An international, multicentre, interventional, randomised, assessor-blinded trial to MAXimise the METHotrexate therapy potential in patients with active rheumatoid arthritis (MethMax trial): study protocol for a randomised controlled trial

(Karolina Anderle et al, Trials, 2026)

What's the MethMax trial about?

Our study tests whether MTX injections under the skin help more patients achieve disease remission compared to MTX pills, when both are given at 25mg per week. Many RA patients don't reach remission on pills alone, and we aim to find out if switching the administration route can improve outcomes.

Key details from the publication:

- Study design: 24 weeks, 182 patients across 7 European countries
- Participants: RA patients on stable oral MTX (10 - 25mg/week) with active disease
- Goals: Compare remission rates, disease activity, quality of life, and side effects
- Innovations: Explores biomarkers (e.g., MTX metabolites, Torque Teno Virus) and adherence tracking (digital tools, questionnaires)

Why this publication matters:

MethMax is one of three trials in the Squeeze project, which focuses on optimizing existing RA therapies. By sharing this protocol openly, we aim to:

- Increase transparency in our clinical research goals
- Inform patients and providers about our methodology
- Advance personalized RA care through evidence-based insights

The article is free to read and highlights our commitment to improving RA treatment strategies. We invite the community to learn about our work and its potential to enhance patient outcomes.

Read the full protocol in the journal Trials: https://link.springer.com/article/10.1186/s13063-026-09519-4

“Can alternative means of phenotyping rheumatoid arthritis reduce its apparent heterogeneity? A comparison of three disease activity classifications with DAS28”

(Simon Steiger et al., RMD Open, 2026)

What the study did:

This study followed people with early rheumatoid arthritis (RA) over time to understand how their disease develops after starting treatment. The researchers used advanced data analysis methods to group patients based on how their symptoms and inflammation changed over time.

What they found:

The researchers identified several distinct patterns of disease progression. Some patients improved quickly and reached remission, while others had ongoing inflammation or slower recovery. These patterns were linked to differences in how inflammation appears in the body, either mainly in the joints or more broadly throughout the body (systemic inflammation). Importantly, simple measurements taken at the first visit, such as blood tests and joint counts, could already help predict which path a patient was likely to follow.

Why it matters for patients:

This study shows that rheumatoid arthritis does not develop the same way in everyone. Recognising early which disease pattern a patient has could help doctors choose the most effective treatment sooner.
In the future, this could lead to more personalised care, better disease control, and improved quality of life for people living with RA.

Access the publication via: https://pubmed.ncbi.nlm.nih.gov/41839530/

“The Effect of Certolizumab Pegol Dose and Dose Changes on Plasma Trough Levels: Data From a Randomized Phase III Trial”

(Gehin et al., Therapeutic Drug Monitoring, 2026)

What the study did:

This study examined how different doses of certolizumab pegol (a biologic drug used to treat rheumatoid arthritis) affect the amount of drug in patients’ blood. Researchers analysed data from a large clinical trial where patients received either a lower or higher dose, and some had their dose increased or decreased over time.

What they found:

- Higher doses led to higher drug levels in the blood, roughly doubling when the dose was increased.
- When the dose was reduced, drug levels dropped accordingly.
- Many patients with low drug levels reached the desired (effective) range after their dose was increased.
- Some patients had very low drug levels due to antibodies against the drug, which reduced its effectiveness.
- Factors such as body weight and inflammation also influenced drug levels, but antibodies had the strongest impact.

Why it matters for patients:

This study shows that adjusting the dose of certolizumab pegol can reliably change how much of the drug is present in the body.
In the future, doctors could use blood tests to measure drug levels and personalise dosing, ensuring patients receive the right amount, not too little (ineffective) and not too much (unnecessary).
This approach, called therapeutic drug monitoring, could improve treatment outcomes while reducing side effects and healthcare costs.

Access the publication via: https://journals.lww.com/drug-monitoring/fulltext/9900/the_effect_of_certolizumab_pegol_dose_and_dose.449.aspx

“Proactive therapeutic drug monitoring of biologic drugs in inflammatory diseases: a clinical practice guideline”

(Kawano-Dourado, Kristianslund, Gehin, Vandvik, et al.; BMJ 2024)

What the study is about:

For diseases such as **rheumatoid arthritis, inflammatory bowel disease, and psoriasis**, biologic drugs (like infliximab or adalimumab) have transformed treatment. But not everyone responds equally: some patients lose effect over time or develop antibodies that make the drug less effective.

This guideline brings together international experts and patient representatives to determine **when it makes sense to measure drug levels in the blood** to personalize treatment, a process called **therapeutic drug monitoring (TDM)**.

What the experts recommend:

1. **For infliximab (given by infusion):**
    - *Weak recommendation in favour* of regularly measuring drug levels during ongoing (maintenance) treatment — this may help maintain remission without extra risk.
2. **For adalimumab (given by injection):**
    - *Weak recommendation against* routine monitoring, as current studies don’t yet prove a clear benefit.
3. **At the start of treatment (induction phase):**
    - *No proven benefit yet* for proactive monitoring.

Why it matters for patients:

These recommendations support **shared decision-making** between patients and doctors.

For infliximab, regular monitoring could help **avoid flares, unnecessary dose increases, or early treatment failure**.

For adalimumab and others, more research is needed before routine monitoring is advised.

This marks a **global step toward personalized biologic therapy**, ensuring patients receive the right dose at the right time.

