The information required by people with inflammatory arthritis to take methotrexate: a mixed-methods systematic review

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Abstract

Objectives. This mixed-methods systematic review aimed to identify and synthesize knowledge of the characteristics, content, and preferred format of information to support people with inflammatory arthritis (IA) to take methotrexate.

Methods. A literature search using MEDLINE, The Cochrane Library, Embase, CINAHL, PsychInfo, GreyEU, Web of Science and Open Dissertation was conducted to identify all studies published from 2000 to December 2022. Included studies detailed factors related to methotrexate (MTX) related information needs of people with inflammatory arthritis > 18 years in English. Joanna Briggs Institute Guidelines (JBI) for convergent integrated mixed-methods systematic reviews were followed using validated tools for data extraction and quality. Data was analysed using reflexive thematic analysis.

Results. Thirteen studies (seven quantitative, two mixed-methods and four qualitative) were included involving 3425 adults, mainly female n=2434 (71%), age 20-84 years. An overarching theme of a requirement for person-centred care was developed with three interlinking themes: 1: Accepting the need for treatment with MTX, 2: Concerns about taking MTX, 3: A need for tailored information and support. Limitations of the evidence were use of heterogeneous outcome measures and instruments to measure information needs.

Conclusion. People with IA have individual, multi-faceted information, and support needs about MTX that are often unresolved when a one-size-fits-all approach is used. The findings can inform rheumatology training to support a person-centred approach to identifying and addressing specific needs, concerns and the development of consistent easy-to-understand accessible MTX information.

Keywords: Inflammatory Arthritis. Methotrexate. Information needs. DMARD counselling. DMARDs.

Rheumatology key messages:
- People with inflammatory arthritis have individual information and support needs when starting methotrexate.
- Addressing these needs supports people to start and continue methotrexate.
- Current one-size-fits-all approaches to providing information about methotrexate do not meet individual needs.
Graphical abstract

Methotrexate information needs of people with IA

We undertook a mixed-methods systematic review to identify the information that people with Inflammatory Arthritis need to take Methotrexate

1. Person-centred
2. Tailored to individual concerns about benefits and risks of treatment
3. Available in easy-to-understand language and accessible formats

Methods

Logan et al. The information required by people with Inflammatory Arthritis to take Methotrexate: A mixed-methods systematic review. Rheumatology

Key findings

Introduction

Guidelines recommend that people with Inflammatory Arthritis (IA) have access to tailored, needs-based information when starting treatment with Methotrexate (MTX) (1). Rheumatoid Arthritis is the most common form of IA, and MTX is recommended as first line DMARD treatment for RA (2). Existing provision of information about MTX varies across and within healthcare provision in quality and content, being available from formal and informal sources. Formal sources include the information produced by healthcare and pharmaceutical organisations, and rheumatology patient associations. Informal sources include peer information such as in-person and digital interactions including social media chat pages, and the internet. Little is known about the perspective of people with IA regarding the information required to start and continue to take MTX. Despite receiving information many people with IA fail to start or continue to take Methotrexate, often due to concerns about the risk-benefit profile of the drug (3) resulting in inadequately controlled disease, worse clinical outcomes, increased risk of disability and reduced quality of life. Furthermore, rheumatology services are experiencing significant workload pressures often with inadequate staffing levels (4) that have been shown to negatively impact care outcomes (5). Therefore, an
evaluation of current methods and materials for providing information about MTX should be undertaken. This would identify whether existing provision of MTX information meets the expectations and needs of people with IA, to support them to start and continue to take MTX and ensure that healthcare resources are being used effectively. This mixed-methods systematic review aimed to identify, appraise, and synthesize existing evidence (6) about the characteristics, content, and format of information about MTX that people with IA require to start and continue to take MTX.

**Methods**

**General methodology**

A mixed-methods systematic review (MMSR) of the characteristics, content, and format of information about MTX required by people with IA to start and continue taking MTX was undertaken. The systematic review protocol is registered in PROSPERO CRD42022325249. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (7) guidelines were followed.

**Search strategy and eligibility**

The literature search strategy was designed with the guidance of an information scientist (NC) and performed by author SL, using comprehensive MEsh and free-text terms for the concepts Inflammatory Arthritis, Information needs, Methotrexate and Disease Modifying Anti-Rheumatic Drugs (DMARDs) and included quantitative, qualitative, and mixed methods literature. The full search was intentionally broad to retrieve all relevant studies and conducted on MEDLINE, Embase, CINAHL, Cochrane Library, PsychInfo, Grey EU, Web of Science and Open Dissertation bibliographic databases and Google search engine. Details of the search strategy are provided in Supplementary Data S1, available at *Rheumatology* online. Studies eligible for inclusion in this systematic review needed to report information needs of people > 18 years in English, with Inflammatory Arthritis starting, taking or with experience of taking DMARDS where MTX was identified as the major conventional synthetic DMARD (csDMARD). Information about MTX included written, audio-visual, and verbal formats. As MTX has been the first line csDMARD of choice for RA since 2000 (8) articles published since 2000 to December 2022 were included.

**Article selection and data extraction**

Title and abstract screening was undertaken by SL against the pre-determined inclusion criteria. Reference lists of included articles were screened by SL for additional studies. Full text articles were obtained where possible, abstracts not including adequate information were excluded. All articles meeting inclusion criteria were screened independently by SL and SR, any discrepancies were
discussed, and consensus achieved. Data was extracted independently by SL and SR, using an adapted version of the JBI Mixed Methods Systematic Review (JBI-MMSR) data extraction tool (9). Data extracted included country of origin, study design, methodology, sample characteristics, relevant statistics and descriptive statistics, details of relevant themes with illustrative qualitative data and consensus achieved.

