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Funding and conclusions of network meta-analyses on targeted therapies in inflammatory diseases: an overview

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Abstract

Objectives: To explore the association between industry funding and network meta-analyses' (NMAs) conclusion, and the use in Clinical Practice Guidelines (CPGs) of NMAs.

Study Design and Setting: This was an overview of NMAs and CPGs. We searched PubMed/MEDLINE, Epistemonikos, and several guideline databases up to February 18th 2023. We included CPGs from the last 5 years and NMAs of randomized controlled trials that evaluated targeted therapies in immune-mediated inflammatory diseases. Data extraction and outcome assessments were done in duplicate by independent authors.

Results: We included 216 NMAs and 99 CPGs. 31% (67/216) were industry-funded. The proportion of industry-funded NMAs that cited one treatment as being best was 44% (25/57) compared to 26% (30/116) for nonindustry-funded (OR = 2.24 [1.15-4.39]; aOR = 1.76 [0.81-3.81]). The abstract's conclusion of 39/67 (58%) industry-funded and 69/149 (46%) nonindustry-funded NMAs were considered unsupported by the results (OR = 1.61 [0.90-2.89]; aOR = 1.40 [0.71-2.78]). All industry-funded NMAs that cited one treatment as best cited their own sponsored drug. 59/99 (60%) CPGs included at least one NMA, with 23/59 (39%) of them citing industry-funded NMAs.

Conclusions: We did not find evidence that industry-funded NMAs were more likely to have unsupported conclusions or to cite only one treatment as being best in their conclusions compared to non-industry-funded NMAs. However, almost all industry-funded NMAs favored their own treatments. Even though 40% of the CPGs did not rely on NMA, over a third of those who did used industry-funded NMAs. Limitations include the possible misclassification due to undisclosed funding and potential confounders that have not been accounted for. © 2024 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Network meta-analysis; Funding; Targeted therapies; Systematic review; Immune-mediated inflammatory diseases; Coherence

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Plain language summary

Network meta-analyses (NMAs) are a type of study that allows to compare in a single analysis many different drugs and can provide a ranking of these drugs from the most desirable to the least desirable (e.g.: from most to least effective). This type of study has become very popular to guide clinical decisions and to help during the writing of practice guidelines. However, some concerns have emerged regarding the potential influence of industry funding on the results and conclusions of published NMAs.

The objective of our study was to assess if there was an influence of funding on the conclusions of the NMAs evaluating innovative drugs in chronic inflammatory diseases. We also evaluated if practice guidelines relied on these studies and if they were industry-funded or not.

Our study shows that industry-funded NMAs largely promoted their own treatment. Yet, even though we had some concerns regarding the relevance or quality of industry-funded studies, we found some flaws in both industry-funded and nonindustry-funded studies. The use of NMAs was modest among guidelines, but a third of those that relied on them cited industry-funded NMAs, which recommended their own treatment.

Our study suggests that efforts are still needed to improve the interpretation and the accurate presentation of NMAs results, both in industry and nonindustry-funded studies. When interpreting the results of a network meta-analysis, bias related to industry funding should be taken into consideration.

1. Introduction

The autoimmune market has been evaluated to increase from \$154 billion worldwide in 2021 up to \$193 billion over the next decade [1], with one of these growth key drivers being the rapid development of biologics and small molecules (eg, JAK inhibitors) to treat chronic immune-mediated inflammatory diseases (IMiDs) [2]. These diseases, including in particular psoriasis, ankylosing spondylitis, rheumatoid arthritis, inflammatory bowel diseases (IBDs), and psoriatic arthritis, constitute a clinically diverse group of conditions with common underlying pathogenetic features [3]. Besides concerns from pharmaceutical companies over economic competitiveness, reliable knowledge on the relative efficacy and safety of these treatments is crucial for clinical practice guidelines (CPGs) developers and clinicians [4–6]. However, most conducted randomized controlled trials used placebo as comparator despite the availability of active treatments [7,8]. To that end, network meta-analysis (NMA) has been useful in addressing some of these gaps in comparative effectiveness research [9].

