metex | metoject

# IMPROVE MTX PATIENT EDUCATION

Addressing possible mild adverse events with an encouraging twist[1]

medac

# Aim and trial design

Most patients are concerned about side effects. What if patients new to methotrexate (MTX) learned to accept mild side effects as a “symptom” that the drug is working? Could a „new way of thinking“ support therapy? This study compared a standard education session with an education where possible “non-severe symptoms” were regarded as positive signal.[1]

47 adult patients with an inflammatory rheumatic disease starting MTX

Randomization (1:1)

**Mindset intervention group** (n = 24)
Educational video: Allocation of symptoms as positive signals

**Standard information group** (n = 23)
Educational video: Allocation of symptoms as side effects

You can find the videos here.

Most of the data from the individual participants was determined using a questionnaire at the respective time points.

**Start** — **Baseline**
Data collection before randomization and after watching the assigned video.

**2 wks** — **Booster session**
Reminder call to adress group-specific messages

**4 wks** — **Outcome analysis**
Primary: Symptome experience
Secondary: Adherence
Motivation for taking MTX

**12 wks** — **Outcome analysis**
Secondary: C-reactive protein
Treatment discontinuation

# Patient characteristics

| | Mindset intervention group (n = 24) | Standard information group (n = 23) |
|---|---|---|
| Age (years), M (SD)<br>Range | 51.8 (15.0)<br>27–78 | 55.6 (16.4)<br>24–80 |
| Gender<br>Female<br>Male<br>Gender Diverse | <br>16 (67%)<br>8 (33%)<br>0 (0%) | <br>19 (83%)<br>3 (13%)<br>1 (4%) |
| Rheumtic conditions treated by MTX<br>Rheumatoid arthritis<br>Psoriatic arthritis<br>Others | <br>10 (42%)<br>7 (29%)<br>7 (29%) | <br>10 (43%)<br>8 (35%)<br>5 (22%) |

## Example of mindset intervention – Reframing the role of side effects

„Methotrexate (MTX) works in your body similarly to how exercise strengthens muscles. Just as soreness after workouts indicates muscle growth, initial symptoms from methotrexate show that the medication is taking effect. Over time, this process helps reduce arthritis symptoms, allowing for better long-term management.“

# Outcome at 4 weeks

## Improved symptome experience

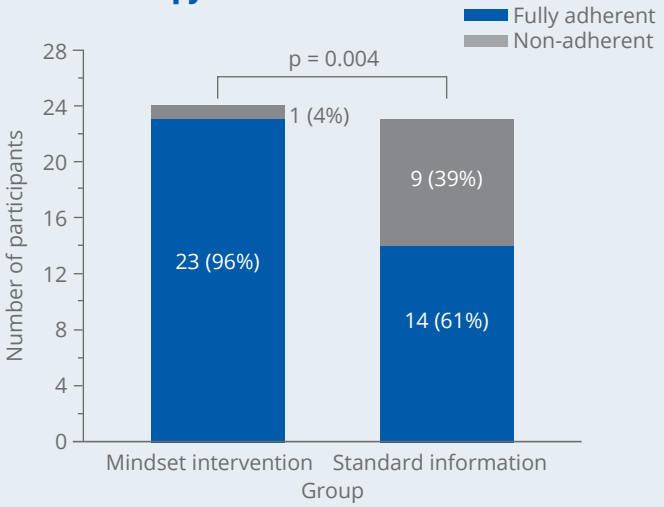
| Symptoms experienced at 4 weeks of MTX therapy | Mindset intervention Mean (SD) [n = 24] | Standard information Mean (SD) [n = 23] | Difference between the groups | |
|---|---|---|---|---|
| | | | P-value | Mean difference (95% CI) |
| Positive mindset to experienced symptoms | 6.75 (1.57) [n = 16] | 2.80 (2.20) [n = 10] | **0.002** | 3.95 (2.46, 5.49) |
| Symptom burden | 4.00 (1.71) [n = 16] | 6.70 (2.75) [n = 10] | **0.005** | -2.70 (-4.50, -0.90) |
| General symptoms experienced by condition | 7.25 (5.01) | 10.78 (6.67) | **0.045** | -3.53 (-6.99, -0.78) |
| MTX specific symptoms attributed as side effects | 3.17(2.46) | 3.96 (2.65) | 0.295 | -0.79 (-2.29, 0.71) |

Although both groups reported similar methotrexate-specific side effects, the patients who received the mindset intervention experienced less symptom burden and fewer general symptoms caused by condition.