Quality assessment of included studies:
Study quality appraisal followed JBI-MMSR methodological guidance (10) using relevant evidence based, peer reviewed, standardised JBI critical appraisal tools (11,12). Critical appraisal criteria are available in Supplementary Data S2, available at Rheumatology online. SL and SR independently appraised the quality of all included studies, SL undertook data extraction, with 20% of studies reviewed to ensure consistency of data extraction by SR.

Analysis
Data analysis followed JBI-MMSR Convergent Integrated guidelines (13). Relevant results from cross-sectional surveys including descriptive statistics such as percentages were transformed into narrative interpretation, i.e. 75% was transformed into three out of four, that answered the review questions (14, 15). Quantitative and qualitative datasets were then combined to produce a unique qualitative dataset for analysis. Data was coded, synthesized, and analysed using reflexive thematic analysis (16). Themes were generated identifying the characteristics, format, and content of MTX information and evaluated whether existing methods of providing information matched expectations and needs of people with IA to take MTX.

Results
The systematic screening process is shown in the PRISMA flow diagram (7), (Figure 1). A total of n= 8468 records were identified, following removal of n= 2393 duplicate records, n= 6075 records were screened and n= 5906 excluded. Eligibility assessment of n=169 records resulted in n=156 being excluded. Thirteen studies were included, seven cross-sectional, four qualitative and two mixed-methods from six countries: Australia (17,18), Canada (19), Japan (20), Netherlands (21,22,23), Spain (24,25) and the UK (26,27,28,29). Detailed information of study design, population, research methods and results of the included studies are included in Supplementary Table S1, available at Rheumatology online.
A total of 3425 adults >18 years, mainly female n=2434 (71%), age 20-84 years were included. Five studies (17,19,24,27,28) included participants diagnosed for less than two years. Most studies (n=8) reported the majority of participants with disease duration of more than ten years (18,20,21,22,23,25,26,29). Six studies (20,22,24,26,28,29) explored aspects of information needs about DMARDs, two (18,27) explored beliefs about MTX information specifically, one (17) explored beliefs about MTX and patient reported use of MTX, two (23,24) explored factors affecting adherence to MTX, and two (19,21) explored strategies to support people to take MTX.

Reflexive thematic analysis of integrated study findings.
An overarching theme of ‘A need for person-centred care,’ (30) was developed, rooted in three main themes; 1) accepting the need to take MTX, 2) concerns about taking MTX, 3: a need for tailored information and support as outlined in Figure 2.

A need for person-centred care: People described individual, far-reaching information and support needs that went beyond information about MTX, to enable them to comprehend and adjust to the life-changing impact of Inflammatory Arthritis, ‘To know what you’re dealing with,’ (19). The level of disruption on normal life and daily activities influenced the information that people need to take MTX.

Accepting the need for Methotrexate: Many people wanted to receive information to help them understand the use of MTX in the context of IA. This included information about IA, drug treatments (19,24), and how IA was likely to affect them in the future (24). Variation existed regarding preferences for the timing (26,27), content and format of information about IA and MTX (18,19,24,27). Some felt overwhelmed when newly diagnosed with IA (19,27) experiencing difficulty in absorbing lots of information, particularly when also receiving MTX information (27). This led some to accept recommendations from rheumatologists to start MTX (24,27), without time to reflect on the information and reduced opportunities for shared decision making (24). Many people were unable to recall information (22,27,28) they received about their diagnosis and MTX whilst some did not recall receiving any information (25). However, receiving information at diagnosis to support acceptance of the need for treatment and development of self-management skills was important for
some 19). Adjusting to a diagnosis of IA was seen as a process (27), some described losing their identity while learning to live with IA. For some this took several years (19) and resulted in difficulty accepting the need for treatment (19).

Treatment with MTX was accepted by others due to the impact upon daily life, seeking relief of pain and improved quality of life (27). Some who witnessed others with IA struggling with pain and disability (19,27), or responding well to treatment with MTX (19,25,27) found it easier to accept MTX. Those experiencing fewer symptoms and less impact from IA sometimes found it difficult to accept the need for MTX, perceiving this to be a ‘strong, toxic drug’ (27). Support from healthcare professionals (HCPs) helped some to understand the rationale for treatment with MTX (27).

Information requirements included why people should take MTX (18, 19,22,24,27), how likely they were to respond to MTX (19, 20), time until they could expect benefit from MTX (23), how MTX works (19, 23), and how to recognise if MTX was working (27). Illustrative quotes are provided in Table 1.

**Table 1: Accepting the need to take Methotrexate here**

**Concerns about taking Methotrexate:** Reticence was expressed by many about taking MTX. Some were concerned that MTX was not helpful for IA (23) and wanted information about possible risks and long-term harms (17,18,20,21,22,23,25,27,29), possible lifestyle restrictions including limiting alcohol intake (19, 22, 25) and alternative treatment options (19, 25).

Receiving verbal and written information around the time of diagnosis, that highlighted the need for care with timing and dosage of MTX, requirements for safety monitoring blood tests and possible side-effects generated more concerns for some (27). Others reported a pragmatic approach balancing concerns about MTX with optimism side-effects would not affect them (27). Satisfaction with information about side-effects (18,22,29) varied, with many seeking reassurance (20) and more information (18, 21, 22, 29), including the likelihood of experiencing side-effects (20,22,25) to support decisions regarding starting MTX (25). Some remained concerned about side effects but decided to start MTX and sought more information (18,22).