Concerns have been raised regarding the increasing number of redundant and discordant NMAs being published [10,11]. A scoping review showed that among a sample of 658 NMAs published between 2013 and 2018, industry-funded NMAs were more likely to suggest favorable conclusions to the sponsor product, with 92% of the 136 included industry-funded NMAs recommending their company's intervention [12]. In a previous study, we showed that industry-funded NMAs on the systemic treatments of psoriasis almost systematically cited their treatment as being best [13].

The objective of our study was to evaluate the effect of funding on the conclusions and the use in CPGs of the NMAs' evaluating the efficacy or safety of the authorized targeted therapies used in a group of chronic IMiDs.

2. Methods

We conducted an overview of the NMAs that evaluated the authorized targeted therapies used in several chronic IMiDs of interest as well as an overview of the CPGs that made recommendations on their management using targeted therapies. Both were based on a protocol registered prior to data collection on the Open Science Framework on February the 18th 2023 (osf.io/wgydt). Reporting was performed according to the Preferred Reporting Items for Overviews of Reviews statement ([Supplementary Table 17](#)) [14].

2.1. Eligibility criteria

2.1.1. Overview of the NMAs

We considered NMAs of randomized controlled trials that included adults with moderate-to-severe IBD, active ankylosing spondylitis, active psoriatic arthritis, moderate-to-severe psoriasis, or active rheumatoid arthritis, and that evaluated the efficacy or safety of the authorized targeted therapies ([Supplementary Table 1](#)) compared to placebo or with an active comparator. We excluded from our overview cost-effectiveness studies, NMAs that only compared biosimilars with their respective originators, and NMAs that used individual patient data (IPD). NMAs that only compared different dosages or regimens of the same intervention were also excluded.

2.1.2. Overview of the CPGs

We carried out a systematic review to include any CPGs published during the last 5 years (i.e., January 2018) concerning adult patients and covering the management with targeted therapies of the IMiDs of interest, developed by local, regional, national, or international groups or affiliated

What is new?**Key findings**

- Industry-funded network meta-analyses (NMAs) largely promoted their own treatment.
- Issues regarding relevance and quality were present in the included studies, irrespective of the source of funding.
- The use of NMA was modest among clinical practice guidelines (CPGs).

What this adds to what was known?

- We assessed the NMAs' abstracts to evaluate if their conclusions were supported by the reported results.
- Source of funding aside, half of the NMAs' conclusions were not supported by the reported results.
- A third of the CPGs that cited NMAs cited industry-funded NMAs, which recommended their own treatment.

What is the implication and what should change now?

- Efforts are still needed to improve the interpretation and the accurate reporting of NMAs' results, both in industry- and nonindustry- funded studies.
- Bias related to funding should be accounted for when appraising the results of a network meta-analysis (NMA).

governmental organizations. Guidelines or consensus statements not informed by systematic review or explicit assessment regarding the body of evidence, editorials and commentaries, consensus based on the opinion of expert panels, guidelines targeting policymakers (eg, health technology assessments) were excluded.

2.2. Study identification

We aimed to identify all relevant NMAs, regardless of language. We searched from inception in PubMed/MEDLINE, Epistemonikos, and International Prospective Register of Systematic Reviews. For psoriasis, we updated our previous literature search from February 2021 [13]. The reference lists of the included studies were also screened.

To identify the guidelines of interest, we searched starting in January 2018, Pubmed/MEDLINE and several guidelines depositories (Supplementary Table 3). We also screened the reference list of the included guidelines and the reference list provided by the Global Guidelines in Dermatology Mapping Project for psoriasis [15]. When

multiple versions of the same CPG were identified, the most updated CPG was considered.

The selection process was conducted through Covidence (<https://www.covidence.org/>) up to February 18, 2023, by the review authors (L.L.C., R.G., T.B., A.M., and G.P.). After excluding duplicates, a single author (R.G.) screened every title and abstract. Independent authors (L.L.C., R.G., A.M., and G.P.) then assessed in duplicate the remaining full texts. In case of missing full text, we contacted studies' authors. Discrepancies were solved through discussion. Full search equations can be found in the [Supplementary Tables 2 and 3](#).

