. Adv Ther. 2018;35(9):1333-55.
71. Yeam CT, Chia S, Tan HCC, Kwan YH, Fong W, Seng JJB. A systematic review of factors affecting medication adherence among patients with osteoporosis. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2018;29(12):2623-37.
72. Fatoye F, Smith P, Gebrye T, Yeowell G. Real-world persistence and adherence with oral bisphosphonates for osteoporosis: a systematic review. BMJ Open. 2019;9(4):e027049.
73. Feldman DE, de Civita M, Dobkin PL, Malleson P, Meshefedjian G, Duffy CM. Perceived adherence to prescribed treatment in juvenile idiopathic arthritis over a one-year period. Arthritis Rheum. 2007;57(2):226-33.
74. De Vera MA, Marcotte G, Rai S, Galo JS, Bhole V. Medication adherence in gout: a systematic review. Arthritis Care Res. 2014;66(10):1551-9.
75. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2014.
76. Boers M KJ, Tugwell P, Beaton D, Bingham CO III, Conaghan PG, D'Agostino M, et al. The OMERACT Handbook [Available from: https://omeracthandbook.org/handbook.
77. Boers M, Kirwan JR, Tugwell P. The OMERACT handbook. Updated April 2019.
78. Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al. The COMET Handbook: version 1.0. Trials. 2017;18(3):280.

79. Buchbinder R, Batterham R, Ciciriello S, Newman S, Horgan B, Ueffing E, et al. Health literacy: what is it and why is it important to measure? J Rheumatol. 2011;38(8):1791-7.
80. Toupin-April K, Barton J, Fraenkel L, Li L, Grandpierre V, Guillemin F, et al. Development of a Draft Core Set of Domains for Measuring Shared Decision Making in Osteoarthritis: An OMERACT Working Group on Shared Decision Making. J Rheumatol. 2015;42(12):2442-7.
81. Tang K, Boonen A, Verstappen SM, Escorpizo R, Luime JJ, Lacaille D, et al. Worker productivity outcome measures: OMERACT filter evidence and agenda for future research. J Rheumatol. 2014;41(1):165-76.
82. Council NR. Crossing the quality chasm: a new health system for the 21st century. 2001. Washington DC: The National Academies Press.
83. Kupfer JM, Bond EU. Patient Satisfaction and Patient-Centered Care: Necessary but Not Equal. Jama. 2012;308(2):139-40.
84. What Is Patient-Centered Care? NEJM Catal. 2017;3(1).
85. Gerteis M, Edgman-Levitan S, Daley J, Delbanco TL. Through the Patient's Eyes: Understanding and Promoting Patient-Centered Care. San Francisco: Wiley; 1993.
86. Kardas P, Lewek P, Matyjaszczyk M. Determinants of patient adherence: a review of systematic reviews. Frontiers in pharmacology. 2013;4:91.
87. Van Den Bemt BJ, Zwikker HE, Van Den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337-51.
88. Kothawala P, Badamgarav E, Ryu S, Miller RM, Halbert R. Systematic review and meta-analysis of real-world adherence to drug therapy for osteoporosis. Mayo Clin Proc. 2007;82(12):1493-501.
89. Son MB, Sergeyenko Y, Guan H, Costenbader KH. Disease activity and transition outcomes in a childhood-onset systemic lupus erythematosus cohort. Lupus. 2016;25(13):1431-9.
90. Hazel E, Zhang X, Duffy CM, Campillo S. High rates of unsuccessful transfer to adult care among young adults with juvenile idiopathic arthritis. Pediatr Rheumatol Online J. 2010;8:2.
91. Ting TV, Kudalkar D, Nelson S, Cortina S, Pendl J, Budhani S, et al. Usefulness of cellular text messaging for improving adherence among adolescents and young adults with systemic lupus erythematosus. J Rheumatol. 2012;39(1):174-9.
92. Hersh AO, Pang S, Curran ML, Milojevic DS, von Scheven E. The challenges of transferring chronic illness patients to adult care: reflections from pediatric and adult rheumatology at a US academic center. Pediatr Rheumatol Online J. 2009;7:13.
93. Galo JS, Mehat P, Rai SK, Avina-Zubieta A, De Vera MA. What are the effects of medication adherence interventions in rheumatic diseases: a systematic review. Ann Rheum Dis. 2016;75(4):667-73.
94. Hilderson D, Moons P, Van der Elst K, Luyckx K, Wouters C, Westhovens R. The clinical impact of a brief transition programme for young people with juvenile idiopathic arthritis: results of the DON'T RETARD project. Rheumatology. 2016;55(1):133-42.
95. Pope C, Mays N. Qualitative research in health care. 3rd ed. Boston: Blackwell Publishing [BMJ books]; 2006.
96. Braun V, Clarke V, Hayfield N, Terry G. Thematic analysis. In: Liamputtong P, editor. Handbook of Research Methods in Health Social Sciences. Singapore: Springer; 2019. p. 843-60.
97. Kuper A, Lingard L, Levinson W. Critically appraising qualitative research. BMJ. 2008;337:a1035.
98. Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, et al. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. Social science & medicine (1982). 2003;56(4):671-84.

99. Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Med Res Methodol. 2012;12:181.
100. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349-57.
101. Jones J, Hunter D. Consensus methods for medical and health services research. BMJ. 1995;311(7001):376.
102. Kelly A, Tong A, Tymms K, March L, Craig JC, De Vera M, et al. Outcome Measures in Rheumatology - Interventions for medication Adherence (OMERACT-Adherence) Core Domain Set for Trials of Interventions for Medication Adherence in Rheumatology: 5 Phase Study Protocol. Trials. 2018;19(1):204.
103. de Wit MP, Berlo SE, Aanerud GJ, Aletaha D, Bijlsma JW, Croucher L, et al. European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects. Ann Rheum Dis. 2011;70(5):722-6.
104. Pasma A, Schenk CV, Timman R, Busschbach JJV, van den Bemt BJF, Molenaar E, et al. Non-adherence to disease-modifying antirheumatic drugs is associated with higher disease activity in early arthritis patients in the first year of the disease. Arthritis Res Ther. 2015;17:281.
105. de Klerk E, van der Heijde D, Landewe R, van der Tempel H, van der Linden S. The compliance-questionnaire-rheumatology compared with electronic medication event monitoring: a validation study. J Rheumatol. 2003;30(11):2469-75.
106. Michaud K, Vrijens B, Tousset E, Pedro S, Schumacher R, Dasic G, et al. Real-World Adherence to Oral Methotrexate Measured Electronically in Patients With Established Rheumatoid Arthritis. ACR Open Rheumatol. 2019;1(9):560-70.
107. Murage MJ, Tongbram V, Feldman SR, Malatestinic WN, Larmore CJ, Muram TM, et al. Medication adherence and persistence in patients with rheumatoid arthritis, psoriasis, and psoriatic arthritis: a systematic literature review. Patient Pref Adherence. 2018;12:1483-503.
108. Grijalva CG, Chung CP, Arbogast PG, Stein CM, Mitchel EF, Jr., Griffin MR. Assessment of adherence to and persistence on disease-modifying antirheumatic drugs (DMARDs) in patients with rheumatoid arthritis. Medical care. 2007;45(10 Supl 2):S66-76.
109. Li L, Cui Y, Yin R, Chen S, Zhao Q, Chen H, et al. Medication adherence has an impact on disease activity in rheumatoid arthritis: a systematic review and meta-analysis. Patient preference and adherence. 2017;11:1343-56.
110. Pascual-Ramos V, Contreras-Yanez I, Villa AR, Cabiedes J, Rull-Gabayet M. Medication persistence over 2 years of follow-up in a cohort of early rheumatoid arthritis patients: associated factors and relationship with disease activity and with disability. Arthritis Res Ther. 2009;11(1):R26.
111. Pasma A, Schenk C, Timman R, van 't Spijker A, Appels C, van der Laan WH, et al. Does non-adherence to DMARDs influence hospital-related healthcare costs for early arthritis in the first year of treatment? PloS one. 2017;12(2):e0171070.
112. Oelke KR, Chambenoit O, Majjhoo AQ, Gray S, Higgins K, Hur P. Persistence and adherence of biologics in US patients with psoriatic arthritis: analyses from a claims database. Journal of comparative effectiveness research. 2019;8(8):607-21.
113. Sauer BC, Teng CC, He T, Leng J, Lu CC, Walsh JA, et al. Treatment patterns and annual biologic costs in US veterans with rheumatic conditions or psoriasis. Journal of medical economics. 2016;19(1):34-43.
114. Walsh JA, Adejoro O, Chastek B, Palmer JB, Hur P. Treatment Patterns Among Patients with Psoriatic Arthritis Treated with a Biologic in the United States: Descriptive Analyses from an Administrative Claims Database. Journal of managed care & specialty pharmacy. 2018;24:623-31.

