Do journals and corporate sponsors back certain views in topics where disagreement prevails?

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Abstract. The article focuses on scientific disagreement about the use of statin-related drugs in the prevention of cardiovascular events. The study forms part of an exploration of the broader principle of research polarization, foremost in medicine. The hypothesis is that statin-positive and statin-critical researchers publish in different committed central journals, and that they are financially supported by different dedicated corporate sources. Methodologically we use Web of Science (WoS) analytic tools to perform publication analysis of a time series covering 1998-2018 in three seven-year windows. For each window data is captured based on sets of known statin-positive and statin-critical articles and researchers, and their primary and secondary co-authors. Standard deviation is used as a focused normalization and visual instrument together with Spearman's correlation coefficient in order to compare frequency distributions of statin-positive and critical journal and sponsor article. Z-test *p*-values are used to assess the probability of error concerning the distributions.

Findings at general topical level showed that a few journals consistently and significantly occupied top positions, two of which, *American Journal of Cardiology* and *Circulation*, published articles from both positions. Besides, *Journal of the American College of Cardiology* served as a major publisher of statin-positive research from 2005, as did *European Heart Journal* from 2012, replacing *American Journal of Cardiology* at the top. From 2012 *Atherosclerosis* and *European Journal of Preventive Cardiology* served as top-publishers of statin-critical articles. Two central US funding agencies, *US Department of Health Human Services* and *National Institutes of Health* (NIH), operated at general topical level across the time series, but the agencies played only a minor role in the divergent research positions. From 2005 statin-positive as well as statin-critical research was mainly sponsored by multinational pharmaceutical companies, predominantly *Merck, AstraZeneca and Pfizer*. In conclusion, the initial hypothesis about dedicated journals and sponsors was entirely substantiated at the general topical level and at the journal level of research disagreement, but not at sponsor level. Distinct dedicated journals were extracted separately from the two divergent statin positions. Since the WoS coverage of sponsor data 1998-2004 was sporadic sponsor data are analyzed from 2005. Only from 2012 the WoS sponsor coverage of the topic is consistently at 60%.

Keywords: Publication analysis; Simvastatin; Atorvastatin; Cardiovascular events; Research disagreement; Statin positive journals; Statin critical journals; Statin sponsors; Scientometric analysis; Frequency distributions

Introduction

In several fields and specialties, particularly in the health sciences, critical disagreements or even polarization (Ploug & Holm, 2015) exist where groups of researchers have opposite views, e.g. on the application of drugs, the use of health monitoring programs or the adverse effects of interventions. Topical examples include the use of statin drugs as primary prevention against cardiovascular events by diminishing cholesterol, HPV (human papilloma virus) prevention by vaccination or breast cancer screening.

The current study forms part of an ongoing scientometric project about polarization in the sciences. The idea is to attempt to establish a methodology which considers a variety of parameters characterizing selected groups of research articles made available by citation indexes, such as Web of Science (WoS) (Clarivate Analytics, 2020) or Scopus (Elsevier, 2020). Such parameters are co-authorships; research groups; sponsorships; publishing journals; research institutions; specific title and abstract terms or concepts; specific indexing keywords; and citations (Rousseau & Egghe, 2018). The aim is to provide journal editors and publishers, research groups, researchers, sponsors and research institutions with a tool that may inform about actual authors, research groups, journals or sponsors that are driving certain research views or stand-points. For instance, the discovery of specific actors promoting a certain critical or positive view of a case, eventually over time, is of interest to the community. From a scientometric perspective such a tool consists of 1) an information retrieval mechanism to extract relevant data in a given time period associated with the topic in question from a given database (e.g., WoS) and 2) a range of well-known analytic instruments, such as frequency distributions; a time series; co-term/author/citation analyses; bibliographic coupling; clustering and network analyses.

In this study we explore the statin issue, including the encapsulation of statin-positive vs. statin-critical research by means of co-author analyses and the application of frequency distributions of journals and sponsors in the form of a time series. The assumption behind co-author analysis is that co-authors to a large extent share the same research perspective. The frequency distributions provide ranked lists of actors (journals and sponsors; positive and critical) which can be compared. Our hypothesis is that aside from the many journals and sponsors that support statin research, irrespectively of viewpoint, one may disclose statin-positive research published in some committed high-ranking journals and being sponsored by a few dedicated corporate units different from other high-ranking journals and sponsors dedicated to statin-critical research.

