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International eDelphi Study to Reach Consensus on the Methotrexate Dosing Regimen in Patients With Psoriasis

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IMPORTANCE A clear dosing regimen for methotrexate in psoriasis is lacking, and this might lead to a suboptimal treatment. Because methotrexate is affordable and globally available, a uniform dosing regimen could potentially optimize the treatment of patients with psoriasis worldwide.

OBJECTIVE To reach international consensus among psoriasis experts on a uniform dosing regimen for treatment with methotrexate in adult and pediatric patients with psoriasis and identify potential future research topics.

DESIGN, SETTING, AND PARTICIPANTS Between September 2020 and March 2021, a survey study with a modified eDelphi procedure that was developed and distributed by the Amsterdam University Medical Center and completed by 180 participants worldwide (55 [30.6%] resided in non-Western countries) was conducted in 3 rounds. The proposals on which no consensus was reached were discussed in a conference meeting (June 2021). Participants voted on 21 proposals with a 9-point scale (1-3 disagree, 4-6 neither agree nor disagree, 7-9 agree) and were recruited through the Skin Inflammation and Psoriasis International Network and European Academy of Dermatology and Venereology in June 2020. Apart from being a dermatologist/dermatology resident, there were no specific criteria for participation in the survey. The participants worked mainly at a university hospital (97 [53.9%]) and were experienced in treating patients with psoriasis with methotrexate (163 [91.6%] had more than 10 years of experience).

MAIN OUTCOMES AND MEASURES In a survey with eDelphi procedure, we tried to reach consensus on 21 proposals. Consensus was defined as less than 15% voting disagree (1-3). For the consensus meeting, consensus was defined as less than 30% voting disagree.

RESULTS Of 251 participants, 180 (71.7%) completed all 3 survey rounds, and 58 participants (23.1%) joined the conference meeting. Consensus was achieved on 11 proposals in round 1, 3 proposals in round 2, and 2 proposals in round 3. In the consensus meeting, consensus was achieved on 4 proposals. More research is needed, especially for the proposals on folic acid and the dosing of methotrexate for treating subpopulations such as children and vulnerable patients.

CONCLUSIONS AND RELEVANCE In this eDelphi consensus study, consensus was reached on 20 of 21 proposals involving methotrexate dosing in patients with psoriasis. This consensus may potentially be used to harmonize the treatment with methotrexate in patients with psoriasis.

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Methotrexate (MTX), a dihydrofolate reductase inhibitor, is one of the 4 available classic systemic treatments for psoriasis and has been widely prescribed for psoriasis for more than 60 years.[1-3] The effectiveness and safety of MTX are acknowledged in psoriasis guidelines worldwide.[4-6] It is also one of the key disease-modifying antirheumatic drugs used in rheumatology.[7]

Methotrexate was approved by the US Food and Drug Administration before dose ranging studies were performed; therefore, a clear dosing regimen is lacking. During the first years of use, Rees et al[8] reported a daily dosage of 1.5 to 2 mg that would be administered for 3 to 12 days consecutively.[8] In 1969, a weekly oral dosage of MTX, 25 mg, was described by Roenigk et al.[9] Three years later, Weinstein and Frost[10] reported a 3 times a week divided dose in which 2.5 to 5 mg of the drug was administered every 36 hours.

Uniformity in the dosing regimen is also lacking in current practice; a global survey study conducted by Psoriasis International Network (which is currently named the Skin Inflammation and Psoriasis International Network [SPIN][11]), showed that starting doses differed from 5 to 22.5 mg per week.[12] Comparable questionnaire results were reported from Iran,[13] and this issue also arose in guidelines.[14] The variability in treatment regimens might have contributed to suboptimal treatment with MTX or early discontinuation of treatment because of limited efficacy or, in the case of overtreatment, adverse effects. Because MTX is available worldwide and the drug is affordable (around $16.17/wk for six 2.5-mg tablets[15]), uniformity in the dosing regimen can potentially contribute to global improvement of the treatment of patients with psoriasis.

The objective of this electronic Delphi (eDelphi) study was to reach international consensus on the dosage of MTX for treating patients with psoriasis and identify existing knowledge gaps. Items included in this eDelphi study were test dose, initiation dose, the increase or decrease of the dose, administration form, maximum dose, administration, and the use of folic acid specified for specific populations (adults, children, and vulnerable patients). This consensus may help to establish uniform MTX dosing in clinical practice, and it can potentially be used to develop a consensus project in other (off-label) dermatoses (eg, atopic dermatitis [AD],[16] morphea,[17] and alopecia areata).[18]

Key Points

Question Can consensus be reached on the dosing of methotrexate in treating patients with psoriasis?

Findings In this consensus statement, after a systematic review of the literature, 21 proposals were formulated involving methotrexate dosing in adults, children, and vulnerable patients. On 20 of these proposals, consensus was reached in 3 eDelphi survey rounds and an online consensus meeting.

Meaning The findings of this study suggest that this consensus can be used in guideline documents as well as further optimization of methotrexate treatment in patients with psoriasis.

Methods

The eDelphi study comprised 3 sequential survey rounds that were conducted in September 2020, November 2020, and February 2021. After the last survey round, an online consensus meeting was organized in June 2021. For the reporting of these results, the Standards for Quality Improvement Reporting Excellence (SQUIRE) 2.0 guidelines[19] were followed. The medical ethics review committee of the Academic Medical Centre in Amsterdam stated that the Medical Research Involving Human Subjects Act did not apply. Participants gave their written informed consent for use of their personal data when registered through email.

Working Group

To determine which items required consensus, an international working group (A.H., S.M., R.G., L.I., R.W., M.H., and P.S.) was formed. Members were selected based on their experience with MTX treatment and psoriasis research. This working group identified 7 items associated with dosage of MTX (test dose, start dose, the increase or decrease of the dose, administration form, maximum dose, administration, and the use of folic acid). They decided to study these items in 3 populations: adults, children, and patients with frailty, such as elderly patients or those with impaired kidney function (patients with frailty was later changed to *vulnerable patients*). Afterwards, a literature search using the same search terms as the systematic review from Menting et al[14] was performed. With this literature review, clinical expertise, and outcomes of the PIN survey,[12] the working group formulated 21 proposals regarding the 7 items. These proposals were used for the first eDelphi round.