2.3. Data extraction

Data extraction was performed in duplicate by independent authors (L.L.C., R.G., and T.B.) following a form previously tested. We extracted the main characteristics of the NMAs, characteristics of the studied population, included interventions, outcomes, number of included studies, of interventions, and of interventions cited as being best in the abstract's conclusion. The study exposure groups were considered industry-funded, if the source of funding was a pharmaceutical company, or nonindustry-funded if the source of funding was either public or academic, if there was no funding or if the source of funding was not reported. In the case of cofunding from different categories (eg, public and industry funding), the study was classified in the category "industry-funded". Authors' financial conflicts of interest (COI) were extracted from the authors' affiliation section and from the publication's COI disclosure. Any types of financial ties with pharmaceutical companies were considered. The financial COI among authors was considered present, absent, or not reported. Additional information on the extracted data regarding Contract Research Organisation (CRO), citation count, journal impact factor (IF), and altmetric attention score (AAS) can be found in [Supplementary Table 4](#). We extracted the main CPG characteristics, including whether they were supported by industry funding, by assessing the funding and acknowledgment section of the CPGs. We explored the CPGs' reference lists and extracted the number of included NMAs and their funding status.

2.4. Outcomes

We assessed the abstracts' conclusions that cited only one treatment as being best and the coherence between the abstracts and the NMAs' results.

Our secondary outcomes were 1/the presence of a registered protocol, 2/the number of included targeted therapies in the NMA over the total number of available targeted therapies at the time of their literature search, 3/the outcomes (efficacy and/or safety) studied in each NMA, 4/the citations per NMA in a 2-year timeframe following the publication, 5/the journal IF at the time of publication, and 6/the NMAs' AAS for the NMAs published in the last 5 years.

2.5. Evaluation of coherence

This evaluation was made in duplicate by independent authors (L.L.C., R.G., and T.B.) following a decisional tree.

The conclusion was divided into propositions, with each sentence corresponding to a proposition. Each proposition that made a statement regarding the relative efficacy or safety of the included intervention was compared to the

