Trends of sources of clinical research funding from 1990 to 2020: a meta-epidemiological study

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ABSTRACT
Evidence has raised concerns regarding the association between funding sources and doubtful data. Our main outcome was to analyze trends on funding sources in articles published from 1990 to 2020 in the more influential journals of internal and general medicine. In this meta-epidemiological study, we included peer-reviewed studies from the 10 highest impact journals in general and internal medicine published between January 1990 and February 2020 based on published original research according to the 2018 InCites Journal of Citation Reports, these consisted of the following: *The New England Journal of Medicine*, *The Lancet*, *JAMA*, *BMJ*, *JAMA Internal Medicine*, *Annals of Internal Medicine*, *PLOS Medicine*, *Cachexia*, *BMC Medicine*, and *Mayo Clinic Proceedings*. Two reviewers working in duplicate extracted data regarding year of publication, study design, and sources of funding. In total, 496 articles were found; of these, 311 (62.7%) were observational studies, 167 (33.7%) were experimental, and 16 (3.2%) were secondary analyses. Percentages of grant sources through the years were predominantly from government (60%), industry (23.83%), and non-governmental (16.06%) organizations. The percentage of industry subsidies tended to decrease, but this was not significant in a linear regression model (r=0.02, p≥0.05). Government and non-government funding sources showed a trend to decrease in the same univariate analysis with both significant associations (r=0.21, p≤0.001 and r=0.10, p≤0.001, respectively). The main funding source in medical research has consistently been government aid. Despite previous reported data, no association was found between the source of funding and statistically significant results favoring study authors' hypothesis.

INTRODUCTION
The only possible way to advance medicine is through clinical research; however, research with human subjects has become increasingly expensive. In fact, an analysis from seven major pharmaceutic companies reported that the median cost of performing a clinical trial from protocol approval to final report was US$3.4 million, US$8.6 million, and US$21.4 million for phase I, II, and III trials.[1–3]

Research funding per se is known to play an essential role in health research and drug development.[2] Thus, clinical research is financed through a combination of different sources.[3] Nevertheless, concerns regarding sources of funding and its association with doubtful data reporting and quality of evidence have been raised.[4 5] For example, Fabbri *et al*[6] found that corporate interest affects the research agendas of many studies, which may lead to publication bias. Funding arrangements have also led to concerns over real or potential conflicts of interest that could arise when researchers face competing allegiances in their work.[7] Moreover, recent evidence suggests that despite the presence of better quality of methods, industry-sponsored research was more prone to disagreement between its results and conclusions.[5 8]

As previously mentioned, funding sources have been evidenced to bias the direction of results in scientific research. This notion triggered the following research question, 'which are the most frequent funding sources of articles published in the more influential medical journals?" In pursuit of these concerns, we have conducted a study with the aim to analyze the trends of research funding among studies published during the last 30 years in the 10 more influential general and internal medicine journals.

MATERIALS AND METHODS
Study design
This study followed a meta-epidemiological design that adheres to the modified Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement for meta-epidemiological studies.[9 10]

Eligibility criteria
Our sample included peer-reviewed studies from the 10 highest impact journals based on impact factor (IF) that published original research in the General and Internal Medicine category according to the 2018 InCites Journal of Citation Reports. These consisted of the following: *The New England Journal of Medicine* (IF: 70.67), *The Lancet* (IF: 59.10), *JAMA* (IF: 51.27), *BMJ* (IF: 27.6), *JAMA Internal Medicine* (IF: 20.76), *Annals of Internal Medicine* (IF:

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19.31), *PLOS Medicine* (IF: 11.04), *Cachexia* (IF: 10.75), *BMC Medicine* (IF: 8.28), and *Mayo Clinic Proceedings* (IF: 7.09). The time interval selected ranged from January 1, 1990, to February 29, 2020. Study designs that were considered for inclusion were prospective and retrospective cohorts, case–control studies, economic evaluations, randomized clinical trials and non-randomized trials.

Sampling

As we did not have a complete list of all the studies that matched the eligibility criteria, a multistage probability sampling was performed.[10] From the selected journals, one volume ranging from January 1, 1990, to February 29, 2020, was randomly selected. In the same way, one issue was chosen at random within each selected journal volume. The number of articles published in each issue journal was counted individually. As each journal published a different frequency of volumes, issues, and number of articles, a weighted analysis was performed to ensure the sample was representative of the population. Finally, one or more articles according to the weighted analysis were selected from each journal issue. We calculated the sample size by employing a formula to estimate proportions in a finite population of 15,000 articles, which was the approximate number of articles published during the last 30 years in the included journals based on our calculation. The total calculated 'n' was 374 articles, which assured a representative sample in that finite population.[11]

Study selection and data collection process

Two reviewers working in duplicate screened each article to assess eligibility and extracted data regarding year of publication, study design, and sources of funding using a standardized web-based form. Prior to each phase, a pilot test was performed to assess disagreements between reviewers.

