A bibliometric analysis of the global research on sofosbuvir
[version 1; referees: 1 approved, 2 approved with reservations]

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Abstract
In this article, we examine the research on sofosbuvir with a bibliometric analysis of global research production. The study of sofosbuvir has been a field of intense research in the past few years, with Latin American contributions playing a modest role. With continued drug development and approval of hepatitis C antivirals, research is expected to increase. Our findings will assist scholars and policy makers in their efforts to improve scientific research policies, with the goal of maximizing the access to treatments, especially in low and middle-income countries.
**Introduction**

Hepatitis C virus (HCV) has a major impact on public health, with around 170 million people in the world being affected. In Latin America, the prevalence of hepatitis C has been estimated to be at around 1.6% of the adult population, and the most common genotypes are 1 and 3. The new treatments for HCV include direct-acting antivirals (DAAs), which shorten length of therapy, improve sustained virologic response rates, and minimize side effects.

Sofosbuvir is one of the most important DAAs in the market today, but high prices have led to a large increase in spending by health systems and can be a barrier to rapid global treatment, especially in low and middle-income countries. The identification of global research on DAAs might lead to new insights into the treatments of HCV and suggest research directions.

Based on the above, our study aimed to identify and explore the worldwide development of sofosbuvir research.

**Methods**

We performed a bibliometric analysis using the original articles indexed in Web of Science. The search strategy used the following MeSH and non-MeSH terms in the title field: Sofosbuvir, Sovaldi, PSI 7977, and GS 7977. The validity of the search strategy was tested by manually reviewing retrieved articles. Bibliometric indicators were investigated by analyzing annual research output, languages, countries, journals, authors, institutions, and citations. Indicators were analyzed with the option “Analyze Results” and “Create Citation Report” in Web of Science. Author co-citation analysis (ACA) was presented as network visualization map using VOSviewer (version 1.6.4) techniques.

**Results**

A total of 341 publications for the period of 2010–2017 (up to March 31, 2017) were retrieved and assessed. There were a total of 126 journals that published research on sofosbuvir. Twenty-four articles were economics-based. The three most prolific journals were Hepatology (31 articles), Gastroenterology (17), and Journal of Hepatology (17), responsible for 19.1% of the total publication output. The retrieved documents were published by 46 different countries. The largest contributors in absolute number of articles were USA (220), France (47), and Germany (43). Only one article was from Latin America (Brazil), and it was about sofosbuvir and Zika. The total number of authors for all articles was 2044. John G. McHutchison from Gilead Science (GS) published the most documents in this field (55), followed by William T. Symonds from GS (30), Diana M. Brainard from GS, and Eric Lawitz from Texas Liver Institute/University of Texas Health Science Center (28). Gilead Sciences (131), Bristol Myers Squibb (38), and Merck (27) were the three major funders. A total of 86 articles were from GS, 30 from Inova Fairfax Hospital, and 26 were from University of Texas. The sum of the citations related to the published articles was 10036. Average citations per item were 29.4, with an h-index of 46.

The number of authors included in the ACA was based on a minimum number of fifteen articles per author. The map produced included 20 authors distributed into three clusters (red, blue, and green), as shown in Figure 1. The red cluster included eleven authors (headed by John G. McHutchison from GS), the blue cluster included five (headed by Eric Lawitz from Texas Liver Institute/University of Texas Health Science Center), and the green cluster included four authors (headed by Zoibar Younossi from Inova Fairfax Hospital).

**Figure 1.** Author co-citation analysis with VOSviewer for sofosbuvir publications. Minimum of fifteen articles per author, 20 authors were included.
Conclusions
According to our bibliometric analysis, the study of sofosbuvir has been a field of intense research in the past few years. Developed countries have had an enormous impact on the global research in the field. Recently, interest has focused on the use of sofosbuvir to treat Zika infection, and an important contribution to the body of sofosbuvir research has been supported by its manufacturer. With continued drug development and approval of hepatitis C antivirals, research is expected to continue increasing.

Data availability
Dataset 1: Data obtained from Web of Science. CSV contained list of studies included. Doi, 10.5256/f1000research.12314.d174424

Competing interests
No competing interests were disclosed.

Grant information
The author(s) declared that no grants were involved in supporting this work.

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7. Sacramento CQ, de Melo GR, de Freitas CS, et al.: The clinically approved antiviral drug sofosbuvir inhibits Zika virus replication. Sci Rep. 2017; 7: 40920. PubMed Abstract | Publisher Full Text | Free Full Text
8. Hernández-Vásquez A, Rosselli D: Dataset 1 in: A bibliometric analysis of the global research on sofosbuvir. F1000Research. 2017. Data Source
The manuscript from Hernández-Vásquez and Rosselli reviews the state of art on sofosbuvir and HCV. This analysis leads to the notion that the contribution of Latin American Institutions to the field is marginal, which is likely an anticipated outcome. The authors move out of the main field of interest of the manuscript, HCV, to Zika virus (ZIKV) to highlight a Latin American contribution to the improved comprehension of the pharmacology of sofosbuvir.