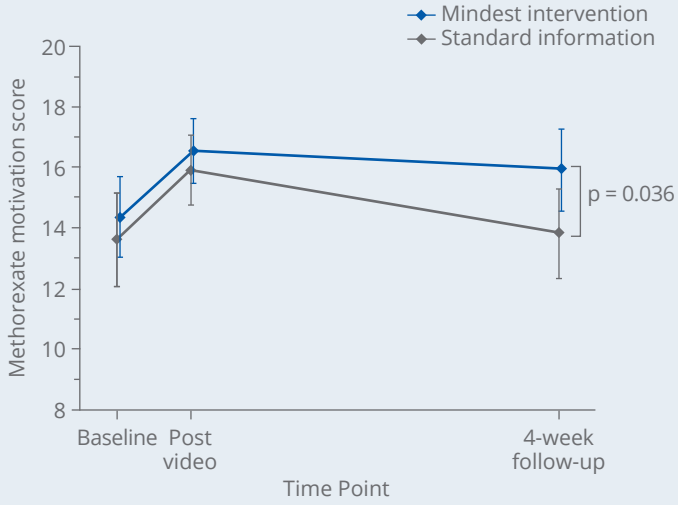
# Outcome at 4 weeks

## Increased adherence and motivation

### a) Self-reported adherence 4 weeks after starting MTX therapy




### b) Change in motivation over time

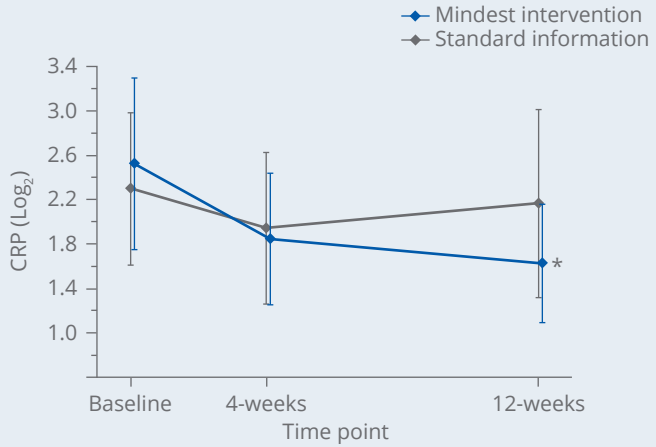



Both adherence and motivation of the participants were improved by mindset intervention.

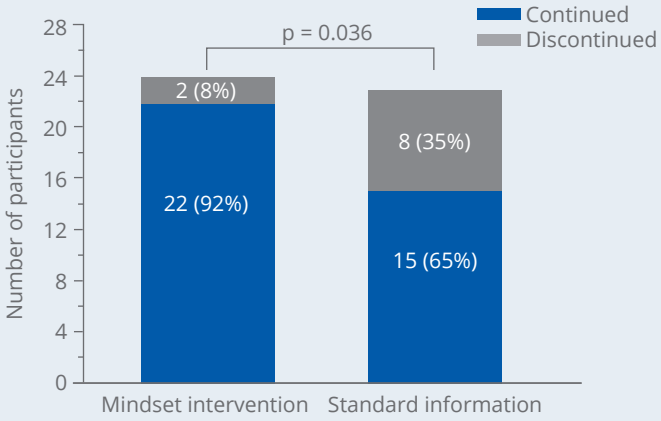
# Outcome at 12 weeks

## Significant reduction of C-reactive protein levels and treatment discontinuations

### a) Change in C-reactive protein levels




### b) Discontinuation of MTX at 12 weeks




CRP was determined from the results of routine clinical blood tests performed near each time point. The data shown here, were collected from a total of 41 participants (standard information n = 20, mindset intervention n = 21).
*Reduction in CRP levels between baseline and 12 weeks in the mindset intervention group ($p < 0.001$)

Only in the mindset intervention group was a significant decrease in CRP observed after three months. In addition, the number of MTX discontinuations was lower in this group.