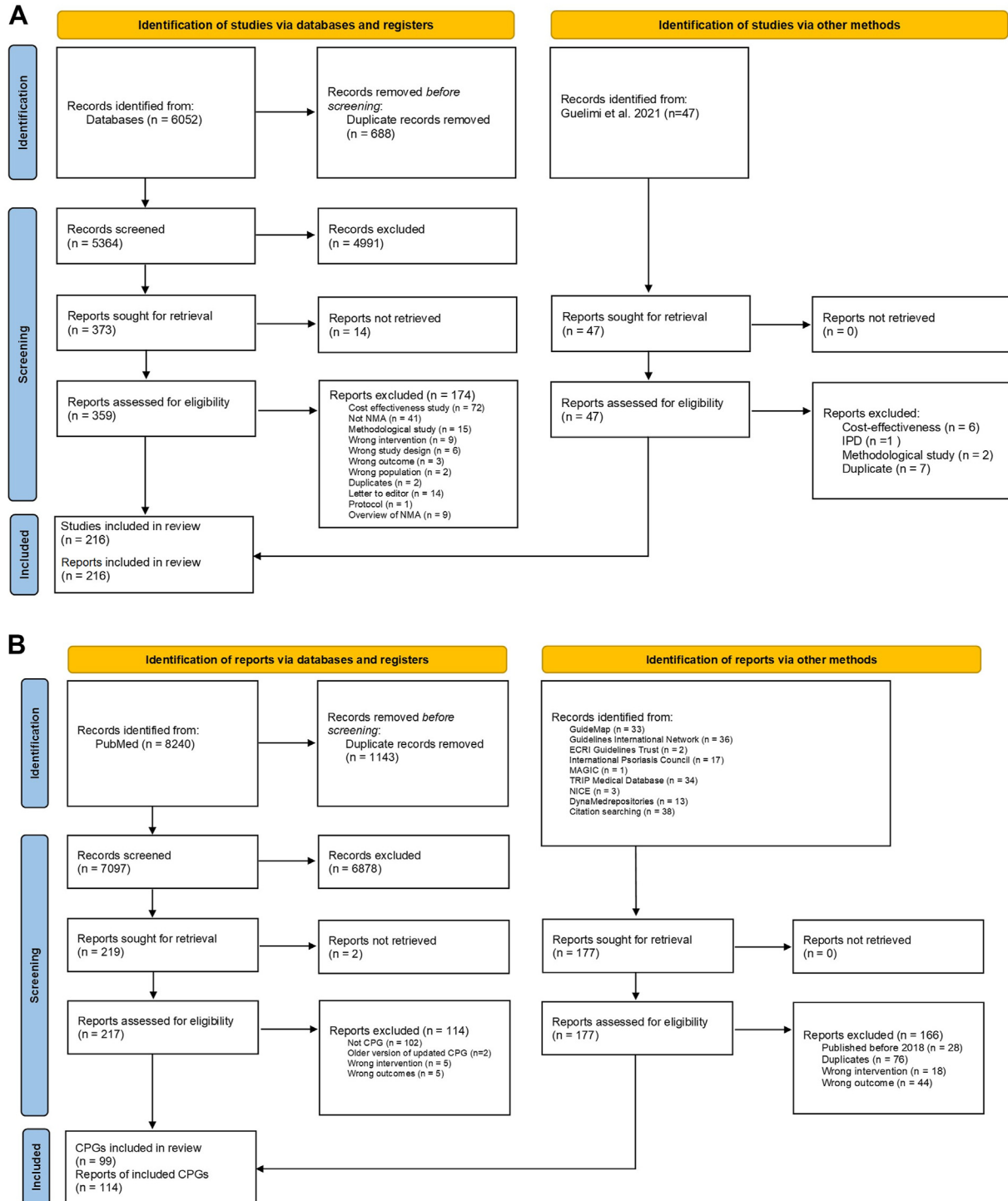


Figure 1. Flow chart of the included NMAs and clinical practice guidelines 1A. Flow chart of the included NMAs, 1B. Flow chart of the included CPGs Abbreviations: NMA, network meta-analysis, CPG, clinical practice guideline, IPD, individual patient data, NICE, National Institute for Health and Care Excellence. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

results and noted as being “true” or “false” depending on whether it was supported by the findings or not (Supplementary Figure 1). We examined in the result section the pairwise relative effect estimates with their confidence intervals to determine whether the interventions cited as best were indeed statistically superior to other uncited interventions. If every proposition of the conclusion were true, the conclusion was considered coherent with the results; if not, the conclusion was considered unsupported by the results (Supplementary Figure 2). If the abstract conclusion did not contain any statement regarding the interventions’ relative efficacy or safety, the same algorithm was applied to the results section of the abstract.

2.6. Statistical analysis

The characteristics of the NMAs were described; overall and according to the type of funding. Associations between outcomes and funding were analysed by univariate and multivariable logistic regression analyses to compute odds ratios (OR) and the associated 95% confidence intervals (95% CI). Models were adjusted for underlying IMIDs, protocol registration, outcomes of the NMA [efficacy alone, safety alone, or both], exhaustivity of included targeted therapies, and year of publication. These variables were chosen according to already-published articles assessing the association between funding and the presence of spin in the abstract [16–20]. We conducted several sensitivity analyses. Firstly, we excluded studies that did not report their funding, which were at risk of misclassification. We also conducted a sensitivity analysis where we only compared funded NMAs, either from industry or public or academic funding. Lastly, for two additional sensitivity analyses, we excluded NMAs having 1/three authors or less and, subsequently, 2/less than three authors. We considered that a minimum of three authors were needed to conduct a systematic review (two for the duplicated study identification and extraction, and one required for consensus in case of disagreement). These analyses aimed to exclude NMAs that were conducted with the 1/bare minimum number of authors or less, 2/less than the minimum. The threshold for statistical significance was set at 0.05. All analyses were performed on R version 4.3.1.

