

of the Use of Productivity Losses/Gains in Cost-Effectiveness Analyses of Immune-Mediated Disorders

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INTRODUCTION

In light of the lack of an agreed international standard for how to conduct cost-effectiveness analyses (CEAs), including cost-utility analyses (CUAs) from a societal perspective, there are differences regarding to what extent the inclusion of productivity losses/gains in economic evaluations can affect cost-effectiveness results and subsequently decisions on whether to recommend new health technologies.

OBJECTIVES

We conducted a systematic literature review of CEAs and CUAs of drugs for chronic immune-mediated disorders to understand how cost elements and cost calculation methods related to productivity losses/gains are used and examine the impact of including productivity costs on economic outcomes.

METHODS

MEDLINE, Embase, and Cochrane Library were searched from January 2010 to October 2020 for all CEAs and CUAs in adults including any of the following conditions: ankylosing spondylitis, chronic idiopathic urticaria, Crohn's disease, fibromyalgia, juvenile idiopathic arthritis, psoriasis, rheumatoid arthritis, systemic lupus erythematosus, and ulcerative colitis. Productivity cost elements including absenteeism, presenteeism, unemployment/early retirement, premature mortality, and informal care were extracted, along with the method used to determine them. Table 1 presents the inclusion and exclusion criteria PICOS (population, intervention, comparator, outcomes, study design) elements used.

Table 1: The inclusion and exclusion criteria PICOS elements used

Category	Details
Population	Adult patients (ages ≥ 18 years old)* with at least one of the following disorders: - Ankylosing spondylitis - Chronic idiopathic urticaria (including chronic spontaneous urticaria) - Crohn's disease - Fibromyalgia - Juvenile idiopathic arthritis - Psoriasis - Rheumatoid arthritis - Systemic lupus erythematosus - Ulcerative colitis
Interventions/comparators	Any drug treatment
Study types	Full economic evaluations: CEAs and CUAs If a study could estimate an ICER (i.e., the study described incremental costs per incremental QALY or life years or cost per response), the study was included.
Outcomes	- Descriptive differences (e.g., publication year, country, type of analysis, model used, time horizon) - Productivity loss elements and approaches - Impact of including productivity costs on ICER
Language	English only
Country	No limits
Publication types	Full-text articles only While there are conference posters and articles that may include cost data, the final data were considered to be uncertain/unverifiable if the full-text article was not available; therefore, only those with full-text articles available were included.
Time-limits	- 2010 to 2020 for full text articles - 2018 to 2020 for the conference abstracts

