

# Potential publication bias in chiropractic and spinal manipulation research listed on clinicaltrials.gov

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*Introduction: Clinical trial registries are used to help improve transparency in trial reporting. Our study aimed to identify potential publication bias in chiropractic and spinal manipulation research by assessing data drawn from published studies listed in clinicaltrials.gov.*

*Methods: We searched the clinicaltrials.gov registry database for completed trials tagged with the key indexing terms chiropractic or spinal manipulation. We assessed if the trial registry had been updated with data, then searched for publications corresponding to the registered trials. Finally, the frequency of positive or negative results was determined from published studies.*

*Results: For the term ‘chiropractic’, 63% of studies supported the intervention and 52% supported the intervention for the term ‘spinal manipulation’.*

*Discussion: Publication bias in chiropractic and spinal manipulation research listed in clinicaltrials.gov*

*Introduction : Les registres des essais cliniques servent à accroître la transparence des rapports sur les essais. Notre étude visait à trouver les éventuels partis pris de publication dans les travaux de recherche sur la chiropratique et les manipulations vertébrales à l’aide de données tirées d’études publiées et répertoriées dans clinicaltrials.gov.*

*Méthodologie : Dans la base de données du registre clinicaltrials.gov, nous avons cherché des essais terminés marqués par les termes d’indexation « chiropratique » et « manipulation vertébrale ». Nous avons cherché à savoir si le registre des essais avait été mis à jour par l’ajout de données, puis nous avons recherché les publications correspondant aux essais répertoriés. Enfin, nous avons établi la fréquence des résultats positifs et négatifs à l’aide des études publiées.*

*Résultats : Avec le terme « chiropratique », 63 % des études étaient en faveur des interventions; avec l’expression « manipulation vertébrale », 52 % des études étaient en faveur des interventions.*

*Discussion : Il semble y avoir un parti pris de publication dans les travaux de recherche sur la chiropratique et les manipulations vertébrales*

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*appears to occur. Further work may help understand why this happens and what may be done to mitigate this moving forward.*

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### Introduction

Publication bias is defined as “the tendency to publish reports of research that appears to support a hypothesis and to refrain from publishing findings that do not, thereby creating opinions about the truth of the intervention that may be unduly optimistic”.<sup>1</sup> This may result from fear of rejection, failure to submit findings with negative results, failure to accept such papers by journal editors, or failure to submit information by those with vested interest in the results. This is important because exclusion of studies at a review or study level may not provide an accurate representation of aggregate study results, which could impact recommendations drawn from systematic reviews and meta-analysis.<sup>2</sup> Additionally, stakeholders need complete information to make decisions about the effectiveness of a given intervention.<sup>3</sup>

Clinical trials are essential for providing information on how treatments compare to one another for a given condition.<sup>4</sup> Researchers in the United States who initiated studies after September 2007 are required to register clinical trials onto registries such as the clinicaltrials.gov website.<sup>5</sup> The International Committee of Medical Journal Editors also recommends this to all authors conducting clinical trials.<sup>6</sup> Trials databases are specifically designed to prevent selective publication and selecting reporting of research outcomes. Trial registries also provide a venue where information from study results can be made public. They are, further, a source of information for non-published, yet completed, clinical trials.<sup>7</sup> However, doubts exist that trial registries are an effective method for reducing publication bias.<sup>8</sup> Approximately half of trials fail to report results in a clinical trial registry.<sup>9</sup>

To study publication bias, one can search an electronic clinical trial registry to identify relevant studies for a

*répertoriés dans clinicaltrials.gov. D'autres travaux pourraient aider à comprendre la cause de ce phénomène et à trouver des moyens de le réduire dans l'avenir.*

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MOTS CLÉS : chiropratique, biais de publication, revues scientifiques

given area of research. This type of search examines what is known as *gray literature*, which includes unpublished studies and studies never submitted to peer review.<sup>2</sup> In one meta-analysis of 28 special education journals, less than half included gray literature and only 33% addressed publication bias.<sup>2</sup> Researchers of this study concluded that not including the gray literature is associated with an increased risk of publication bias.<sup>2</sup>

Goldacre encourages others to explore publication bias for specific interventions to identify its prevalence.<sup>9</sup> We could locate no information about the prevalence of publication bias in chiropractic and spinal manipulation clinical trials. The primary objective of our study was to identify potential publication bias related to *chiropractic* and *spinal manipulation* trials.

