

Background: Comparative effectiveness studies using observational data are increasingly used. Despite their high potential for bias, there are no detailed recommendations on how these studies should best be analysed and reported in rheumatology.

Objectives: To conduct a systematic literature review of comparative effectiveness research in rheumatology to inform the EULAR task force developing points to consider when analysing and reporting comparative effectiveness research with observational data.

Methods: All original articles comparing drug effectiveness in longitudinal observational studies of ≥ 100 patients published in key rheumatology journals (Scientific Citation Index > 2) between 1.01.2008 and 25.03.2019 available in Ovid MEDLINE® were included. Titles and abstracts were screened by two reviewers for the first 1000 abstracts and independently checked to ensure sufficient agreement has been reached. The main information extracted included the types of outcomes used to assess effectiveness, and the types of analyses performed, focusing particularly on confounding and attrition.

Results: 9969 abstracts were screened, with 218 articles proceeding to full-text extraction (Figure 1), representing a number of rheumatic and musculoskeletal diseases. Agreement between the two reviewers for the first 1000 abstracts was 92.7% with a kappa of 0.6. The majority of the studies used several outcomes to evaluate effectiveness (Figure 2A). Most of the studies did not explain how they addressed missing data on the covariates (70%) (Figure 2B). When addressed (30%), 44% used complete case analysis and 10% last observation carried forward (LOCF). 25% of studies did not adjust for confounding factors and there was no clear correlation between the number of factors used to adjust and the number of participants in the studies. An important number of studies selected covariates using bivariate screening and/or stepwise selection. 86% of the studies did not acknowledge attrition (Figure 2C). When trying to correct for attrition (14%), 38% used non-responder (NR) imputation, 24% used LUNDEX¹, a form of NR imputation, and 21% LOCF.

Figure 2: Results of the Systematic Literature Review

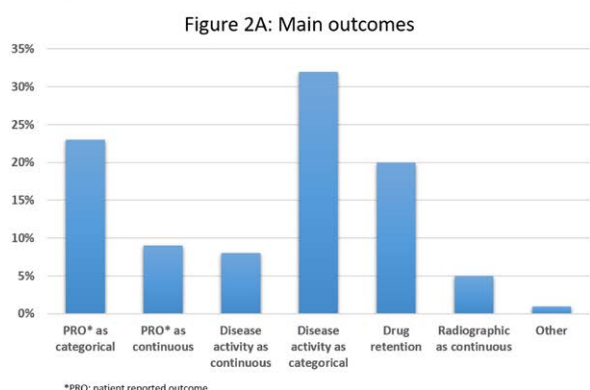


Figure 2B: Missing Data

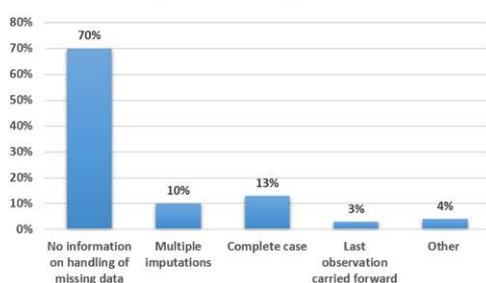
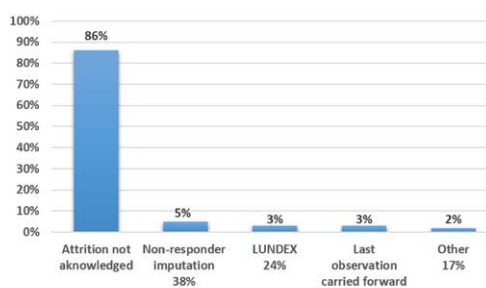


Figure 2C: Attrition



Conclusion: Most of studies used multiple outcomes. However, the vast majority did not acknowledge missing data and attrition, and a quarter did not adjust for any confounding factors. Moreover, when attempting to account for attrition, several studies used methods which potentially increase bias (LOCF, complete case analysis, bivariate screening...). This systematic review confirms the need for the development of recommendations for the assessment and reporting of comparative drug effectiveness in observational data in rheumatology.

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OP0199

POINTS TO CONSIDER WHEN ANALYSING AND REPORTING COMPARATIVE EFFECTIVENESS RESEARCH WITH OBSERVATIONAL DATA IN RHEUMATOLOGY

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Background: Comparing drug effectiveness in observational settings is hampered by several major threats, among them confounding and attrition bias bias

(patients who stop treatment no longer contribute information, which may overestimate true drug effectiveness).