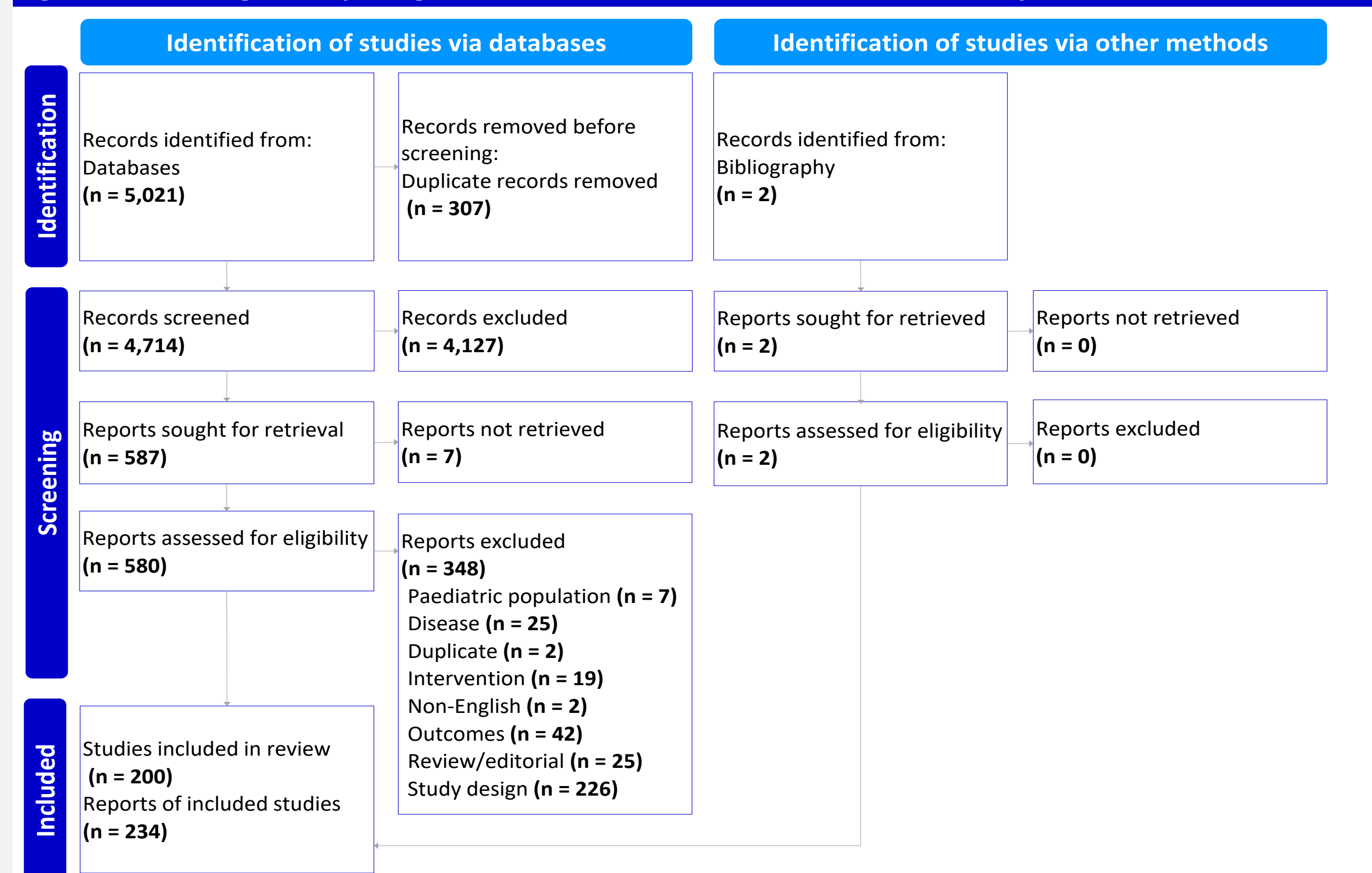
Key: ICER, incremental cost-effectiveness ratio; PICOS, population, intervention, comparator, outcomes, study design; QALY, quality-adjusted life year. Note: *If it was unclear in a study whether adults or children were assessed, then the study was included based on the assumption that all the indications examined are more prevalent in adults, especially when it comes to economic studies. Moreover, if a study included both adult and paediatric patients, it was included if subgroup data for adult patients were reported. In a second instance, if adult patients constituted ≥ 80% of the total population, then the study was included and data were extracted for the complete study population.

RESULTS

1. Study selection

- Our searches identified 5,021 records, identified 200 unique studies from 234 publications following screening (Figure 1).

Figure 1: Flow diagram depicting search results and selection of studies for analysis



Notes: One of the studies – Liu et al., 2012 – reported data for three separate indications (Crohn's disease, psoriasis, and rheumatoid arthritis). For the purposes of narrative synthesis and qualitative analysis, this was counted three times, once for each respective indication. Thus, the number of studies included in review was 200.