Participant Recruitment

All SPIN members (4500 professionals on chronic inflammatory skin diseases) worldwide were invited to participate.[11] We sent an additional email to the national representatives (n = 108) and scientific committee members (n = 35) of SPIN that asked them to recruit at least 10 psoriasis experts in their countries. The European Academy of Dermatology and Venereology promoted the eDelphi study through social media (Twitter). We also asked the working group to share the eDelphi study in their network. Only dermatologists, dermatology residents, and researchers (who were participating in psoriasis research or guideline development) were allowed to participate. The sample size was not predefined, but we set the minimum on 100 participants as a representative number of psoriasis experts.

eDelphi Rounds 1 to 3

The software chosen for this eDelphi study was LimeSurvey (LimeSurvey GmbH). This questionnaire software fulfills all privacy requirements from the Amsterdam University Medical Centers from which this eDelphi study was sent to the participants.[20] It was pretested by an independent data manager and 2 authors (A.H. and P.S.). The eDelphi was conducted in 3 rounds, which took approximately 3 months each. In every round, all participants received an email with a link to the survey and their personal token. In the survey, they voted on a proposal using a 9-point scale in which 1 to 3 indicated disagree, 4 to 6 neither agree nor disagree, and 7 to 9 agree. Beneath every proposal, relevant references could be found.

During the first round of the eDelphi study, alternative proposals for consensus could be added by the participants, preferably supported by evidence. The proposals in which no consensus was met were slightly adjusted by the working group according to the most frequently sent alternative proposals.

Table 1. Baseline Characteristics

Characteristic	No. (%)		
	Participants completed first round (n = 201)	Participants completed 3 rounds (n = 180)	Participants in consensus meeting (n = 58)
Age, y			
20-29	1 (0.5)	1 (0.5)	0
30-39	31 (15.4)	25 (13.9)	10 (17.2)
40-49	57 (28.4)	52 (28.9)	18 (31.05)
50-59	65 (32.3)	57 (31.7)	18 (31.05)
60-69	42 (20.9)	40 (22.2)	11 (19.0)
≥70	5 (2.5)	5 (2.8)	1 (1.7)
Country of residence (per continent)			
Africa	5 (2.5)	4 (2.2)	2 (3.4)
Asia	27 (13.4)	24 (13.3)	10 (17.3)
Europe	114 (56.7)	102 (56.7)	34 (58.6)
North America	18 (9.0)	15 (8.4)	4 (6.9)
Oceania[a]	9 (4.5)	8 (4.4)	0
South America	28 (13.9)	27 (15)	8 (13.8)
Current position			
University hospital	104 (51.7)	97 (53.9)	34 (58.6)
Nonuniversity hospital	12 (6.0)	7 (3.9)	3 (5.2)
Private practice	26 (12.9)	23 (12.8)	5 (8.6)
Combination of 2 or 3 mentioned previously	59 (29.4)	53 (29.4)	16 (27.6)
Member of international dermatology society/psoriasis interest group (yes/no)			
Yes	180 (89.6)	162 (90.0)	54 (93.1)
No	21 (10.4)	18 (10.0)	4 (6.9)
Experience with MTX in psoriasis (y)			
<10	20 (10)	17 (9.4)	6 (10.3)
10-20	66 (32.8)	59 (32.8)	21 (36.2)
20-30	61 (30.3)	54 (30)	22 (37.9)
30-40	46 (22.9)	43 (23.9)	8 (13.8)
40-49	8 (4.0)	7 (3.9)	1 (1.7)
>100 Patients treated with MTX (yes/no)			
No	28 (13.9)	24 (13.3)	9 (15.5)
Yes	173 (86.1)	156 (86.7)	49 (84.5)
Participation in psoriasis research or guideline development (yes/no)			
Yes	163 (81.1)	145 (80.6)	51 (87.9)
No	38 (18.9)	35 (19.4)	7 (12.1)

Abbreviation: MTX, methotrexate.

[a] Oceania includes Australia and New Zealand.

During the second round, participants were able to vote on the remaining proposals. They could also view the distribution of the scores per proposal together with the alternative proposals. During the third round, participants who disagreed with the proposal could vote on the different alternatives that were collected in the first round.

All eDelphi questions were mandatory to answer, and participants were encouraged to choose the option of 4 to 6 (neither agree nor disagree) as little as possible. Weekly reminder emails were sent to increase the response rate.

Consensus Meeting

To resolve potentially remaining disagreements and adjust the final proposals for which no consensus was reached, we organized an online consensus meeting. The consensus meeting was held June 17, 2021, through the videoconference setting of Zoom (Zoom Video Communications).[21] Participants were asked to register themselves before this meeting. Because of participants' different time zones, it was not possible to make this meeting mandatory for everyone. Participants who could not attend the meeting had the possibility to share their opinions through email in advance.