### Methods

We used a 4-step process to meet our primary objective. The first step determined the number of completed trials in clinicaltrials.gov listed under the key indexing terms *chiropractic* and *spinal manipulation* research. A second step determined if any results were posted on the clinicaltrials.gov database. Third, we looked at the publication section on clinicaltrials.gov to determine if there were any publications associated with the studies. Finally, we determined the proportion of publications whose results favored the intervention.

### Search strategy

Data collection took place from May 2018-August 2018 for the term *chiropractic* and from February 2019-April 2019 for the term *spinal manipulation*. To complete our first objective, identifying potential publication bias, we searched clinicaltrials.gov looking for studies with

the term *chiropractic* or *spinal manipulation*, using the *advanced search* category. In the 'other terms' box, we first searched the term *chiropractic* and then conducted a second search for the term *spinal manipulation*. In the *study type and study results* box, we choose *all studies*. In the targeted search box, for intervention/treatment, we searched *chiropractic* and then *spinal manipulation*. For locations, we selected studies in the USA. We searched all funder types, phases, ages, genders, and start dates. We included all studies that provided results using this search strategy. We restarted the search in [clinicaltrials.gov](http://clinicaltrials.gov) each time we began to search for articles to ensure all studies available were included by the end of data collection. Finally, the results of the spreadsheet and the article abstracts were compared between two reviewers.

Article eligibility criteria were based on criteria from a prevalence study of clinical trials on [clinicaltrials.gov](http://clinicaltrials.gov) by Fleming and Goldacre.<sup>7</sup> We considered a clinical trial still in progress if it had one of the following statuses: 'Active, not recruiting,' 'Available,' 'Enrolling by invitation,' 'Not yet recruiting,' 'Recruiting,' or 'Suspended.' Articles in progress were excluded from the additional comparison search for published articles but were still tallied. Studies with a status of 'Withdrawn,' 'Withheld,' 'No longer available,' and 'Temporarily not available' were also excluded.<sup>7</sup> Trials were considered completed if they had a status of 'Completed' or 'Terminated.'<sup>7</sup>

#### *Updated results*

To determine if results were posted on [clinicaltrials.gov](http://clinicaltrials.gov) database, we looked under the results tab to see if it had results or if it said, 'no results posted'. If there was any information in the results section, we considered it to have provided results.

#### *Search for publications*

To find publications linked to the studies posted in the database, we examined the publication section of [clinicaltrials.gov](http://clinicaltrials.gov). If there were any publications listed, we tallied the number on the spreadsheet. If the publication was a study protocol, we still counted it as a publication, but did not use it in our assessment of publication bias.

#### *Assessment of potential publication bias*

After completing the [clinicaltrials.gov](http://clinicaltrials.gov) search for eligible articles, we determined if results from included trials were

published. To do this, we analyzed all articles associated with those trials posted on the [clinicaltrials.gov](http://clinicaltrials.gov) database. We developed a spreadsheet that noted if the trial had posted results, the number of published papers related to the trial, and whether or not the published paper favored the effectiveness of the experimental intervention. We also had a category called *mixed results*, for when the results of the study did not appear to favor or reject the intervention. Thus, the conclusions were classified as in favor of, against, or mixed results. This was determined by reading the abstract, results and conclusions of each study. Results were tallied and verified by 2 independent coders and placed on an Excel spreadsheet.

#### **Results**

For our primary objective, we found 65 studies under the key term *chiropractic*. Six studies had been terminated; 59 were complete. Ten of those studies posted results on [clinicaltrials.gov](http://clinicaltrials.gov). There were 64 total published articles, eight of which were study protocols. As noted above, we did not include the study protocols in the analysis, leaving 56 articles to analyze. Thirty-five studies supported the intervention, eight did not, and 13 had mixed results.

Searching *spinal manipulation* showed similar results. There were 76 total studies. Five studies had been terminated, and 71 were complete. Thirteen of the 71 studies posted results on [clinicaltrials.gov](http://clinicaltrials.gov). There were 97 total publications from the 71 studies. Twenty-five of the studies were study protocols, and were not included, leaving 72 total articles. Forty-nine of the studies supported the intervention, five did not and 18 had mixed results. Complete search results are shown in Table 1.

