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## Replication of Systematic Reviews: Is It to the Benefit or Detriment of Methodological Quality?

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1 **Replication of Systematic Reviews: Is It to the Benefit or Detriment of Methodological**  
2 **Quality?**

3  
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31

## 32 **Abstract**

33 **Objective:** To perform an overview of the overlap of systematic reviews (SR) assessing direct  
34 oral anticoagulants (DOACs) and characterise these reviews in terms of bias and  
35 methodological quality (PROSPERO: CRD42022316273).

36 **Study design and setting:** A PubMed-indexed search was performed from inception to 31  
37 January 2022 to identify SR evaluating DOACs in patients treated for an acute venous  
38 thromboembolism. The risk of bias of these SR was assessed according to the Risk Of Bias In  
39 Systematic reviews (ROBIS) tool. Redundancy was defined as overlap in terms of the type of  
40 population considered, the interventions compared and the studies included.

41 **Results:** A total of 144 SR were evaluated, of which 26 (18.1%) were classified as original, 87  
42 (60.4%) as conceptual replications and 31 (21.5%) as excessive replications. The risk of bias  
43 was high in 19 (73.1%) of the original SR, 65 (74.7%) of the conceptual replications and 21  
44 (67.7%) of the excessive replications. Compared to the original SR, the overall methodological  
45 quality was not improved in either conceptual or excessive replications.

46 **Conclusion:** A large number of SR were classified as replications, a fifth constituted excessive  
47 replications. The replications showed no improvement in overall methodological quality  
48 compared to the original SR.

49 **Keywords:** systematic review; bias; methodological quality; replication; redundancy

50

51 **Running title: Replication and Risk of Bias In Systematic Reviews**

52 **Word count: 3293**

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**What is new?****Key findings**

- More than 80% of the systematic reviews analysed were replications and were considered as being of poor methodological quality; a fifth of these reviews constituted excessive replications, showing overlap of population types, interventions compared and studies included.

**What this adds to what is known**

- Methodological quality tended to improve in excessive replications compared to original systematic reviews or conceptual replications but the differences were not statistically significant.

**What is the implication and what should change now**

- Systematic reviews replications of poor methodological quality represent a considerable waste of effort and resources.
- Authors, publishers and reviewers should be vigilant and carefully scrutinise already existing reviews to avoid wasteful replication.

## 57 1. Introduction

58 For many years now, a race to publish seems to have been underway. However, the increasing  
59 number of scientific articles published each year raises issues in terms of scientific integrity and  
60 value. Specifically, the notion of “publish or perish” [1] and the mass production of trials of  
61 poor methodological quality that ultimately fail to provide reliable results [2,3] and represent a  
62 waste of research resources [4–6], have become a harsh reality. In view of their high level of  
63 evidence, systematic reviews and meta-analyses have become a common feature of clinical  
64 research, and therefore do not escape this rush to publish [7,8]. In particular, meta-analyses of  
65 aggregate data (i.e. those based on effect estimates of studies reported in the literature) have  
66 dramatically increased due to the facility of obtaining aggregate data and the development of  
67 free and easy-to-use statistical software.

68  
69 Meta-analytical methods were originally developed to quantitatively synthesise an abundance  
70 of published data and produce a readily comprehensible and concise overview of a therapeutic  
71 field to facilitate decision-making. However, the validity of meta-analyses depends mainly on  
72 the quality of their development and reporting. Many systematic reviews and meta-analyses are  
73 of poor quality, principally due to methodological weaknesses in their execution [7]. Given the  
74 mass of systematic reviews and meta-analyses published, it is difficult to distinguish the most  
75 reliable, relevant and least biased results. This is especially true when these systematic reviews  
76 and meta-analyses are redundant or show contradictory results [7,9], and when their number  
77 exceeds that of individual studies [10,11]. Overlap, replication and redundancy have already  
78 been observed in many fields of medical research [12–26]. Various arguments have been  
79 invoked to justify replication and redundancy, such as the wish to update an earlier systematic  
80 review and meta-analysis by including data from new high-quality trials not evaluated  
81 previously, reluctance to extrapolate the results obtained to all patients in the absence of  
82 subgroup analyses, the need to assess an endpoint not evaluated in other systematic reviews  
83 and meta-analyses, or a change in endpoint definition. In fact, redundancy might be acceptable  
84 if its sole aim was to produce a less biased meta-analysis. Redundancy may also be  
85 unintentional, especially when similar systematic reviews and meta-analyses are accepted for  
86 publication by different journals during the same period, but this could be avoided by pre-  
87 registration of systematic reviews. In addition, Tugwell et al. developed a checklist and  
88 guidance to aid assessment of whether or not replication of systematic reviews would be useful

89 [27]. Up to now, this mechanism of replication has never been described, especially with  
90 regards to the links between the authors of such successive systematic reviews.