We have chosen to analyze the statin issue covering the period 1998-2018 across three seven-year periods. Simvastatin was originally produced by Merck Company and the patent ran out in 2006. Fundamentally, the research community currently agrees to apply statins (Simvastatin or Atorvastatin and similar drugs) as *secondary* prevention, that is, in cases where patients already have experienced

heart failure and other serious cardiovascular events (Godlee, 2014; Demasi, 2018). However, statin drugs used as *primary* prevention in people that shows no or minor indications of cardiovascular problems, has given rise to much disagreement (Olsson, 2009; Redberg & Katz, 2017; Akyea, 2019).

For the period 1998-2018 we searched Web of Science (WoS) for scientometric analyses of disagreement or polarization in research work in order to find similar studies. We found that scientometric analyses of divergence phenomena concentrate on publication patterns and gender issues, demographic and topical divergence, management positions and productivity or differences in citation and publishing patterns. One study investigated the spread of research supported by one funding agency (Folbe et al., 2014). Vinnik et al. (2012) aimed at identifying factors predicting high-quality cardiovascular research. Very few scientometric studies deal with different research views on the same topic, e.g. Nestorowicz & Anacka (2019) on migration literature, and we have discovered no attempts to do such analyses in medical topics.

We have used WoS, Science Citation Index and its analytic tools as the source for collecting data (Clarivate Analytics, 2020). Statin-positive and statin-critical authors were initially detected through researcher statements in classic media, such as the BBC, and other science associated sources in the public domain. We applied levels of standard deviation (STDV) as a normalization tool in order visually to compare the frequency distributions of journals and sponsors within each seven-year period, regardless of their size. Non-parametric statistical tests, i.e, Spearman's *Rho*, were applied to assess the strength of difference between statin-positive and critical distributions.

Following the Methodology section, the paper provides general findings on the statin topic, followed by findings associated with the journals and sponsors for each period and comparisons between statin-positive and critical research. The paper ends with a concluding discussion of study biases, limitations and findings.

Methodology

Initially, we isolated a basic set from WoS on the topic 'simvastatin OR atorvastatin OR statin*', combined with 'cardiovascular' covering 1998-2018, Table 1. This retrieval profile covers a large variety of cardiovascular issues, such as heart failure and other coronary issues and include adverse phenomena, also in patients with diabetes or renal diseases. The set was then divided into three seven-year sets, 1998-2004; 2005-2011; 2012-2018, to form a time series on the topic. For each period set we applied WoS analytic tools to produce ranked frequency distributions of the publishing journals and supporting institutions (named sponsors) associated with the topic, Tables 2-3.

We applied three independent data sources in order to capture statin-positive and statin-critical articles from each analysis window: 1) knowledge of known statin-positive/critical researchers derived from various media; 2) manually monitoring and selecting top-cited articles from each of the three

period sets in a systematic way; 3) manually checking review articles from within each period set retrieved by search terms like 'controversy', 'debate', 'risk*' 'efficacy', 'benefit*', 'adverse effect*', 'primary prevention'.

1. We consulted Wikipedia (UK) and other classic media associated with scientific issues, such as TV documentaries, newspapers and Scandinavian medical journals not indexed in WoS, in order to find statin-positive and statin-critical researchers and articles. For instance, the well-known and highly cited statin-positive researcher *Collins R* was extracted from a BBC health program (2013); later BBC programs have also been dedicated the use of statin treatments. The Swedish medical journal *Läkaertidningen* provided us with the researcher, *Olsson AC* (2009) and other statin-critical or unconvinced international researchers from article references. This mode of data gathering from non-academic sources is not to be regarded as systematic but helped to get hold on the divergent issues in question. From the selected key researchers, we extracted their articles and actual co-authors, providing us with two sets of statin-positive/critical articles. We name these small sets of authors 'Key-Researcher Sets'.
2. Each of the three period sets were sorted by citations and top-cited articles manually checked for statin-positive and critical/uncertain statements found in titles, abstracts or conclusions. Because older articles in each set may obtain more citations than younger articles the lower limit of citations to articles monitored was set to 50 during 1998-2011 and ≥ 20 citations for 2012-2018. An article was regarded statin-positive if it promotes the use of statin treatment in cases of low LDL/HDL values, in primary prevention of cardiovascular events and in cases where the benefits of treatment are emphasized to outdo observed adverse phenomena. Most articles of this kind were cohort or placebo-controlled studies and meta-analyses. Statin-critical articles were items pointing to adverse issues interpreted as more serious for patients than benefits, arguing against the use of statins in primary prevention or casting doubt about or pointing to outcomes of studies where statin treatment did not demonstrate substantial effects. Cohort analyses as well as opinion papers, review articles and letters to the editor/comments and replies considering studies constituted many of such items. Discussions of biases in cohort vs. placebo studies were often interwoven into the argumentation. The selected statin-positive/critical articles and their authors were checked against the already captured two Key Researcher Sets of co-authors retrieved from each topical period.
3. Further, we identified some few additional authors to articles not retrieved previously deemed statin-positive or critical from title words and abstract statements traced in WoS during the three analysis periods defined by the search terms outlined above.