115. Dalen J, Svedbom A, Black CM, Lyu R, Ding Q, Sajjan S, et al. Treatment persistence among patients with immune-mediated rheumatic disease newly treated with subcutaneous TNF-alpha inhibitors and costs associated with non-persistence. Rheumatol Int. 2016;36(7):987-95.
116. de Klerk E, van der Linden SJ. Compliance monitoring of NSAID drug therapy in ankylosing spondylitis, experiences with an electronic monitoring device. British journal of rheumatology. 1996;35(1):60-5.
117. Cheng LI, Durden E, Limone B, Radbill L, Juneau PL, Spangler L, et al. Persistance and Compliance with Osteroporosis Therapies Among Women in a Commercially Insured Population in the United States. Journal of managed care & specialty pharmacy. 2015;21(9):824-33, 33a.
118. Chodick G, Moser SS, Goldshtein I. Non-adherence with bisphosphonates among patients with osteoporosis: impact on fracture risk and healthcare cost. Expert review of pharmacoeconomics & outcomes research. 2016;16(3):359-70.
119. Walsh CA, Cahir C, Tecklenborg S, Byrne C, Culbertson MA, Bennett KE. The association between medication non-adherence and adverse health outcomes in ageing populations: A systematic review and meta-analysis. Br J Clin Pharmacol. 2019;85(11):2464-78.
120. Yin R, Li L, Zhang G, Cui Y, Zhang L, Zhang Q, et al. Rate of adherence to urate-lowering therapy among patients with gout: a systematic review and meta-analysis. BMJ Open. 2018;8(4):e017542-e.
121. Tan C, Teng GG, Chong KJ, Cheung PP, Lim A, Wee HL, et al. Utility of the Morisky Medication Adherence Scale in gout: a prospective study. Patient Pref Adherence. 2016;10:2449-57.
122. Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. Pharmacotherapy. 2008;28(4):437-43.
123. Halpern R, Mody RR, Fuldeore MJ, Patel PA, Mikuls TR. Impact of noncompliance with urate-lowering drug on serum urate and gout-related healthcare costs: administrative claims analysis. Current medical research and opinion. 2009;25(7):1711-9.
124. Janssen CA, Oude Voshaar MAH, Vonkeman HE, Krol M, van de Laar M. A retrospective analysis of medication prescription records for determining the levels of compliance and persistence to urate-lowering therapy for the treatment of gout and hyperuricemia in The Netherlands. Clinical rheumatology. 2018;37(8):2291-6.
125. Zandman-Goddard G, Amital H, Shamrayevsky N, Raz R, Shalev V, Chodick G. Rates of adherence and persistence with allopurinol therapy among gout patients in Israel. Rheumatology. 2013;52(6):1126-31.
126. Rapoff MA, Belmont JM, Lindsley CB, Olson NY. Electronically monitored adherence to medications by newly diagnosed patients with juvenile rheumatoid arthritis. Arthritis Rheum. 2005;53(6):905-10.
127. Marshall A, Gupta K, Pazirandeh M, Bonafede M, McMorrow D. Treatment patterns and economic outcomes in patients with juvenile idiopathic arthritis. ClinicoEconomics and outcomes research : CEOR. 2019;11:361-71.
128. Lee WJ, Briars L, Lee TA, Calip GS, Suda KJ, Schumock GT. Use of Tumor Necrosis Factor-Alpha Inhibitors in Children and Young Adults With Juvenile Idiopathic Arthritis or Rheumatoid Arthritis. Pharmacotherapy. 2016;36(12):1201-9.
129. Feldman DE, De Civita M, Dobkin PL, Malleson PN, Meshefedjian G, Duffy CM. Effects of adherence to treatment on short-term outcomes in children with juvenile idiopathic arthritis. Arthritis Rheum. 2007;57(6):905-12.
130. Sturge C, Garralda ME, Boissin M, Dore CJ, Woo P. School attendance and juvenile chronic arthritis. British journal of rheumatology. 1997;36(11):1218-23.
131. Barry MJ, Edgman-Levitan S. Shared decision making--pinnacle of patient-centered care. The New England journal of medicine. 2012;366(9):780-1.

132. Voshaar MJ, Nota I, van de Laar MA, van den Bemt BJ. Patient-centred care in established rheumatoid arthritis. Best practice & research Clinical rheumatology. 2015;29(4-5):643-63.
133. Downe S, Finlayson KW, Lawrie TA, Lewin SA, Glenton C, Rosenbaum S, et al. Qualitative Evidence Synthesis (QES) for Guidelines: Paper 1 - Using qualitative evidence synthesis to inform guideline scope and develop qualitative findings statements. Health research policy and systems. 2019;17(1):76.
134. Kuper A, Reeves S, Levinson W. An introduction to reading and appraising qualitative research. BMJ. 2008;337:a288.
135. Giacomini MK, Cook DJ. Users' guides to the medical literature: XXIII. Qualitative research in health care A. Are the results of the study valid? Evidence-Based Medicine Working Group. Jama. 2000;284(3):357-62.
136. Johnson SR, O'Brien KK. Qualitative Methods in Systemic Sclerosis Research. J Rheumatol. 2016;43(7):1265-7.
137. Paley J, Lilford R. Qualitative methods: an alternative view. BMJ. 2011;342:d424.
138. Saketkoo LA, Pauling JD. Qualitative Methods to Advance Care, Diagnosis, and Therapy in Rheumatic Diseases. Rheumatic diseases clinics of North America. 2018;44(2):267-84.
139. Borreani C, Miccinesi G, Brunelli C, Lina M. An increasing number of qualitative research papers in oncology and palliative care: does it mean a thorough development of the methodology of research? Health and quality of life outcomes. 2004;2:7.
140. Tong A, Winkelmayer WC, Craig JC. Qualitative research in CKD: an overview of methods and applications. Am J Kidney Dis. 2014;64(3):338-46.
141. Goguen J, Knight M, Tiberius R. Is it science? A study of the attitudes of medical trainees and physicians toward qualitative and quantitative research. Advances in health sciences education : theory and practice. 2008;13(5):659-74.
142. Hsu CY, Lin YS, Cheng TT, Syu YJ, Lin MS, Lin HF, et al. Adherence to hydroxychloroquine improves long-term survival of patients with systemic lupus erythematosus. Rheumatology. 2018;57(10):1743-51.
143. Jaleel A, Saag KG, Danila MI. Improving drug adherence in osteoporosis: an update on more recent studies. Ther Adv Musc Dis. 2018;10(7):141-9.
144. Scheepers L, Burden AM, Arts ICW, Spaetgens B, Souverein P, de Vries F, et al. Medication adherence among gout patients initiated allopurinol: a retrospective cohort study in the Clinical Practice Research Datalink (CPRD). Rheumatology. 2018;57(9):1641-50.
145. Kelly A, Tymms K, Tunnicliffe D, Sumpton D, Perera C, Fallon K, et al. Patients' attitudes and experiences of disease-modifying anti-rheumatic drugs in rheumatoid arthritis and spondyloarthritis; a qualitative synthesis. Arthritis Care Res. 2018;70(4):525-32.
146. Rai SK, Choi HK, Choi SHJ, Townsend AF, Shojania K, De Vera MA. Key barriers to gout care: a systematic review and thematic synthesis of qualitative studies. Rheumatology. 2018;57(7):1282-92.
147. Shaw Y, Metes ID, Michaud K, Donohue JM, Roberts MS, Levesque MC, et al. Rheumatoid Arthritis Patients' Motivations for Accepting or Resisting Disease-Modifying Antirheumatic Drug Treatment Regimens. Arthritis Care Res. 2018;70(4):533-41.
148. van Tuyl LH, Hewlett S, Sadlonova M, Davis B, Flurey C, Hoogland W, et al. The patient perspective on remission in rheumatoid arthritis: 'You've got limits, but you're back to being you again'. Ann Rheum Dis. 2015;74(6):1004-10.
149. Nota I, Drossaert CH, Taal E, van de Laar MA. Patients' considerations in the decision-making process of initiating disease-modifying antirheumatic drugs. Arthritis Care Res. 2015;67(7):956-64.
150. Salt E, Rowles GD, Reed DB. Patient's perception of quality patient--provider communication. Orthop Nurs. 2012;31(3):169-76.

151. van Tuyl LH, Plass AM, Lems WF, Voskuyl AE, Kerstens PJ, Dijkmans BA, et al. Discordant perspectives of rheumatologists and patients on COBRA combination therapy in rheumatoid arthritis. Rheumatology. 2008;47(10):1571-6.
152. Shaw Y, Bradley M, Zhang C, Dominique A, Michaud K, McDonald D, et al. The development of resilience among rheumatoid arthritis patients: a qualitative study. Arthritis Care Res. 2019.
153. Pasma A, van 't Spijker A, Luime JJ, Walter MJ, Busschbach JJ, Hazes JM. Facilitators and barriers to adherence in the initiation phase of Disease-modifying Antirheumatic Drug (DMARD) use in patients with arthritis who recently started their first DMARD treatment. J Rheumatol. 2015;42(3):379-85.
154. Salt E, Peden A. The complexity of the treatment: the decision-making process among women with rheumatoid arthritis. Qual Health Res. 2011;21(2):214-22.
155. Tattersall R, McDonagh JE. Transition: a rheumatology perspective. Br J Hosp Med. 2010;71(6):315-9.
156. Howland S, Fisher K. Looking through the patient lens - Improving best practice for young people with juvenile idiopathic arthritis transitioning into adult care. SpringerPlus. 2015;4:111.
157. Hersh A, von Scheven E, Yelin E. Adult outcomes of childhood-onset rheumatic diseases. Nature reviews Rheumatology. 2011;7(5):290-5.
158. Ostlie IL, Dale O, Moller A. From childhood to adult life with juvenile idiopathic arthritis (JIA): a pilot study. Disability and rehabilitation. 2007;29(6):445-52.
159. Wells C. Wellness in the Midst of Disease: A Narrative Analysis of Growing Up with Rheumatic Conditions [dissertation]. Minneapolis: University of Minnesota; 2015.
160. Hilderson D, Eyckmans L, Van der Elst K, Westhovens R, Wouters C, Moons P. Transfer from paediatric rheumatology to the adult rheumatology setting: experiences and expectations of young adults with juvenile idiopathic arthritis. Clinical rheumatology. 2013;32(5):575-83.
161. Shaw KL, Southwood TR, McDonagh JE. User perspectives of transitional care for adolescents with juvenile idiopathic arthritis. Rheumatology. 2004;43(6):770-8.
162. Tunnicliffe DJ, Singh-Grewal D, Chaitow J, Mackie F, Manolios N, Lin MW, et al. Lupus Means Sacrifices: Perspectives of Adolescents and Young Adults With Systemic Lupus Erythematosus. Arthritis Care Res. 2016;68(6):828-37.
163. Wolfe F, Hawley DJ, Wilson K. The prevalence and meaning of fatigue in rheumatic disease. J Rheumatol. 1996;23(8):1407-17.
164. Repping-Wuts H, van Riel P, van Achterberg T. Rheumatologists' knowledge, attitude and current management of fatigue in patients with rheumatoid arthritis (RA). Clinical rheumatology. 2008;27(12):1549-55.
165. Fautrel B, Alten R, Kirkham B, de la Torre I, Durand F, Barry J, et al. Call for action: how to improve use of patient-reported outcomes to guide clinical decision making in rheumatoid arthritis. Rheumatol Int. 2018;38(6):935-47.
166. Hewlett S, Cockshott Z, Byron M, Kitchen K, Tipler S, Pope D, et al. Patients' perceptions of fatigue in rheumatoid arthritis: overwhelming, uncontrollable, ignored. Arthritis Rheum. 2005;53(5):697-702.
167. Hewlett S, Chalder T, Choy E, Cramp F, Davis B, Dures E, et al. Fatigue in rheumatoid arthritis: time for a conceptual model. Rheumatology. 2011;50(6):1004-6.
168. Nicklin J, Cramp F, Kirwan J, Urban M, Hewlett S. Collaboration with patients in the design of patient-reported outcome measures: capturing the experience of fatigue in rheumatoid arthritis. Arthritis Care Res. 2010;62(11):1552-8.
169. Hewlett S, Almeida C, Ambler N, Blair PS, Choy EH, Dures E, et al. Reducing arthritis fatigue impact: two-year randomised controlled trial of cognitive behavioural approaches by rheumatology teams (RAFT). Ann Rheum Dis. 2019;78(4):465-72.
170. Tesch R. Types of qualitative analysis. In: Qualitative research: Analysis types and software. London: Routledge; 1990:77-92.: Routledge.

