The effects of disease-modifying anti-rheumatic drugs (DMARDs) on patient-reported outcome (PRO) domains in rheumatoid arthritis (RA): a systematic review and network meta-analyses (NMA)

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INTRODUCTION

- Despite low disease activity, many RA patients continue to experience residual symptoms and disease burden that can be captured through PROs.
- Head-to-head comparisons of DMARDs based on PROs are limited or lacking.
- **NMA** enables such comparisons by integrating direct and indirect evidence.

OBJECTIVE

- This **NMA** enables to evaluate the relative effects of DMARDs on the most relevant PRO domains for RA patients:
  - Pain: VAS
  - Fatigue: FACIT-F
  - Activity limitation: HAQ(-DI)
  - Physical health: SF-36 PCS
  - Mental health: SF-36 MCS

METHODS

- **Systematic review with AI-assisted screening (ASReview) including randomized controlled trials (RCTs) that:**
  - Compared a DMARD vs another DMARD or placebo.
  - Reported PROs aligned with the International Consortium for Health Outcomes Measurement (ICHOM) RA-relevant domains.
- **NMA:** to evaluate direct and indirect evidence within each PRO domain.
  - **Network plots** to visualize network characteristics
  - **Forest plots** presented relative effects of DMARDs on each PRO domain.
- **Sensitivity and subgroup analyses:** to assess robustness of results.
- **Variance-weighted clustered linear regression**: to explore effects of disturbing factors on mean PRO change scores.
  - early RA (<3 years diagnosis), DMARD naivety, follow-up duration, and baseline PRO score.

RESULTS

- 99 records included (I^2=0-96%) among 5 PRO domains.

Table 1. *Characteristics of included studies of each PRO domain.*

PRO domain	RCTs (arms)	Sample size	Paired comparisons (direct)	DMARDs classes	DMARD classes not reported
Pain	47 (102)	20,013	36 (17)	9	
Fatigue	28 (63)	15,213	15 (9)	6	ANA, ABA, CSD
Activity limitation	**63 (138)**	**27,189**	**36 (18)**	**9**	
Physical health	33 (72)	16,709	28 (14)	8	ANA
Mental health	28 (59)	11,491	28 (14)	8	ANA

- JAKi, IL6i and CSD were significantly better at reducing activity limitation compared to TNFi.
- Sensitivity and subgroup analyses confirmed result robustness.
- Early RA and worse baseline PRO scores predicted larger PRO improvements (p<0.05).

PRO domain: activity limitation

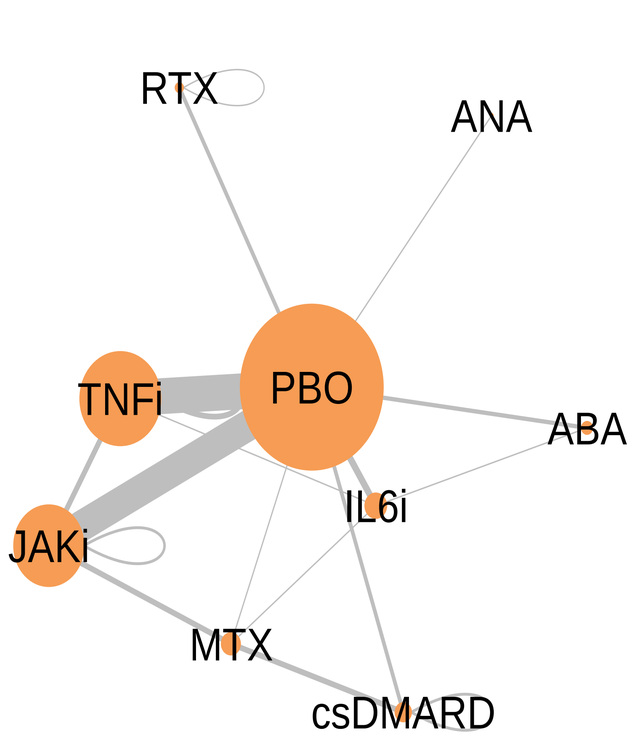

Figure 1. *Network diagram for activity limitation.*

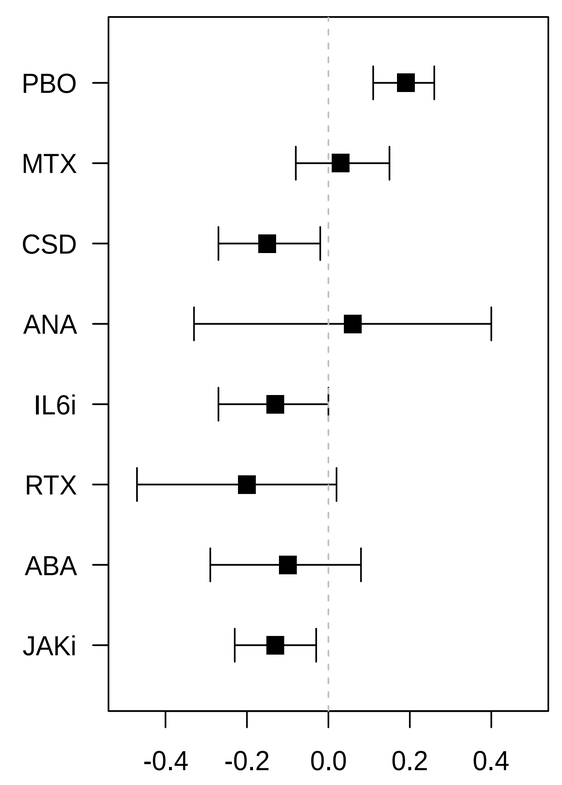

Figure 2. *Forest plot for activity limitation.*

CONCLUSIONS

- The use of NMA allows the inclusion of more studies, enabling comparisons between DMARDs that have not been directly compared in individual trials.
- However, substantial heterogeneity within the comparisons limits the strength of the evidence.
- To identify more differences, future RCTs should use PROs as primary outcomes.

CONTACT INFORMATION

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Abbreviations

ABA: abatacept; ANA: anakinra; CSD/csDMARD: conventional synthetic disease-modifying anti-rheumatic drugs; FACIT-F: Functional Assessment of Chronic Illness Therapy: Fatigue; HAQ(-DI): Health Assessment Questionnaire(-Disability Index); IL6i: interleukin 6 inhibitor; JAKi: janus kinase inhibitors; MTX: methotrexate; N/A: not applicable; PBO: placebo; PRO: relevant patient-reported outcome RTX: rituximab; SF-36 PCS/MCS: 36-Item Short Form Health Survey: Physical/Mental Component Score; TNFi: tumor necrosis factor inhibitor; VAS: visual analogue scale.