Objectives: To present points to consider (PtC) when analysing and reporting comparative effectiveness with observational data in rheumatology (EULAR-funded taskforce).

Methods: The task force comprises 18 experts: epidemiologists, statisticians, rheumatologists, patients, and health professionals.

Results: A systematic literature review of methods currently used for comparative effectiveness research in rheumatology and a statistical simulation study were used to inform the PtC (table). Overarching principles focused on defining treatment effectiveness and promoting robust and transparent epidemiological and statistical methods increase the trustworthiness of the results.

Points to consider

Reporting of comparative effectiveness observational studies must follow the STROBE guidelines

Authors should prepare a statistical analysis plan in advance

To provide a more complete picture of effectiveness, several outcomes across multiple health domains should be compared

Lost to follow-up from the study sample must be reported by the exposure of interest

The proportion of patients who stop and/or change therapy over time, as well as the reasons for treatment discontinuation must be reported

Covariates should be chosen based on subject matter knowledge and model selection should be justified

The study baseline should be at treatment initiation and a description of how covariate measurements relate to baseline should be included

The analysis should be based on all patients starting a treatment and not limited to patients remaining on treatment at a certain time point

When treatment discontinuation occurs before the time of outcome assessment, this attrition should be taken into account in the analysis.

Sensitivity analyses should be undertaken to explore the influence of assumptions related to missingness, particularly in case of attrition

Conclusion: The increased use of real-world comparative effectiveness studies makes it imperative to reduce divergent or contradictory results due to biases. Having clear recommendations for the analysis and reporting of these studies should promote agreement of observational studies, and improve studies' trustworthiness, which may also facilitate meta-analysis of observational data.

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Multiple issues in inherited connective tissues - more than 'just' hypermobility

OP0200

PATIENTS WITH HYPERMOBILITY RELATED DISORDERS HAVE A SIGNIFICANT NUMBER OF ORTHOPAEDIC INTERVENTIONS ON MULTIPLE SITES AND AT A YOUNG AGE: DATA FROM A TERTIARY REFERRAL CENTRE

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Background: Mechanisms of pain associated with joint hypermobility are poorly understood and include nociceptive pain from structural joint changes along with soft tissue injuries linked to impaired proprioception; central sensitisation associated with chronic pain and muscle weakness alongside deconditioning. Anxiety and depression are also thought to play a role in patients presenting with pain and hypermobility. We have observed an increase in the rate of orthopaedic surgical procedures undertaken in patients attending the hypermobility clinics compared to those attending the general rheumatology and chronic pain clinics. There is limited published data regarding orthopaedic interventions in patients with hypermobility related disorders especially those with confirmed genetic mutations.

Objectives: We aimed to evaluate the characteristics of patients in our hypermobility cohort focusing on those who had received prior surgical intervention in order to understand the underlying mechanism behind their presentations.

Methods: A retrospective review of medical records was conducted of patients attending a hypermobility clinic at our tertiary referral centre, University College London Hospital, between January 2018 and December 2018.

Results: There were 350 patients (300 females, 50 males) with a mean age of 36 years (range 18-71 years). 63% had a diagnosis of Hypermobility Spectrum Disorder or Hypermobility Syndrome and 37% had a type of Ehlers-Danlos Syndromes (EDS) (hypermobility, classical, vascular or other rare type). 46 patients (13%) had documented genetic mutations. 83 patients (24%) had undergone orthopaedic interventions including 9 who had EDS with confirmed genetic mutations. 54% of patients who had surgical intervention were under the age of 40. The total number of surgical procedures in the cohort was 227 (equating to 0.6485 interventions per patient). Of those requiring operative intervention, the average number of interventions per patient was 2.73. One third of patients had surgery on two or more joint groups, including 8 patients (2%) who had surgery in four or more joint groups. Knees (24%) and hips (23%) were the most common sites for operative intervention with 9% having surgery on their shoulders. 29% of pts had significant hypermobility with a Beighton score of 7 and above but there was no correlation between Beighton score and number of surgical procedures. Only 2% of cases were referred from an orthopaedic team thereby excluding a referral bias.

Conclusion: Patients with hypermobility related disorders have a significant number of orthopaedic surgical procedures on multiple sites and at a young age, with indication of mechanical pathology playing an important role in their symptoms. The Beighton score does not appear to be a reliable predictor of surgical intervention. This is not surprising given that the score only covers 5 joint areas and excludes common surgical sites such as the hips and shoulders. Early diagnosis and a holistic non-operative approach combining physiotherapy and chronic pain management is essential to reduce the need for multiple surgical procedures.

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