171. Creswell JW, Creswell JD. Qualitative methods. In: Salmon H, Neve C, Felts DC, Marks A, editors. Research design: Qualitative, quantitative, and mixed methods approaches. Los Angeles, SAGE publications; 2018:179-211.
172. Creswell J, Poth C. Qualitative inquiry and research design: choosing among five approaches. 4th Ed. Los Angeles (CA): SAGE Publications; 2017.
173. Corbin J, Strauss A. Basics of qualitative research: Techniques and Procedures for Developing Grounded Theory. 3rd ed. Thousand Oaks CA: Sage Publications; 2008.
174. Reeves S, Kuper A, Hodges BD. Qualitative research methodologies: ethnography. BMJ. 2008;337:a1020.
175. Atkinson P, Coffey A, Delamont S, Lofland J, Lofland L. Handbook of ethnography. London, UK: Sage Publication; 2001.
176. Hammond M, Howarth J, Keat R. Understanding phenomenology. Oxford, UK: Blackwell Publishing; 1991.
177. Moustakas C. Phenomenological research methods. Virding A, editor. California, SAGE Publications; 1994.
178. Van Manen M. Phenomenology of practice: Meaning-giving methods in phenomenological research and writing. Morse J, editor. Walnut Creek: Left Coust Press Inc; 2014.
179. Yin RK. Case study research : design and methods. 5th edition. Los Angeles: SAGE Publications; 2014.
180. Riessman CK. Narrative methods for the human sciences. Los Angeles: SAGE Publications; 2008.
181. Thurston WE, Coupal S, Jones CA, Crowshoe LF, Marshall DA, Homik J, et al. Discordant indigenous and provider frames explain challenges in improving access to arthritis care: a qualitative study using constructivist grounded theory. International journal for equity in health. 2014;13:46.
182. Kottak N, Tesser J, Leibowitz E, Rosenberg M, Parenti D, DeHoratius R. Ethnographic Observational Study of the Biologic Initiation Conversation Between Rheumatologists and Biologic-Naive Rheumatoid Arthritis Patients. Arthritis Care Res (Hoboken). 2018;70(7):997-1004.
183. Rose G. Why do patients with rheumatoid arthritis use complementary therapies? Musculoskeletal Care. 2006;4(2):101-15.
184. Grant M. Mothers with arthritis, child care and occupational therapy: Insight through case studies. Br J Occup Ther. 2001;64(7):322-9.
185. Stamm T, Lovelock L, Stew G, Nell V, Smolen J, Machold K, et al. I have a disease but I am not ill: A narrative study of occupational balance in people with rheumatoid arthritis. OTJR Occup Particip Health. 2009;29(1):32-9.
186. Morse J. Determining sample size. Qual Health Res. 2000;10(1):3-5.
187. Morgan DL. Focus groups as qualitative research. 2nd ed. Thousand Oaks CA: Sage publications; 1996.
188. Bowen GA. Document analysis as a qualitative research method. Qual Res J. 2009;9(2):27-40.
189. Reeves S, Albert M, Kuper A, Hodges BD. Why use theories in qualitative research? BMJ. 2008;337:a949.
190. Creswell JW, Creswell JD. Mixed methods procedures. In: Salmon H, Neve C, Felts DC, Marks A, editors. Research design: Qualitative, quantitative, and mixed methods approaches. Los Angeles, SAGE publications; 2018:213-46.
191. Kelly A, Tymms K, de Wit M, Bartlett SJ, Cross M, Dawson T, et al. Patient and caregiver priorities for medication adherence in gout, osteoporosis and rheumatoid arthritis: nominal group technique. Arthritis Care Res. 2019 Jul 19 [E-pub ahead of print].
192. Tunnicliffe DJ, Singh-Grewal D, Craig JC, Howell M, Tugwell P, Mackie F, et al. Healthcare and Research Priorities of Adolescents and Young Adults with Systemic Lupus Erythematosus: A Mixed-methods Study. J Rheumatol. 2017;44(4):444-51.

193. Carr ECJ, Ortiz MM, Patel JN, Barber CEH, Katz S, Robert J, et al. Models of Arthritis Care: A Systems-Level Evaluation of Acceptability as a Dimension of Quality of Care. J Rheumatol. 2019 Nov 15 (E-pub ahead of print).
194. Mahmood S, Hazes JMW, Veldt P, van Riel P, Landewé R, Bernelot Moens H, et al. The Development and Evaluation of Personalized Training in Shared Decision-making Skills for Rheumatologists. J Rheumatol. 2020;47(2):290-7.
195. Nicklin J, Cramp F, Kirwan J, Greenwood R, Urban M, Hewlett S. Measuring fatigue in rheumatoid arthritis: a cross-sectional study to evaluate the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional questionnaire, visual analog scales, and numerical rating scales. Arthritis Care Res (Hoboken). 2010;62(11):1559-68.
196. Dures EK, Hewlett SE, Cramp FA, Greenwood R, Nicklin JK, Urban M, et al. Reliability and sensitivity to change of the Bristol Rheumatoid Arthritis Fatigue scales. Rheumatology (Oxford, England). 2013;52(10):1832-9.
197. Lewin S, Glenton C, Oxman AD. Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. BMJ. 2009;339:b3496.
198. Onwuegbuzie AJ, Leech NL. Linking research questions to mixed methods data analysis procedures 1. Qual Report. 2006;11(3):474-98.
199. Oakley A, Strange V, Bonell C, Allen E, Stephenson J. Process evaluation in randomised controlled trials of complex interventions. BMJ. 2006;332(7538):413-6.
200. Singh JA, Herbey I, Bharat A, Dinnella JE, Pullman-Mooar S, Eisen S, et al. Gout Self-Management in African American Veterans: A Qualitative Exploration of Challenges and Solutions From Patients' Perspectives. Arthritis Care Res. 2017;69(11):1724-32.
201. Craig ET, Orbai AM, Mackie S, Bartlett SJ, Bingham CO, 3rd, Goodman S, et al. Advancing Stiffness Measurement in Rheumatic Disease: Report from the Stiffness Special Interest Group at OMERACT 2018. J Rheumatol. 2019;46(10):1374-8.
202. Lima K, Phillip CR, Williams J, Peterson J, Feldman CH, Ramsey-Goldman R. Factors Associated with Participation in Rheumatic Disease-Related Research among Underrepresented Populations: A Qualitative Systematic Review. Arthritis Care Res. 2019.
203. Karp DR, Chong BF, James JA, Arriens C, Ishimori M, Wallace DJ, et al. Mock Recruitment for the Study of Antimalarials in Incomplete Lupus Erythematosus Trial. Arthritis Care Res. 2019;71(11):1425-9.
204. Lawford BJ, Delany C, Bennell KL, Hinman RS. "I Was Really Pleasantly Surprised": Firsthand Experience and Shifts in Physical Therapist Perceptions of Telephone-Delivered Exercise Therapy for Knee Osteoarthritis-A Qualitative Study. Arthritis Care Res. 2019;71(4):545-57.
205. Critical Appraisal Skills Programme (2018). CASP Qualitative Checklist. [Available from: https://casp-uk.net/casp-tools-checklists/.
206. Guba EG. Criteria for Assessing the Trustworthiness of Naturalistic Inquiries. Educ Tech Res Develop. 1981;29(2):75-91.
207. Levitt HM, Bamberg M, Creswell JW, Frost DM, Josselson R, Suárez-Orozco C. Journal article reporting standards for qualitative primary, qualitative meta-analytic, and mixed methods research in psychology: The APA Publications and Communications Board task force report. The American psychologist. 2018;73(1):26-46.
208. Greenhalgh T, Taylor R. Papers that go beyond numbers (qualitative research). BMJ. 1997;315(7110):740-3.
209. Sandelowski M. Rigor or rigor mortis: the problem of rigor in qualitative research revisited. ANS Advances in nursing science. 1993;16(2):1-8.
210. Lincoln YS, Guba EG. Naturalistic inquiry. Newberry Park. London, UK: Sage Publications; 1985.
211. Flurey CA, Hewlett S, Rodham K, White A, Noddings R, Kirwan JR. "You Obviously Just Have to Put on a Brave Face": A Qualitative Study of the Experiences