Those with more concerns often used multiple information sources seeking to resolve concerns and gain reassurance about the necessity to take MTX (18,23). Using multiple information sources could result in conflicting information that increased concerns (21,29), creating a barrier to starting MTX.
Information avoidance was described by some who chose not to read “official” information (27) in a bid to minimise concerns about side-effects, whereas others rationalised concerns accepting that all drugs have side-effects (27). Information about alternative treatment options was important for those concerned that the risk of side-effects outweighed potential benefits of MTX, however many reported not receiving such information (24).

Many were concerned about possible adverse effects and implications on lifestyle (19,22,25). Specific concerns included the impact of MTX on sex life, which some felt was not adequately addressed (22). The risk of or experiencing MTX related nausea was undesirable leading to concerns about potential long-term harms from taking MTX (19). Some identified concerns about the risk of developing side-effects when taking multiple medications (19), and whether MTX was the cause of hair loss (25). Fears about the possibility of MTX causing drowsiness were not always adequately addressed (22). Conflicting guidelines about restricting alcohol intake frequently led to anxieties (19,22,25), appeared to increase concerns about the toxicity of MTX, deemed patronizing (23), and created a burden of treatment for some. Many wanted information about possible drug interactions (19,21,22,25), dietary restrictions or interactions between food and MTX (25). Practical aspects such as deciding which day of the week to take MTX, organising MTX supplies, problems opening packaging, managing sub-cutaneous MTX injection devices and side-effects such as local injection site reactions, managing associated toxic waste (19,21,23,25,27) and the importance of safety monitoring (27) also resulted in concerns and difficulties. Illustrative quotes are provided in Table 2.

**[Table 2: Concerns about taking Methotrexate here]**

**The need for tailored information and support:** Access to, and perceptions of information about MTX varied, reflective in part of differing access to healthcare provision including whether people access to a broader multi-disciplinary team (MDT) or solely a rheumatologist. Provision of routine, standardised information that did not meet information needs was frequently reported (19,21,23,24), whilst many expressed preferences to receive verbal, tailored information about MTX from HCPs (18,21,24). Information provided by rheumatologists (17,18,21,22,25,26,28,29) and HCPs (24,26,27) was often valued (27). Varying satisfaction was reported with the quality of information provided (25,26,29), including the use and action of MTX (22). Access to HCPs varied, information from hospital pharmacists was helpful for some (19,26). Rheumatology nurses provided valuable information (19,26), that was seen to support people to gain a better understanding of IA, and the need for treatment with MTX (27).
Information about the likelihood of improvement from taking MTX together with the risk of disease progression (27) if IA was left untreated helped people to understand the rationale for taking MTX. Perceptions about the quantity and timing of MTX information varied (18,22,24,26,27). Some felt overloaded (27) with information whilst others recalled receiving little, or no information in (25,29) in the consultation. However, unmet information needs were commonly reported (17,18,19,21,22,23,24,27,28,29) after receiving information about MTX. This included wanting to understand more about IA, the rationale for taking MTX (29), the likelihood of treatment response and experiencing side-effects to enable people to be involved in decisions about taking MTX (24).

People varied as to how much involvement they wanted in decisions about IA treatment (21,24,25,27,29). Around the time of diagnosis some relied upon rheumatologist recommendations (27), whilst others wanted the opportunity to be more involved (24,29). Time constraints resulting from workload pressures were recognised as limiting the time spent with each person (24).

Many reported unmet information needs (21,24,29), requiring information and support to develop self-management skills to cope with IA (23) and manage practical issues around taking MTX (23). This included how to safely manage MTX during intercurrent illness including infection, action to be taken when experiencing side-effects (21,24) and managing disease flares. Direct access to rheumatology services in-between appointments (25) for information, from rheumatologists (23) and HCPs via telephone or digital helplines was important for many (21), particularly as safety information could be difficult to remember (28). Disparity in access to such services was reported (20,24), some perceived rheumatology HCPs to be gate-keepers of information, controlling when and how people accessed or received information about IA and MTX which impacted upon the ability to be involved in SDM (24). Written information received ahead of consultations supported involvement in care for some (24). Person-centred care involving two-way discussions where people felt listened to (21,29) and had opportunities to ask questions (29) were valued. However, few reported person-centred care, some felt unheard, reporting dismissed concerns resulting in frustration (23) about unmet information needs. Varying perceptions of written MTX information leaflets provided by HCPs (25,26,27,28) were reported, being helpful in reinforcing verbal information (19,25) for some. Others reported concerns generated by the emphasis on safety information (27), and lacking detail about the benefits of MTX, mechanism of action and duration of treatment (27). The Patient Information leaflet (PIL) within MTX packaging was the only source of information for some. Technical language used in PILs was difficult to understand for some (25). Long lists of potential drug interactions,
including the risk of death generated concerns about the safety of MTX (24). Others chose to avoid written information to avoid further anxiety or concerns (27).