2.7. Deviation from the protocol

Before starting our review, we excluded from our eligibility criteria cost-effectiveness studies and NMAs that used IPD. We amended the decision tree assessing coherence between the abstracts and the results. Instead of assessing the conclusions in their entirety we assessed the conclusions by proposition to minimize subjective interpretation. For our primary outcomes, the multivariable logistic regressions were added *post-hoc* to account for possibly confounding variables.

3. Results

3.1. NMAs overview

3.1.1. Included studies

Of the 6099 potentially eligible studies, 216 were included (Fig 1A). We failed to retrieve the full text of 13 studies, despite requests to authors (Supplementary Table 6). The full list of the included NMAs is available in Supplementary Table 7. Reference list with reasons for exclusion at full-text stage are reported in Supplementary Table 5.

3.2. CPGs overview

3.2.1. Included CPGs

Of the 8417 potentially eligible reports, 99 CPGs were included (Fig 1B). We failed to retrieve the full texts of two reports despite the authors’ solicitation. The full list of included CPGs is available in the Supplementary Table 15.

3.3. Characteristics of the included studies

3.3.1. NMAs’ characteristics

The 216 included NMAs were published between 2003 and 2023. All were written in English. A majority studied rheumatoid arthritis (78/216, 36%) followed by psoriasis (52/216, 24%) and IBD (50/216, 23%) (Table 1, Fig 2). 47/216 NMA (22%) registered a protocol, and a clear definition of a primary outcome was available in 40% (86/216) (Table 1). Half of the NMAs assessed both efficacy and safety outcomes (111/216, 52%). Regarding funding, 67/216 (31%) were industry-funded, and among them, 52/67 (78%) declared the assistance of a CRO. Among the nonindustry-funded NMAs, 65/149 (44%) received public or academic funding, 48/149 (32%) did not receive any funding, and 36/149 (24%) did not report whether they received any funding. Characteristics for each study can be found in Supplementary Table 7.

3.3.2. CPGs’ characteristics

We identified 32 CPGs on IBD, 11 on psoriatic arthritis, 19 on psoriasis, 22 on rheumatoid arthritis, and 15 on ankylosing spondylitis. The majority of CPGs were national (81/99, 82%) and originated from Europe (42/99, 42%). In all, 20/99 (20%) CPGs were supported by either one (9/20, 45%) or several (11/20, 55%) pharmaceutical companies.

3.4. Number of treatments reported as being best

Overall, 173/216 NMAs made a statement regarding the relative efficacy or safety of the included interventions in their abstract’s conclusion. Among them, 57/173 (33%) were industry-funded and 116/173 (67%) were not. The proportion of industry-funded NMAs that cited one treatment as being the best was 44% (25/57) compared with 26% (30/116) (Fig 3). Industry-funded NMAs presented a

Table 1. Main NMAs' characteristics given the source of funding

NMA's characteristics	Overall <i>n</i> (%) (total = 216)	Industry-funded NMAs <i>n</i> (%) (total = 67)	Non industry-funded NMAs <i>n</i> (%) (total = 149)	<i>P</i> -value ^a for secondary outcomes
Protocol registration	47 (22)	7 (10)	40 (27)	.01
Financial COI among authors ^b				-
Yes	117 (54)	67 (100)	50 (34)	
No	86 (40)	0	86 (58)	
Not reported	13 (6)	0	13 (9)	
Assistance of a CRO	56 (26)	52 (78)	4 (3)	-
Author from CRO	46 (21)	43 (64)	3 (2)	-
Author from pharmaceutical companies	57 (26)	57 (85)	0	-
Studied population				-
Psoriasis	52 (24)	27 (40)	25 (17)	
Psoriatic arthritis	22 (10)	8 (12)	14 (9)	
IBD	50 (23)	8 (12)	42 (28)	
Ankylosing spondylitis	14 (6)	3 (4)	11 (7)	
Rheumatoid arthritis	78 (36)	21 (31)	57 (38)	
Outcome of interest				<.001
Efficacy alone	85 (39)	43 (64)	42 (28)	
Safety alone	20 (9)	1 (1)	19 (13)	
Both efficacy and safety	111 (51)	23 (34)	88 (59)	
Definition of a primary outcome	86 (40)	9 (12)	77 (52)	<.001
Inclusion of all available targeted therapies	64 (30)	21 (31)	43 (29)	.83
Proportion of included targeted therapies over the number of available targeted therapies	80 (50–71)	85 (67–79)	75 (38–67)	.02
Median number of included targeted therapies, median (IQR)	5 (4–8)	8 (5–10)	5 (3–8)	-
Median number of included studies, median (IQR)	17 (8–33)	20 (10–39)	16 (8–31)	-
Median number of efficacy outcome, median (IQR)	3 (2–4)	3 (3–5)	3 (2–4)	-
Median number of safety outcome, median (IQR)	2 (1–3)	2 (2–3)	2 (1–3)	-

