

Lay language summaries of SQUEEZE publications

1. "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.

Access the publication via: https://www.nature.com/articles/s41746-025-01997-1

2. "Therapeutic serum level for adalimumab in rheumatoid arthritis"

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.

Access the publication via: https://rmdopen.bmj.com/content/10/4/e004888

3. "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.

Access the publication via: https://osf.io/2h9en

4. "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):
 - o 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.

Access the publication via: https://www.bmj.com/content/387/bmj-2024-079830

5. "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 Al-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.

Access the publication via: https://ard.eular.org/article/S0003-4967(25)00900-8/fulltext