During the consensus meeting, the results from the 3 eDelphi rounds were presented by Dr van Huizen. Then, the 5 remaining proposals for which no consensus was achieved during the 3 eDelphi rounds were discussed. For every proposal, Dr van Huizen provided an overview of the literature and proposed alternatives, after which Dr Menting and Prof Spuls led the discussion with the participants. If needed, the proposals were adjusted further. Afterwards,

Table 2. Proposals and Voting Percentages in eDelphi Rounds 1, 2, and 3 and Consensus Meeting

Proposal	References	%		
		Disagree	Neither agree nor disagree	Agree
eDelphi round 1[a]				
1. The MTX dose can be decreased to the lowest effective dose according to treatment goals.	22-24	3.5	2.5	94
2. Folic acid should be supplemented in all patients.	4,6,14,25-43	3.5	2.5	94
3. MTX should be tried, if needed with increased dosage, at least 3-4 mo before the effect can be assessed, according to treatment goals.	6,22,24,30,44,45	5	5	90
4. In case of gastrointestinal adverse events, it is preferred to switch the MTX route of administration from oral to subcutaneous.	4,29,30,46	5	3.5	91.5
5. Folic acid should be dosed in 4-6 mg (depending on availability) when prescribing <15 mg MTX.	4,6,27,31,37,39,43,47-50	8.4	5.5	86.1
6. The maximum weekly dose of MTX in adults is 25 mg/wk.	14,27-30,44,51,52	9	4.4	86.6
7. For MTX, there is no maximum treatment duration unless there are safety concerns.	30	9.5	3.4	87.1
8. Usually, MTX is administered in a single weekly dose.	4,6,25,27-31,34,36,49,53-56	10.4	2.5	87.1
9. When initiating treatment with MTX in children, a dosage of around 10 mg/m^2/wk is prescribed.	4,30,57,58	10.9	9.5	79.6
10. The maximum weekly dose of MTX in children is 15 mg/m^2/wk.	4,30,57,58	13.9	12	74.1
11. When initiating treatment with MTX in vulnerable patients, start with a dosage of 7.5-10 mg/wk.	4	14.9	5	80.1
eDelphi round 2[a]				
1. When initiating treatment with MTX in adults, no test dosage is needed.	4,14,31	11.1	2.6	86.3
2. Usually, MTX is administered orally.	25-28,36,55,59,60	14.7	6.8	78.5
3. Folic acid should be administered 24 h after MTX intake.	4,6,14,37,39,41,47,50,61	12.6	4.2	83.2
eDelphi round 3[a]				
1. When initiating treatment with MTX in adults, start with a dosage of 15 mg/week.	4,6,14,25,26,31,47,62,63	14.4	2.2	83.3
2. In case of inefficacy or insufficient effect according to the treatment goals, it is preferred to switch the MTX route of administration from oral to subcutaneous.	6,27,28,30,64	10	3.3	86.7
Consensus meeting[b]				
1. A test dosage is not needed in vulnerable patients.	4	16	2	82
2. The maximum dosage for vulnerable patients is the same as in adults (25 mg/week).[c]	(Expert opinion)	26	7	67
3. When initiating treatment with MTX in children, a test dosage is not needed.	65-67	5	2	93
4. The dosage of folic acid should be increased when increasing the dosage of MTX.[d]	4,68	93	2	5
5. Folic acid should be administered once a week.	4,6,14,37,39,41,47,50,61	14	7	79

Abbreviations: eDelphi, electronic Delphi, MTX, methotrexate.

[a] For the eDelphi round, consensus was defined as <15% disagree.

[b] For the consensus meeting, consensus was defined as <30% disagree.

[c] Adjusted to passive voice after the consensus meeting, some subpopulations were changed to vulnerable patients.

[d] For this proposal no consensus was reached. Adjusted to passive voice after the consensus meeting.

participants could vote on these proposals in 3 categories; disagree, neither agree nor disagree, and agree.

Definition of Consensus

Consensus was defined as less than 15% of scores of 1 to 3 (disagree) during the eDelphi rounds. For the consensus meeting, consensus was defined as less than 30% of scores of 1 to 3 (disagree). The results were analyzed with SPSS, version 26.0 (IBM).

Privacy and Data Management

A privacy officer was consulted before the start of the project. A data privacy effect assessment was written to identify potential privacy risks and take adequate measurements according to the Dutch Privacy Law.

Data were pseudonymized and collected through tokens. The eDelphi results were password protected. Only Dr van Huizen and Prof Spuls could access the online results.

Results

Participant Characteristics and Response Rates

In total, 251 participants registered themselves for the first round (contact rate, 5.6% [251/4500]), of whom 180 participants (71.7%)

completed all eDelphi rounds. Participants were working mainly at university hospitals, were members of an international dermatology society or psoriasis interest group, and had 10 to 20 years of experience in treating patients with psoriasis with MTX. Two patients participated in the eDelphi study incidentally but did not finish the first round and were excluded from further participation. Baseline characteristics are presented in **Table 1**.

eDelphi Rounds 1 to 3

In total, 21 proposals were included in round 1 (**Table 2**[4,6,14,22-68]). Consensus was reached on 11 proposals (52.4%). On the remaining 10 proposals, participants added 41 (deduplicated) alternative proposals. These alternative proposals were summarized beneath the involving proposals in the next rounds. A total of 201 of the 251 participants (response rate, 80.1%) completed round 1.

During the second round, participants voted on the 10 remaining original proposals, and consensus was reached on 3 of them. Of the remaining 201 participants, 190 people (response rate, 94.5%) completed this eDelphi round.

During the third round, 7 original proposals were included, of which consensus was reached on 2 proposals. To collect information for the discussion during the consensus meeting, participants also voted on alternative proposals. A total of 180 of the 190 participants (response rate, 94.7%) completed this last round. The numbers of consensus per eDelphi round can be found in **Figure 1**.

Consensus Meeting

The 5 remaining proposals were discussed in a consensus meeting (Table 2). Not all participants could join the consensus meeting throughout the entire meeting. The maximum number of attendees was 58. Five proposals were discussed, and consensus was reached on 4 proposals.

Most participants agreed that a test dosage for vulnerable patients and children was not needed when administering treatment with low-dose MTX. Idiosyncratic hepatotoxicity could be prevented by lowering the initial dose. Physicians generally are very careful when treating this population with MTX.

Remarks made on the proposals about patients with frailty concerned a lack of a clear definition of this population. Therefore, this description was changed to vulnerable patients. It was concluded that no specific maximum dosage in vulnerable patients was needed and this dose could be equal to the maximum dosage in adults.