Clear, easy to understand, comprehensive written information (23,25) was seen to support MTX use (23), visual aids including infographs supported understanding of both written and verbal information provided by HCPs (19,24). Digital sources of information including social media, internet search engines and websites, reinforced verbal and written information provided by HCPs (18,19,21,24,26,29). However, perceptions of internet-based information differed, with some concerns about the reliability of information (21,24), others reported helpful information and educational websites (18) that supported MTX use. Others reported ‘scary’ information (27) that generated concerns, leading to avoidance of such sources. Signposting to reliable websites and sources of digital information (24) by HCPs supported development of self-management skills including use of complementary therapies (24). Many people valued support from friends, family, carers, and other people with IA, helping them come to terms with a diagnosis of IA (19,24,27), living with IA, accepting treatment with MTX, and successfully taking MTX (19,23,25,27). A clear need for adequate, reliable information for family and friends was identified (19) to help them understand the impact of IA, and the need and complexities of treatment with MTX. Peer support from other people with IA was helpful for some (19, 25), particularly when unable to get the information they wanted from HCPs and other formal sources to resolve concerns. Learning of other people’s positive experiences of living with IA and taking MTX was reported to be helpful in supporting people to start and persevere with MTX (19,27). Conversely, hearing similar worries or poor experiences of taking MTX often reinforced concerns, making it difficult for people to accept the need for MTX, and did not support people to take MTX (27). Table 3 presents illustrative quotes.

**Table 3: The need for tailored information and support here**

**Strength of evidence**

In line with JBI methodological guidance for MMSR an assessment of the strength of the evidence was not made due to the complexities of integrating quantitative and qualitative data and data transformation (8).

**Discussion**

This study provided a thematic synthesis of the information people with IA require to take MTX. The results of this review demonstrated individual multi-faceted information needs about the diagnosis
of IA and treatment with MTX that change during the course of the disease (34). These findings correlate with findings from previous studies (3, 33, 34) identifying how the relationship between beliefs and concerns about taking medication influences whether people will start and continue to take MTX (33).

Wide variation was reported regarding access to, and provision of information about MTX from rheumatology departments across included studies, specifically regarding whether rheumatologists provided information about MTX or access to MDT care was available. Some studies reported rheumatology nurses or pharmacists providing information. Most people preferred to receive information in person, verbally from rheumatologists and HCPs supported by written information. Although practices may have evolved through requirements for remote care delivery during the COVID-19 pandemic no data had been published regarding this at the time of the review. Reported methods of providing information about MTX were not always person-centred or needs-based, many reported difficulty with recall and unmet information needs. Inconsistent information sources and use of technical language could increase rather than allay concerns whilst use of infographics could support understanding. The internet and digital sources were frequently used to supplement information provided by healthcare services, although some reported reservations about reliability. Patient associations, friends and family played an important role in supporting some people with IA. However, the need for additional information, education, and support from HCPs to enable people to develop self-management skills (1,35,36) for both IA and MTX treatment was identified.

The review findings are in contrast to existing guidelines recommending that people with IA receive tailored information when starting MTX (1,2). This suggests that a move from one-size-fits-all information provision to a needs-based, person-centred approach is required. Increased access to a multi-disciplinary team could support people to resolve information needs, develop self-management skills (1,35,36), improve satisfaction, and potentially enhance care outcomes (31, 32). It is important to note that barriers exist as to date there are no agreed coproduced recommendations regarding the content and format of such information (37).

Furthermore, European rheumatology guidelines recommend that HCPs provide person-centred care (38), and the value of nurses providing education for people starting and taking MTX is recognised (37). However, a lack of formal training to support delivery of information about MTX has been identified, therefore development of appropriate training to support HCPs is recommended (37,39,40). Training should support shared decision-making, promote two-way discussion, and use of
easy-to-understand language in consultations to enable individual needs and concerns about treatment of IA with MTX to be elicited and addressed (41). Increasing HCPs awareness of factors that may affect information needs including individual (age (42), sex (42,43,44)), health literacy (1,36,45), disease specific factors (disease activity and duration), and psychological factors such as low mood is warranted (1,36,41). This could support HCPs to elicit and provide tailored information to resolve concerns such as reproductive health in younger females (43), and the complexity of treatment in older people (21). Vigilance in identification of poor mental health is imperative as those with depression are at greater risk of non-adherence (34). Appropriate referral and signposting to mental health services offers potential to increase patient satisfaction, adherence to MTX (34) and improve IA and mental health outcomes. Findings from the review have been adapted into practical recommendations for adopting a person-centred approach to providing information about MTX presented in Table 4.

[Table 4: Recommendations to support person-centred information about Methotrexate here]

These could inform the content of training for HCPs, development of patient-facing resources and delivery of person-centred information about MTX across differing healthcare service provision. Strategies to minimise duplication of, and provision of inconsistent information regarding MTX such as guidance about alcohol intake could be considered. A consistent approach across rheumatology departments to signposting people to reliable sources of written and digital information, and social media sites (47) could reduce uncertainty about treatment with MTX.

Opportunities also exist for joined-up working with rheumatology, pharmaceutical and patient associations to coproduce and implement consistent, easy-to-understand information in a range of accessible formats to meet varying literacy and communication needs (41). Such an approach could promote a positive message about the benefits of MTX, allay common concerns about potential risks of harms and side-effects (48).

This review identified a paucity of evidence regarding the information needs of people with IA at the point of commencing MTX, therefore future research should explore and identify information needs at this timepoint.
Limitations
This study has several limitations, firstly the review did not identify any randomised controlled trials that would have provided stronger evidence about the information needs of people starting MTX. Secondly, the majority of participants had been diagnosed for several years, so there was often a significant time interval between people starting MTX and data collection. This may have resulted in recall bias about information needs and service provision at the time of starting MTX. Thirdly, none of the included studies explored the provision of information about MTX by rheumatology nurses in dedicated DMARD counselling consultations commonly provided in the UK.