2. Characteristics of the included studies

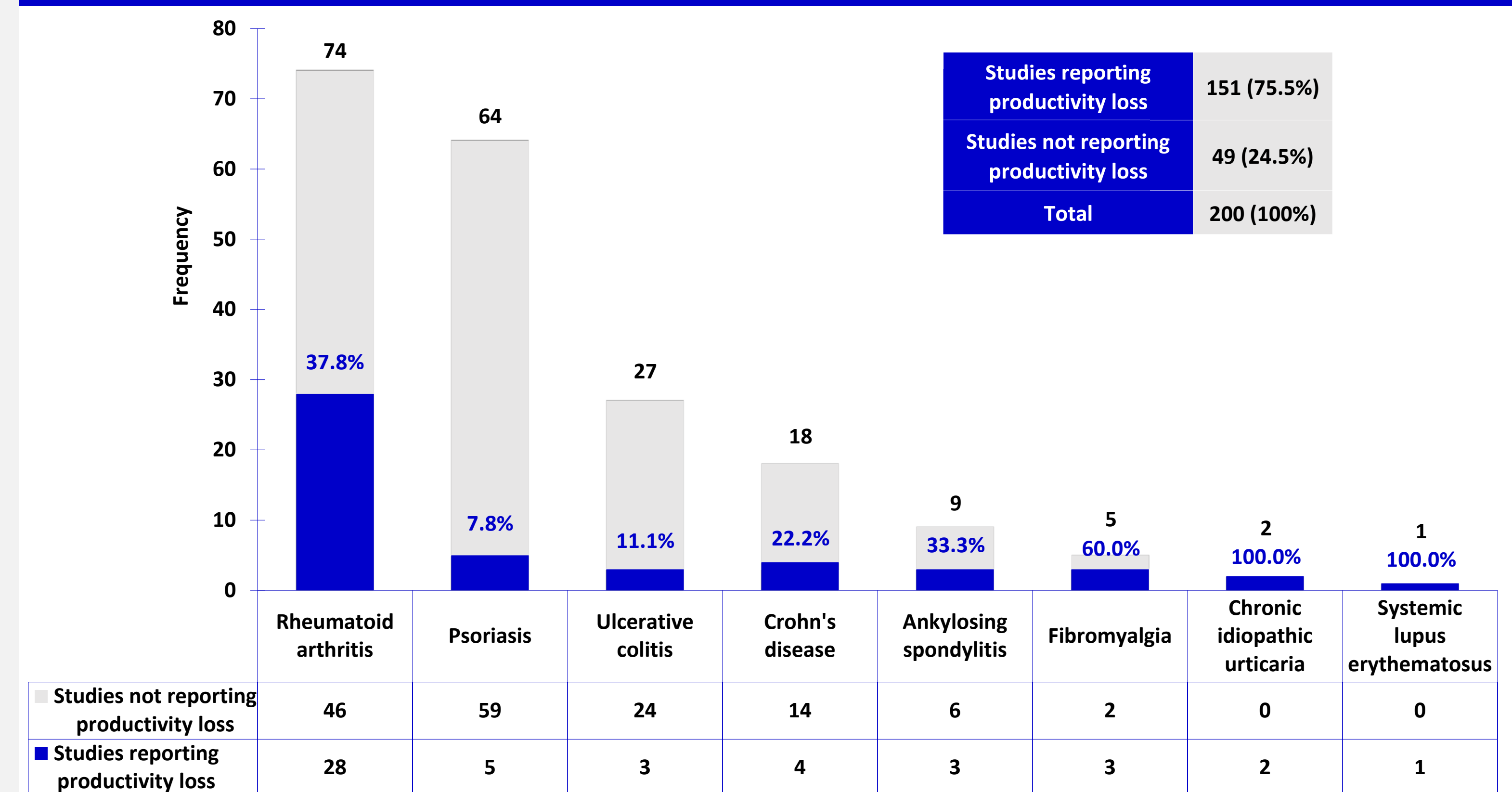
- Most of the studies investigated rheumatoid arthritis (74; 37.0%) or psoriasis (64; 32.0%). The majority were CUAs (146; 73.0%), with some including both a CEA and a CUA (Table 2).
- 49 studies were identified that considered productivity loss, the majority of which investigated rheumatoid arthritis followed by psoriasis, Crohn's disease (Figure 2)

Table 2: Characteristics of included studies

Disease	Total	Rheumatoid arthritis*	Psoriasis*	Ulcerative colitis	Crohn's disease*	Ankylosing spondylitis	Fibromyalgia	Chronic idiopathic urticaria	Systemic lupus erythematosus
Number of studies	200 (100%)	74 (37.0%)	64 (32.0%)	27 (13.5%)	18 (9.0%)	9 (4.5%)	5 (2.5%)	2 (1.0%)	1 (0.5%)
Economic analysis									
CEA	54 (27.0%)	13 (6.5%)	32 (16.0%)	3 (1.5%)	3 (1.5%)	1 (0.5%)	2 (1.0%)	0 (0.0%)	0 (0.0%)
CUA	137 (68.5%)	58 (29.0%)	31 (15.5%)	23 (11.5%)	15 (7.5%)	7 (3.5%)	0 (0.0%)	2 (1.0%)	1 (0.5%)
CEA + CUA	9 (4.5%)	3 (1.5%)	1 (0.5%)	1 (0.5%)	0 (0.0%)	1 (0.5%)	3 (1.5%)	0 (0.0%)	0 (0.0%)
Interventions and comparators									
Biologics and/or JAKi	171 (85.5%)	70 (35.0%)	51 (25.5%)	24 (12.0%)	16 (8.0%)	7 (3.5%)	0 (0.0%)	2 (1.0%)	1 (0.5%)
Others [†]	29 (14.5%)	4 (2.0%)	13 (6.5%)	3 (1.5%)	2 (1.0%)	2 (1.0%)	5 (2.5%)	0 (0.0%)	0 (0.0%)