## Literature

[1] Yielder R, Leibowitz K, Crum AJ et al. Changing mindsets about methotrexate in the rheumatology clinic to reduce side effects and improve adherence: a randomized controlled trial. Ann Behav Med. 2025;59(1):kaae089.

**Metoject® PEN / metex® Pen 7.5 mg / 10 mg / 12.5 mg / 15 mg / 17.5 mg / 20 mg / 22.5 mg/ 25 mg/ 27.5 mg / 30 mg solution for injection in pre-filled pen**
**Qualitative and quantitative composition:** 1 pre-filled pen with 0.15 ml (0.20 ml; 0.25 ml; 0.30 ml; 0.35 ml; 0.40 ml; 0.45 ml; 0.50 ml; 0.55 ml; 0.60 ml) contains 7.5 mg (10 mg; 12.5 mg; 15 mg; 17.5 mg; 20 mg; 22.5 mg; 25 mg; 27.5 mg; 30 mg) methotrexate. *Excipients:* NaCl, NaOH, HCl, water for injections.
**Metoject® / metex® 50 mg/ml solution for injection, pre-filled syringe**
**Qualitative and quantitative composition:** 1 ml of solution contains 50 mg methotrexate (as methotrexate disodium). 1 pre-filled syringe of 0.15 ml (0.20 ml; 0.25 ml; 0.30 ml; 0.35 ml; 0.40 ml; 0.45 ml; 0.50 ml; 0.55 ml; 0.60 ml) contains 7.5 mg (10 mg; 12.5 mg; 15 mg; 17.5 mg; 20 mg; 22.5 mg; 25 mg; 27.5 mg; 30 mg) methotrexate. *Excipients:* NaCl, NaOH, water for injections.
**Therapeutic indications:** Active rheumatoid arthritis in adult patients; polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate; severe psoriatic arthritis in adult patients; mild to moderate Crohn's disease either alone or in combination with corticosteroids in adult patients refractory or intolerant to thiopurines. *PEN additionally:* moderate to severe psoriasis in adult patients who are candidates for systemic therapy. *Syringe additionally:* severe recalcitrant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, PUVA and retinoids. **Posology and method of administration:** Should only be prescribed by physicians who are familiar with the various characteristics of the medicinal product and its mode of action. Patients must be educated to use the proper injection technique. The first injection of Metoject PEN should be performed under direct medical supervision. *Adults, rheumatoid arthritis:* The recommended initial dose is 7.5 mg of Metoject once weekly, administered subcutaneously. Depending on the individual activity of the disease and tolerability, the dose may be increased gradually by 2.5 mg per week. A weekly dose of 25 mg should in general not be exceeded. *Polyarthritic forms of juvenile idiopathic arthritis:* The recommended dose is 10-15 mg/m² body surface area (BSA)/once weekly, administered subcutaneously. In therapy-refractory cases the weekly dosage may be increased up to 20 mg/m² BSA/once weekly. Use in children < 3 years of age is not recommended as insufficient data on efficacy and safety is available for this population. *Psoriasis vulgaris, psoriatic arthritis:* Test dose of 5 – 10 mg should be administered parenterally, one week prior to therapy to detect idiosyncratic adverse reactions. The recommended initial dose is 7.5 mg of methotrexate once weekly, administered subcutaneously. The dose is to be increased gradually but should not, in general, exceed a weekly dose of 25 mg of methotrexate. *Crohn's disease:* Induction treatment: 25 mg/week administered subcutaneously. Response to treatment can be expected after approximately 8 -12 weeks. Maintenance treatment: 15 mg/week. *Elderly:* Dose reduction should be considered due to reduced liver and kidney function as well as lower folate reserves. If changing the oral to parenteral administration a reduction of dose may be required due to the variable bioavailability. **Contraindications:** Hypersensitivity to methotrexate or any of the excipients; severe liver impairment; alcohol abuse; severe renal impairment (creatinine clearance < 30 ml/min); pre-existing blood dyscrasias (bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anaemia); serious, acute or chronic infections such as tuberculosis, HIV, other immunodeficiency syndromes; ulcers of the oral cavity and known active gastrointestinal ulcer disease; pregnancy, breastfeeding; concurrent vaccination with live vaccines. **Special warnings and precautions for use:** In the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn's disease, Metoject PEN (methotrexate) must only be used once a week. Dosage errors in the use can result in serious adverse reactions, including