The two groups of statin-positive/critical co-author data per analysis period, originating from the three modes of data capture, were searched against the three original period sets of topical publications. The resulting 2 x 3 set combinations form the first round of co-authors searching. For each set WoS analytics was used to produce six new ranked distributions of co-authors. The distributions were sorted alphabetically in order to detect previously found author names. New authors not detected previously were extracted and added to the previous author search profiles by Boolean OR. The lower limit of author frequency on the co-author distributions was set to ≥ 4. As an extra benefit we could carry out name form control and selection of less used name forms for the same authors (e.g., Ridker PM & Ridker P). This second and final round of co-author searching augmented the size of the original statin-positive/critical sets. Each of the 2 x 3 sets was refined by WoS analytics to exclude statin-positive authors from the statin-critical sets and *vice versa*. A third round of co-authorship searching was avoided for fear of extracting non-relevant authors and because the authors on the lists tended to be the same as on previous lists. The total number of statin-positive articles was twice as large as the number of critical articles for the entire period (817 vs. 393). For each analysis period we used WoS analytic tools to produce frequency distributions of journals and sponsors from the two divergent sets of articles, Tables 4-7.

Thus, first we compared the journal or sponsor rank distributions in the three original sets on the general statin topic, Tables 2-3, with the statin-positive and the statin-critical distributions, Tables 4-5 and Tables 6-7, respectively. Secondly, we carried out time series analysis as well as comparisons between statin-positive and critical journal and sponsor distributions. Since the data are non-parametric, we applied one-tailed Z-test when comparing the statin-divergent distributions with the original topical sets, but only to demonstrate the calculated degree of effect and probability of error (the *z* and *p* values). We do not state anything about the (non)significance of the statin-divergent sets. We are aware of the significance discussions by Schneider (2015) and Amrhein et al. (2019) and recognize that by using our described methodology several biases are introduced in the study. In order to compare statin-positive journal and sponsor distributions we used Spearman's *Rho* and visual comparisons.

To visually detect if a (group of) journal(s) or sponsor(s) stand out on the general and particular distribution lists observed for the selected periods we applied standard deviation (STDV) statistics, so that data elements (analysis units) located by frequency equal to or above *average frequency + 3-4 STDV* in distributions are marked across the time series. As such the STDV indicator functions as a focused normalization instrument in the comparisons. WoS analytics allows analysis of max. 100,000 units per set of articles, which in the current study did not pose a problem, since the number of units in all analyses was below that limit. Sponsor name forms were checked for different versions, resulting in altered frequencies for some sponsors. WoS controlled and verified the indexed journal names.

Findings

Table 1 demonstrates the development of research production 1998-2018 on the statin topic. The productivity was slow and without highly cited articles and few review articles during the initial period 1998-2004 compared to later. The following 7-year period saw a vast increase in productivity – from a total of 1,413 to 4,809 items and more than tripling from 300 to 1,070 review articles. 29 articles became highly cited 2005-2011. As noted above the patent held by Merck for Simvastatin ran out in 2006, making the drug free to pursue and study further by various companies and state agencies from then on. In the third and most recent period the research production increased further with respect to all document types. Many meta-analyses, cohort and large-scale clinical studies also emerged.

Table 1. Annual and 7-year development of research production 1998-2018 on statin drugs related to cardiovascular events. **Bold** signifies highest activity. WoS, July 25, 2020.