and Coping Styles of Men With Rheumatoid Arthritis. Arthritis Care Res. 2017;69(3):330-7.
212. Hart RI, McDonagh JE, Thompson B, Foster HE, Kay L, Myers A, et al. Being as Normal as Possible: How Young People Ages 16-25 Years Evaluate the Risks and Benefits of Treatment for Inflammatory Arthritis. Arthritis Care Res. 2016;68(9):1288-94.
213. Sumpton D, Thakkar V, O'Neill S, Singh-Grewal D, Craig JC, Tong A. "It's Not Me, It's Not Really Me." Insights From Patients on Living With Systemic Sclerosis: An Interview Study. Arthritis Care Res. 2017;69(11):1733-42.
214. Hewlett S, Sanderson T, May J, Alten R, Bingham CO, 3rd, Cross M, et al. 'I'm hurting, I want to kill myself': rheumatoid arthritis flare is more than a high joint count--an international patient perspective on flare where medical help is sought. Rheumatology. 2012;51(1):69-76.
215. Kelly A, Bartlett SJ, de Wit MP, Beaton DE, Dawson T, Evans V, et al. Addressing Challenges in Developing a Core Domain Set in Adherence Interventions in Rheumatology: A Report from the OMERACT-Adherence Group. J Rheumatol. 2019 Jan 15 [E-pub ahead of print].
216. Hiligsmann M, Salas M, Hughes DA, Manias E, Gwadry-Sridhar FH, Linck P, et al. Interventions to improve osteoporosis medication adherence and persistence: a systematic review and literature appraisal by the ISPOR Medication Adherence & Persistence Special Interest Group. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2013;24(12):2907-18.
217. Hartman L, Lems WF, Boers M. Outcome measures for adherence data from a medication event monitoring system: A literature review. Journal of clinical pharmacy and therapeutics. 2019;44(1):1-5.
218. Cranney A, Welch V, Tugwell P, Wells G, Adachi JD, McGowan J, et al. Responsiveness of endpoints in osteoporosis clinical trials--an update. J Rheumatol. 1999;26(1):222-8.
219. Taibanguay N, Chaiamnuay S, Asavatanabodee P, Narongroeknawin P. Effect of patient education on medication adherence in patient with rheumatoid arthritis: a randomized controlled trial. Patient Pref Adherence. 2019;13:119-29.
220. Conn VS, Ruppar TM, Enriquez M, Cooper PS. Patient-Centered Outcomes of Medication Adherence Interventions: Systematic Review and Meta-Analysis. Value Health. 2016;19(2):277-85.
221. Clowes J, Peel N, Eastell R. The impact of monitoring on adherence and persistence with antiresorptive treatment for postmenopausal osteoporosis: a randomized controlled trial. J Clin Endocrinol Metab. 2004;89(3):1117-23.
222. Delmas P, Vrijens B, Eastell R, Roux C, Pols H, Ringe J, et al. Effect of monitoring bone turnover markers on persistence with risedronate treatment of postmenopausal osteoporosis. J Clin Endocrinol Metab. 2007;92(4):1296-304.
223. Gorai I, Tanaka Y, Hattori S, Iwaoki Y. Assessment of adherence to treatment of postmenopausal osteoporosis with raloxifene and/or alfacalcidol in postmenopausal Japanese women. J Bone Miner Metab. 2010;28(2):176-84.
224. Kendler D, McClung M, Freemantle N, Lillestol M, Moffett A, Borenstein J, et al. Adherence, preference, and satisfaction of postmenopausal women taking denosumab or alendronate. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2011;22(6):1725-35.
225. McAlister FA, Ye C, Beaupre LA, Rowe BH, Johnson JA, Bellerose D, et al. Adherence to osteoporosis therapy after an upper extremity fracture: a pre-specified substudy of the C-STOP randomized controlled trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2019;30(1):127-34.

226. Tüzün Ş, Akyüz G, Eskiyurt N, Memi A, Kuran B, İçağasıoğlu A, et al. Impact of the training on the compliance and persistence of weekly bisphosphonate treatment in postmenopausal osteoporosis: a randomized controlled study. Int J Med Sci. 2013;10(13):1880-7.
227. Ganda K, Schaffer A, Pearson S, Seibel M. Compliance and persistence to oral bisphosphonate therapy following initiation within a secondary fracture prevention program: a randomised controlled trial of specialist vs. non-specialist management. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2014;25(4):1345-55.
228. Gonnelli S, Caffarelli C, Rossi S, Munno O, Malavolta N, Isaia G, et al. How the knowledge of fracture risk might influence adherence to oral therapy of osteoporosis in Italy: the ADEOST study. Aging Clin Exp Res. 2016;28(3):459-68.
229. Guilera M, Fuentes M, Grifols M, Ferrer J, Badia X. Does an educational leaflet improve self-reported adherence to therapy in osteoporosis? The OPTIMA study. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2006;17(5):664-71.
230. Kung A, Rachman I, Adam J, Roeshadi D, Torralba T, Navarra S, et al. Impact of bone marker feedback on adherence to once monthly ibandronate for osteoporosis among Asian postmenopausal women. International journal of rheumatic diseases. 2009;12(3):216-24.
231. Lai P, Chua S, Chew Y, Chan S. Effects of pharmaceutical care on adherence and persistence to bisphosphonates in postmenopausal osteoporotic women. Journal of clinical pharmacy and therapeutics. 2011;36(5):557-67.
232. Muratore M, Quarta E, Quarta L. Intramuscular neridronate in patients with rheumatoid arthritis using corticosteroids: evaluation of treatment adherence in a randomized, open-label comparison with other bisphosphonates. Acta Biomed. 2013;84(1):23-9.
233. Oral A, Lorenc R. Compliance, persistence, and preference outcomes of postmenopausal osteoporotic women receiving a flexible or fixed regimen of daily risedronate: A multicenter, prospective, parallel group study. Acta Orthop Traumatol Turc. 2015;49(1):67-74.
234. Roh YH, Noh JH, Gong HS, Baek GH. Comparative adherence to weekly oral and quarterly intravenous bisphosphonates among patients with limited heath literacy who sustained distal radius fractures. J Bone Miner Metab. 2018;36(5):589-95.
235. Roux C, Giraudeau B, Rouanet S, Dubourg G, Perrodeau E, Ravaud P. Monitoring of bone turnover markers does not improve persistence with ibandronate treatment. Joint Bone Spine. 2012;79(4):389-92.
236. LeBlanc A, Wang A, Wyatt K, Branda M, Shah N, Houten H, et al. Encounter decision aid vs. clinical decision support or usual care to support patient-centered treatment decisions in osteoporosis: the Osteoporosis Choice randomized trial II. PloS one. 2015;10(5).
237. Silverman S, Nasser K, Nattrass S, Drinkwater B. Impact of bone turnover markers and/or educational information on persistence to oral bisphosphonate therapy: a community setting-based trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2012;23(3):1069-74.
238. Solomon DH, Iversen MD, Avorn J, Gleeson T, Brookhart MA, Patrick AR, et al. Osteoporosis telephonic intervention to improve medication regimen adherence: a large, pragmatic, randomized controlled trial. Arch Intern Med. 2012;172(6):477-83.
239. Akarirmak U, Kocyigit H, Eskiyurt N, Esmaeilzadeh S, Kuru O, Yalcinkaya E, et al. Influence of patient training on persistence, compliance, and tolerability of different dosing frequency regimens of bisphosphonate therapy: an observational study in Turkish

patients with postmenopausal osteoporosis. Acta Orthop Traumatol Turc. 2016;50(4):415-23.
240. Briot K, Ravaud P, Dargent-Molina P, Zylberman M, Liu-Leage S, Roux C. Persistence with teriparatide in postmenopausal osteoporosis; impact of a patient education and follow-up program: the French experience. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2009;20(4):625-30.
241. Nielsen D, Ryg J, Nielsen W, Knold B, Nissen N, Brixen K. Patient education in groups increases knowledge of osteoporosis and adherence to treatment: a two-year randomized controlled trial. Patient education and counseling. 2010;81(2):155-60.
242. Majumdar SR, Johnson JA, Lier DA, Russell AS, Hanley DA, Blitz S, et al. Persistence, reproducibility, and cost-effectiveness of an intervention to improve the quality of osteoporosis care after a fracture of the wrist: results of a controlled trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2007;18(3):261-70.
243. Bianchi M, Duca P, Vai S, Guglielmi G, Viti R, Battista C, et al. Improving adherence to and persistence with oral therapy of osteoporosis. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2015;26(5):1629-38.
244. Cizmic A, Heilmann R, Milchak J, Riggs C, Billups S. Impact of interactive voice response technology on primary adherence to bisphosphonate therapy: a randomized controlled trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2015;26(8):2131-6.
245. Ducoulombier V, Luraschi H, Forzy G, Vandecandelaere M, Houvenagel E. Contribution of phone follow-up to improved adherence to oral osteoporosis treatment. Am J Pharm Benefits. 2015;7(3):e81-e9.
246. Montori V, Shah N, Pencille L, Branda M, Houten H, Swiglo B, et al. Use of a decision aid to improve treatment decisions in osteoporosis: the osteoporosis choice randomized trial. Am J Med. 2011;124(6):549-56.
247. Naranjo A, Ojeda-Bruno S, Bilbao-Cantarero A, Quevedo-Abeledo J, Diaz-González B, Rodríguez-Lozano C. Two-year adherence to treatment and associated factors in a fracture liaison service in Spain. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2015;26(11):2579-85.
248. Robbins B, Rausch KJ, Garcia RI, Prestwood KM. Multicultural medication adherence: a comparative study. J Gerontol Nurs. 2004;30(7):25-32.
249. Schousboe J, DeBold R, Kuno L, Weiss T, Chen Y-T, Abbott IT. Education and phone follow-up in postmenopausal women at risk for osteoporosis: effects on calcium intake, exercise frequency, and medication use. Dis Manag Health Outcomes. 2005;13(6):395-404.
250. Shu AD-H, Stedman MR, Polinski JM, Jan SA, Patel M, Truppo C, et al. Adherence to osteoporosis medications after patient and physician brief education: post hoc analysis of a randomized controlled trial. Am J Manag Care. 2009;15(7):417-24.
251. Stephens MH, Grey A, Fernandez J, Kalluru R, Faasse K, Horne A, et al. 3-D bone models to improve treatment initiation among patients with osteoporosis: A randomised controlled pilot trial. Psychol Health. 2016;31(4):487-97.
252. Stuurman-Bieze A, Hiddink E, Boven J, Vegter S. Proactive pharmaceutical care interventions decrease patients' nonadherence to osteoporosis medication. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2014;25(6):1807-12.