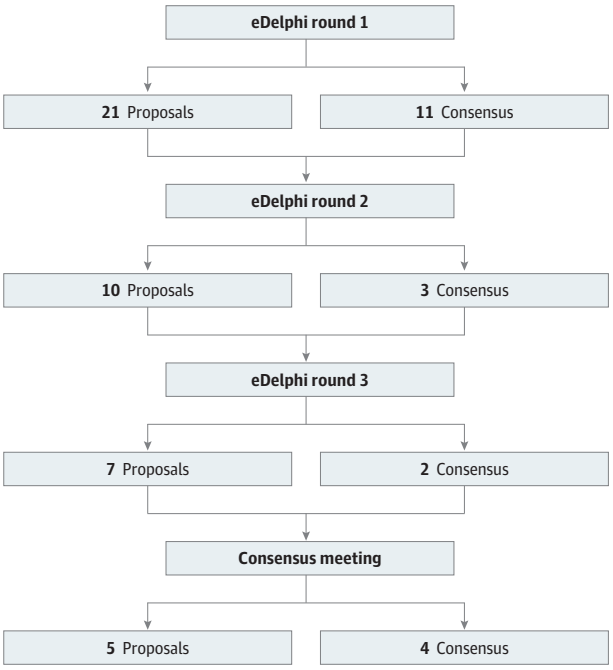
The last proposals discussed during the consensus meeting involved the use of folic acid and whether the dose should be increased when increasing the dose of MTX. Participants stated that the evidence is controversial; therefore, consensus on this proposal was not possible. Consensus was reached on the proposal involving the weekly administration of folic acid.

For 2 proposals, the definition of patients with frailty had to be adjusted, and the sentence had to be rewritten in active voice. This was done by the working group after voting. In total, we achieved consensus on 7 items involving 20 proposals (Table 2; **Figure 2**).

Future Research

The identification of potential future research was one of the aims of this project. Based on the findings in our systematic literature review, the eDelphi study, and discussion during the consensus meeting, we identified a few potential future research topics. We suggest focusing potential future research on MTX dosing in specific populations (eg, children of different ages)and elderly or patients with an impaired kidney function). For folic acid, different doses (increased with higher dosages of MTX) and schedules should be studied.

Figure 1. Consensus per Electronic Delphi (eDelphi) Round



Number of proposals on which participants could vote and on which consensus was reached.

Discussion

During this project, consensus was reached on 20 of 21 proposals involving MTX dosage in patients with psoriasis; 10 proposals during the first round, 3 during the second, and 3 during the third, with 4 reaching consensus during the consensus meeting. This consensus may help clinicians to optimize treatment for patients with psoriasis with MTX worldwide because MTX is an important drug, being affordable and globally accessible. This consensus can be used in current practice and guidelines. The identified knowledge gaps can potentially be the basis for future research.