		Annual		7-year period		
Year	Articles	High cits.	Review art.	Artticles	High cits.	Review art.
1998	49		17			
1999	83		17			
2000	114		19			
2001	187		31			
2002	236		56			
2003	341		73			
2004	403		87	1413	0	300
2005	523		121			
2006	595		146			
2007	651		147			
2008	711		153			
2009	731	5	159			
2010	787	12	166			
2011	811	12	178	4809	29	1070
2012	816	7	174			
2013	810	6	145			
2014	930	11	177			
2015	934	**13**	178			
2016	**973**	10	204			
2017	941	9	**219**			
2018	932	8	207	6336	64	1304
Total	**12558**	**93**	**2674**	12558	93	2674

Tables 2 and 3 demonstrate the distributions of mainstream journals and sponsors used in statin research. We plotted the frequencies and the average plus triple, quadruple and ≥ 5 x STDV values, based on all elements of the distributions. Table 2 shows that *American Journal of Cardiology*, *Atherosclerosis* and *Circulation* were the most important journals used for publication on the topic 1998-2011. During the third period 2012-2018 one journal entered as top-journal: *PLOS One.* Also, *Journal of Clinical Lipidology* and *International Journal of Cardiology* entered the top-5 rankings as central sources, pushing *American Journal of Cardiology* downwards on the list. In comparison, Tables 4 and 6 display the distributions of journals used for publication by statin-positive and critical researchers.

As can be observed in Table 3 WoS does not index all sponsoring agencies in the initial analysis period. Only 8 % of the records contain sponsors, hence the short list. No commercial companies are

indexed. The indexing begins to be more effective from 2007. For sponsors the analyses therefore concentrated on the two 7-year periods, 2005-2011 and 2012-2018, in which the coverage of sponsors is substantially higher, 30% and 59%, respectively. Thus, for the period 1998-2011 Table 3 only demonstrates *clues* as to top supporters.

Table 2. Top-35 journals publishing on statin drugs in relation to cardiovascular events 1998-2018. WoS, July 25, 2020.