Sources of funding were categorized as industry, government, and non-governmental; this classification was performed using a stepwise method. First, if the study had at least one source of funding from the industry, it was classified as such. Second, if an industry source of funding was not present, we looked for government funding and if found the study was classified as 'government'. If none of the previous sources of funding were present, the study was classified as 'non-government'. Original investigation was classified as experimental, observational, secondary research, and other.

Studies that evaluated a hypothesis were also classified as having statistically significant results or not. Results were considered as statistically significant if they fulfilled any of the following criteria: the p value for the study main hypothesis was less than 0.05, the CI suggested a statistically significant effect or association toward authors' hypothesis according to the provided measure of effect (HR, relative ratio, OR), or in the case of non-inferiority studies, when the CI did not cross the non-inferiority prespecified margin.

Statistical analysis

Analysis was divided into a univariate, bivariate, and multivariate analysis. In the univariate analysis, we described the funding sources in gross numbers and proportions and performed a subgroup analysis to evaluate if these proportions varied according to the study design. In a bivariate analysis, we evaluated if each funding source showed a statistically significant increase or decrease throughout the years, as evaluated by a bivariate linear regression model. Furthermore, in a multivariate analysis, we performed a logistic regression model to evaluate if there was an association between the funding source (independent variable) and the presence of statistically significant results in each included study (dependent variable), previously adjusted to study design.

RESULTS

Characteristics of included studies

We obtained 496 articles that were published as original research between January 1990 and February 2020. Of these, 311 (62.7%) were observational studies, 167 (33.7%) were experimental, and 16 (3.2%) were secondary analyses from primary studies. The remaining 2 (0.4%) studies were categorized as a different design. A total of 386 articles were included in the analysis, as 41 articles were not funded and 69 articles did not report funding sources. Furthermore, geographic variations were observed in the data analysis where 55.6% of studies were from North America, 35.3% from Europe, 4.2% from Asia, 3.4% from Oceania, and the remaining 1% were from Africa and 0.4% were from Central and South America.

Sources of clinical research funding

Most grant sources from 1990 to 2020 came from government agencies (60%), followed by industry sources (23.83%), and lastly by non-governmental sources (16.06%) (figure 1, online supplemental figure 1). Furthermore, industry was the most common source of funding in 1993, 2007, and 2008. In 2020, most grants also came from government (77.7%) and industry organizations (22.22%).

Subgroup analysis according to study design

When evaluating funding sources stratified by study design, we observed that, in observational studies, government organizations were the main funding source on most occasions (73.23%), followed by non-governmental organizations (18.30%) and industry organizations (8.4%). Non-governmental organizations were the most common source of funding in 2011 (figure 2, online supplemental figure 2).

Regarding experimental studies, we observed that, from 1990 to 1999, most funding sources mainly came from industry organizations (46.49%), followed by government (40%) and non-governmental organizations (13.37%). Still, government organizations were the most common source of funding in 2014, 2018, and currently in 2020 (online supplemental figures 3 and 4).

Current sources of funding

Currently in 2020, most grants came from government (77.7%) and industry organizations (22.22%). When stratifying it according to study design, a large proportion of grant sources are mainly from government organizations both in observational and in experimental study designs.