COI, conflict of interest; CRO, contract research organization; IBD, inflammatory bowel disease; IQR, interquartile range; NMA, network meta-analysis.

^a *P* values from χ^2 -test or Fisher's exact test for categorical variables or Mann–Whitney *U* test for continuous variables.

^b Financial COI of any type were extracted from the authors' affiliation and the disclosure of conflict of interest section of the publication.

statistically significant risk of citing one treatment as being best before adjustment (OR = 2.24 [1.15–4.39], *P* = .02), but not after adjustment (aOR = 1.76 [0.81–3.81], *P* = .15) (variables adjusted for were: underlying IMIDs, protocol registration, NMA's outcomes, exhaustivity of included targeted therapies, and year of publication). These results were consistent across all sensitivity analyses (Supplementary Table 13). For the industry-funded NMAs, the treatment cited as best was always the sponsored intervention (25/25). When several treatments were cited as being best, the sponsored intervention was almost always cited among the best (31/32 [97%]).

3.5. Coherence between the abstracts and the reported results

Half of the abstract's conclusions were labeled as coherent (108/216) and the other half as "unsupported". Agreement between the assessors was fair (percentage agreement = 70%, Cohen's κ = 0.40). The main reason behind the lack of support was the omission of citing a treatment not statistically different from those listed as the most effective in 93/108 (86%) cases, followed by the statement of a proposition that was true for some but not all the outcomes in 11/108 (10%) cases (Supplementary

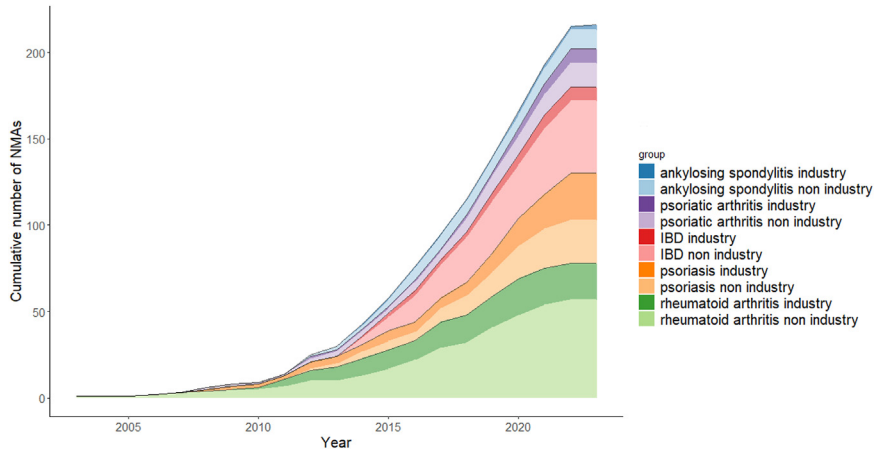


Figure 2. Cumulative number of industry and nonindustry-funded NMAs published every year for each IMIDs Abbreviations: NMA, network meta-analysis; IBD, inflammatory bowel disease. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 12). NMAs with industry-funding presented a nonsignificant risk of presenting unsupported conclusions before (OR = 1.61 [0.90–2.89], $P = .11$) and after adjustment (aOR = 1.40 [0.71–2.78], $P = .33$). These results were consistent in all sensitivity analyses (Supplementary Table 13).