Top-30 journals 1998-2004; N=388	Freq.	Top-30 Journals 2005-2011; N=963	Freq.	Journals 2012-2018; N= 1216	Freq.
**** CIRCULATION***	***59***	**** AMERICAN JOURNAL OF CARDIOLOGY***	***150***	**** ATHEROSCLEROSIS***	***176***
**** AMERICAN JOURNAL OF CARDIOLOGY***	***54***	**** ATHEROSCLEROSIS***	***134***	**** CIRCULATION***	***159***
**** ATHEROSCLEROSIS***	***51***	**** CIRCULATION***	***103***	**** PLOS ONE***	***148***
CURRENT OPINION IN LIPIDOLOGY	***33***	**** JOURNAL OF THE AMERICAN COLLEGE OF CARDIO.***	***100***	**** JOURNAL OF CLINICAL LIPIDOLOGY***	***129***
AMERICAN HEART JOURNAL	***29***	**** CURRENT MEDICAL RESEARCH AND OPINION***	***98***	**** INTERNATIONAL JOURNAL OF CARDIOLOGY***	***124***
EUROPEAN HEART JOURNAL SUPPLEMENTS	***29***	**** INTERNATIONAL JOURNAL OF CARDIOLOGY***	***69***	**** JOURNAL OF THE AMERICAN COLLEGE OF CARDIO.***	***121***
INTERNATIONAL JOURNAL OF CLINICAL PRACTICE	**23**	***AMERICAN HEART JOURNAL***	***59***	**** AMERICAN JOURNAL OF CARDIOLOGY***	***100***
ARTERIOSCLEROSIS THROMBOSIS AND VASC. BIOL.	22	***EUROPEAN HEART JOURNAL***	***57***	**** EUROPEAN HEART JOURNAL***	***88***
EUROPEAN HEART JOURNAL	21	***ATHEROSCLEROSIS SUPPLEMENTS***	***52***	**** CURRENT PHARMACEUTICAL DESIGN***	***76***
INTERNATIONAL JOURNAL OF CARDIOLOGY	21	***EXPERT OPINION ON PHARMACOTHERAPY***	***51***	***JOURNAL OF THE AMERICAN HEART ASSOCIATION***	***71***
DIABETES CARE	19	***JOURNAL OF CLINICAL LIPIDOLOGY***	***51***	***CURRENT ATHEROSCLEROSIS REPORTS***	***69***
JOURNAL OF THE AMERICAN COLLEGE OF CARDIO.	19	***INTERNATIONAL JOURNAL OF CLINICAL PRACTICE***	***50***	***EUROPEAN JOURNAL OF PREVENTIVE CARDIO.***	***67***
ARCHIVES OF INTERNAL MEDICINE	18	**CLINICAL THERAPEUTICS**	**43**	***CURRENT VASCULAR PHARMACOLOGY***	***59***
CURRENT MEDICAL RESEARCH AND OPINION	17	**CURRENT PHARMACEUTICAL DESIGN**	**41**	***CURRENT OPINION IN LIPIDOLOGY***	***58***
ATHEROSCLEROSIS SUPPLEMENTS	16	**CIRCULATION JOURNAL**	**39**	**JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS**	**52**
JAMA JOURNAL OF THE AMERICAN MEDICAL ASS.	16	CURRENT ATHEROSCLEROSIS REPORTS	38	**LIPIDS IN HEALTH AND DISEASE**	**50**
CLINICAL CARDIOLOGY	15	CURRENT OPINION IN LIPIDOLOGY	37	**CURRENT MEDICAL RESEARCH AND OPINION**	**46**
KIDNEY INTERNATIONAL	14	DIABETES CARE	35	**BMJ OPEN**	**45**
CARDIOVASCULAR DRUGS AND THERAPY	13	AMERICAN JOURNAL OF CARDIOVASCULAR DRUGS	34	CLINICAL THERAPEUTICS	40
ANNALS OF PHARMACOTHERAPY	12	EUROP. JOURN. OF CARDIOVASC. PREVENT. REHAB.	34	AMERICAN HEART JOURNAL	39
CANADIAN JOURNAL OF CARDIOLOGY	12	CANADIAN JOURNAL OF CARDIOLOGY	33	AMERICAN JOURNAL OF CARDIOVASCULAR DRUGS	38
HERZ	12	CURRENT OPINION IN CARDIOLOGY	33	CARDIOVASCULAR DRUGS AND THERAPY	38
ARCHIVES DES MALAD.DU COEUR ET DES VAISSEAUX	11	JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS	33	CIRCULATION JOURNAL	38
CURRENT OPINION IN CARDIOLOGY	11	VALUE IN HEALTH	32	CARDIOVASCULAR DIABETOLOGY	37
THERAPIE	11	CARDIOVASCULAR THERAPY AND PREVENTION	30	CLINICAL LIPIDOLOGY	37
CLINICAL THERAPEUTICS	10	CURRENT VASCULAR PHARMACOLOGY	29	CLINICAL CARDIOLOGY	36
DRUGS	10	LANCET	28	CURRENT CARDIOLOGY REPORTS	36
EXPERT OPINION ON INVESTIGATIONAL DRUGS	10	AMERICAN JOURNAL OF MEDICINE	27	BMC CARDIOVASCULAR DISORDERS	35
JOURNAL OF CARDIOVASCULAR RISK	10	HEART	27	ANGIOLOGY	34
LANCET	10	NEW ENGLAND JOURNAL OF MEDICINE	26	CANADIAN JOURNAL OF CARDIOLOGY	32
Average all 388 journals:	**3.67**	**Average all 963 journals:**	**5.01**	**Average all 1216 journals:**	**5.22**
Standard deviation (STDV) all 388 journals:	**6.33**	**Standard deviation (STDEV) all 963 journals::**	**11.10**	**Standard deviation (STDEV) all 1216 journals:**	**13.01**

Legend: *****: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV

Table 3. Top-30 sponsors of research on statin drugs related to cardiovascular events 1998-2018. WoS, July 25, 2020.