91  
92 Our study aimed in particular to investigate replication and its characteristics in terms of the  
93 biases and methodological quality of the systematic reviews concerned. With this objective in  
94 mind, and to illustrate the phenomenon of replication, we chose the example of direct oral  
95 anticoagulants (DOACs) used for the acute treatment of venous thromboembolism (VTE), in  
96 view of the recent development of these medicinal products and the large number of systematic  
97 reviews published on this topic.

98

## 99 **2. Material and Methods**

### 100 ***2.1. Identification and Selection of Systematic Reviews and Data Extraction***

101 The study protocol was prospectively registered in the International prospective register of  
102 systematic reviews (PROSPERO, <https://www.crd.york.ac.uk/PROSPERO>, registration  
103 number CRD42022316273).

104

105 We sought to identify all relevant published systematic reviews including randomised  
106 controlled trials or observational studies evaluating DOACs in relation to any comparator in  
107 patients treated for VTE during the acute and/or extended phase of anticoagulation, including  
108 patients receiving acute treatment for VTE in the context of cancer. A literature search was  
109 performed on PubMed from inception to January 31, 2022 using keywords and medical subject  
110 headings (MeSH) terms with no restrictions on language or publication period. Initially, the  
111 search was not restricted to the treatment of VTE in order to include systematic reviews  
112 addressing several indications. The full electronic search equation is presented in Appendix  
113 Table 1.

114

115 One of the authors (CC) screened the titles and abstracts of publications for possible inclusion.  
116 Then, two of the authors (CC, PB) independently screened the full-text articles, discrepancies  
117 between reviewers being resolved by discussion. To be eligible, the systematic reviews had to  
118 meet the following criteria: 1) include randomised controlled trials or observational studies; 2)  
119 evaluate DOACs in relation to any comparator (active standard treatment: vitamin-K  
120 antagonists, aspirin, or low-molecular-weight heparin; non-active treatment: placebo or control;  
121 or other DOACs); 3) include patients treated for an acute VTE during the acute or extended

122 phase of anticoagulation. Pairwise (individual patient data or aggregated data) and network  
123 meta-analyses were included. Systematic reviews including only one study assessing DOACs  
124 in acute VTE patients were excluded. In order to characterise replication, only full-text articles  
125 were included in this review.

126  
127 Data were independently extracted by two of the authors (CC and PB). In the event of  
128 discrepancies between reviewers, a consensus was reached by discussion. The following data  
129 were extracted from each systematic review: publication details (author names, year of  
130 publication, journal, free-access journal, impact factor of the journal), details of the meta-  
131 analysis (pairwise or network design, statistical model, registration, number of studies included,  
132 names and designs of the studies included, treatments, method used to assess the risk of bias of  
133 the included studies [tool employed and use of this tool to assess the effect of bias on the  
134 results]), and citations of previous systematic reviews in the field. A systematic review was  
135 defined as having no overlap in authorship if it shared no common author with other systematic  
136 reviews. Two systematic reviews were considered as having an overlap in authorship if they  
137 shared at least one common author.

138

## 139 ***2.2. Description of the Phenomenon of Replication***

140 Systematic reviews are first classified according to their PICO (Population, Intervention,  
141 Comparison and Outcome) question. Each systematic review is then assigned to one of three  
142 replication categories according to the definitions used by Tugwell et al. [27]: original,  
143 conceptual replication or excessive replication. The original category comprises both original  
144 and updated systematic reviews, i.e. both the original systematic review published on a  
145 particular topic and any updates published by the same team [28]. Conceptual replication  
146 corresponds to replication in order to broaden or narrow the research question, while  
147 maintaining the same objectives as the original systematic reviews, but 1) adding new  
148 randomised studies, 2) focusing on a comparator or an intervention, 3) highlighting patient  
149 subgroups, 4) investigating other outcomes or 5) adding non-randomised studies. Finally,  
150 excessive replication is defined as overlap in terms of the type of population, the interventions  
151 compared and the studies included. If several systematic reviews are published at the same time,  
152 the first systematic review registered is considered as the original one. Two of the authors (CC,  
153 SL) assigned each systematic review to one of the three categories, discrepancies being resolved  
154 by discussion.

### 2.3. *Quality Assessment of the Systematic Reviews*

Two authors (CC and PB) independently assessed the risk of bias of the systematic reviews according to the Risk of Bias in Systematic Reviews (ROBIS) tool, discrepancies between reviewers being resolved by discussion. Using this tool, the assessment of the risk of bias of the systematic reviews was accomplished in two phases: 1) identification of concerns regarding the review process and 2) appraisal of the overall risk of bias [29]. Phase 1 covered four domains: study eligibility criteria, study identification and selection, data collection and study appraisal and synthesis and findings. Each of the four domains was subjectively assessed as having a low, unclear or high risk of bias, based on the questions specified in the tool. In the second phase, the overall risk of bias of the systematic reviews was assessed as low, unclear or high, based on assessment of the four domains in phase 1.