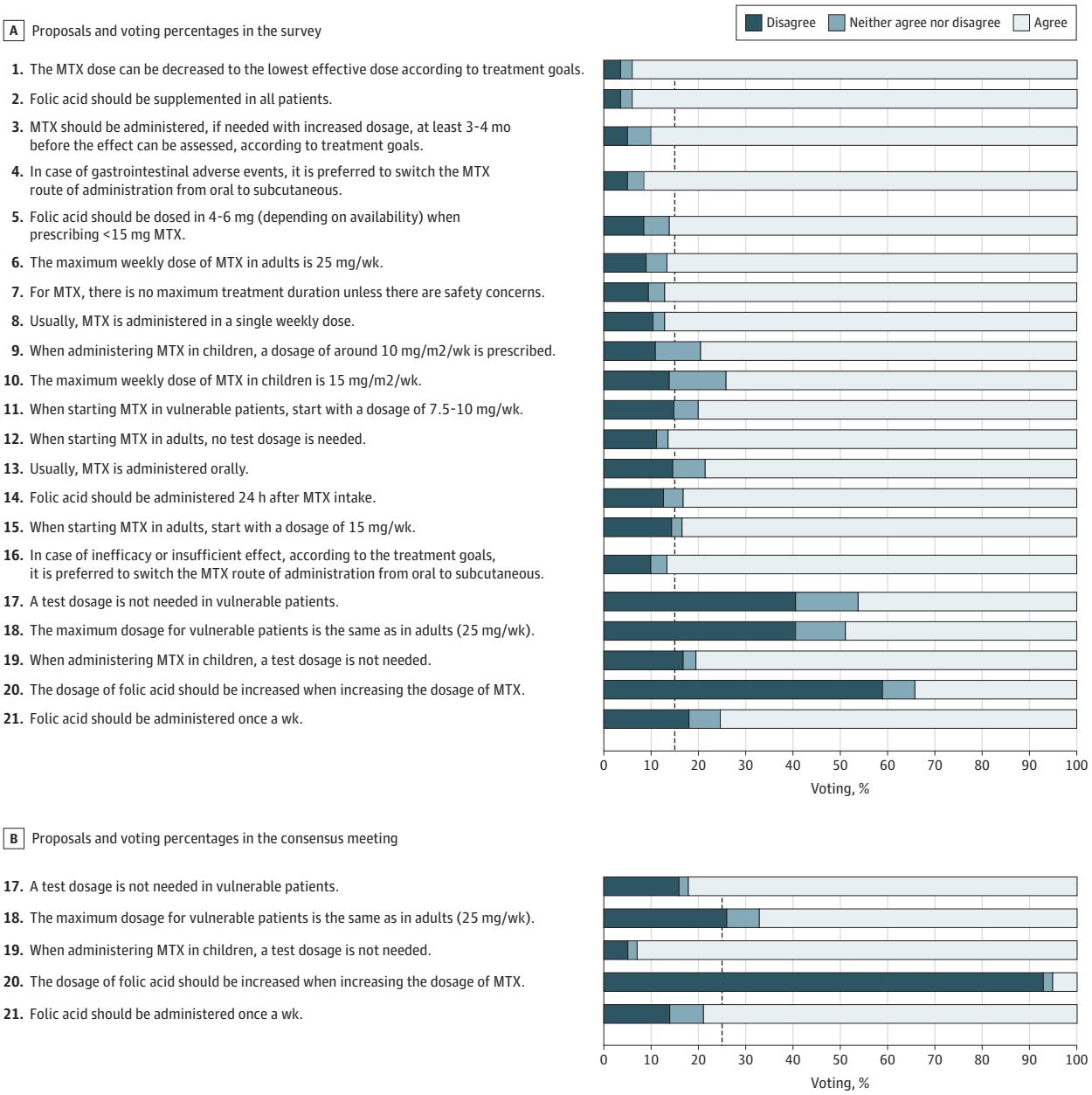
Consensus

No consensus was achieved on the proposal of an increased dosage of folic acid when increasing the dosage of MTX. During the consensus meeting, it was discussed that there was a lack of evidence and the available evidence was inconclusive. Therefore, we could not adjust the proposal in a manner that consensus was a possibility.

We eventually reached consensus on all items involving children and MTX dosing. However, most proposals were based on studies from rheumatology because of a lack of evidence in dermatology.

The proposals on patients with frailty sparked the most discussion. The working group decided to keep the definition broad and added a definition of patients with frailty to the eDelphi study that

Figure 2. Proposals and Voting Percentages in the Survey and Consensus Meeting



Percentage of those who voted disagree, neither agree nor disagree, and agree during the eDelphi rounds. Black vertical dashed line indicates cutoff for consensus, defined as less than 15% (A) and less than 30% (B) voting disagree. MTX indicates methotrexate.

included elderly individuals and individuals with kidney renal dysfunction, liver disorders (eg, nonalcoholic steatohepatitis), ulcerative colitis, history of hepatitis, lack of compliance, gastritis, diabetes, previous cancer, and congestive heart failure. However, many participants stated that this definition was too broad. During the consensus meeting, we deviated from the protocol and the term *patients with frailty* was changed to *vulnerable patients*, which only included elderly patients and patients with impaired kidney function. The participants believed vulnerable patients were the subpopulation for whom special cautions for MTX dosing were needed.

Strengths and Limitations

A strength of the consensus study was that it was supported by randomized clinical trials and guidelines because we updated the systematic literature review from Menting et al.[14] Second, we recruited different participants from all 7 continents. The participants were mainly academic dermatologists with an experience in treating patients with MTX. Third, because of frequent reminders, we reached a high total response rate of 71.7% (180 of 251 participants). Another strength is the design of this study; the anonymous eDelphi study avoided the possibility of dominance by any of

the participants, but during the consensus meeting the proposals could also be discussed live.

Some limitations remain; for the consensus, we decided to define the percentage of participants that scored 1-3 (disagree). Other studies have also defined the percentage of scores 6 to 9 (agree) during an eDelphi exercise,[69] but we expected a consensus would not be reached with a predefined percentage for agree. In retrospect, (see Table 2) setting a minimum of 70% agree did not change the consensus.

Another limitation is the method of recruitment. We choose to recruit patients among SPIN and European Academy of Dermatology and Venereology members and decided not to limit our selection to psoriasis experts only. Eventually, it turned out that most physicians were experienced in treating this population with MTX (90% treated patients with psoriasis with the drug for more than 10 years).

The scope of this survey project is a limitation as well, because we did not include proposals on the screening and safety monitoring of patients treated with the drug. An example of the screening is the use of transient elastography and measurement of procollagen III N-terminal peptide for assessing liver fibrosis.[70] We decided to focus on the dosing of MTX to prevent the survey being too extensive, because this could discourage participants from completing the survey rounds.

Lastly, we aimed for a global consensus, but most participants were from Europe. The overrepresentation of Western nationalities may have limited the generalizability of this consensus, because MTX is an important drug in non-Western countries because of less availability of biologics.[71]

Conclusions

Although we achieved consensus in this eDelphi survey study, more high-quality studies could support our proposals. Randomized clinical trials or prospective observational studies focusing on the use of folic acid and dosing in different subpopulations (children and vulnerable patients) are needed. It should also be defined for which subpopulation (elderly patients or those with impaired kidney function or liver disorders) a specific dosing schedule is required. We do not think this consensus is translatable to other inflammatory disease. For AD, we found studies arguing that the dose MTX for AD should be higher compared with psoriasis because the systemic T-cell subsets show a higher activation status in AD than in psoriasis[72] and the immunosuppressive effect of MTX is mediated by its ability to induce apoptosis and clonal deletion of activated T cells.[73] Therefore, separate consensus should be achieved for other (off-label) disease, such as AD, morphea, and alopecia areata. Other consensus projects can focus on the screening and monitoring of this drug,[74] how often and which tests should be performed, and whether special precautions are needed in children, elderly individuals, and other subpopulations.[75]

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REFERENCES

1. Gubner R, August S, Ginsberg V. Therapeutic suppression of tissue reactivity: II: effect of aminopterin in rheumatoid arthritis and psoriasis. *Am J Med Sci*. 1951;221(2):176-182. doi:10.1097/00000441-195102000-00009

2. Edmundson WF, Guy WB. Treatment of psoriasis with folic acid antagonists. *AMA Arch Derm*. 1958;78(2):200-203. doi:10.1001/archderm.1958.01560080060010

3. Said S, Jeffes EW, Weinstein GD. Methotrexate. *Clin Dermatol*. 1997;15(5):781-797. doi:10.1016/S0738-081X(97)00014-X

4. Van Der Kraaij GE, Spuls PhI, Balak DMW, et al. Update richtlijn psoriasis 2017. *Ned Tijdschr Dermatol Venereol*. 2017;27(4):170-173.

5. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol*. 2020;82(6):1445-1486. doi:10.1016/j.jaad.2020.02.044

6. Mrowietz U, Nast A. The EuroGuiDerm guideline for the systemic treatment of psoriasis vulgaris—1.4 methotrexate (MTX) https://www.edf.one/dam/jcr:04c2fd28-be9b-48ac-89de-0d52f1b2d573/8_Methotrexate_Aug_2020.pdf European Dermatology Forum; 2020 [

7. Coates LC, Gossec L, Ramiro S, et al. New GRAPPA and EULAR recommendations for the management of psoriatic arthritis. *Rheumatology (Oxford)*. 2017;56(8):1251-1253. doi:10.1093/rheumatology/kew390

8. Rees RB, Bennett JH, Bostick WL. Aminopterin for psoriasis. *AMA Arch Derm*. 1955;72(2):133-143. doi:10.1001/archderm.1955.03730320035005

9. Roenigk HH Jr, Fowler-Bergfeld W, Curtis GH. Methotrexate for psoriasis in weekly oral doses. *Arch Dermatol*. 1969;99(1):86-93. doi:10.1001/archderm.1969.01610190092018

10. Weinstein GD, Frost P. Methotrexate for psoriasis. a new therapeutic schedule. *Arch Dermatol*. 1971;103(1):33-38. doi:10.1001/archderm.1971.04000130035004

11. Skin Inflammation and Psoriasis International Network. SPIN dermatology. Accessed August 12, 2021. https://www.spindermatology.org/2021

12. Gyulai R, Bagot M, Griffiths CEM, et al. Current practice of methotrexate use for psoriasis: results of a worldwide survey among dermatologists. *J Eur Acad Dermatol Venereol*. 2015;29(2):224-231. doi:10.1111/jdv.12495

13. Zargari O, Hejazi S, Shahidi-Dadras M, et al. Considerable variation among Iranian dermatologists in the dosing and monitoring of methotrexate for treating psoriasis. *Int J Dermatol*. 2014;53(3):385-389. doi:10.1111/ijd.12201

14. Menting SP, Dekker PM, Limpens J, Hooft L, Spuls PI. Methotrexate dosing regimen for plaque-type psoriasis: a systematic review of the use of test-dose, start-dose, dosing scheme, dose adjustments, maximum dose and folic acid supplementation. *Acta Derm Venereol*. 2016;96(1):23-28. doi:10.2340/00015555-2081

15. Drugs.com. Methotrexate prices, coupons and patient assistance programs. Accessed August 6, 2021. https://www.drugs.com/price-guide/methotrexate

16. Schram ME, Roekevisch E, Leeflang MM, Bos JD, Schmitt J, Spuls PI. A randomized trial of methotrexate versus azathioprine for severe atopic eczema. *J Allergy Clin Immunol*. 2011;128(2):353-359. doi:10.1016/j.jaci.2011.03.024

17. Zulian F, Martini G, Vallongo C, et al. Methotrexate treatment in juvenile localized scleroderma: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2011;63(7):1998-2006. doi:10.1002/art.30264

18. Hammerschmidt M, Mulinari Brenner F. Efficacy and safety of methotrexate in alopecia areata. *An Bras Dermatol*. 2014;89(5):729-734. doi:10.1590/abd1806-4841.20142869

19. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. SQUIRE 2.0 (Standards for QUality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. *BMJ Qual Saf*. 2016;25(12):986-992. doi:10.1136/bmjqs-2015-004411

20. LimeSurvey. Home page. Accessed August 6, 2021. https://www.limesurvey.org/

21. ZOOM. Home page. Accessed August 6, 2021. https://zoom.us/

22. Mahil SK, Wilson N, Dand N, et al; BADBIR study group and the PSORT consortium. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study (the British Association of Dermatologists Biologics and Immunomodulators Register, BADBIR). *Br J Dermatol*. 2020;182(5):1158-1166. doi:10.1111/bjd.18333

23. Mrowietz U, Kragballe K, Nast A, Reich K. Strategies for improving the quality of care in psoriasis with the use of treatment goals--a report on an implementation meeting. *J Eur Acad Dermatol Venereol*. 2011;25(suppl 3):1-13. doi:10.1111/j.1468-3083.2011.04033.x

24. European Dermatology Forum. The EuroGuiDerm guideline for the systemic treatment of psoriasis vulgaris—VII: disease severity and treatment goals. Accessed July 14, 2020. https://www.edf.one/dam/jcr:99d22233-88de-4dbe-8ee5-c0062a3ed8cc/2_Disease_severity_treatment_goals_Aug_2020.pdf

25. Ranjan N, Sharma NL, Shanker V, Mahajan VK, Tegta GR. Methotrexate versus hydroxycarbamide (hydroxyurea) as a weekly dose to treat moderate-to-severe chronic plaque psoriasis: a comparative study. *J Dermatolog Treat*. 2007;18(5):295-300. doi:10.1080/09546630701499291

26. Mahbub MS, Khondker L, Khan SI, Hazra SC. Comparative efficacy of hydroxyurea and methotrexate in treating psoriasis. *Mymensingh Med J*. 2013;22(1):116-130.

27. Paul C, Gallini A, Maza A, et al. Evidence-based recommendations on conventional systemic treatments in psoriasis: systematic review and expert opinion of a panel of dermatologists. *J Eur Acad Dermatol Venereol*. 2011;25(suppl 2):2-11. doi:10.1111/j.1468-3083.2011.03990.x

28. Raaby L, Zachariae C, Østensen M, et al. Methotrexate use and monitoring in patients with psoriasis: a consensus report based on a Danish expert meeting. *Acta Derm Venereol*. 2017;97(4):426-432. doi:10.2340/00015555-2599

29. Menter A, Cordoro KM, Davis DMR, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. *J Am Acad Dermatol*. 2020;82(1):161-201. doi:10.1016/j.jaad.2019.08.049

30. Warren RB, Weatherhead SC, Smith CH, et al. British Association of Dermatologists' guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. *Br J Dermatol*. 2016;175(1):23-44. doi:10.1111/bjd.14816

31. Rademaker M, Gupta M, Andrews M, et al. The Australasian Psoriasis Collaboration view on methotrexate for psoriasis in the Australasian setting. *Australas J Dermatol*. 2017;58(3):166-170. doi:10.1111/ajd.12521

32. Karamata VV, Gandhi AM, Patel PP, Sutaria A, Desai MK. A study of the use of drugs in patients suffering from psoriasis and their impact on quality of life. *Indian J Pharmacol*. 2017;49(1):84-88.