253. Waalen J, Bruning A, Peters M, Blau E. A telephone-based intervention for increasing the use of osteoporosis medication: a randomized controlled trial. Am J Manag Care. 2009;15(8):e60-70.
254. Alhefny A, El-Rahman M, El-Moteleb S, Shedid N, Sakr H, Hassan R. Evaluation of adherence to drug treatment in patients with rheumatoid arthriits. Egypt J Rheumatol Clin Immunol. 2016;4(1):81-92.
255. Miedany Y, Gaafary M, Arousy N, Ahmed I, Youssef S, Palmer D. Arthritis education: the integration of patient-reported outcome measures and patient self-management. Clinical and experimental rheumatology. 2012;30(6):899-904.
256. Brus H, Laar M, Taal E, Rasker J, Wiegman O. Effects of patient education on compliance with basic treatment regimens and health in recent onset active rheumatoid arthritis. Ann Rrheum Dis. 1998;57(3):146-51.
257. Ferguson A, Ibrahim F, Thomas V, Weinman J, Simpson C, Cope A, et al. Improving medication adherence in rheumatoid arthritis (RA): A pilot study. Psychol Health Med. 2015;20(7):781-9.
258. Hill J, Bird H, Johnson S. Effect of patient education on adherence to drug treatment for rheumatoid arthritis: a randomised controlled trial. Ann Rheum Dis. 2001;60(9):869-75.
259. Ravindran V, Jadhav R. The effect of rheumatoid arthritis disease education on adherence to medications and followup in Kerala, India. J Rheumatol. 2013;40(8):1460-1.
260. Joplin SK, van der Zwan R, Bagga H, Joshua F, Wong PK. Pilot study assessing the novel use of musculoskeletal ultrasound in patients with rheumatoid arthritis to improve patient attitudes and adherence to medication. International journal of rheumatic diseases. 2016;19(7):658-64.
261. Stockl KM, Shin JS, Lew HC, Zakharyan A, Harada AS, Solow BK, et al. Outcomes of a rheumatoid arthritis disease therapy management program focusing on medication adherence. J Manag Care Pharm. 2010;16(8):593-604.
262. Unk JA, Brasington R. Efficacy study of multimedia rheumatoid arthritis patient education program. Journal of the American Association of Nurse Practitioners. 2014;26(7):370-7.
263. van den Bemt BJ, den Broeder AA, van den Hoogen FH, Benraad B, Hekster YA, van Riel PL, et al. Making the rheumatologist aware of patients' non-adherence does not improve medication adherence in patients with rheumatoid arthritis. Scandinavian journal of rheumatology. 2011;40(3):192-6.
264. Clifford S, Barber N, Elliott R, Hartley E, Horne R. Patient-centred advice is effective in improving adherence to medicines. Pharm World Sci. 2006;28(3):165-70.
265. Abhishek A, Jenkins W, La-Crette J, Fernandes G, Doherty M. Long-term persistence and adherence on uratelowering treatment can be maintained in primary care--5-year follow-up of a proof-of-concept study. Rheumatology. 2017;56(4):529-33.
266. Mikuls TR, Cheetham TC, Levy GD, Rashid N, Kerimian A, Low KJ, et al. Adherence and Outcomes with Urate-Lowering Therapy: A Site-Randomized Trial. Am J Med. 2018;132(3):354-61.
267. Miedany Y, Gaafary M, Palmer D. Assessment of the utility of visual feedback in the treatment of early rheumatoid arthritis patients: a pilot study. Rheumatol Int. 2012;32(10):3061-8.
268. Homer D, Nightingale P, Jobanputra P. Providing patients with information about disease-modifying anti-rheumatic drugs: individually or in groups? A pilot randomized controlled trial comparing adherence and satisfaction. Musculoskeletal Care. 2009;7(2):78-92.
269. Feldman CH, Wohlfahrt A, Campos A, Gagne JJ, Iversen MD, Massarotti E, et al. Can Patient Navigators Improve Adherence to Disease-Modifying Antirheumatic Drugs? Quantitative Findings From a Six-Month Single-Arm Pilot Intervention. Arthritis Care Res. 2018;70(9):1400-5.

270. Rudd R, Blanch D, Gall V, Chibnik L, Wright E, Reichmann W, et al. A randomized controlled trial of an intervention to reduce low literacy barriers in inflammatory arthritis management. Patient education and counseling. 2009;75(3):334-9.
271. Bond CA, Monson R. Sustained improvement in drug documentation, compliance, and disease control. A four-year analysis of an ambulatory care model. Arch Intern Med. 1984;144(6):1159-62.
272. Pincus T, Callahan LF. What is the natural history of rheumatoid arthritis? Rheumatic diseases clinics of North America. 1993;19(1):123-51.
273. Orchard TR, Wordsworth BP, Jewell DP. Peripheral arthropathies in inflammatory bowel disease: their articular distribution and natural history. Gut. 1998;42(3):387-91.
274. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis. 2005;64 Suppl 2:ii14-7.
275. Sieper J, Braun J, Rudwaleit M, Boonen A, Zink A. Ankylosing spondylitis: an overview. Ann Rheum Dis. 2002;61 Suppl 3:iii8-18.
276. Singh JA, Saag KG, Bridges SL, Jr., Akl EA, Bannuru RR, Sullivan MC, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheum. 2016;68(1):1-26.
277. Contreras-Yanez I, Ponce De Leon S, Cabiedes J, Rull-Gabayet M, Pascual-Ramos V. Inadequate therapy behavior is associated to disease flares in patients with rheumatoid arthritis who have achieved remission with disease-modifying antirheumatic drugs. The American journal of the medical sciences. 2010;340(4):282-90.
278. Smolen JS, Landewe R, Breedveld FC, Buch M, Burmester G, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2014;73(3):492-509.
279. Pound P, Britten N, Morgan M, Yardley L, Pope C, Daker-White G, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. Social science & medicine (1982). 2005;61(1):133-55.
280. Goodacre LJ, Goodacre JA. Factors influencing the beliefs of patients with rheumatoid arthritis regarding disease-modifying medication. Rheumatology. 2004;43(5):583-6.
281. Townsend A, Backman CL, Adam P, Li LC. A qualitative interview study: patient accounts of medication use in early rheumatoid arthritis from symptom onset to early postdiagnosis. BMJ Open. 2013;3(2).
282. Fraenkel L, Seng EK, Cunningham M, Mattocks K. Understanding how patients (vs physicians) approach the decision to escalate treatment: a proposed conceptual model. Rheumatology. 2015;54(2):278-85.
283. Ahlmen M, Nordenskiold U, Archenholtz B, Thyberg I, Ronnqvist R, Linden L, et al. Rheumatology outcomes: the patient's perspective. A multicentre focus group interview study of Swedish rheumatoid arthritis patients. Rheumatology. 2005;44(1):105-10.
284. Sanderson T, Calnan M, Morris M, Richards P, Hewlett S. The impact of patient-perceived restricted access to anti-TNF therapy for rheumatoid arthritis: a qualitative study. Musculoskeletal Care. 2009;7(3):194-209.
285. Stamm TA, Machold KP, Smolen J, Prodinger B. Life stories of people with rheumatoid arthritis who retired early: how gender and other contextual factors shaped their everyday activities, including paid work. Musculoskeletal Care. 2010;8(2):78-86.
286. Sanderson T, Calnan M, Morris M, Richards P, Hewlett S. Shifting normalities: Interactions of changing conceptions of a normal life and the normalisation of symptoms in rheumatoid arthritis. Sociol Health Illn. 2011;33(4):618-33.

287. Choi HK, Hernan MA, Seeger JD, Robins JM, Wolfe F. Methotrexate and mortality in patients with rheumatoid arthritis: a prospective study. Lancet. 2002;359(9313):1173-7.
288. de La Forest Divonne M, Gottenberg JE, Salliot C. Safety of biologic DMARDs in RA patients in real life: A systematic literature review and meta-analyses of biologic registers. Joint Bone Spine. 2017;84(2):133-40.
289. Zolnierek KBH, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. Medical care. 2009;47(8):826-34.
290. O'Connor AM, Rostom A, Fiset V, Tetroe J, Entwistle V, Llewellyn-Thomas H, et al. Decision aids for patients facing health treatment or screening decisions: systematic review. BMJ. 1999;319(7212):731-4.
291. Coates LC, Kavanaugh A, Ritchlin CT. Systematic review of treatments for psoriatic arthritis: 2014 update for the GRAPPA. J Rheumatol. 2014;41(11):2273-6.
292. Zwar N, Richmond R, Borland R, Stillman S, Cunningham M, Litt J. Smoking cessation guidelines for Australian general practice. Australian family physician. 2005;34(6):461-6.
293. Whitlock EP, Orleans CT, Pender N, Allan J. Evaluating primary care behavioral counseling interventions: an evidence-based approach. American journal of preventive medicine. 2002;22(4):267-84.
294. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. Medical care. 2004;42(3):200-9.
295. Kumar K, Gordon C, Barry R, Shaw K, Horne R, Raza K. 'It's like taking poison to kill poison but I have to get better': a qualitative study of beliefs about medicines in Rheumatoid arthritis and Systemic lupus erythematosus patients of South Asian origin. Lupus. 2011;20(8):837-44.
296. Yagasaki K, Komatsu H, Takahashi T. Inner conflict in patients receiving oral anticancer agents: a qualitative study. BMJ Open. 2015;5(4):e006699.
297. Fagbami O, Oluwasanjo A, Fitzpatrick C, Fairchild R, Shin A, Donato A. Factors Supporting and Inhibiting Adherence to HIV Medication Regimen in Women: A Qualitative Analysis of Patient Interviews. The open AIDS journal. 2015;9:45-50.
298. Vervoort SC, Borleffs JC, Hoepelman AI, Grypdonck MH. Adherence in antiretroviral therapy: a review of qualitative studies. AIDS (London, England). 2007;21(3):271-81.
299. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health. 1999;14(1):1-24.
300. Ajzen I. From intentions to actions: A theory of planned behavior. Action control: Springer; 1985. p. 11-39.
301. Selvaag AM, Aulie HA, Lilleby V, Flato B. Disease progression into adulthood and predictors of long-term active disease in juvenile idiopathic arthritis. Ann Rheum Dis. 2016;75(1):190-5.
302. Wipff J, Sparsa L, Lohse A, Quartier P, Kahan A, Deslandre CJ. Impact of juvenile idiopathic arthritis on quality of life during transition period at the era of biotherapies. Joint Bone Spine. 2016;83(1):69-74.
303. Felsenstein S, Reiff AO, Ramanathan A. Transition of Care and Health-Related Outcomes in Pediatric-Onset Systemic Lupus Erythematosus. Arthritis Care Res. 2015;67(11):1521-8.
304. Christie D, Viner R. Adolescent development. BMJ. 2005;330(7486):301-4.
305. Blum RW, Garell D, Hodgman CH, Jorissen TW, Okinow NA, Orr DP, et al. Transition from child-centered to adult health-care systems for adolescents with chronic conditions. A position paper of the Society for Adolescent Medicine. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 1993;14(7):570-6.