### 2.4. *Statistical Analysis*

The descriptive analysis was performed according to the category of replication (original, conceptual replication, other type of replication or excessive replication) using numbers and percentages for qualitative data, and means with their standard errors, as well as medians with interquartile range (IQR) for quantitative data.

Network diagrams were used to visualise the links between authors of the systematic reviews. To visualise the number of replications of systematic reviews associated with the original systematic review, we used alluvial diagrams. To analyse whether the methodological quality of the systematic reviews differed between the original, conceptual replication and excessive replication categories, a logistic regression analysis was performed, taking the replication category (original, conceptual replication or excessive replication) as the covariate and the risk of bias in each domain and overall (high vs low) as the dependent variable. The coefficient of the covariate was expressed as a ratio.

All analyses were performed using R statistical software (R Foundation for Statistical Computing). Network diagrams were plotted using igraph and network packages [30].



### 185 3. Results

#### 186 3.1. Study Selection

187 The search procedure identified 1,258 potentially eligible systematic reviews, of which 988  
188 were excluded after a scan of their titles and abstracts (Appendix Figure 1). After assessment  
189 of the full texts, 91 additional references were excluded. Finally, 144 systematic reviews were  
190 included in the review (references listed in the Appendix).

#### 191 192 3.2. Description of the Systematic Reviews Included According to the Category of 193 Replication

194 Among these 144 systematic reviews, 26 were classified as original, 87 as conceptual  
195 replications and 31 as excessive replications. For 19 (73.1%) of the 26 original systematic  
196 reviews we identified at least one other systematic review showing overlap, i.e., either a  
197 conceptual replication, an excessive replication or both (Figure 1). Some original systematic  
198 reviews exhibited extensive overlap with up to 15 conceptual replications and 12 excessive  
199 replications.

200  
201 The characteristics of the 144 systematic reviews included are summarised in Table 1 and fully  
202 described in Appendix Table 2 and Table 3. Most of the systematic reviews had a pairwise  
203 design and had been performed in Europe and North America. The majority of the conceptual  
204 replications (54.0%) were published in a free-access format compared to 42.3% and 45.2% of  
205 the original systematic reviews and excessive replications, respectively. A protocol of the  
206 systematic review had been registered in 46.1%, 27.6% and 19.3% of the original reviews,  
207 conceptual replications and excessive replications, respectively, mainly in the PROSPERO  
208 database. A quarter of the excessive replications indicated protocol registration within 10 days  
209 prior to submission of the systematic review for publication, compared to 2 months for original  
210 systematic reviews and 3 months for conceptual replications. Twenty (64.5%) excessive  
211 replications had assessed the risk of bias of the studies included, compared with over 70% in  
212 the original systematic reviews and conceptual replications. No overlap in authorship with other  
213 systematic reviews was observed in 14 (45.2%) of the 31 excessive replications, 35 (40.2%) of  
214 the 87 conceptual replications and 7 (26.9%) of the 26 original systematic reviews. Of the 734  
215 authors of systematic reviews, 537 (73.2%) had published an original systematic review and/or  
216 a conceptual replication (Appendix Figure 2). The remaining 197 authors (26.8%) had

217 published at least one excessive replication, of which 51 (25.9%) had also published at least  
218 one original systematic review or a conceptual replication.

219  
220 Forty-one (47.1%) of the 87 conceptual replications cited a previous systematic review, of  
221 which 17 included a justification for the replication, and 27 cited another conceptual replication  
222 (Table 2). Twenty-one (67.7%) of the 31 excessive replications cited a previous systematic  
223 review, of which 14 included a justification for the replication, and 15 cited the original  
224 systematic review. Eight of the 31 excessive replications cited the systematic review they  
225 duplicated.

226  
227 The reasons for conceptual replication were to add new randomised studies (26.4%), to  
228 highlight particular patient subgroups (20.7%), to investigate other outcomes (19.5%), to focus  
229 on a comparator or an intervention (17.2%) and to add non-randomised studies (16.1%). The  
230 characteristics of the 87 conceptual replications are summarised in Appendix Table 4.

### 231 **3.3. Risk of Bias of the Systematic Reviews**

232 Overall, the risk of bias was assessed as high in 99 (68.7%) systematic reviews and low in 39  
233 (27.1%) systematic reviews (Table 1). A high risk of bias was observed in almost 70% of the  
234 original and conceptual replications but in 61.3% of the excessive replications. The high overall  
235 risk of bias of the systematic reviews was mainly due to the high risk of bias in domain 4 of the  
236 ROBIS tool regarding study synthesis and findings (Figure 2, Appendix Table 5).

237

### 238 **3.4. Comparison of Risk of Bias**

239 Compared to original systematic reviews, the overall methodological quality was not improved  
240 in replications (Figure 3).

