

## 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 Earlier reviews were subtype-specific or outdated and often omitted direct non-healthcare or carer components, limiting comparability.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

~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.

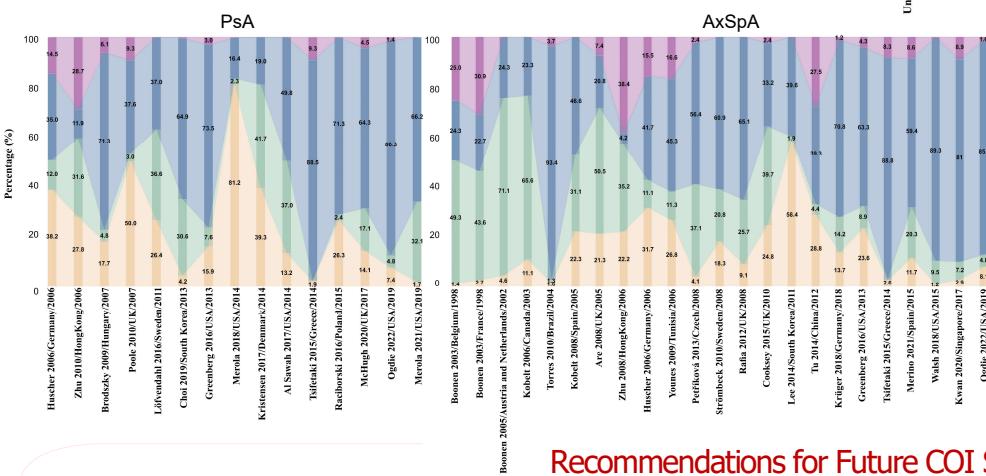
## Proportions & Temporal Trends

### 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  $\uparrow$  ( $Z = 2.88$ ,  $p = 0.0020$ ); Productivity  $\downarrow$  ( $Z = -2.85$ ,  $p = 0.0022$ ). Within direct (AxSpA): Medication  $\uparrow$  ( $Z = 2.42$ ,  $p = 0.0078$ ).
- PsA: Inpatient  $\downarrow$  ( $Z = -1.76$ ,  $p = 0.0310$ ).
- Pattern mirrors RA: higher drug share, lower inpatient.



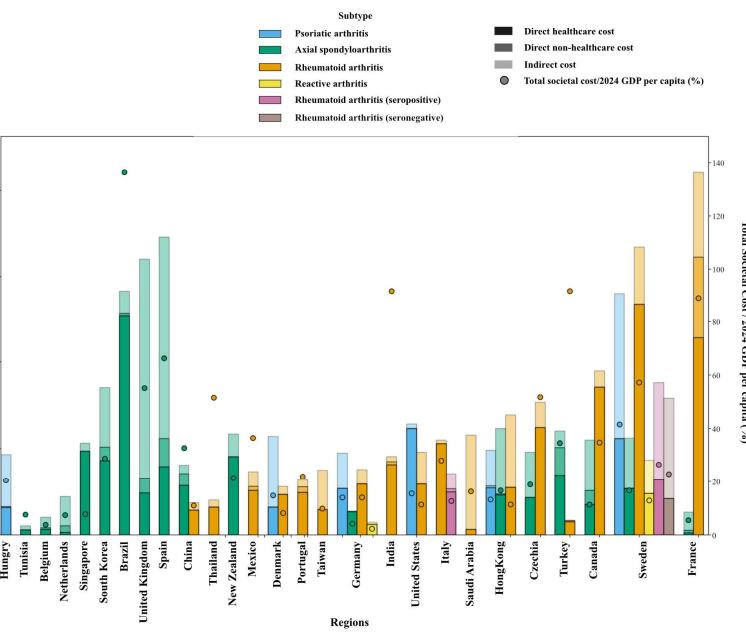
## Recommendations for Future COI Studies

### 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.



## 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.

### 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