306. White PH, Cooley WC. Supporting the Health Care Transition From Adolescence to Adulthood in the Medical Home. Pediatrics. 2018 published on 22 October 2018. doi:10.1542/peds.2018-2587;142(5).
307. Foster HE, Minden K, Clemente D, Leon L, McDonagh JE, Kamphuis S, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. Ann Rheum Dis. 2017;76(4):639-46.
308. Rosen DS, Blum RW, Britto M, Sawyer SM, Siegel DM. Transition to adult health care for adolescents and young adults with chronic conditions: position paper of the Society for Adolescent Medicine. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2003;33(4):309-11.
309. Clemente D, Leon L, Foster H, Minden K, Carmona L. Systematic review and critical appraisal of transitional care programmes in rheumatology. Seminars in arthritis and rheumatism. 2016;46(3):372-9.
310. Clemente D, Leon L, Foster H, Carmona L, Minden K. Transitional care for rheumatic conditions in Europe: current clinical practice and available resources. Pediatr Rheumatol Online J. 2017;15(1):49.
311. Chira P, Ronis T, Ardoin S, White P. Transitioning youth with rheumatic conditions: perspectives of pediatric rheumatology providers in the United States and Canada. J Rheumatol. 2014;41(4):768-79.
312. Shaw KL, Southwood TR, McDonagh JE. Young people's satisfaction of transitional care in adolescent rheumatology in the UK. Child: care, health and development. 2007;33(4):368-79.
313. Jensen PT, Karnes J, Jones K, Lehman A, Rennebohm R, Higgins GC, et al. Quantitative evaluation of a pediatric rheumatology transition program. Pediatr Rheumatol Online J. 2015;13:17.
314. McDonagh JE, Southwood TR, Shaw KL. Unmet education and training needs of rheumatology health professionals in adolescent health and transitional care. Rheumatology. 2004;43(6):737-43.
315. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Med Res Methodol. 2008;8:45.
316. Tuchman LK, Slap GB, Britto MT. Transition to adult care: experiences and expectations of adolescents with a chronic illness. Child: care, health and development. 2008;34(5):557-63.
317. Stinson JN, Toomey PC, Stevens BJ, Kagan S, Duffy CM, Huber A, et al. Asking the experts: Exploring the self-management needs of adolescents with arthritis. Arthritis Care Res. 2008;59(1):65-72.
318. Dickinson AR, Blamires J. Moving on: the experience of young people with juvenile idiopathic arthritis transferring from paediatric to adult services. Neonatal Paediatr Child Health Nurs. 2013;16(2):2.
319. Applebaum MA, Lawson EF, von Scheven E. Perception of transition readiness and preferences for use of technology in transition programs: teens' ideas for the future. International journal of adolescent medicine and health. 2013;25(2):119-25.
320. Raunsbaek Knudsen L, de Thurah A, Bjerrum M. Transition from child to adult care in an outpatient clinic for adolescents with juvenile idiopathic arthritis: An inductive qualitative study. Nursing open. 2018;5(4):546-54.
321. van Staa AL, Jedeloo S, van Meeteren J, Latour JM. Crossing the transition chasm: experiences and recommendations for improving transitional care of young adults, parents and providers. Child: care, health and development. 2011;37(6):821-32.
322. Knight A, Vickery M, Fiks AG, Barg FK. The illness experience of youth with lupus/mixed connective tissue disease: a mixed methods analysis of patient and parent perspectives. Lupus. 2016;25(9):1028-39.
323. Lugasi T, Achille M, Stevenson M. Patients' perspective on factors that facilitate transition from child-centered to adult-centered health care: a theory integrated

metasummary of quantitative and qualitative studies. The Journal of adolescent health : official publication of the Society for Adolescent Medicine. 2011;48(5):429-40.
324. Fegran L, Hall EO, Uhrenfeldt L, Aagaard H, Ludvigsen MS. Adolescents' and young adults' transition experiences when transferring from paediatric to adult care: a qualitative metasynthesis. International journal of nursing studies. 2014;51(1):123-35.
325. Tong A, Wong G, Hodson E, Walker RG, Tjaden L, Craig JC. Adolescent views on transition in diabetes and nephrology. European journal of pediatrics. 2013;172(3):293-304.
326. Colver A, McConachie H, Le Couteur A, Dovey-Pearce G, Mann KD, McDonagh JE, et al. A longitudinal, observational study of the features of transitional healthcare associated with better outcomes for young people with long-term conditions. BMC Med. 2018;16(1):111.
327. Glenton C, Lewin S, Lawrie TA, Barreix M, Downe S, Finlayson KW, et al. Qualitative Evidence Synthesis (QES) for Guidelines: Paper 3 - Using qualitative evidence syntheses to develop implementation considerations and inform implementation processes. Health research policy and systems. 2019;17(1):74.
328. Lewin S, Glenton C, Lawrie TA, Downe S, Finlayson KW, Rosenbaum S, et al. Qualitative Evidence Synthesis (QES) for Guidelines: Paper 2 - Using qualitative evidence synthesis findings to inform evidence-to-decision frameworks and recommendations. Health research policy and systems. 2019;17(1):75.
329. Katz JD, Mamyrova G, Agarwal S, Jones OY, Bollar H, Huber AM, et al. Parents' perception of self-advocacy of children with myositis: an anonymous online survey. Pediatr Rheumatol Online J. 2011;9(1):10.
330. Lawson EF, Hersh AO, Applebaum MA, Yelin EH, Okumura MJ, von Scheven E. Self-management skills in adolescents with chronic rheumatic disease: A cross-sectional survey. Pediatr Rheumatol Online J. 2011;9(1):35.
331. Bingham CA, Scalzi L, Groh B, Boehmer S, Banks S. An assessment of variables affecting transition readiness in pediatric rheumatology patients. Pediatr Rheumatol Online J. 2015;13(1):42.
332. Stollon N, Zhong Y, Ferris M, Bhansali S, Pitts B, Rak E, et al. Chronological age when healthcare transition skills are mastered in adolescents/young adults with inflammatory bowel disease. World J Gastroenterol. 2017;23(18):3349-55.
333. Cruikshank M, Foster HE, Stewart J, Davidson JE, Rapley T. Transitional care in clinical networks for young people with juvenile idiopathic arthritis: current situation and challenges. Clinical rheumatology. 2016;35(4):893-9.
334. Shaw K, Hackett J, Southwood T, McDonagh J. The prevocational and early employment needs of adolescents with juvenile idiopathic arthritis: the adolescent perspective. Br J Occup Ther. 2006;69(3):98-105.
335. Tong A, Jones J, Speerin R, Filocamo K, Chaitow J, Singh-Grewal D. Consumer perspectives on pediatric rheumatology care and service delivery: a qualitative study. J Clin Rheumatol. 2013;19(5):234-40.
336. Cai RA, Chaplin H, Livermore P, Lee M, Sen D, Wedderburn LR, et al. Development of a benchmarking toolkit for adolescent and young adult rheumatology services (BeTAR). Pediatr Rheumatol Online J. 2019;17(1):23.
337. Hanghoj S, Boisen KA, Schmiegelow K, Holge-Hazelton B. Feasibility of a transition intervention aimed at adolescents with chronic illness. International journal of adolescent medicine and health. 2018;30(3):1-8.
338. Knudsen LR, de Thurah A, Bjerrum M. Transition from child to adult care in an outpatient clinic for adolescents with juvenile idiopathic arthritis: An inductive qualitative study. Nursing open. 2018;5(4):546-54.
339. Grande SW, Longacre MR, Palmblad K, Montan MV, Berquist RP, Hager A, et al. Empowering Young People Living With Juvenile Idiopathic Arthritis to Better Communicate With Families and Care Teams: Content Analysis of Semistructured Interviews. JMIR mHealth and uHealth. 2019;7(2):e10401.

340. Harry O, Crosby LE, Smith AW, Favier L, Aljaberi N, Ting TV, et al. Self-management and adherence in childhood-onset systemic lupus erythematosus: what are we missing? Lupus. 2019;28(5):642-50.
341. Reiss JG, Gibson RW, Walker LR. Health care transition: youth, family, and provider perspectives. Pediatrics. 2005;115(1):112-20.
342. Stinson J, McGrath P, Hodnett E, Feldman B, Duffy C, Huber A, et al. Usability testing of an online self-management program for adolescents with juvenile idiopathic arthritis. Journal of medical Internet research. 2010;12(3):e30.
343. O'Sullivan G, O'Higgins S, Caes L, Saetes S, McGuire BE, Stinson J. Self-management needs of Irish adolescents with Juvenile Idiopathic Arthritis (JIA): How can a Canadian web-based programme meet these needs? Pediatr Rheumatol Online J. 2018;16(1):68.
344. Secor-Turner M, Scal P, Garwick A, Horvath K, Wells CK. Living with juvenile arthritis: adolescents' challenges and experiences. Journal of pediatric health care : official publication of National Association of Pediatric Nurse Associates & Practitioners. 2011;25(5):302-7.
345. Wells G, Cranney A, Shea B, Tugwell P. Responsiveness of endpoints in osteoporosis clinical trials. J Rheumatol. 1997;24(6):1230-3.
346. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2006;17(12):1726-33.
347. Sattui SE, Saag KG. Fracture mortality: associations with epidemiology and osteoporosis treatment. Nature reviews Endocrinology. 2014;10(10):592-602.
348. Uhlig T, Moe RH, Kvien TK. The burden of disease in rheumatoid arthritis. PharmacoEconomics. 2014;32(9):841-51.
349. Kanis JA, Johnell O, Oden A, Sembo I, Redlund-Johnell I, Dawson A, et al. Long-term risk of osteoporotic fracture in Malmo. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2000;11(8):669-74.
350. Melton LJ, 3rd, Atkinson EJ, O'Connor MK, O'Fallon WM, Riggs BL. Bone density and fracture risk in men. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 1998;13(12):1915-23.
351. Center JR, Bliuc D, Nguyen ND, Nguyen TV, Eisman JA. Osteoporosis medication and reduced mortality risk in elderly women and men. J Clin Endocrinol Metab. 2011;96(4):1006-14.
352. Singh JA, Christensen R, Wells GA, Suarez-Almazor ME, Buchbinder R, Lopez-Olivo MA, et al. Biologics for rheumatoid arthritis: an overview of Cochrane reviews. Sao Paulo Med J. 2010;128(5):309-10.
353. Jacobsson LT, Turesson C, Nilsson J-Å, Petersson IF, Lindqvist E, Saxne T, et al. Treatment with TNF blockers and mortality risk in patients with rheumatoid arthritis. Ann Rheum Dis. 2007;66(5):670-5.
354. Terkeltaub R. Update on gout: new therapeutic strategies and options. Nature reviews Rheumatology. 2010;6(1):30-8.
355. Aggarwal B, Liao M, Mosca L. Medication adherence is associated with having a caregiver among cardiac patients. Ann Behav Med. 2013;46(2):237-42.
356. Urquhart-Secord R, Craig JC, Hemmelgarn B, Tam-Tham H, Manns B, Howell M, et al. Patient and Caregiver Priorities for Outcomes in Hemodialysis: An International Nominal Group Technique Study. Am J Kidney Dis. 2016;68(3):444-54.
357. Manera KE, Johnson DW, Craig JC, Shen JI, Ruiz L, Wang AY, et al. Patient and Caregiver Priorities for Outcomes in Peritoneal Dialysis: Multinational Nominal Group Technique Study. Clinical journal of the American Society of Nephrology : CJASN. 2019;14(1):74-83.