241 Comparison of conceptual replications versus original systematic reviews revealed no  
242 difference in either overall methodological quality (OR 1.09, 95% CI [0.38-2.85]) or the risk of  
243 bias in each domain (Figure 3A). The risk of bias of the individual items within each domain  
244 are presented in Appendix Figure 3.

245 Comparison of excessive replications versus original systematic reviews suggested a better  
246 overall methodological quality (OR 0.77, 95% CI [0.24-2.42]), although the difference was not  
247 statistically significant (Figure 3B). The risk of bias of individual items within each of these  
248 domains are presented in Appendix Figure 4.

249 Comparison of excessive replications versus conceptual replications suggested a better overall  
250 methodological quality of excessive replication, although the difference was not statistically  
251 significant (Figure 3C). The risk of bias of individual items within each domain are presented  
252 in Appendix Figure 5.

253

#### 254 **4. Discussion**

255 This systematic overview included 144 systematic reviews evaluating DOACs versus any  
256 comparator in patients treated for VTE, of which 87 (60.4%) were conceptual replications and  
257 31 (21.5%) were excessive replications. Compared with other systematic reviews, excessive  
258 replications assessed the risk of bias of the included studies to a lesser extent and barely 20%  
259 registered the protocol of the systematic review (19.3%). However, excessive replications  
260 showed a trend towards a lower risk of bias than the other types of systematic review.

261

262 To the best of our knowledge, this is the first study analysing replications among systematic  
263 reviews assessing DOACs in the acute treatment of VTE and evaluating the methodological  
264 quality of excessive replications compared to original systematic reviews. Overlap of  
265 systematic reviews assessing DOACs has previously been evaluated only with regard to stroke  
266 prevention in atrial fibrillation [23]. In that context, the extent of overlap was substantial,  
267 possibly owing to the small number of trials compared to the number of systematic reviews.  
268 Several other studies have also observed overlap and redundancy of systematic reviews in many  
269 fields of medical research [10,13–22,24–26]. A quarter of the excessive replications included  
270 in the present review cited the systematic review they duplicated, indicating that these  
271 systematic reviews were performed despite awareness of other systematic reviews with a  
272 similar PICO question, suggesting deliberate redundancy. The justifications for replication  
273 advanced by the authors of systematic reviews included, for example, the assessment of an  
274 outcome not previously evaluated or of the separate components of composite outcomes, the  
275 need for subgroup analyses, the availability of new data or the inclusion of a larger number of  
276 studies and patients. Other non-valid justifications were also advanced, such as to “have a clear  
277 presentation and summarization of the study and sensitivity analysis”. Ioannidis [7] and Siontis  
278 and colleagues [12] also noted that the authors of redundant systematic reviews and meta-  
279 analyses did not systematically cite previous systematic reviews and meta-analyses concerning

280 the same topic. They found that only 3% of these prior meta-analyses “were cited by subsequent  
281 studies claiming to be replications addressing the same question”.

282 Based on the ROBIS quality assessment tool, more than 70% of the systematic reviews included  
283 in this overview were considered to be at high risk of bias. For this reason, despite the level of  
284 evidence of these systematic reviews and meta-analyses, they were not always synonymous  
285 with high-quality research. Even assuming that when a systematic review is replicated, the  
286 methodological quality might be improved, this was not the case and these replications retained  
287 a high overall risk of bias. Most of the systematic reviews evaluated were therefore of low  
288 methodological quality, replications decreasing their quality still further. The quality of  
289 systematic reviews needs to be improved through prospective registration of the protocol, an  
290 exhaustive search strategy, reporting of the methods and results of additional analyses, and  
291 assessment of the potential impact of the risk of bias of the studies included in the meta-analysis  
292 of the results obtained. This conclusion is consistent with those of studies evaluating the  
293 methodological quality of systematic reviews and meta-analyses concerning many other  
294 clinical issues and finding this to be generally poor [26,31–41]. As we have seen, some authors  
295 registered their systematic reviews only a few weeks prior to publication, which does not  
296 comply with PROSPERO requirements and suggests retrospective rather than prospective  
297 registration. The prospective registration of a systematic review protocol has two objectives.  
298 The first is to avoid excessive replication and therefore redundancy. The second is to avoid any  
299 inductive approach and thus to declare the research objective once the results have been  
300 obtained. Registration does not imply a prospective evaluation process if it precedes publication  
301 by only a few weeks. Nowadays, it is not only registration that is important, but also the date  
302 of this registration.