Conclusion
In conclusion, this systematic review demonstrates that people with IA have diverse, multi-faceted information needs about taking MTX. Significant unmet needs frequently remain after receiving information using a routine one-size-fits-all approach. A person-centred, needs-based approach to elicit and address person-specific information needs and concerns about MTX considering age, sex, disease activity, lifestyle, and psychological factors such as low mood is recommended. Training to support HCPs may be required to support provision of person-centred information. Development of easy-to-understand information, consistent across sources, available in accessible formats offers potential to resolve concerns, support acceptance and adherence to MTX treatment, thereby potentially improving outcomes for people with IA.

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Data availability: The data underlying this article are available in the article and in its online supplementary material.
References


Figure 1

Records identified from*: Databases (n = 8468)

Records removed before screening: Duplicate records removed (n = 2363)

Records screened (n = 6075)

Records excluded**: (n = 5906)

Reports sought for retrieval
1 Full paper

Reports not retrieved
Full Paper – Study excluded on basis of abstract included in no below

Reports assessed for eligibility (n = 169)

Papers excluded: 156
Reason 1 (n = 2 conference abstracts reporting included study
Reason 2 (n = 149 Numbers taking MTX not stated/not MTX info needed
Reason 3 (n = 2 pre 2000)
Reason 4 (n = 2 age under 18yrs.)
Reason 5 (n = 2 no differentiation of participants below and above age 18)

Studies included in review (n = 13)
Overarching theme: A need for person-centred care

Theme 1: Accepting the need for Methotrexate

Theme 2: Concerns about taking Methotrexate

Theme 3: The need for tailored information and support

Figure 2

77x27mm (300 x 300 DPI)
Table 1: Accepting the need to take Methotrexate

| ‘This is something arthritis but can you spend 15-20 minutes explaining to me a disease that is going to affect me for the rest of my life.’ (19) |
| ‘I listened to the important bits and the rest of it was all just a blur really. [...] when he was explaining it to me I was just like, just clouded over and I was just not really listening’ (27) |
| ‘I finally gripped that I’ve got this for life []). So that was the real turning point for me where I finally started to be more accepting of it’ (19) |
| ‘I’d got to do something because as I say the pains in my hands, arms and everywhere, I just couldn’t wait to get something to get rid of that pain.’ (27) |
| ‘The thought that I could end up in a wheelchair, or my perception of it was ‘gnarled up’, [...] was on sticks and she’d only just got this rheumatoid arthritis [] she was really in a terrible state.’ (27) |
| ‘It sort of contradicted that I’d got a few joint pain in my hands—because that’s all it was at that point—to, well I’m starting on a chemotherapy drug!’ (27) |
Table 2: Concerns about taking Methotrexate

I just had a quick look at the leaflet. [...] I saw that somehow it is very dangerous to take this medicine, like there are more side-effects than the good [effects].’ (27)
‘I was scared, definitely scared. But you always hope that you’re one of the ones who don’t get the symptoms.’ (27)
‘I also read the effects of each drug, and you decide, no, well... I can risk these side effects but not those. And also the patient has the right to make his choice ,’ (25)
‘[I] felt assured But I was very scared at the side-effects.’ (27)

‘Sometimes you also search for information yourself. Then you do sometimes see that there’s a difference in side effects, the way you have to administer it ... So, it’s different to the information leaflets or what you read in the brochures’ (21)

‘I think sometimes you can worry yourself reading things [] if you read the leaflets in the tablets—any tablet— you wouldn’t take them, would you? Because they’ve all got side effects, haven’t they?’ (27)

‘I mean because, well, absolutely no alcohol—I understand—() Is this truly compatible.’ (24)

‘I worry about long-term effects, being nauseous pretty well all the time.’ (19)
Table 3: The need for tailored information and support

‘That they (healthcare providers) really give you the information they know. And that they also give you tips on what you have to watch out for’ (21).

‘I’d like the doctor to tell me the pros and cons, and I can decide, too, because after all... it’s my body, and it’s my life.’ (24)

‘helpful to have handouts...not just in their head information because my head gets overloaded.’ (19).

‘It just says that it reduces inflammation, it’s not a pain-killer, it reduces inflammation. How it does that? I’m not very sure about really. [] If I stopped taking it, would it still be raging on or would it be, would it be enough, you know, to stop it?’ (27)

‘you need to know how the medication works [] surely it must be achievable to translate this information in a simple way.’ (23)

‘I don’t get his vocabulary, so I think the graphics... help me understand him better... ‘ (24)

‘I use my rheumatologist and then we go through pros and cons. Then I go away and I always do research on the internet.’(19)

‘I thought ‘I’m not going to look on the internet’ because I made a decision years ago not to do that because it just scares the living daylights out of you.’ (27)
Table 4: Recommendations to support person-centred information about Methotrexate