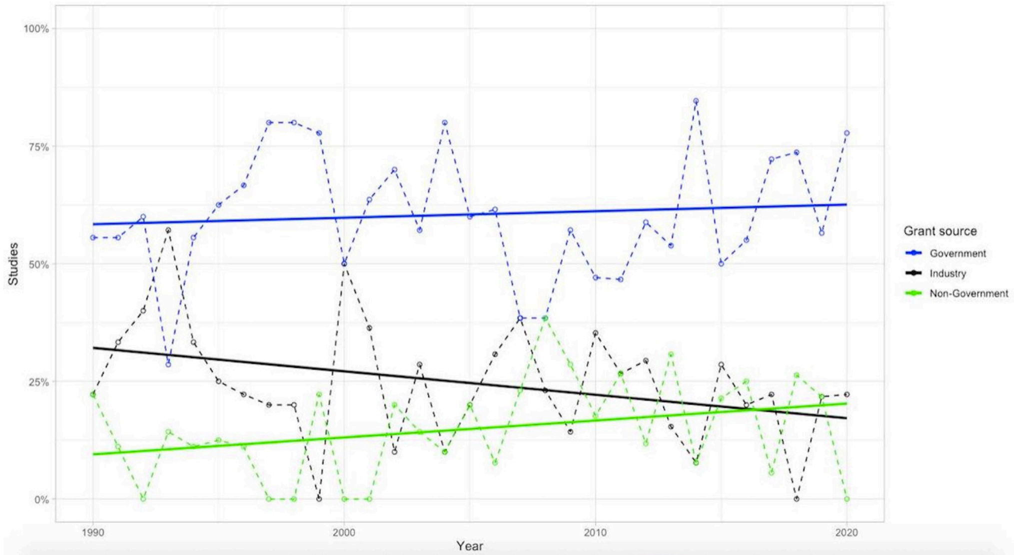

Figure 1 Percentage of total funding by year from 1990 to 2020.

Trends in funding through the years

As years went by, the percentage of industry subsidies tended to decrease; however, this trend was not significant in a linear regression model (r=0.02, p≥0.05). In the same manner, government and non-government sources showed a trend toward decreasing in the same univariate analysis with both significant associations (r=0.21, p≤0.001 and r=0.10, p≤0.001, respectively).

Predictors of statistically significant results

We found no association between the source of funding and the presence of statistically significant results. Experimental studies were less likely to have statistically significant results (OR 0.25 (CI 0.13 to 0.48), p≤0.001) compared with observational studies.

DISCUSSION

Main findings

This is the first study to report the trends of sources of research grants worldwide in the last 30 years. Our main finding was that government subsidies were the most prevalent grant source in the last 30 years, followed by industry and non-government sources. Despite the study design, the source of grant was primarily provided by a government organization. Notably, in experimental studies the trend was different only in earlier years where the leading funding sources were industry organizations since 1990 until nearly 1999. However, in more recent years, government organizations were the largest source of funding. Statistically significant results were not associated with any type of funding source, but it was associated with experimental study designs.

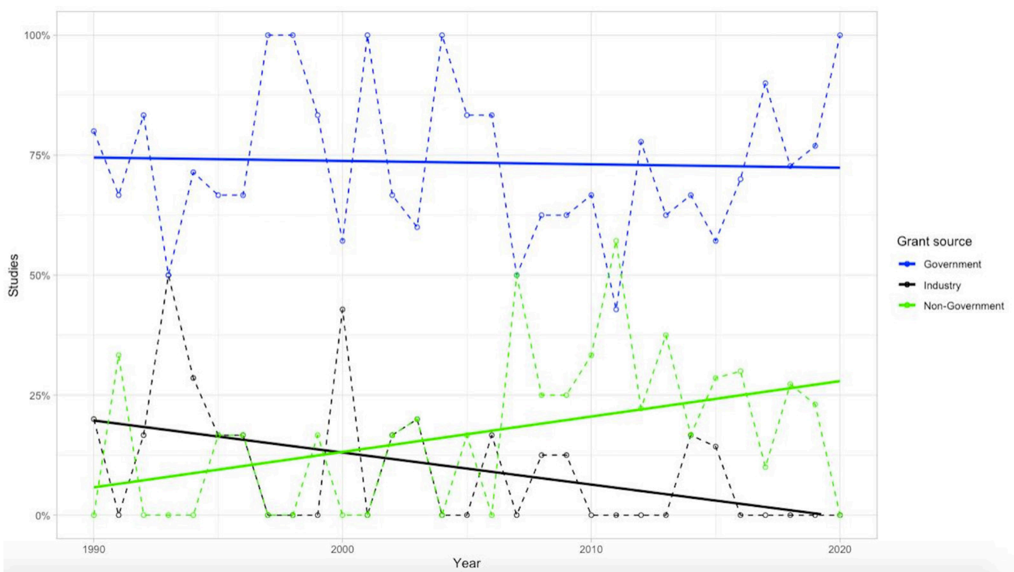

Figure 2 Percentage of total observational funding by year from 1990 to 2020.

Comparison with previous studies

Currently, just one study has achieved similar results to ours, reporting the money invested in medical research from different grant sources in the USA from 1994 to 2012. The results shown by Moses *et al*[12] demonstrate that the largest sources of funding in US medical research were the foundations, charities, and other private funds. Despite this, the sample of this study was only based in US grant sources and does not include the wide time interval and the inclusion of international studies of our study.[13–15]

The government's role in medical research funding is to finance healthcare security programs to achieve the global well-being of its population.[16] This can be achieved by supporting health security programs to improve their scientific production. Currently, this role has been increasing in many parts of the world, since improving medical research has had priority in several governments.[16 17] This increment of governmental interest in public health can be also seen in our findings.