358. Hughes LD, Done J, Young A. A 5 item version of the Compliance Questionnaire for Rheumatology (CQR5) successfully identifies low adherence to DMARDs. BMC Musculoskelet Disord. 2013;14:286.
359. Haag H, Liang T, Avina-Zubieta JA, De Vera MA. How do patients with systemic autoimmune rheumatic disease perceive the use of their medications: a systematic review and thematic synthesis of qualitative research. BMC Rheumatol. 2018;2(1):9.
360. Conn VS, Hafdahl AR, Cooper PS, Ruppar TM, Mehr DR, Russell CL. Interventions to improve medication adherence among older adults: meta-analysis of adherence outcomes among randomized controlled trials. The Gerontologist. 2009;49(4):447-62.
361. Mazzuca SA. Does patient education in chronic disease have therapeutic value? Journal of chronic diseases. 1982;35(7):521-9.
362. Conn VS, Ruppar TM. Medication adherence outcomes of 771 intervention trials: Systematic review and meta-analysis. Prev Med. 2017;99:269-76.
363. Khan AA, Morrison A, Hanley DA, Felsenberg D, McCauley LK, O'Ryan F, et al. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2015;30(1):3-23.
364. Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2014;29(1):1-23.
365. Harrold LR, Mazor KM, Velten S, Ockene IS, Yood RA. Patients and providers view gout differently: a qualitative study. Chronic illness. 2010;6(4):263-71.
366. Iversen MD, Vora RR, Servi A, Solomon DH. Factors affecting adherence to osteoporosis medications: a focus group approach examining viewpoints of patients and providers. J Geriatr Phys Ther. 2011;34(2):72-81.
367. Kelly A, Sumpton D, O'Sullivan C, Meara A, Nieuwlaat R, Tugwell P, et al., editors. Scope and Consistency of Adherence Related Outcomes in Randomized Controlled Trials of Interventions for Improving Medication Adherence. 2018 ACR/ARHP Annual Meeting; 2017; San Diego, California: Arthritis Rheumatol.
368. Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino MA, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. Journal of clinical epidemiology. 2014;67(7):745-53.
369. De Geest S, Zullig LL, Dunbar-Jacob J, Helmy R, Hughes DA, Wilson IB, et al. ESPACOMP Medication Adherence Reporting Guideline (EMERGE). Ann Intern Med. 2018;169(1):30-5.
370. Blaschke TF, Osterberg L, Vrijens B, Urquhart J. Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. Annu Rev Pharmacol Toxicol. 2012;52:275-301.
371. Yadav K, Vock DM, Matas AJ, Robiner WN, Nevins TE. Medication adherence is associated with an increased risk of cancer in kidney transplant recipients: a cohort study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2018:364-70.
372. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Journal of clinical epidemiology. 2009;62(10):1006-12.
373. Singh JA. Challenges faced by patients in gout treatment: a qualitative study. J Clin Rheumatol. 2014;20(3):172.
374. Fair C, Cuttance J, Sharma N, Maslow G, Wiener L, Betz C, et al. International and Interdisciplinary Identification of Health Care Transition Outcomes. JAMA pediatrics. 2016;170(3):205-11.

375. Hilderson D, Westhovens R, Wouters C, Van der Elst K, Goossens E, Moons P. Rationale, design and baseline data of a mixed methods study examining the clinical impact of a brief transition programme for young people with juvenile idiopathic arthritis: the DON'T RETARD project. BMJ Open. 2013;3(12):e003591.
376. Demonceau J, Ruppar T, Kristanto P, Hughes DA, Fargher E, Kardas P, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. Drugs. 2013;73(6):545-62.
377. Glenton C, Lewin S, Norris S, Norris S. WHO handbook for guideline development. 2nd ed. Switzerland. World Health Organization; 2014. Chapter 15: Using evidence from qualitative research to develop WHO guidelines; p183-200.
378. DiMatteo MR. Social support and patient adherence to medical treatment: a meta-analysis. Health Psychol. 2004;23(2):207-18.
379. Mongkhon P, Ashcroft DM, Scholfield CN, Kongkaew C. Hospital admissions associated with medication non-adherence: a systematic review of prospective observational studies. BMJ quality & safety. 2018;27(11):902-14.
380. McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. The Annals of pharmacotherapy. 2002;36(9):1331-6.
381. Senst BL, Achusim LE, Genest RP, Cosentino LA, Ford CC, Little JA, et al. Practical approach to determining costs and frequency of adverse drug events in a health care network. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2001;58(12):1126-32.
382. Pharmaceutical Group of the European Union. https://www.pgeu.eu/en/policy/5-adherence.html (accessed 29/2/2019).
383. Oecd. Health at a glance: Europe 2016: State of health in the EU cycle: OECD; 2016.
384. Bosworth HB, Granger BB, Mendys P, Brindis R, Burkholder R, Czajkowski SM, et al. Medication adherence: a call for action. Am Heart J. 2011;162(3):412-24.
385. Marie-Schneider P, Aslani P. Adherence policy, education and practice - an international perspective. Pharm Pract. 2010;8(4):209-12.
386. Smith E, Hoy DG, Cross M, Vos T, Naghavi M, Buchbinder R, et al. The global burden of other musculoskeletal disorders: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014;73(8):1462-9.
387. Tak PP, Kalden JR. Advances in rheumatology: new targeted therapeutics. Arthritis Res Ther. 2011;13(1):S5.
388. Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. Lancet. 2011;377(9773):1276-87.
389. Schumacher Jr H, Becker M, Lloyd E, MacDonald P, Lademacher C. Febuxostat in the treatment of gout: 5-yr findings of the FOCUS efficacy and safety study. Rheumatology. 2009;48(2):188-94.
390. Sale JE, Gignac MA, Hawker G, Frankel L, Beaton D, Bogoch E, et al. Decision to take osteoporosis medication in patients who have had a fracture and are'high'risk for future fracture: a qualitative study. BMC Musculoskelet Disord. 2011;12(1):92.
391. Linn AJ, van Weert JC, Schouten BC, Smit EG, van Bodegraven AA, van Dijk L. Words that make pills easier to swallow: a communication typology to address practical and perceptual barriers to medication intake behavior. Patient preference and adherence. 2012;6:871-85.
392. Kirkham JJ, Clarke M, Williamson PR. A methodological approach for assessing the uptake of core outcome sets using ClinicalTrials. gov: findings from a review of randomised controlled trials of rheumatoid arthritis. BMJ. 2017;357:j2262.
393. Cheung PP, de Wit M, Bingham CO, 3rd, Kirwan JR, Leong A, March LM, et al. Recommendations for the Involvement of Patient Research Partners (PRP) in OMERACT Working Groups. A Report from the OMERACT 2014 Working Group on PRP. J Rheumatol. 2016;43(1):187-93.