33. Roenigk HH Jr, Auerbach R, Maibach H, Weinstein G, Lebwohl M. Methotrexate in psoriasis: consensus conference. *J Am Acad Dermatol*. 1998;38(3):478-485. doi:10.1016/S0190-9622(98)70508-0

34. Stiff KM, Glines KR, Porter CL, Cline A, Feldman SR. Current pharmacological treatment guidelines for psoriasis and psoriatic arthritis. *Expert Rev Clin Pharmacol*. 2018;11(12):1209-1218. doi:10.1080/17512433.2018.1548277

35. Smith CH, Jabbar-Lopez ZK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol*. 2017;177(3):628-636. doi:10.1111/bjd.15665

36. Yousefzadeh H, Azad FJ, Banihashemi M, et al. Clinical efficacy and quality of life under micronutrients in combination with methotrexate therapy in chronic plaque of psoriatic patients. *Zhonghua Pifuke Yixue Zazhi*. 2017;35(4):187-194. doi:10.1016/j.dsi.2017.06.005

37. Lindqvist T, Salah LA, Gillstedt M, Wennberg AM, Osmancevic A. Methotrexate management in psoriasis: are we following the guidelines? *Acta Derm Venereol*. 2018;98(4):449-451. doi:10.2340/00015555-2857

38. Armstrong AW, Aldredge L, Yamauchi PS. Managing patients with psoriasis in the busy clinic: practical tips for health care practitioners. *J Cutan Med Surg*. 2016;20(3):196-206. doi:10.1177/1203475415623508

39. Drach M, Papageorgiou K, Maul JT, et al. Effectiveness of methotrexate in moderate to

severe psoriasis patients: real-world registry data from the Swiss Dermatology Network for Targeted Therapies (SDNTT). *Arch Dermatological Res*. 2019; 8:8. doi:10.1007/s00403-019-01945-6

40. Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol*. 2009;60(5):824-837. doi:10.1016/j.jaad.2008.11.906

41. Mijuskovic ZP, Kandolf-Sekulovic L, Tiodorovic D, et al. Serbian association of dermatovenereologists' guidelines for the diagnosis and treatment of psoriasis. *Serbian J Dermatol Venereol*. 2016;8(2): 61-78. doi:10.1515/sjdv-2016-0006

42. Salim A, Tan E, Ilchyshyn A, Berth-Jones J. Folic acid supplementation during treatment of psoriasis with methotrexate: a randomized, double-blind, placebo-controlled trial. *Br J Dermatol*. 2006;154 (6):1169-1174. doi:10.1111/j.1365-2133.2006.07289.x

43. Attwa EM, Elkot RA, Abdelshafey AS, Hafez AR. Subcutaneous methotrexate versus oral form for the treatment and prophylaxis of chronic plaque psoriasis. *Dermatol Ther*. 2019;32(5):e13051. doi:10.1111/dth.13051

44. National Institute for Health and Clinical Excellence. Guidance: psoriasis: assessment and management of psoriasis. Accessed July 14, 2020. https://www.nice.org.uk/guidance/cg153

45. Saurat JH, Langley RG, Reich K, Unnebrink K, Sasso EH, Kampman W. Relationship between methotrexate dosing and clinical response in patients with moderate to severe psoriasis: subanalysis of the CHAMPION study. *Br J Dermatol*. 2011;165(2):399-406. doi:10.1111/j.1365-2133.2011.10399.x

46. Mrowietz U, de Jong EM, Kragballe K, et al. A consensus report on appropriate treatment optimization and transitioning in the management of moderate-to-severe plaque psoriasis. *J Eur Acad Dermatol Venereol*. 2014;28(4):438-453. doi:10.1111/jdv.12118

47. Nast A, Amelunxen L, Augustin M, et al. S3 Guideline for the treatment of psoriasis vulgaris, update—Short version part 1—systemic treatment. *J Dtsch Dermatol Ges*. 2018;16(5):645-669. doi:10.1111/ddg.13516

48. Reich K, Augustin M, Thaci D, et al. A 24-week multicentre, randomised, open-label, parallel-group study comparing the efficacy and safety of ixekizumab to fumaric acid esters and methotrexate in patients with moderate-to-severe plaque psoriasis naive to systemic treatment. *Br J Dermatol*. 2019;3:3.

49. Warren RB, Mrowietz U, von Kiedrowski R, et al. An intensified dosing schedule of subcutaneous methotrexate in patients with moderate to severe plaque-type psoriasis (METOP): a 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017; 389(10068):528-537. doi:10.1016/S0140-6736(16)32127-4

50. Kolios AGA, Yawalkar N, Anliker M, et al. Swiss S1 guidelines on the systemic treatment of psoriasis vulgaris. *Dermatology*. 2016;232(4):385-406. doi:10.1159/000445681

51. Chakravarty K, McDonald H, Pullar T, et al; British Society for Rheumatology, British Health Professionals in Rheumatology Standards, Guidelines and Audit Working Group; British Association of Dermatologists. BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. *Rheumatology (Oxford)*. 2008;47(6):924-925. doi:10.1093/rheumatology/kel216a

52. National Institute for Health and Care Excellence. Surveillance report 2017—psoriasis: assessment and management (2012). Accessed July 14, 2020. https://www.ncbi.nlm.nih.gov/books/NBK550979/

53. Noor SM, Ayub N, Paracha MM. Efficacy and safety of methotrexate versus acitretin in chronic plaque psoriasis. *J Postgrad Med Inst*. 2017;31(1):4-7. https://jpmi.org.pk/index.php/jpmi/article/view/2031

54. Tichý M, Zapletalova J. Experience with the systemic treatment of severe forms of psoriasis. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2012;156(1):29-40. doi:10.5507/bp.2012.007

55. Yan K, Zhang Y, Han L, et al. Safety and efficacy of methotrexate for Chinese adults with psoriasis with and without psoriatic arthritis. *JAMA Dermatol*. 2019;155(3):327-334. doi:10.1001/jamadermatol.2018.5194

56. Yesudian PD, Leman J, Balasubramaniam P, et al. Effectiveness of subcutaneous methotrexate in chronic plaque psoriasis. *J Drugs Dermatol*. 2016; 15(3):345-349.