As sofosbuvir became an antiviral of major interest, not only towards HCV and ZIKV, but also for Dengue virus (DENV) – my suggestion is to compare the studies on the pharmacology of this drug on HCV and Flavivirus members. The study on ZIKV and sofosbuvir cited in this manuscript (https://www.nature.com/articles/srep40920) was preceded by a pre-print, which was the first contribution to open the field of sofosbuvir against flaviviruses (https://www.biorxiv.org/content/early/2016/07/06/061671; https://www.the-scientist.com/?articles.view/articleNo/46585/title/Sofosbuvir-Shows-Anti-Zika-Activity-In-Vitro/) – around six months after the ZIKV outbreak. I presume that the proposed comparison will demonstrate the installed capacity of response to novel (re)emergent viruses in Latin America.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
Yes
Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Referee Report 25 September 2017

doi:10.5256/f1000research.13329.r26177

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Curriculum Development Unit, College of Medicine, King Saud University, Riyadh, Saudi Arabia

I read with great interest the above titled article. However there are several issues/problems that need to be improved.

Abstract
The whole abstract should be rewritten. We need first to know the rationales of the study, or why is this study needed? What is the research question? What is the aim of the study? Then under state the search engine used and key words used in the search, and briefly state how did you process findings. Then state the bibliometric parameters that you aimed to study. State key results that answered your research question and stated under methods (follow the same sequence). Then state 2-3 lines summarizing key lessons learnt from your findings or what we can conclude from your study findings or take home messages. Ask your-self, “did the study answer my research question?” If yes, in what way...

What are the bibliometric parameters that you examined? State them under methods and include the findings for each one.

There are several redundant words in the abstract such as “In this study”, “we examined the research on sofosbuvir with a bibliometric analysis..” but you did not mention, even under methods in the manuscript, which type of research did you include in your analysis. Did you include only human or animal studies as well? Did you include only basic research or clinical research and clinical trials or both? Did you only include randomized controlled studies only or also you did include observational studies, controlled studies, reviews, and meta-analysis? Which of which did you include?

Introduction

Please note the following regarding “Second paragraph” under Introduction:

- What do you mean by “most important DAAs”? You may omit this
- We need to know why did you chose Sofosbuvir and not other drugs in this group
- What are the advantages of Sofosbuvir over other drugs in this group and add references.
- Not clear about the sentence “high prices have led to a large increase in spending by health systems and can be a barrier to global treatment…” how this is related to the bibliometric analysis you are aiming at? Focus on the study purpose.
- State the rationale of the study
• State the bibliometric parameters you aim to analyze.
• State clearly the research question
• Add appropriate references for each item
• The statement “based on the above….” Is meaningless and should be omitted.

Methods:
• State the study design. Add a reference
• State the date of searching the Web of Science, and who conducted such search. Did both researchers share this responsibility?
• It is not clear what do you mean by MeSH and non-MeSH? Did you use PubMed as well? Explain why?
• What do you mean by PSI 7977 and GS7977, if these are the codes for the drug before its marketing. State this and the references for this.
• What were the inclusion and exclusion criteria?
• Did you include only basic research or clinical research and clinical trials or both? Did you only include randomized controlled studies only or also you did include observational studies, controlled studies, reviews, and meta-analysis? Which of which did you include?
• Did you include editorials? Did you include letter to the Editor? Did you include animal studies? Did you include review studies and meta-analysis? All these details are needed.
• What were the bibliometric parameters that you analyzed?
• I cannot see any description of how did you analyse the data gathered. How did you reach to agreement to include or not to include an article?
• Did you calculate the degree of agreement between researchers?

Results
• This section needs a lot of work
• The results should mirror the subtitles under methods
• Provide results for each subitem in the bibliometric analysis you did.
• The assessment is superficial and more in depth analysis is needed.
• Use subtitles
• You may create 2-3 tables summarizing key findings/analysis.
• What does Figure 1 mean?

Discussion
• I cannot see a section for “the discussion”. You should add a discussion.
• Remind the research of your research question, briefly state your key findings
• Discuss the agreement and disagreement with other researchers.
• Discuss the meaning of your findings.
• Discuss the limitation of the study
• Discuss the significance of your findings
• Future directions in this area

Conclusion
• This should be rewritten in light of your findings.
• Your statement about bibliometric analysis is misleading. I cannot see any bibliometric analysis from what I have read.
References

Only 8 references. Please read the literature in this area and improve this section

Supplementary data

I would advice also submitting the raw data of the material collected in a table showing the author (first author and year), title of article, journal detail, type of article (research, review, meta-analysis, article, editorial etc), and name of university/country involved.

References

1. Hernández-Vásquez A, Rosselli D: A bibliometric analysis of the global research on sofosbuvir. *F1000Research*. 2017; 6. Publisher Full Text

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No

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

No

**Competing Interests:** No competing interests were disclosed.

**Referee Expertise:** Medical education, bibliometrics, clinical pharmacology, gastroenterology hepatology

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Juliana Gonçalves Reis
Postgraduate Program in Public Health and Environment, National School of Public Health Sergio Arouca (ENSP/Fiocruz), Niterói, Brazil

Methods
- Was it necessary to clean and standardize the data?
- Describe the option of the bibliographic database wos.
- Why was it used a high limit for the number of documents per author?

Results
- I suggest a chart of the distribution number of documents per year.
- I suggest a network of articles keywords with the description of the clusters.

Conclusions
- What are the main gaps?
- What are the possibilities for future research?

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Yes

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Competing Interests: No competing interests were disclosed.

Referee Expertise: Bibliometric analysis, public health, VOSviewer.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
Your article is published within days, with no editorial bias

- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

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