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<thead>
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<th>Recommendations to support a person-centred approach to providing information about Methotrexate</th>
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<tbody>
<tr>
<td>1. Use of a biopsychosocial approach to elicit information needs and concerns about Inflammatory Arthritis and Methotrexate (17,18,20,21,23,24,25,26,27,29). Two-way discussion supports a person-centred approach to care, meeting information needs with shared decision-making (1,17,20,21,23,24,25,27,29,30)</td>
</tr>
<tr>
<td>2. Use clear, easy to understand language in verbal, written and digital information, avoiding technical terms. Images or infographics may support understanding (18,21,23,24,25,26,27,29)</td>
</tr>
<tr>
<td>3. Elicit and address information needs and concerns with consideration of factors including age, sex, disease activity and duration (1,17,18,20,22,23,27,21,24,25,28,26,27,29) regarding: Rationale for treatment with MTX (18,20,23,24,27,29) Time to effect and likely duration of treatment (18, 20,23,24,27,29) Likelihood of experiencing, and management of side-effects (17,18,20,22,23,24,25,26,27,29) Risk of long-term harms i.e. potential impact upon liver function (17,21,23,24,25,26,27,29) Potential drug interactions (22,21,24,25,29) Managing MTX at times of illness/infection/surgery (23,24,25,26,29) Practical aspects of taking MTX/Folic Acid dosage, i.e. self-injection (17,21,22,23,24,25,29) Concerns regarding MTX and cancer (26) Lifestyle implications i.e. alcohol guidance, pregnancy, family planning, breastfeeding and immunisation guidelines to reduce the risk of infection (17,21,22,23,25,26,29)</td>
</tr>
<tr>
<td>4. Clear guidance as to who and how to contact in case of concerns i.e. Rheumatology adviceline (21,22,23,24,25,26)</td>
</tr>
<tr>
<td>5. Check understanding of information discussed, consider use of teach-back (46) strategies (21,22,23,25,26)</td>
</tr>
<tr>
<td>6. Practical advice and signposting to additional reliable sources of information about Inflammatory Arthritis, MTX and to support self-management (18,20,21,23,24,25,26,27,29) such as VersusArthritis, National Rheumatoid Arthritis Society (NRAS), Psoriasis and Psoriatic Arthritis Alliance (papaa.org), National Axial Spondyloarthritis Society (NASS), NHS.UK and related moderated Health Unlocked social media platforms in the UK</td>
</tr>
<tr>
<td>7. Practical and emotional support from rheumatology healthcare professionals, family, friends, and others with IA can support people to take MTX (18,21,23,24,25,26,27,29)</td>
</tr>
</tbody>
</table>
Supplementary Data S1: OVID MEDLINE SR Search Strategy

