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## Background & Methods

Inflammatory arthritis (IA) leads to high direct healthcare and indirect costs across regions. Earlier reviews were subtype-specific or outdated and often omitted direct non-healthcare or carer components, limiting comparability. We provide an updated, multi-subtype synthesis with methodological appraisal.

- Protocol & search:** PRISMA; PROSPERO CRD42023452485; MEDLINE, Embase, Cochrane Database of Systematic Reviews, HMIC; last search 5 July 2025.
- Standardisation:** All costs standardised to 2024 US dollar values using the CCEMG-EPPi Centre cost converter.
- Eligibility & outcomes:** Adults with AxSpA, PsA, ReA, seropositive/seronegative RA where available. Outcomes: **direct healthcare costs, direct non-healthcare costs, indirect costs when reported.**
- Synthesis & statistics:** Narrative synthesis; **Cochran–Armitage test** for trends in **proportions** of cost components (e.g. medication, inpatient).

### Study characteristics

n=82 studies; 28 countries; designs mainly **prevalence-based (96.3%)** with **bottom-up (93.9%)** costing; data largely **retrospective databases (86.1%)**. Perspectives: **healthcare system 48.8%, societal 41.5%, patients and families 8.5%**. HCA ~90% for productivity loss valuation; FCA seldom used.

## Key drivers

- Medication** is the primary driver of **direct healthcare costs**, reflecting wider use of **bDMARDs**.
- Hospitalisation** and **outpatient visits** remain major but declining contributors.
- Productivity losses** from **work disability** and **absenteeism** dominate **indirect costs**.
- Carer productivity losses** - up to 65% of total productivity losses - substantially adds to the societal burden.
- Comorbidities**, especially depression, cardiovascular and respiratory diseases, markedly increase total and direct healthcare costs.

## Proportions & Temporal Trends

### Proportions

- Indirect costs > 60% of total societal costs in 14/31 estimates.
- Productivity losses reported in ~50% studies; **presenteeism** rarely captured.
- Carer productivity losses reported in ~33% studies; contributes **1.3–65%** of indirect costs.

### Temporal trends (Cochran–Armitage)

- AxSpA: Direct ↑ (Z = 2.88, p = 0.0020); Productivity ↓ (Z = -2.85, p = 0.0022). Within direct (AxSpA): Medication ↑ (Z = 2.42, p = 0.0078).
- PsA: Inpatient ↓ (Z = -1.76, p = 0.0310).
- Pattern mirrors RA: **higher drug share, lower inpatient.**