3.6. Comparison between industry-funded and nonindustry-funded NMAs

We found that industry-funded NMAs were less likely to register a protocol ($P = .01$), less likely to define primary outcomes ($P < .001$), less likely to evaluate both efficacy and safety outcomes ($P < .001$), and more likely to evaluate solely efficacy outcomes compared to nonindustry-

funded NMAs ($P < .001$). Industry-funded NMAs included a higher proportion of the available treatments; however, we found no difference between the sources of funding regarding the proportion of NMAs that included all the available targeted therapies (Table 1).

3.7. Effect of funding on NMAs dissemination and use in CPGs

We did not find any difference in NMAs’ dissemination between industry-funded and nonindustry-funded NMAs in terms of the median number of citations, median AAS, and median journal IF (Supplementary Table 18).

Regarding their use in CPGs, 59/99 (60%) cited at least 1 NMA, with a median number of cited NMAs of 2

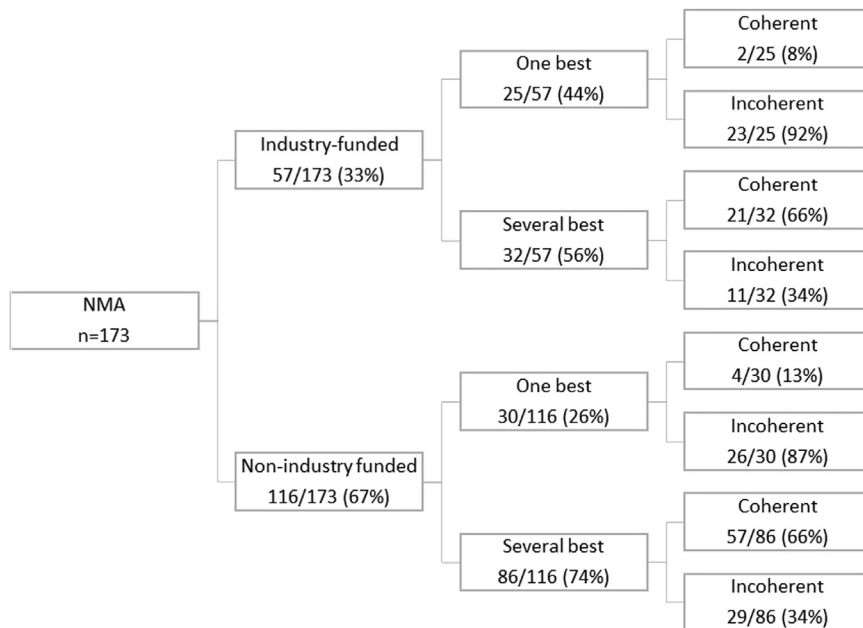


Figure 3. Coherence of the abstract conclusion given the number of treatments cited as best and the source of funding Abbreviation: NMA, network meta-analysis. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

(IQR = 1-4). All the NMAs cited in the CPGs were included in our review of NMAs, except for 7 that did not fit our inclusion criteria. Among the CPGs that referenced NMAs, 6/59 (10%) cited industry-funded NMAs only, 36/59 (61%) cited nonindustry-funded NMAs only, and 17/59 (29%) cited both. We did not find any association between the funding of CPGs by the industry and the presence of NMAs in the reference list ($P = .60$) or the citation of industry-funded NMAs ($P = .71$).

4. Discussion

Given the expansion of therapeutic options, NMA stands out as a valuable tool for clinical decision-makers and CPG developers. This method, however, may be an opportunity for pharmaceutical companies to use it as a marketing tool to promote their drugs. In our study, a third of the included NMAs were industry-funded.