303 The reporting of systematic reviews and meta-analyses should be further regulated and authors  
304 should follow the guidelines issued. In particular, the consistency of the publication with the  
305 protocol should be carefully assessed and reported in order to enable identification of any  
306 sources of bias and explanation of disparities between the results of different meta-analyses.  
307 Bolland and Grey reviewed meta-analyses evaluating the effects of vitamin D supplementation  
308 on bone fractures and found their results to be discordant owing to substantial disparities in trial  
309 selection, outcome definition and statistical methodology [14]. Among the seven meta-analyses  
310 included in their review, only four included all eligible trials and two even included trials that  
311 did not meet their eligibility criteria. Finally, assessment of the quality of the methodology and  
312 results of redundant systematic reviews and meta-analyses is crucial to ensure that these do not  
313 convey misleading, inaccurate, or biased information.

314

315 Our overview has some limitations. First, we performed an umbrella review and restricted our  
316 search to a single database. Even though the list of systematic reviews indexed by PubMed is  
317 comprehensive, we may have missed some additional published and unpublished systematic  
318 reviews. The extent of replication is therefore potentially even greater than that we describe  
319 here. A second limitation is that we based our analysis of replication on the date of registration  
320 of the protocol whenever possible, but otherwise on the date of publication of the systematic  
321 reviews (online or in printed issues) without considering the delay in editorial and publication  
322 procedures. The third limitation concerns evaluation of the level of bias present within a  
323 systematic review. We chose to use the ROBIS tool which requires substantial reflection to  
324 complete, an issue that could become problematic in the context of a larger review.  
325 Furthermore, the assessment of each risk of bias domain requires careful analysis of the  
326 systematic review concerned in order to correctly rate the risk of bias, adding to the difficulty  
327 of using this tool. Finally, even when used by experienced methodologists, the ROBIS tool  
328 remains subjective.

329

## 330 **5. Conclusion**

331 The massive production of systematic reviews has led to a considerable waste in the form of  
332 excessive replicated publications of poor methodological quality. This waste could be avoidable  
333 in most cases if authors, publishers and reviewers were sufficiently vigilant. Authors have a  
334 role to play before starting their review, first by systematically checking the evidence already  
335 existing or likely to be published soon and then, if a further systematic review and meta-analysis  
336 is considered necessary, by systematically registering its protocol, assuming that excessive  
337 replication is not deliberate. In that case, publishers and reviewers should scrutinise the existing  
338 evidence to avoid wasteful excessive replication and should ensure that the recommendations  
339 of well-established guidelines for the reporting of systematic reviews and meta-analyses are  
340 fully respected in order to improve the publication quality.

341

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346

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350

**351 Declaration of interest**

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354 **Laporte** has received personal fees from Bayer for consulting, personal fees continuing medical  
355 education lectures from Pfizer, and personal fees for continuing medical education lectures  
356 from Eli Lilly.

357

**358 Reproducible Research Statement**

359 Study protocol: Registered in PROSPERO (registration no. CRD42022316273)  
360 ([https://www.crd.york.ac.uk/prospero/display\\_record.php?RecordID=316273](https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=316273))

361 Statistical code and data set: The analysis scripts and data set may be requested from Céline  
362 Chapelle (e-mail address: [celine.chapelle@chu-st-etienne.fr](mailto:celine.chapelle@chu-st-etienne.fr)).

363

**364 CRediT author statement**

365 **Céline Chapelle:** Conceptualization, Methodology, Data curation, Formal analysis, Software,  
366 Writing - Original Draft, Writing - Review & Editing. **Edouard Ollier:** Conceptualization,  
367 Methodology, Formal analysis, Software, Supervision, Validation, Writing - Original Draft,  
368 Writing - Review & Editing. **Paul Bonjean:** Data curation, Writing - Review & Editing.  
369 **Clara Locher:** Conceptualization, Writing - Review & Editing. **Paul Jacques Zufferey:**  
370 Conceptualization, Writing - Review & Editing. **Michel Cucherat:** Conceptualization,  
371 Writing - Review & Editing. **Silvy Laporte:** Conceptualization, Methodology, Supervision,  
372 Writing - Original Draft, Writing - Review & Editing.

373 All authors approved the manuscript prior to submission.

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**Table 1. Summary of the characteristics of the systematic reviews included according to the replication category.** Values are numbers (percentages) unless stated otherwise.