## Study landscape

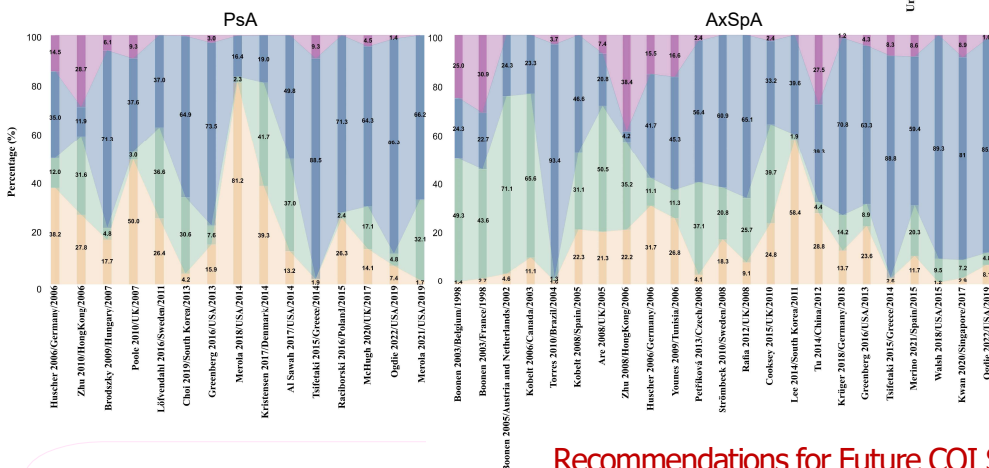
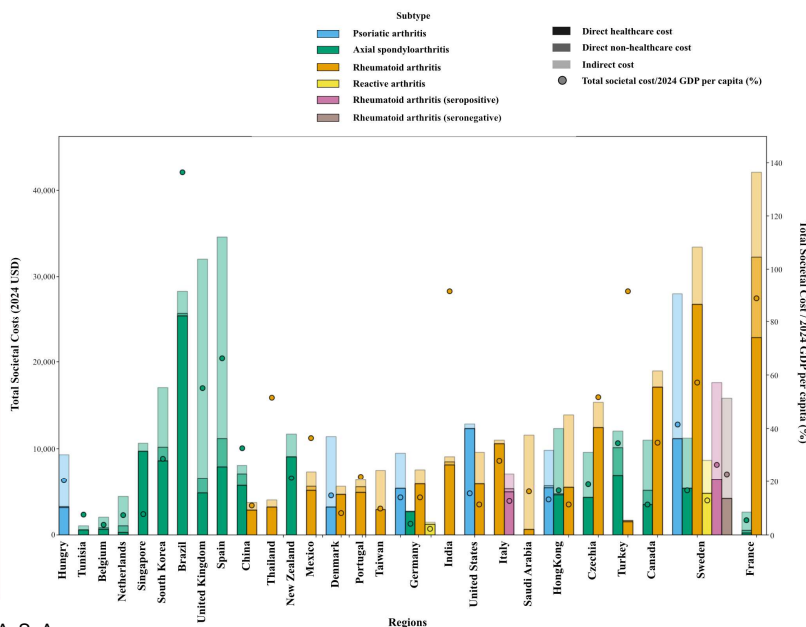
- Subtypes:** AxSpA n=49, PsA n=30, ReA n=2; RA update n=13; 8 studies separated serostatus.
- Regions:** Europe 39.0%, North America 26.8%, Asia 25.6%.

## Cost ranges & benchmarking

Per-patient annual costs (2024 USD)

- Direct healthcare costs: US\$222–71,518 (AxSpA/PsA/ReA); RA recent: US\$502–84,260.
- Direct non-healthcare costs: US\$53–3,272.
- Indirect costs (productivity losses): US\$79–25,456.

Benchmark to **GDP per capita**: 2.1%–136.4% overall; most estimates 10–30%.



## Methodological Heterogeneity

- Perspective / horizon** unclear in many studies.
- Indirect cost methods** inconsistent (HCA vs FCA); **carer / non-healthcare** often omitted.
- < 50% report uncertainty (**modified CHEERS checklist**).
- 70% omit sensitivity analysis (**Larg & Moss checklist**).
- Evidence dominated by **prevalence-based (96%), bottom-up (94%), retrospective data**.

## Recommendations for Future COI Studies

### Reporting

- State **price year + currency** clearly.
- Specify **perspective** and **time horizon**.
- Disaggregate **direct healthcare, direct non-healthcare, indirect, carer** components.

### Productivity methods

- Report and justify **HCA / FCA**; test impact in sensitivity scenarios.

### Scope & design

- Adopt **societal perspective** where possible.
- Include **comorbidities, technical examinations**, and **all-cause costs** for incremental burden.

### Quality assurance

- Follow **modified CHEERS checklist** and **Larg & Moss checklist**; conduct **uncertainty and heterogeneity** analyses.

## References

- P.-H. Hsieh, O. Wu, C. Geue, E. McIntosh, I. B. McInnes, and S. Siebert, '02 Economic burden of rheumatoid arthritis: a systematic review of literature in biologic era', Ann. Rheum. Dis., vol. 79, no. 6, pp. 771–777, Jun. 2020, doi: 10.1136/annrheumdis-2019-216243.
- Larg and J. R. Moss, 'Cost-of-Illness Studies: A Guide to Critical Evaluation', Pharmacoeconomics, vol. 29, no. 8, pp. 653–671, Aug. 2011, doi: 10.2165/11588380-000000000-00000.
- D. Husereau et al., 'Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement', BMJ, vol. 346, no. mar25 1, pp. f1049–f1049, Mar. 2013, doi: 10.1136/bmj.f1049.