Industry-funded NMAs had a 40% increase in odds to have conclusions unsupported by the results and a 76% increase in odds to cite only one treatment as being best in their conclusions. However, there was uncertainty about these associations. Still, almost all favored their own treatments, either as a unique option or as one of the best options. The main reason behind unsupported conclusions was the omission of citing a treatment not statistically different from those listed as the most effective, which was more often the case when only one treatment was cited as the best. This observation could be considered a form of spin for NMAs. Nevertheless, even though previous studies have shown that industry funding had an influence on the results and conclusion of systematic reviews and meta-analyses, no statistically significant association was found between industry funding and the occurrence of spin [13,17–19].

Beyond that, we found that no matter the type of funding, a majority of the NMAs failed to meet important methodological requirements. Most of them did not register a protocol, and less than half defined a primary outcome. Moreover, 40% did not evaluate the safety of the included interventions. While found no matter the type of funding, these flaws were more likely to be observed in industry-funded NMAs. Additionally, less than a third of the NMAs included all available targeted therapies at the time of their review. Even though 10% of the NMAs in our overview focused on subpopulation of interest for which the inclusion of all available targeted therapies may have been unnecessary or unreasonable, most of them dismissed valuable information from important interventions.

Our results agreed with the ones presented by Veroniki et al. [12]. One methodological difference is that we assessed the coherence of the reported results. Ultimately, the prevalence of unsupported conclusions was high irrespective of funding, with a bias toward sponsored drugs

for industry-funded NMAs. However, the absence of protocol or predefined primary outcomes did not allow us to exclude cases of selective reporting or publication bias. As previously pointed out, the industry often commissions many NMAs through CRO, with most of them not being registered and published after analyses [21]. This raises some concerns that these publications are biased and open to *post-hoc* manipulation of results.

Lastly, only 60% of the included CPGs relied on NMAs, with 39% of them citing industry-funded NMAs, either alone (14%), or with nonindustry-funded NMAs (25%). The proportion of CPGs that included NMAs remained stable over time, despite the more recent incentives for using them to guide recommendations [22,23]. Based on our results, it is possible that guideline developers are reluctant to include industry-funded NMAs and/or biased or poor-quality NMAs, even if this would mean ignoring useful data. A future study will further aim to assess CPGs' financial ties with the industry and the impact of the NMAs on their recommendation.

Our study has several limitations. Firstly, a quarter of the nonindustry-funded NMAs did not report their funding status, which may have led to some misclassification. Additionally, financial COI among authors may have been underestimated as they were extracted from the publications self-reported disclosures [24]. Secondly, the review authors were not blinded to the funding status when assessing the abstracts' coherence. To limit subjective interpretation, the authors followed a decision tree independently and in duplicate. The agreement between assessors was classified as fair, which could be mainly explained by one of the assessors missing nonsignificant differences for some comparisons. All cases of disagreement were resolved through discussions. Thirdly, we focused our attention on the abstracts rather than on the discussion or the main conclusion. We assumed that the abstract would be more impactful on readers. Lastly, we included in our logistic models relevant variables previously acknowledged in the literature [18–20]. Still, there may be some concern regarding the mediation role of some variables, questioning their classification as true confounders. While the inclusion of these potentially mediating variables could theoretically introduce bias, their incorporation tended to shift estimations toward the null.

5. Conclusion

Although there was no evidence that industry-funded NMAs were more likely to have unsupported conclusions or to cite only one treatment as best in their conclusions, almost all favored their own treatments either as a unique option or as one of the best options. Even though the use of NMA was modest in the included CPGs, over a third of those who did use industry-funded NMAs.

Patient and public involvement

There was no patient or public involvement during the conduct of this study.

Ethics approval

No ethics approval was required for this study.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

CRedit authorship contribution statement

Robin Guelimi: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Sivem Afach:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Thomas Bettuzzi:** Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation. **Antoine Meyer:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Data curation. **Guillaume Padern:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Data curation. **Zenas Yiu:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Florian Naudet:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Emilie Sbidian:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Conceptualization. **Laurence Le-Cleach:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Conceptualization.

Data availability

Data and code underlying this article are available on Open Science Framework (osf.io/wgydt).

Declaration of competing interest

Robin Guelimi reports financial support was provided by Public Assistance Hospitals Paris. and the Association for

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Supplementary data

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