	Original (N = 26)	Conceptual replication (N = 87)	Excessive replication (N = 31)
Type of meta-analysis			
Individual patient data meta-analysis	3 (11.5)	3 (3.4)	0 (0.0)
Pairwise meta-analysis	18 (69.2)	62 (71.3)	23 (74.2)
Network meta-analysis	5 (19.2)	22 (25.3)	8 (25.8)
Median (IQR) number of authors of the publication	6 (4-9)	6 (5-8)	6 (4-8)
Free-access publication	11 (42.3)	47 (54.0)	14 (45.2)
Journal not indexed for MEDLINE*	0 (0.0)	4 (4.6)	4 (12.9)
Median (IQR) impact factor of the journal	5.24 (3.06-7.66)	3.50 (2.77-5.72)	3.00 (2.32-5.33)
Geographic location of the first author			
Europe	10 (38.5)	34 (39.1)	16 (51.6)
North America	10 (38.5)	28 (32.2)	11 (35.5)
Asia	5 (19.2)	22 (25.3)	2 (6.4)
Other	1 (3.8)	3 (3.4)	2 (6.4)
Design of the included studies			
RCTs only	23 (88.5)	72 (82.8)	30 (96.8)
Observational studies only	0 (0.0)	3 (3.4)	1 (3.2)
RCTs and observational studies	3 (11.5)	12 (13.8)	0 (0.0)
Assessment of the risk of bias of the included studies			
Descriptive (table/figure)	16	52	16
Analysis according to risk of bias	4	13	4
Registration of the protocol			
PROSPERO	10	22	5
Cochrane database	2	1	0
Open Science Framework	0	1	1
Median time (IQR) from registration to submission of the publication (months)	2.6 (2.2-3.2)	5.8 (3.1-8.7)	0.4 (0.3-12.7)

No overlap in authorship	7 (26.9)	35 (40.2)	14 (45.2)
Risk of bias of the systematic reviews (ROBIS tool)			
Low	7 (26.9)	22 (25.3)	10 (32.3)
Unclear	1 (3.9)	3 (3.4)	2 (6.4)
High	18 (69.2)	62 (71.3)	19 (61.3)

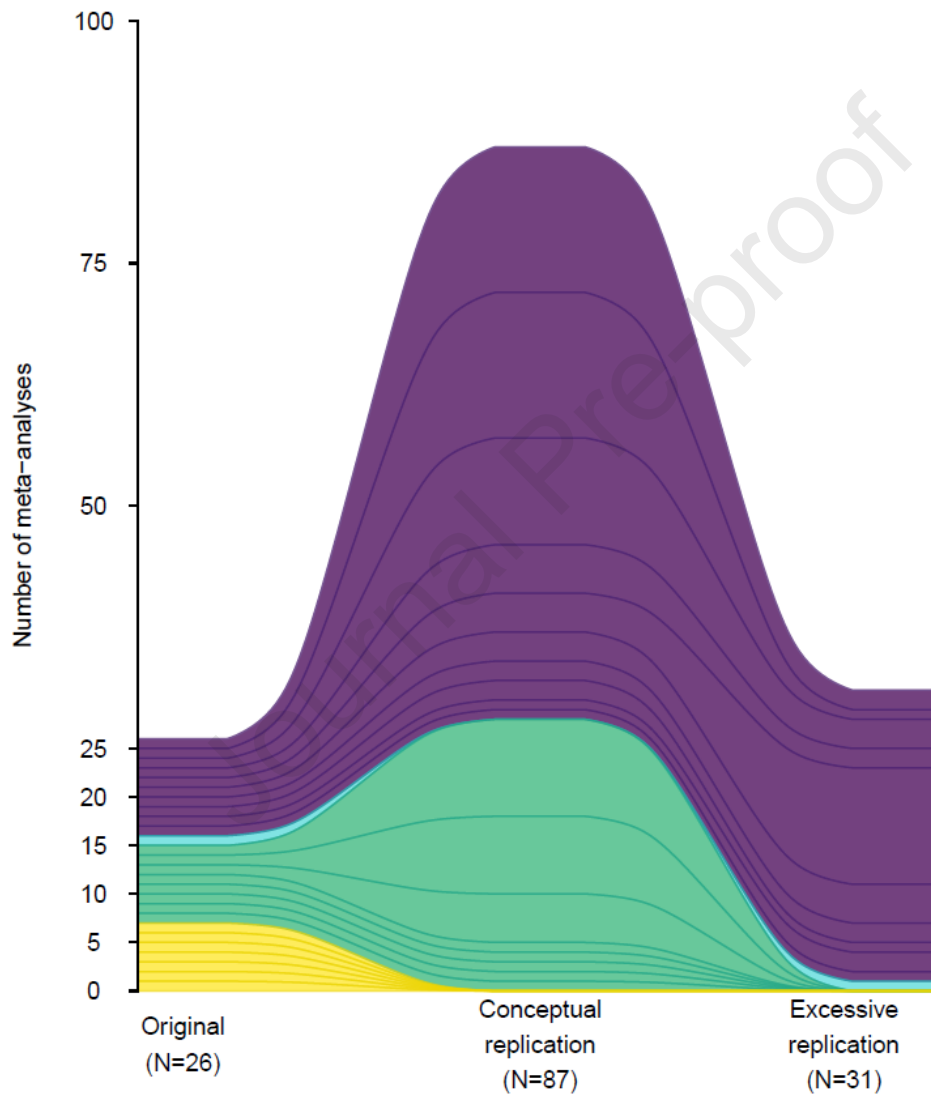
\* At the time of the publication.

IQR = interquartile range; RCT = randomised controlled trial.