394. Richards P, De Wit M. The OMERACT glossary for patient research partners. URL: https://wwwomeractorg/pdf/OMERACT_Glossarypdf. 2004.
395. Song Initiative. The SONG Handbook. Version 1.0 June 2017, Sydney, Australia. Available at songinitiative.org/reports-and-publications/.
396. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77-101.
397. Urquhart-Secord R, Craig JC, Hemmelgarn B, Tam-Tham H, Manns B, Howell M, et al. Patient and caregiver priorities for outcomes in hemodialysis: an international nominal group technique study. Am J Kidney Dis. 2016;68(3):444-54.
398. Fried BJ, Boers M, Baker PR. A method for achieving consensus on rheumatoid arthritis outcome measures: the OMERACT conference process. J Rheumatol. 1993;20(3):548-51.
399. Orbai AM, de Wit M, Mease P, Shea JA, Gossec L, Leung YY, et al. International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Ann Rheum Dis. 2017;76(4):673-80.
400. Linstone HA, Turoff M. The Delphi method: Techniques and applications: Addison-Wesley Reading, MA; 1975.
401. Bartlett SJ, Hewlett S, Bingham CO, 3rd, Woodworth TG, Alten R, Pohl C, et al. Identifying core domains to assess flare in rheumatoid arthritis: an OMERACT international patient and provider combined Delphi consensus. Ann Rheum Dis. 2012;71(11):1855-60.
402. Taylor WJ, Schumacher HR, Jr., Baraf HS, Chapman P, Stamp L, Doherty M, et al. A modified Delphi exercise to determine the extent of consensus with OMERACT outcome domains for studies of acute and chronic gout. Ann Rheum Dis. 2008;67(6):888-91.
403. Gazi H, Pope JE, Clements P, Medsger TA, Martin RW, Merkel PA, et al. Outcome measurements in scleroderma: results from a delphi exercise. J Rheumatol. 2007;34(3):501-9.
404. Bartlett SJ, Hewlett S, Bingham CO, Woodworth TG, Alten R, Pohl C, et al. Identifying core domains to assess flare in rheumatoid arthritis: an OMERACT international patient and provider combined Delphi consensus. Ann Rheum Dis. 2012;71(11):1855-60.
405. Akins RB, Tolson H, Cole BR. Stability of response characteristics of a Delphi panel: application of bootstrap data expansion. BMC Med Res Methodol. 2005;5(1):37.
406. Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. PLoS Med. 2011;8(1):e1000393.
407. Flynn TN, Louviere JJ, Peters TJ, Coast J. Best–worst scaling: What it can do for health care research and how to do it. J Health Econ. 2007;26(1):171-89.
408. Mokkink LB, Prinsen CA, Bouter LM, de Vet HC, Terwee CB. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) and how to select an outcome measurement instrument. Braz J Phys Ther. 2016;20(2):105-13.
409. Arkell P, Ryan S, Brownfield A, Cadwgan A, Packham J. Patient experiences, attitudes and expectations towards receiving information about anti-TNF medication–"It could give me two heads and I'd still try it!". BMC Musculoskelet Disord. 2013;14(1):165.
410. Backman CL, Smith LdF, Smith S, Montie PL, Suto M. Experiences of mothers living with inflammatory arthritis. Arthritis Rheum. 2007;57(3):381-8.
411. Bath J, Hooper J, Steel D, Reed E, Giles M, Woodland J. Patient perceptions of rheumatoid arthritis. Nurs Stand. 1999;14(3):35-8.
412. Boonen A, van Berkel M, Cieza A, Stucki G, van der Heijde D. Which aspects of functioning are relevant for patients with ankylosing spondylitis: results of focus group interviews. J Rheumatol. 2009;36(11):2501-11.

413. Chilton F, Collett RA. Treatment choices, preferences and decision-making by patients with rheumatoid arthritis. Musculoskeletal Care. 2008;6(1):1-14.
414. Cinar FI, Cinar M, Yilmaz S, Simsek I, Erdem H, Pay S. Thoughts and perceptions of ankylosing spondylitis patients with regard to TNF inhibitors. Rheumatol Int. 2014;34(7):979-86.
415. Donovan JL, Blake DR. Patient non-compliance: deviance or reasoned decision-making? Social science & medicine (1982). 1992;34(5):507-13.
416. Edwards J. An exploration of patients' experiences of anti-TNF therapy. Musculoskeletal Care. 2004;2(1):40-50.
417. Flurey CA, Morris M, Pollock J, Richards P, Hughes R, Hewlett S. A Q-methodology study of flare help-seeking behaviours and different experiences of daily life in rheumatoid arthritis. BMC Musculoskelet Disord. 2014;15:364.
418. Flurey CA, Morris M, Richards P, Hughes R, Hewlett S. It's like a juggling act: rheumatoid arthritis patient perspectives on daily life and flare while on current treatment regimes. Rheumatology. 2014;53(4):696-703.
419. Popa-Lisseanu MGG, Greisinger A, Richardson M, O'Malley KJ, Janssen NM, Marcus DM, et al. Determinants of treatment adherence in ethnically diverse, economically disadvantaged patients with rheumatic disease. J Rheumatol. 2005;32(5):913-9.
420. Grønning K, Lomundal B, Koksvik HS, Steinsbekk A. Coping with arthritis is experienced as a dynamic balancing process. A qualitative study. Clinical rheumatology. 2011;30(11):1425-32.
421. Hart RI, Foster HE, McDonagh JE, Thompson B, Kay L, Myers A, et al. Young people's decisions about biologic therapies: who influences them and how? Rheumatology. 2015;54:1294-301.
422. Headland M. Using a website containing patient narratives to understand people's experiences of living with arthritis. J Orthop Nurs. 2006;10(2):106-12.
423. Hirsh D, Clerehan R, Staples M, Osborne RH, Buchbinder R. Patient assessment of medication information leaflets and validation of the Evaluative Linguistic Framework (ELF). Patient education and counseling. 2009;77(2):248-54.
424. Hofmann D, Ibrahim F, Rose D, Scott DL, Cope A, Wykes T, et al. Expectations of new treatment in rheumatoid arthritis: developing a patient-generated questionnaire. Health Expect. 2015;18(5):995-1008.
425. Kett C, Flint J, Openshaw M, Raza K, Kumar K. Self-management strategies used during flares of rheumatoid arthritis in an ethnically diverse population. Musculoskeletal Care. 2010;8(4):204-14.
426. Kristiansen TM, Primdahl J, Antoft R, Hørslev-Petersen K. It Means Everything: Continuing Normality of Everyday Life for People with Rheumatoid Arthritis in Early Remission. Musculoskeletal Care. 2012;10(3):162-70.
427. Larsson I, Bergman S, Fridlund B, Arvidsson B. Patients' dependence on a nurse for the administration of their intravenous anti-TNF therapy: A phenomenographic study. Musculoskeletal Care. 2009;7(2):93-105.
428. Lempp H, Scott D, Kingsley G. The personal impact of rheumatoid arthritis on patients' identity: A qualitative study. Chronic illness. 2006;2(2):109-20.
429. Lempp H, Hofmann D, Hatch SL, Scott DL. Patients' views about treatment with combination therapy for rheumatoid arthritis: a comparative qualitative study. BMC Musculoskelet Disord. 2012;13:200.
430. Li LC, Adam PM, Backman CL, Lineker S, Jones CA, Lacaille D, et al. Proof-of-concept study of a Web-based methotrexate decision aid for patients with rheumatoid arthritis. Arthritis Care Res 2014;66(10):1472-81.
431. Lindblad AK, Hartzema AG, Jansson L, Feltelius N. Patients' views of priority setting for new medicines. A qualitative study of patients with rheumatoid arthritis. Scandinavian journal of rheumatology. 2002;31(6):324-9.

432. Linden C, Bjorklund A. Living with rheumatoid arthritis and experiencing everyday life with TNF-alpha blockers. Scand J Occup Ther. 2010;17(4):326-34.
433. Lorish CD, Richards B, Brown S. Perspective of the patient with rheumatoid arthritis on issues related to missed medication. Arthritis Care Res. 1990;3(2):78-84.
434. Markusse IM, Akdemir G, Huizinga TW, Allaart CF. Drug-free holiday in patients with rheumatoid arthritis: a qualitative study to explore patients' opinion. Clinical rheumatology. 2014;33(8):1155-9.
435. Marshall NJ, Wilson G, Lapworth K, Kay LJ. Patients' perceptions of treatment with anti-TNF therapy for rheumatoid arthritis: a qualitative study. Rheumatology. 2004;43(8):1034-8.
436. McArthur MA, Birt L, Goodacre L. "Better but not best": A qualitative exploration of the experiences of occupational gain for people with inflammatory arthritis receiving anti-TNFalpha treatment. Disability and rehabilitation. 2015;37(10):854-63.
437. Meade T, Sharpe L, Hallab L, Aspanell D, Manolios N. Navigating Motherhood Choices in the context of Rheumatoid Arthritis: Women's Stories. Musculoskeletal Care. 2013;11(2):73-82.
438. Meyfroidt S, Van der Elst K, De Cock D, Joly J, Westhovens R, Hulscher M, et al. Patient experiences with intensive combination-treatment strategies with glucocorticoids for early rheumatoid arthritis. Patient education and counseling. 2015;98(3):384-90.
439. Minnock P, Ringnér A, Bresnihan B, Veale D, FitzGerald O, McKee G. Perceptions of the cause, impact and management of persistent fatigue in patients with rheumatoid arthritis following tumour necrosing factor inhibition therapy. Musculoskeletal care. 2016:23-35.
440. O'Hare R, Muir A, Chapman S, Watson A, Hudson SA. Identification of the pharmaceutical care issues of rheumatoid arthritis patients in secondary care. Pharm World Sci. 2001;23(5):183-4.
441. Sanderson T, Morris M, Calnan M, Richards P, Hewlett S. What outcomes from pharmacologic treatments are important to people with rheumatoid arthritis? Creating the basis of a patient core set. Arthritis Care Res. 2010;62(5):640-6.
442. Sanderson T, Morris M, Calnan M, Richards P, Hewlett S. 'It's this whole picture, this well-being': Patients' understanding of 'feeling well' with rheumatoid arthritis. Chronic illness. 2010;6(3):228-40.
443. Sanderson T, Hewlett S, Richards P, Morris M, Calnan M. Utilizing qualitative data from nominal groups: Exploring the influences on treatment outcome prioritization with rheumatoid arthritis patients. J Health Psychol. 2012;17(1):132-42.
444. Sandhu S, Veinot P, Embuldeniya G, Brooks S, Sale J, Huang S, et al. Peer-to-peer mentoring for individuals with early inflammatory arthritis: Feasibility pilot. BMJ Open. 2013;3(3):e002267.
445. Schildmann J, Grunke M, Kalden JR, Vollmann J. Information and participation in decision-making about treatment: A qualitative study of the perceptions and preferences of patients with rheumatoid arthritis. J Med Ethics. 2008;34(11):775-9.
446. Stockdale J, Goodacre L. 'It's magic stuff': the experiences of patients with ankylosing spondylitis taking anti-TNF-alpha medication. Musculoskeletal Care. 2009;7(3):162-77.
447. Stockdale J, Selfe J, Roddam H. An Exploration of the Impact of Anti-TNFα Medication on Exercise Behaviour in Patients with Ankylosing Spondylitis. Musculoskeletal Care. 2014;12(3):150-9.
448. van der Elst K, Meyfroidt S, De Cock D, De Groef A, Binnard E, Moons P, et al. Unraveling patient-preferred health and treatment outcomes in early rheumatoid arthritis: A longitudinal qualitative study. Arthritis Care Res. 2016;68(9):1278-87.
449. Zhang J, Verhoef MJ. Illness management strategies among Chinese immigrants living with arthritis. Social science & medicine (1982). 2002;55(10):1795-802.