In contrast to our study, Logeman *et al*[18] reported that the most influential people in healthcare research belong to industry organizations, a trend observed in their sample from 2002 through 2018. Fabbri *et al*[19] discovered that industry grants have also influenced non-government organizations, with grants provided to patient groups ranging from 20% to 83%; they also found that industry-funded patient groups tended to have positions favorable to the sponsors. However, this influence of private funding was not found in our multivariate analysis.

Implications for future research

Investment in healthcare is evolving as time passes by, and in the same way, the interest of different grant sources is changing as well. Funding provided by the industry has implications in medical scientific production, such as conflicts of interest and their influence in research decisions. This is associated with significant results both in original and in secondary studies.[4 5] Therefore, industry subsidies are expected to be the largest source of funding for medical research. The decrease in this type of funding may reflect the awareness of these issues. Conversely, our results reflect that the main sources of funding in our wide sample are the government grants. The effect of government funding in medical research on study results is unknown and is of interest to have a better understanding on what other important implications government grants have through more meta-epidemiological research.

Strengths and limitations

The strengths of our study include that we analyzed a wide variety of studies, incorporating studies from different countries, years, and with diverse study designs. Our multistage probability sampling helped us collect a properly stratified sample from a large population. Our main limitations are that we did not search for the exact investment amount provided by each source of funding, including a limited number of journals and focusing our analysis on the last three decades.

CONCLUSIONS

The main funding source in medical research in the last 30 years has consistently been government aid. Despite previous reported data, no association was found between the source of funding and statistically significant results. Further studies are needed to state what association government funding could have with the results of studies.

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REFERENCES

1 Martin L, Hutchens M, Hawkins C, *et al*. How much do clinical trials cost? *Nat Rev Drug Discov* 2017;16:381–2.
2 Ebadi A, Schiffauerova A. How to receive more funding for your research? get connected to the right people! *PLoS One* 2015;10:e0133061–19.
3 Squitieri L, Chung KC. Funding research in the twenty-first century: current opinions and future directions. *Hand Clin* 2014;30:367–76.
4 Hansen C, Lundh A, Rasmussen K. Financial conflicts of interest in systematic reviews: associations with results, conclusions, and methodological quality. *Emergencias* 2021;33:220–1.
5 Lundh A, Lexchin J, Mintzes B, *et al*. Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2017;2:MR000033.
6 Fabbri A, Lai A, Grundy Q, *et al*. The influence of industry sponsorship on the research agenda: a scoping review. *Am J Public Health* 2018;108:e9–16.
7 McComas KA. Researcher views about funding sources and conflicts of interest in nanotechnology. *Sci Eng Ethics* 2012;18:699–717.
8 Packalen M, Bhattacharya J. Nih funding and the pursuit of edge science. *Proc Natl Acad Sci U S A* 2020;117:12011–6.
9 Murad MH, Wang Z. Guidelines for reporting meta-epidemiological methodology research. *Evid Based Med* 2017;22:139–42.
10 Sedgwick P. Multistage sampling. *BMJ* 2015;31:h4155.
11 Giraudeau B, Higgins JPT, Tavernier E, *et al*. Sample size calculation for meta-epidemiological studies. *Stat Med* 2016;35:239–50.
12 Moses H, Matheson DHM, Cairns-Smith S, *et al*. The anatomy of medical research: US and international comparisons. *JAMA* 2015;313:174–89.
13 Rodríguez-Padial L, Fernández Lozano I, Hidalgo Urbano R, *et al*. Trends and bibliometric impact of research grants of the Spanish Society of Cardiology/

Spanish heart Foundation (2007-2012). *Revista Española de Cardiología* 2019;72:1012–9.
14 Bernstein M, Desy NM, Matache BA, *et al*. A ten-year analysis of the research funding program of the orthopaedic trauma association. *J Bone Joint Surg Am* 2013;95:e142.
15 Crockett SD, Dellon ES, Bright SD, *et al*. A 25-year analysis of the American College of gastroenterology research grant program: factors associated with publication and advancement in academics. *Am J Gastroenterol* 2009;104:1097–105.
16 Boddie C, Sell TK, Watson M. Federal funding for health security in FY2016. *Health Secur* 2015;13:186–206.
17 Dieleman J, Campbell M, Chapin A. Evolution and patterns of global health financing 1995-2014: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *Lancet* 2017;389:1981–2004.
18 Logeman AL, Ponce O, Álvarez-Villalobos N, *et al*. Who influences health care in the United States? A study of trends from 2002 to 2018. *Mayo Clin Proc* 2019;94:2360–1.
19 Fabbri A, Parker L, Colombo C, *et al*. Industry funding of patient and health consumer organisations: systematic review with meta-analysis. *BMJ* 2020;368:l6925.