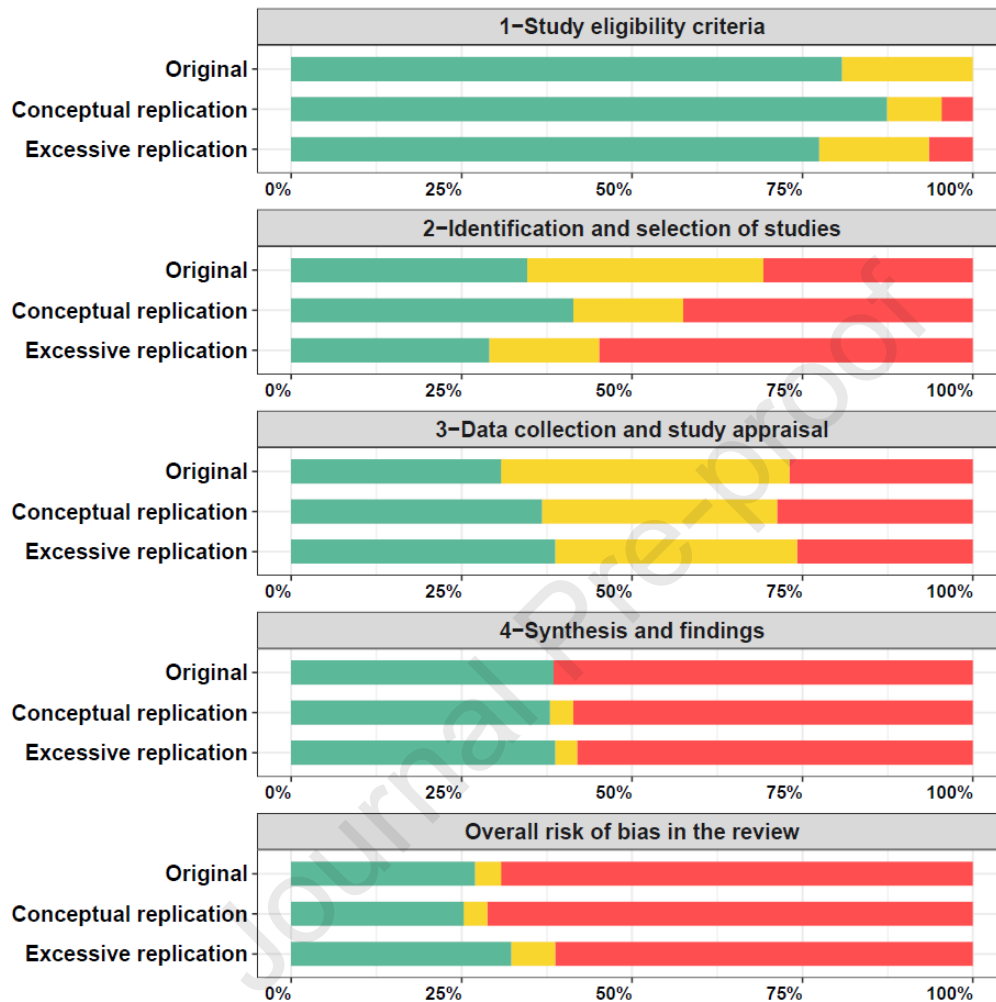
**Table 2. Citations of the systematic reviews included according to the replication category.** Values are numbers (percentages) unless stated otherwise.

	Conceptual replication (N = 87)	Excessive replication (N = 31)
Citations of previous systematic reviews	41 (47.1)	21 (67.7)
Inclusion of a justification	17	14
Citations of the original systematic review	10 (24.4)	15 (71.4)
Inclusion of a justification	2	9
Citations of a conceptual replication	27 (65.8)	10 (47.6)
Inclusion of a justification	13	7
Citations of an excessive replication	11 (26.8)	8 (38.1)
Inclusion of a justification	4	5