57. Nederlandse Vereniging voor Kindergeneeskunde. Richtlijn medicamenteuze behandeling van kinderen met juveniele idiopathische artritis. Accessed July 14, 2020. https://richtlijnendatabase.nl/richtlijn/juveniele_idiopathische_artritis_jia/startpagina_-_jia.html

58. Fortina AB, Bardazzi F, Berti S, et al. Treatment of severe psoriasis in children: recommendations of an Italian expert group. *Eur J Pediatr*. 2017;176(10): 1339-1354. doi:10.1007/s00431-017-2985-x

59. Kumar B, Saraswat A, Kaur I. Short-term methotrexate therapy in psoriasis: a study of 197 patients. *Int J Dermatol*. 2002;41(7):444-448. doi:10.1046/j.1365-4362.2002.01530.x

60. Hroch M, Chladek J, Simkova M, Vaneckova J, Grim J, Martinkova J. A pilot study of pharmacokinetically guided dosing of oral methotrexate in the initial phase of psoriasis treatment. *J Eur Acad Dermatol Venereol*. 2008;22 (1):19-24.

61. Chládek J, Simková M, Vanecková J, Hroch M, Vávrová J, Hůlek P. Assessment of methotrexate hepatotoxicity in psoriasis patients: a prospective evaluation of four serum fibrosis markers. *J Eur Acad Dermatol Venereol*. 2013;27(8):1007-1014. doi:10.1111/j.1468-3083.2012.04643.x

62. Barker J, Hoffmann M, Wozel G, et al. Efficacy and safety of infliximab vs. methotrexate in patients with moderate-to-severe plaque psoriasis: results of an open-label, active-controlled, randomized trial (RESTORE1). *Br J Dermatol*. 2011; 165(5):1109-1117. doi:10.1111/j.1365-2133.2011.10615.x

63. Heydendael VM, Spuls PI, Opmeer BC, et al. Methotrexate versus cyclosporine in moderate-to-severe chronic plaque psoriasis. *N Engl J Med*. 2003;349(7):658-665. doi:10.1056/NEJMoa021359

64. Haustein UF, Rytter M. Methotrexate in psoriasis: 26 years' experience with low-dose long-term treatment. *J Eur Acad Dermatol Venereol*. 2000;14(5):382-388. doi:10.1046/j.1468-3083.2000.00058.x

65. Ferrara G, Mastrangelo G, Barone P, et al; Rheumatology Italian Study Group. Methotrexate in juvenile idiopathic arthritis: advice and recommendations from the MARAJIA expert consensus meeting. *Pediatr Rheumatol Online J*. 2018;16(1):46. doi:10.1186/s12969-018-0255-8

66. Papp K, Thaçi D, Marcoux D, et al. Efficacy and safety of adalimumab every other week versus methotrexate once weekly in children and adolescents with severe chronic plaque psoriasis: a randomised, double-blind, phase 3 trial. *Lancet*. 2017;390(10089):40-49. doi:10.1016/S0140-6736(17)31189-3

67. Tangtatco JAA, Lara-Corrales I. Update in the management of pediatric psoriasis. *Curr Opin Pediatr*. 2017;29(4):434-442. doi:10.1097/MOP.0000000000000517

68. Visser K, Katchamart W, Loza E, et al. Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. *Ann Rheum Dis*. 2009;68(7): 1086-1093. doi:10.1136/ard.2008.094474

69. Schlessinger DI, Iyengar S, Yanes AF, et al. Development of a core outcome set for clinical trials in basal cell carcinoma: study protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. *Trials*. 2017;18(1):490. doi:10.1186/s13063-017-2244-5

70. Frankowski M, Świerkot J, Gomułkiewicz M, Korman L, Skoczyńska M, Starba A. Usefulness of noninvasive diagnostic procedures for assessment of methotrexate hepatotoxicity in patients with rheumatoid arthritis. *Rheumatol Int*. 2021. doi:10.1007/s00296-021-05059-z

71. Al Hammadi A, Al-Sheikh A, Ammoury A, et al. Experience and challenges for biologic use in the treatment of moderate-to-severe psoriasis in Africa and the Middle East region. *J Dermatolog Treat*. 2017;28(2):129-135. doi:10.1080/09546634.2016.1183763

72. Czarnowicki T, Malajian D, Shemer A, et al. Skin-homing and systemic T-cell subsets show higher activation in atopic dermatitis versus psoriasis. *J Allergy Clin Immunol*. 2015;136(1):208-211. doi:10.1016/j.jaci.2015.03.032

73. Genestier L, Paillot R, Fournel S, Ferraro C, Miossec P, Revillard JP. Immunosuppressive properties of methotrexate: apoptosis and clonal deletion of activated peripheral T cells. *J Clin Invest*. 1998;102(2):322-328. doi:10.1172/JCI2676

74. Clary DD, Reid AT, Kiani R, Fanciullo J. Methotrexate hepatotoxicity monitoring guidelines in psoriasis and rheumatoid arthritis: is there a consensus? *S D Med*. 2021;74(8):363-366.

75. van Huizen AM, Vermeulen FM, Bik CMJM, et al. On which evidence can we rely when prescribing off-label methotrexate in dermatological practice?—a systematic review with GRADE approach. *J Dermatolog Treat*. 2021:1-20. doi:10.1080/09546634.2021.1961999