#### **Discussion**

The existence of publication bias in chiropractic and spinal manipulation research cannot be ruled out. There are trials with results not yet posted on [clinicaltrials.gov](http://clinicaltrials.gov), as well as completed studies without published results. Additionally, results often skew in favor of the intervention. Our results harmonize with existing literature that also show publication bias exists in research for other professions.<sup>8</sup> A study investigating the evidence of publication bias in oncology research found that it was more likely to report positive findings when the trial was registered in advance. Larger sample sizes, with non-stringent blinding, were more likely to report that the drug had favorable results<sup>8</sup>

Table 1.  
Results from searching chiropractic and spinal manipulation on clinicaltrials.gov.

|  | Chiropractic | Spinal Manipulation |
|--|--------------|---------------------|
| Total studies  | 65           | 76                  |
| Completed  | 59           | 71                  |
| Terminated   | 6            | 5                   |
| Results posted                                       | 10           | 13                  |
| Studies that published                               | 22           | 38                  |
| Total published articles from studies that published | 64           | 97                  |
| Studies that only published study protocols          | 8            | 3                   |
| Total study protocols                                | 19           | 25                  |
| Articles in favor of hypothesis                      | 35           | 49                  |
| Articles against hypothesis                          | 8            | 5                   |
| Mixed conclusions                                    | 13           | 18                  |

Publication bias occurs across disciplines. It has been seen in anesthesiology<sup>10</sup>, gastroenterology<sup>11</sup>, dermatology<sup>12</sup>, again in oncology<sup>13</sup>, and even organizational sciences<sup>14</sup>. Hermann and colleagues examined publication bias in clinical oncology reviews. They examined systematic reviews published in the top five highest impact factor oncology journals, for the years 2007-2015. Out of 182 reviews, only 57 reported publication bias evaluations.<sup>15</sup> It is fair to say this is now both an endemic and epidemic problem.

In addition to publication bias present in research from other professions, it is also present in other countries. A retrospective study analyzing data in the European Clinical Trials Register revealed that out of 7274 trials, only 49.5% reported results. To comply with the European Commission, trials are required to post results within 12 months of the completion date, but half of trials fail to do this. Large studies with a commercial sponsor were more likely to post positive results than those without a commercial sponsor.<sup>16</sup> This correlates with another study stating that for-profit funded research is associated with publication bias as well as with non-publication of trial results.<sup>17</sup>

Possible reasons for failure to publish are that researchers need time to analyze and report their data. Studies that have not completed recruiting would not be expected to publish. Goldacre and Powell Smith argue that live, ongoing monitoring of trials and the imposition of negative

consequences for withholding trial results may help decrease publication bias.<sup>9</sup> A study exploring methods to reduce publication bias found that editors thought mandatory publication would be the most effective method, while researchers thought a two-stage review would be more effective.<sup>2,18</sup> As early as 1990, Kay Dickersin argued in *JAMA* that publication bias was a growing problem.<sup>19</sup>

The presence of publication bias is responsible for the growth of clinical trials registries.<sup>20</sup> The continued reporting of trials with statistically significant results and not those without skews the results of a systematic review or meta-analysis.<sup>21,22</sup> Some have argued that the prestigious Cochrane Collaboration- which is well aware of the many issues surrounding publication bias- may actually help amplify the effects of bias. Jefferson has argued that one can identify “subtle distortions, discrepancies and missing information” when reading a short synopsis of a huge data set, which Cochrane creates for each report.<sup>23</sup> However it may be, what is clear is that if nonsignificant or unfavorable findings are withheld from publication, results of any review or meta-analysis will skew in favor of the intervention under study.

The International Committee of Medical Journal Editors recommends that editors should be careful when assessing research to ensure the results are valid and there are no additional outcomes added. They also urge editors to avoid not publishing articles because of lack of statistical significance.<sup>24</sup> Negative studies are every bit as

important as positive ones; publishing null findings can identify ineffective practices and inform and produce new theories and research. It also is a more accurate representation of the current state of knowledge. Thus, being aware of null findings is crucial when examining the effectiveness and limitations of a given intervention. Authors and editors should publish their research, whether or not the results are statistically significant. Publishing null findings are important because they help shape the knowledge base and guide clinical practice.<sup>3</sup>

### Limitations

We limited our assessment of publication bias in chiropractic and spinal manipulation to the sole US trials database, [clinicaltrials.gov](http://clinicaltrials.gov).<sup>25</sup> In the United States, it is a legal requirement to update a registry after completion within one year of completion of a trial. We studied abstracts of articles, rather than the full paper. We searched the terms *chiropractic* and *spinal manipulation* and did not exclude studies from other professions; thus, the results are not specific to just chiropractic. Additionally, only two reviewers analyzed the data; more reviewers might provide a more well-rounded picture of publication bias.

### Conclusion

There is evidence of possible publication bias in chiropractic and spinal manipulation research. Action steps should be taken to reduce publication bias, including publishing completed research regardless of the outcome and timely posting of results to [clinicaltrials.gov](http://clinicaltrials.gov). Future research should focus on the reasons why this bias exists and what may be done to mitigate its presence in our literature.

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