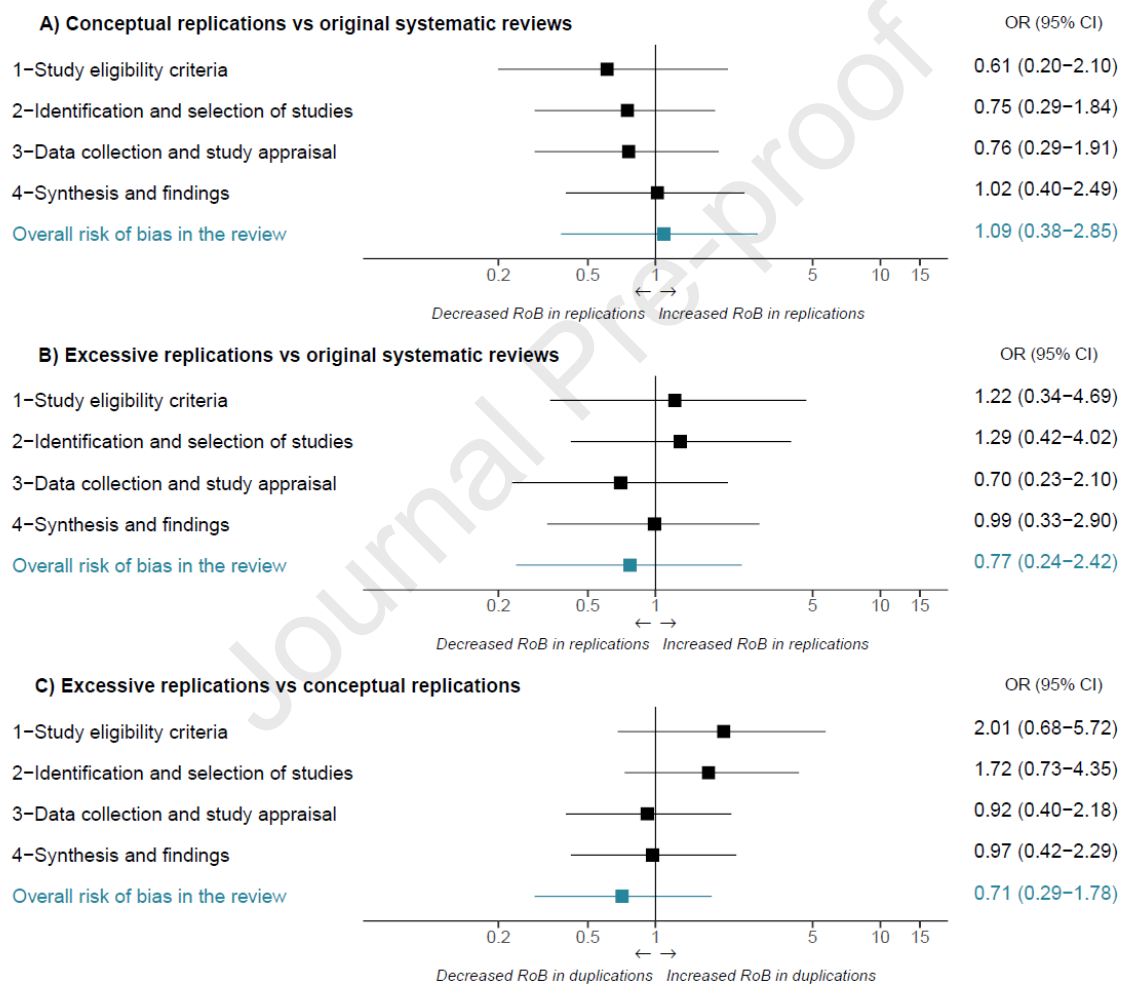
**Figure 1. Alluvial diagram of the number of replications associated with the corresponding original systematic review. Yellow: no associated conceptual or excessive replication; green: at least one conceptual and no excessive replication associated; blue: at least one excessive and no conceptual replication associated; purple: at least one conceptual and one excessive replication associated.**



**Figure 2. Risk of bias of the systematic reviews for each ROBIS tool domain according to the replication category (original, conceptual replication or excessive replication) presented as percentages across all systematic reviews included. Green: low risk of bias; orange: unclear risk of bias; red: high risk of bias.**



**Figure 3. Comparison of the risk of bias for each ROBIS tool domain between A) conceptual replications and original systematic reviews (reference: original systematic reviews); B) excessive replications and original systematic reviews (reference: original systematic reviews); C) excessive replications and conceptual replications (reference: conceptual replications). An OR < 1 denotes a lower risk of bias compared to the reference, an OR of 1 denotes no difference, and an OR > 1 denotes a higher risk of bias compared to the reference.**



95% CI = 95% confidence interval; OR = odds ratio; RoB = risk of bias.

**What is new?**

**Key findings**

- More than 80% of the systematic reviews analysed were replications and were considered as being of poor methodological quality; a fifth of these reviews constituted excessive replications, showing overlap of population types, interventions compared and studies included.

**What this adds to what is known**

- Methodological quality tended to improve in excessive replications compared to original systematic reviews or conceptual replications but the differences were not statistically significant.

**What is the implication and what should change now**

- Systematic reviews replications of poor methodological quality represent a considerable waste of effort and resources.
- Authors, publishers and reviewers should be vigilant and carefully scrutinise already existing reviews to avoid wasteful replication.



## **Declaration of interest**

**Céline Chapelle:** none

**Edouard Ollier:** none

**Paul Bonjean:** none

**Clara Locher:** none

**Paul Jacques Zufferey:** none

**Michel Cucherat:** personal fees from Bayer and BMS for consulting

**Silvy Laporte:** personal fees from Bayer for consulting, personal fees for continuing medical education lectures from Pfizer, and personal fees for continuing medical education lectures from Eli Lilly.

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