“Therapeutic serum level for adalimumab in rheumatoid arthritis: explorative analyses of data from a randomized phase III trial”

(Gehin et al., RMD Open, 2024)

What the study did:

This study looked at patients with active RA who started treatment with **adalimumab** (Humira® or its biosimilar Hyrimoz®), one of the most commonly used biologic drugs.
The researchers measured how much adalimumab was in patients’ blood over 48 weeks and compared those levels with how well their RA was controlled.

What they found:

- Patients whose blood levels of adalimumab were **above 4 milligrams per liter (mg/L)** were **more likely to reach remission or low disease activity** during the first year of treatment.
- Those with lower levels often responded poorly.
- Some patients developed **antibodies against the drug** (“antidrug antibodies”), which reduced the amount of active adalimumab in their blood and made the treatment less effective.
- Blood levels tended to stay stable over time, but people with antibodies had much lower drug levels and worse outcomes.

Why it matters for patients:

This study helps define what counts as an *effective blood level* of adalimumab.
Knowing this threshold (around **4 mg/L**) could allow doctors to use **therapeutic drug monitoring (TDM)**, measuring blood levels and adjusting doses if they are too low or if antibodies are detected.
This can make treatment more efficient, avoid unnecessary drug use, and help patients who aren’t responding find out *why*, whether it’s due to dose, antibodies, or other factors.
It’s a step toward **personalized dosing** and smarter, more sustainable use of biologic therapies in RA.

“Time-independent disease state identification defines distinct trajectories determined by localised vs systemic inflammation in early rheumatoid arthritis”

(Steinz, Knevel, et al. Annals of the Rheumatic Diseases, 2025)

What the study is about:

Not all patients with newly diagnosed rheumatoid arthritis (RA) follow the same path after starting treatment. Some improve quickly, others slowly, and some continue to have inflammation despite therapy.
Researchers from Leiden University, King’s College London, Newcastle University, and industry partners used **advanced data analysis and AI-based clustering** to follow over **1,400 patients** with early RA over 1.5 years.

What they found:

They identified **four main disease patterns (trajectories)**:

1. **Systemic inflammation (high ESR or white blood cells):** slower improvement and worse long-term wellbeing.
2. **Fast responders:** many swollen joints at first but rapid remission.
3. **Persistent joint inflammation (localized):** continuing symptoms despite treatment.
4. **Mixed or poor outcomes:** both joint and systemic inflammation with lower chances of remission.

These patterns were consistent in two large cohorts from the Netherlands and the UK.
Importantly, **blood tests and joint counts at the first visit could already predict most patients’ future trajectory**.

Why it matters for patients:

This research suggests that RA isn’t one single disease course: it can behave differently in different people, depending on whether inflammation is **mostly in the joints** or **systemic (throughout the body)**.
Recognizing these patterns early may help rheumatologists **personalize treatment intensity**, preventing long-term damage and improving quality of life.
It also shows the value of using **big data and AI** to understand and predict how RA evolves in real life.

“Location and amount of joint involvement differentiates rheumatoid arthritis into different clinical subsets”

(Maarseveen et al., Digital Medicine (npj), 2025)

What the study did:

Researchers analyzed data from over 1,000 people with newly diagnosed rheumatoid arthritis (RA) to see if the *pattern* of affected joints could reveal different “types” of RA, with the help of artificial intelligence algorithms. They wanted to understand why some patients respond better to treatment than others.

What they found:

They discovered **four main forms of RA**, based on which joints were inflamed at diagnosis:

1. **Foot-dominant RA**: mainly affects the feet and ankles.
2. **Oligoarticular RA**: few joints involved, often with positive antibodies (seropositive).
3. **Hand-dominant RA**: mainly affects the hands, often without antibodies (seronegative).
4. **Polyarthritis RA**: many joints affected across hands and feet.

People with **hand-dominant RA** tended to respond *better* to the first-line treatment (methotrexate) and reached remission more often than those with foot- or polyarthritis patterns.
These differences were confirmed in several independent patient groups and linked to distinct patterns of inflammation seen in joint tissue samples.

Why it matters for patients:

This study shows that *where* RA starts in your joints may influence *how the disease behaves* and *how well you respond to treatment*.
In the future, doctors might use this kind of analysis to **personalize therapy**, for example, by identifying early which patients may need stronger or faster treatment based on their joint pattern.
It also highlights that **foot joints**, often overlooked in standard joint counts, deserve more attention in both diagnosis and monitoring.

“Prevalence and correlates of adherence to disease-modifying antirheumatic drugs (DMARDs) in adults with rheumatoid arthritis – a scoping review protocol”

(Kocher et al., 2024)

What the study is about:

People with rheumatoid arthritis (RA) often need to take DMARDs (disease-modifying antirheumatic drugs) regularly to control inflammation and prevent joint damage. However, many patients find it difficult to take these medications exactly as prescribed, for example, skipping doses, stopping early, or forgetting doses.
The problem is that research results on how common this is, why it happens, and what it leads to have been inconsistent.

What the project will do:

This research team, including experts from Switzerland, Austria, Spain, the Netherlands, and EULAR, will review all studies published since 1998 on how well adults with RA adhere to their DMARD treatments.
They will look at:

- How often non-adherence happens
- What factors influence it (such as beliefs, side effects, cost, or communication with doctors)
- What health or economic consequences it has
- How adherence is measured in research

Why it matters for patients:

Understanding why people with RA may not always take their medication as prescribed is essential to improving long-term outcomes.
The results will help identify the biggest barriers and inform new solutions, including digital tools and care models, such as those being developed in our EU Horizon SQUEEZE project.
Ultimately, this research aims to make it easier for patients to stick with their treatments and maintain remission safely.