death. **Undesirable effects:** Most serious adverse reactions of methotrexate include bone marrow suppression, pulmonary toxicity, hepatotoxicity, renal toxicity, neurotoxicity, thromboembolic events, anaphylactic shock and Stevens-Johnson syndrome. Most frequently (very common) observed adverse reactions of methotrexate include gastrointestinal disorders e.g. stomatitis, dyspepsia, abdominal pain, nausea, loss of appetite and abnormal liver function tests e.g. increased ALAT, ASAT, bilirubin, alkaline phosphatase. Other frequently (common) occurring adverse reactions are leukopenia, anaemia, thrombopenia, headache, tiredness, drowsiness, pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia, oral ulcers, diarrhoea, exanthema, erythema and pruritus. *Effects:* Pharyngitis, infection (incl. reactivation of inactive chronic infection), sepsis, conjunctivitis. Lymphoma. Leukopenia, anaemia, thrombopenia, pancytopenia, agranulocytosis, severe courses of bone marrow depression, lymphoproliferative disorders, eosinophilia. Allergic reactions, anaphylactic shock, hypogammaglobulinaemia. Precipitation of diabetes mellitus. Depression, confusion, mood alterations. Headache, tiredness, drowsiness, dizziness, pain, muscular asthenia or paraesthesia/ hypoaesthesia, changes in sense of taste (metallic taste), convulsions, meningism, acute aseptic meningitis, paralysis, encephalopathy/ leukoencephalopathy. Visual disturbances, impaired vision, retinopathy. Pericarditis, pericardial effusion, pericardial tamponade. Hypotension, thromboembolic events. Pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia. Symptoms indicating potentially severe lung injury (interstitial pneumonitis) are: dry, not productive cough, short of breath and fever, pulmonary fibrosis, Pneumocystis jirovecii pneumonia, shortness of breath and bronchial asthma, pleural effusion, epistaxis, pulmonary alveolar haemorrhage. Stomatitis, dyspepsia, nausea, loss of appetite, abdominal pain, oral ulcers, diarrhoea, gastrointestinal ulcers and bleeding, enteritis, vomiting, pancreatitis, gingivitis, haematemesis, haematorrhea, toxic megacolon. Abnormal liver function tests (increased ALAT, ASAT, alkaline phosphatase and bilirubin), cirrhosis, fibrosis and fatty degeneration of the liver, decrease in serum albumin, acute hepatitis, hepatic failure. Exanthema, erythema, pruritus, photosensitivity reactions, loss of hair, increase in rheumatic nodules, skin ulcer, herpes zoster, vasculitis, herpetiform eruptions of the skin, urticarial, increased pigmentation, acne, petechiae, ecchymosis, allergic vasculitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), increased pigmentary changes of the nails, acute paronychia, furunculosis, telangiectasia, skin exfoliation/ dermatitis exfoliative. Arthralgia, myalgia, osteoporosis, stress fracture, osteonecrosis of jaw (secondary to lymphoproliferative disorders). Inflammation and ulceration of the urinary bladder, renal impairment, disturbed micturition, renal failure, oliguria, anuria, electrolyte disturbances, proteinuria. Inflammation and ulceration of the vagina, loss of libido, impotence, gynaecomastia, oligospermia, impaired menstruation, vaginal discharge. Fever, wound-healing impairment, asthenia, injection site necrosis, oedema. Local damage (formation of sterile abscess, lipodystrophy) of injection site following intramuscular or subcutaneous administration. Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, pruritus, severe itching, pain) were observed, decreasing during therapy. **Overdose:** Calcium folinate is the specific antidote for neutralising the toxic undesirable effects of methotrexate. **Legal classification:** POM **Marketing authorisation holder:** medac GmbH, Theaterstr. 6, 22880 Wedel, Germany.
**Date of revision of text:** 19.09.2024
**PEN or syringe are registered in the following countries:** Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Latvia, Lithuania, Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

# Optimizing MTX therapy

- Mindset intervention is a promising approach to improve symptom experience in patients who are at an early stage of diagnosis.
- By applying this approach in daily practice, patients' adherence and persistence can be achieved by simple means.

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