(rheumat* adj3 (arthrit* or diseas* or condition* or nodule*)).ti,ab,kf.
exp Arthritis, Rheumatoid/
exp spondylarthritis/
(Inflamm* adj3 Arthritis).ti,ab,kf.
(Psoriat* adj3 (arthr* or polyarthr* or poly arthr* or oligoarthr* or oligo arthr* or mono arthr* or rheumat*)).ti,ab,kf.
(psoriat* adj3 (arthrit* or diseas* or condition*)).ti,ab,kf.
Spondylarthropath*.ti,ab,kf.
(ankyl* adj3 spon*).ti,ab,kf.
(spon* adj3 arthr*).ti,ab,kf.
reactive arthr*.ti,ab,kf.
Felty Syndrome.ti,ab,kf.
caplan* syndrome.ti,ab,kf.
Sjogren*.ti,ab,kf.
Sicca syndrome.ti,ab,kf.
Still* disease*.ti,ab,kf.
or/1-15
Methotrexate/
(Methotrexate or MTX).mp.
(methotrexate or MTX).ti,ab,kf.
DMARD*.ti,ab,kf.
csDMARD*.ti,ab,kf.
tDMARD*.ti,ab,kf.
sDMARD*.ti,ab,kf.
disease modifying anti*.ti,ab,kf.
tsdmard.ti,ab,kf.
antirheumatic agents/
(((Antirheumatic* or anti rheumatic*) adj3 (drug* or medic* or agent*)).ti,ab,kf.
or/17-27
"medication use".ti,ab,kf.
teaching materials/ or audiovisual aids/ or medical illustration/
(teaching material$ or audiovisual aid$ or audio visual aid$ or medical illustration$).ti,ab,kf.
Digital Technology/
digital technolog$.ti,ab,kf.
smartphone/ or text messaging/
(smartphon$ or smart phon$ or textmessag$ or text messag$).ti,ab,kf.
Computers, Handheld/
(handheld computer$ or hand held computer$ or mobile device$).ti,ab,kf.
Self-Management/
patient self management.ti,ab,kf.
health knowledge, attitudes, practice/
(patient$ adj4 (belief$ or concern$)).ti,ab,kf.
medication information seeking behavio?r.ti,ab,kf.
(((MTX or methotrexate) adj3 (informat* or advi* or guid*or educat* or knowledge)).ti,ab,kf.
(((Drug* or medicin* or medication*) adj3 (informat* or advi* or guid* or educat* or knowledg*)) and (methotrexate or MTX)).ti,ab,kf.
internet/ or social media/
(internet or world wide web or worldwideweb or www or social media or socialmedia).ti,ab,kf.
(facebook or twitter or youtube or instagram or healthunlocked or whatsapp or
snapchat).ti,ab,kf.
(social networking site$ or SNS).ti,ab,kf.
or/29-48
Epidemiologic studies/
exp case control studies/
exp cohort studies/
Case control.ti,ab,kf.
(cohort adj (study or studies)).ti,ab,kf.
Cohort analy$.ti,ab,kf.
(Follow up adj (study or studies)).ti,ab,kf.
(observational adj (study or studies)).ti,ab,kf.
Longitudinal.ti,ab,kf.
Retrospective.ti,ab,kf.
Cross sectional.ti,ab,kf.
Cross-sectional studies/
interview/
Qualitative Research/
(theme* or thematic).ab,ti,kf.
qualitative.ab,ti,kf.
nursing methodology research/
questionnaire*.ab,ti,kf.
ethnological research.ab,ti,kf.
ethnograph*.ab,ti,kf.
ethnonursing.ab,ti,kf.
phenomenol*.ab,ti,kf.
(grounded adj (theor* or study or studies or research or analys?s)).ab,ti,kf.
(life stor* or women* stor* or men* stor*).ti,ab,kf.
Focus Group/
focus group*.ti,ab,kf.
(emic or etic or hermeneutic* or heuristic* or semiotic*).ab,ti,kf.
((data adj1 saturat*) or participant observ*).ab,ti,kf.
(social construct$ or postmodern* or post modern* or poststructural* or post structural* or
feminis* or interpret*).ab,ti,kf.
(action research or cooperative inquir* or co operative inquir*).ab,ti,kf.
(humanistic or existential or experiential or paradigm*).ab,ti,kf.
(field adj (study or studies or research)).ti,ab,kf.
biographical method.ab,ti,kf.
theoretical sampl*.ab,ti,kf.
observational method*.ab,ti,kf.
content analysis.ab,ti,kf.
(constant adj (comparative or comparison)).ab,ti,kf.
((discourse* or discurs*) adj3 analys?s).ti,ab,kf.
narrative analys?s.ab,ti,kf.
merleau ponty.ti,ab,kf.
(account or accounts or unstructured or open ended or text* or narrative*).ti,ab,kf.
(mix* adj2 (method* or design*)).ab,ti,kf.
or/50-91
16 and 28 and 49 and 92
<table>
<thead>
<tr>
<th>First Author/Year/Country</th>
<th>Sample size, female: male</th>
<th>Age</th>
<th>Diagnosis/% taking MTX/Duration of MTX</th>
<th>Cross-sectional Study Research Design</th>
<th>Key findings/Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson, 2015 UK (single site)</td>
<td>43:34:9</td>
<td>Median 58yrs Range 29-84 yrs.</td>
<td>43 people IA, MTX median treatment duration 48 months (3-240 months)</td>
<td>Clinic survey exploring knowledge of side-effects, monitoring and access to help</td>
<td>People with IA taking MTX had poor recall of the side-effects of MTX. Few people sought additional information from hcp, although the reasons for this were unclear. Access to specialist advice and support was seen as important to avoid harm.</td>
</tr>
<tr>
<td>Funahashi, 2012 Japan (single site)</td>
<td>165:139:16</td>
<td>Most aged 70+ (n59, 36%)No further details</td>
<td>165 RA /76% taking MTX 110 taking only DMARD - 80 taking MTX 55 taking bDMARD - 42 also taking MTX</td>
<td>Clinic survey exploring information needs when starting new treatment/expectations new DMARD</td>
<td>Before starting new MTX/DMARD treatment: most people wanted to know about the types and frequency of side effects, likelihood of responding to treatment, safety profile, cost, frequency of use.</td>
</tr>
<tr>
<td>Leonardo 2020 Australia (national RA database survey)</td>
<td>742:564:178</td>
<td>Average age 59 yrs.</td>
<td>742 RA and experience of taking MTX 494 taking MTX</td>
<td>National RA database online survey via SurveyMonkey - perception and selection of information about MTX</td>
<td>Most people with RA reported receiving helpful information from Rheumatologists. Other information sources used included: family doctors (55%), internet search engines (39%), educational websites (38%), pharmacists (37%). People with RA use several sources of information to try and resolve concerns about MTX. Positive information obtained from rheumatologists and educational websites supported people’s information needs to take MTX.</td>
</tr>
<tr>
<td>First Author/Year/Country</td>
<td>Sample size. female: male</td>
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<tr>
<td>Lim 2007 UK (Single unit)</td>
<td>319 206:113</td>
<td>No data</td>
<td>319 participants 252 (79%) IA of these 210 RA, 221 taking MTX Median disease duration 9 (IQR 4-17 yrs.)</td>
<td>Clinic postal survey of satisfaction with service/information and shared decision making re DMARDs</td>
<td>Conflicting information may result in higher concerns and lead to non-use of MTX and other DMARDs</td>
</tr>
<tr>
<td>Nash 2013 Australia (National)</td>
<td>1313 944:325:44 no answer</td>
<td>Mean age 58.4 yrs.</td>
<td>RA 1313 1034 currently taking MTX</td>
<td>Clinic survey Use and perceptions of methotrexate (MTX)</td>
<td>Concerns or experiences of adverse events (AE) resulted in some people not starting or stopping MTX. Perceptions and concerns about use, tolerance and efficacy of MTX should be addressed regularly with people taking MTX</td>
</tr>
<tr>
<td>Oton 2022b Spain</td>
<td>294 241:53</td>
<td>75% aged 31-60 yrs. No further data</td>
<td>People with immune mediated rheumatic disease taking MTX 42% Psoriatic Arthritis 16% RA 6% Ankylosing Spondylitis.</td>
<td>Internet 51 item survey in Spanish via Twitter/snowballing Information, care needs and satisfaction</td>
<td>Most people wanted more information about MTX and living with IA, than currently provided and value written information, that includes a thorough explanation, written in understandable language, with diagrams to aid understanding. Most people value patient centred care. Development of accessible methods of reliable, patient-centred information remains an unmet need.</td>
</tr>
<tr>
<td>Packham 2017 UK</td>
<td>264 174:90</td>
<td>Median Age 65 yrs. (55-71yrs)</td>
<td>264 RA MTX n75</td>
<td>Postal survey Attitudes and experience of information received during drug counselling for DMARDs</td>
<td>Education provided by rheumatology nurses is valued by most people with RA. Ensuring people have a nominated key worker and a direct point of access may improve satisfaction and provide access to further information, as required, to support people taking MTX and other DMARDs.</td>
</tr>
<tr>
<td>First Author</td>
<td>Year/Date</td>
<td>Sample size</td>
<td>Age</td>
<td>Diagnosis/No.:/% taking MTX/duration of MTX</td>
<td>Qualitative Study Research design</td>
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<tr>
<td>Hayden</td>
<td>2015 UK</td>
<td>15:11:4</td>
<td>Age range 20-79 yrs.</td>
<td>People diagnosed with Inflammatory Arthritis &lt;2years taking MTX</td>
<td>Semi-structured interviews</td>
</tr>
<tr>
<td>Mathijsen</td>
<td>2018 Netherlands</td>
<td>28:19:9</td>
<td>Median age 67.5 yrs.</td>
<td>Adults over 18 with RA with experience of taking at least one DMARD54% taking MTX</td>
<td>Focus groups</td>
</tr>
<tr>
<td>Oton</td>
<td>2022a Spain</td>
<td>12:7:5</td>
<td>Adults over 18 years</td>
<td>People with rheumatic diseases taking MTX for at least four weeks</td>
<td>Focus Groups</td>
</tr>
<tr>
<td>Rai</td>
<td>2018 Canada</td>
<td>27:17:10</td>
<td>Age range 20-79</td>
<td>Individuals with rheumatologist diagnosis of IA</td>
<td>Focus Group with activity to develop tool or strategy to support medication use</td>
</tr>
<tr>
<td>Author</td>
<td>Sample female: male</td>
<td>Age</td>
<td>Diagnosis</td>
<td>Mixed-Method Study Research Design</td>
<td>Key findings/Study outcomes</td>
</tr>
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</tbody>
</table>
| Voshaar 2016, Netherlands | Phase 1: n=120 72:48  Phase 2: n=21 17:4 | Mean age: 59.6 years | Inflammatory Arthritis (IA) IA of which, 18 (88%) RA | Qualitative theory based mixed methods  
Phase 1: Cross sectional  
18 item postal survey  
Phase 2: Focus group (sub-group of Phase 1 participants)  
To assess and exploring barriers and facilitators to take DMARDs. | People with IA had individual information needs to support them to take MTX/DMARDs. Authors recommend that interventions to support use of DMARDs including Methotrexate using the domains of capability, opportunity and motivation should be developed to provide tailored support for people with IA. |
| Hegeman 2021, Netherlands | Phase 1  
n=12.  9:3  
Phase 2  
n=61  
44:17  
Phase 1:  
Average age 62.5 years  
Phase 2:  
Average age 67 yrs. | RA  
MTX 5 (42%)  
MTX 28 (47%) | Phase 1:  
12 people with RA structured consultation observation  
Phase 2: Postal survey | People with RA are generally very satisfied with information about MTX and other DMARDs. Unmet information needs included information about possible side effects, influence on sex life, alcohol intake, drug interactions, drowsiness, managing side effects and missed doses and risks from MTX.  
Using Satisfaction with Information about Medication questionnaire in clinical practice may help identify concerns and unmet information needs. |
STUDY QUALITY APPRAISAL CRITERIA