Key: CEA, cost-effectiveness analysis; CUA, cost-utility analysis; JAKi, Janus kinase inhibitor. Notes: *A single study reported data for three indications: Crohn's Disease, psoriasis, and rheumatoid arthritis (Liu et al., 2012). [†] Interventions other than biologics and JAKi were listed as "Others".

Figure 2: Studies reporting the impact of productivity loss



3. Analysis of productivity loss elements and approaches

- Of the 49 studies incorporating productivity losses/gains, 42 reported the type of cost element used; all of these used patient absenteeism, either alone or in addition with other elements.
- Only 16 studies reported the method used to value productivity changes, of which 8 used a human capital approach, 4 used a friction cost approach, and 4 used both approaches.

4. Qualitative analysis of impact of including productivity costs on ICER

- 28 of the 49 studies (57.1%) reported inclusion of productivity losses/gains as contributing to more favourable cost-effectiveness, while 12 (24.5%) reported no significant impact. 9 (18.4%) studies did not report information regarding the potential impact on the incremental cost-effectiveness ratio (ICER). None of the studies reported inclusion to contribute to less favourable outcomes (Table 3).

Table 3: Studies reporting the impact of productivity loss/gain inclusion on the ICER

	Total	Rheumatoid arthritis	Psoriasis	Ulcerative colitis	Crohn's disease	Ankylosing spondylitis	Fibromyalgia	Chronic idiopathic urticaria	Systemic lupus erythematosus
Studies reporting productivity loss	49 (100%)	28 (100%)	5 (100%)	3 (100%)	4 (100%)	3 (100%)	3 (100%)	2 (100%)	1 (100%)
Reported impact of inclusion of productivity losses/gains on the ICER (percentage of number of studies for each disease)									
More favourable	28 (57.1%)	12 (42.9%)	3 (60.0%)	3 (100%)	3 (75.0%)	3 (100%)	1 (33.3%)	2 (100%)	1 (100%)
No significant impact	12 (24.5%)	8 (28.6%)	2 (40.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (66.7%)	0 (0.0%)	0 (0.0%)
Less favourable	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Impact not reported	9 (18.4%)	8 (28.6%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Discussion

- For diseases where the impact of productivity loss is already widely reported, such as rheumatoid arthritis, many CEAs incorporate productivity loss.
- The identified evidence base suggests that including productivity elements into an economic evaluation leads to generally more favourable outcomes in terms of cost-effectiveness, but less favourable cost-effectiveness outcome resulting from inclusion of productivity changes may not have been reported due to non-reporting bias.

Conclusion

- This study suggests that incorporating productivity cost elements may positively affect cost-effectiveness outcomes in evaluations for chronic immune-mediated disorders. Our work highlights the continued need for clarity when reporting how CEAs and CUAs in this disease area are conducted.

Abbreviations: CEA: cost-effectiveness analysis; CEAs: cost-effectiveness analyses; CUA: cost-utility analysis; CUAs: cost-utility analyses; PICOS: population, intervention, comparator, outcomes, study design; ICER: Incremental cost-effectiveness ratio; QALY: quality-adjusted life year; JAKi: Janus kinase inhibitor; CI: confidence interval

Declaration of conflicting interests: The authors declare the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Akira Yuasa, Naohiro Yonemoto, and Kazumasa Kamei are full-time employees of Pfizer Japan Inc. Akira Yuasa, Naohiro Yonemoto, and Kazumasa Kamei hold stocks and stock options from Pfizer Inc. Toshiaki Murofushi and Michael LoPresti are full-time employees of INTAGE Healthcare Inc. which received funding from Pfizer Japan Inc. Shunya Ikeda declares no conflicts of interest associated with this manuscript.

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