<table>
<thead>
<tr>
<th>JBI Cross-sectional studies critical appraisal criteria (11)</th>
<th>JBI Qualitative studies critical appraisal criteria (12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Were inclusion criteria clearly stated</td>
<td>1: Is there congruity between stated philosophical perspective and research methodology</td>
</tr>
<tr>
<td>2: Were study subjects and setting described in detail</td>
<td>2: Is there congruity between research methodology and the research question or objectives</td>
</tr>
<tr>
<td>3: Exposure measure reliable and valid</td>
<td>3: Is there congruity between the research methodology and the methods used to collect data</td>
</tr>
<tr>
<td>4: Objective standard criteria used for measurement of condition</td>
<td>4: Is there congruity between research methodology and the representation and analysis of data</td>
</tr>
<tr>
<td>5: Confounding factors identified</td>
<td>5: Is there congruity between the research methodology and the interpretation of results</td>
</tr>
<tr>
<td>6: Strategies to deal with confounding factors identified</td>
<td>6: Is there a statement locating the researcher culturally or theoretically</td>
</tr>
<tr>
<td>7: Outcomes measured in reliable and valid way</td>
<td>7: Is the influence of the researcher on the research, and vice-versa, addressed</td>
</tr>
<tr>
<td>8: Was appropriate statistical analysis used</td>
<td>8: Are participants, and their voices, adequately represented</td>
</tr>
<tr>
<td></td>
<td>9: Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body</td>
</tr>
<tr>
<td></td>
<td>10: Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data</td>
</tr>
</tbody>
</table>
Methotrexate information needs of people with IA

We undertook a mixed-methods systematic review to identify the information that people with Inflammatory Arthritis need to take Methotrexate

- 13 studies involving 3425 adults
- 20-84 years
- 71% female
- Thematic analysis of studies

Information about Methotrexate should be

1. Person-centred
2. Tailored to individual concerns about benefits and risks of treatment
3. Available in easy-to-understand language and accessible formats

Methods

<table>
<thead>
<tr>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logan et al., The information required by people with Inflammatory Arthritis to take Methotrexate: A mixed-methods systematic review. Rheumatology</td>
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</tbody>
</table>

Methotrexate information needs of people with IA

127x95mm (300 x 300 DPI)