Sponsors 1998-2004; N= 31 (from 8% publ.)	Freq.	Sponsors 2005-2011; N=1576 (from 30% of publ.)	Freq.	Sponsors 2012-2018; N=4,688 (from 59% of publ.)	Freq.
UNITED STATES DEP. OF HEALTH HUMAN SERVICES	**93**	**** UNITED STATES DEP. OF HEALTH HUMAN SERVICES***	***375***	**** UNITED STATES DEP. OF HEALTH HUMAN SERVICES***	***591***
NATIONAL INSTITUTES OF HEALTH NIH USA	**90**	**** NATIONAL INSTITUTES OF HEALTH NIH USA***	***360***	**** NATIONAL INSTITUTES OF HEALTH NIH USA***	***567***
NIH NAT. HEART LUNG BLOOD INSTITUTE NHLBI	57	**** PFIZER***	***190***	**** ASTRAZENECA***	***397***
NIH NAT. INST. OF DIABET. DIGEST. KIDNEY DISEASES	16	**** ASTRAZENECA***	***175***	**** PFIZER***	***368***
NIH NAT. CENTER FOR RESEARCH RESOURCES NCRR	14	**** MERCK COMPANY***	***171***	**** MERCK COMPANY***	***336***
NIH NAT. INST. OF NEUROL. DISORD. STROKE NINDS	10	**** NIH NAT. HEART LUNG BLOOD INSTITUTE NHLBI***	***154***	**** AMGEN***	***309***
NIH NATIONAL INSTITUTE ON AGING NIA	10	**** SANOFI AVENTIS***	***87***	**** SANOFI AVENTIS***	***246***
UNITED STATES PUBLIC HEALTH SERVICE	5	***NOVARTIS***	***75***	**** NIH NAT. HEART LUNG BLOOD INSTITUTE NHLBI***	***225***
AGENCY FOR HEALTHCARE RESEARCH QUALITY	4	***GLAXOSMITHKLINE***	***73***	**** NOVARTIS***	***174***
MEDICAL RESEARCH COUNCIL UK MRC	4	***BRISTOL MYERS SQUIBB***	***71***	**** NAT. NATURAL SCIENCE FOUNDATION OF CHINA***	***168***
NIH NAT. CENTER FOR COMPL. ALTERNAT. MED.	4	***ABBOTT LABORATORIES***	***70***	**** ELI LILLY***	***157***
NIH EUN. KENNEDY SHRIVER NAT. INST. OF CHILD …	3	**SCHERING PLOUGH CORPORATION**	**65**	**** BRISTOL MYERS SQUIBB***	***148***
NIH NATIONAL CANCER INSTITUTE NCI	3	**ROCHE HOLDING**	**54**	**** ROCHE HOLDING***	***131***
NIH NAT. INST. OF ARTHRIT. MUSCUL. SKIN DIS. NIAMS	3	NIH NAT. INST. OF DIABET. DIGEST. KIDNEY DISEASES	48	**** ABBOTT LABORATORIES***	***127***
NIH NATIONAL EYE INSTITUTE NEI	2	TAKEDA PHARMACEUTICAL COMPANY LTD	45	**** MEDICAL RESEARCH COUNCIL UK MRC***	***124***
NIH NAT. INST. OF ALLERGY INFECT. DISEASES NIAID	2	BRITISH HEART FOUNDATION	41	**** GLAXOSMITHKLINE***	***123***
BHP HRSA HHS	1	NIH NAT. CENTER FOR RESEARCH RESOURCES NCRR	39	**** BOEHRINGER INGELHEIM***	***106***
DANISH HEART FOUNDATION	1	MEDICAL RESEARCH COUNCIL UK MRC	38	**** NATIONAL INSTITUTE FOR HEALTH RESEARCH NIHR***	***105***
DANISH MEDICAL RESEARCH COUNSIL	1	GENZYME CORPORATION	33	**** BRITISH HEART FOUNDATION***	***97***
ELSE AND MOGENS WEDELL WEDELLSB. FOUND. CPH DK	1	ELI LILLY	31	***TAKEDA PHARMACEUTICAL COMPANY LTD***	***94***
FDA HHS	1	NIH NATIONAL INSTITUTE ON AGING NIA	31	***DAIICHI SANKYO COMPANY LIMITED***	***89***
INSTITUTE OF BIOMEDICAL SCIENCE UK	1	CANADIAN INSTITUTES OF HEALTH RESEARCH CIHR	30	***NOVO NORDISK***	***87***
KING CHRISTIAN X S FOUNDATION	1	DAIICHI SANKYO COMPANY LIMITED	30	***GENZYME CORPORATION***	***86***
NIH NAT. INST. OF ENVIRONM. HEALTH SCIENCES NIEHS	1	MIN. OF EDU. CULT. SPORTS SC. AND TECH. JAPAN	30	***CANADIAN INSTITUTES OF HEALTH RESEARCH CIHR***	***85***
NIH NAT. INST. OF GENERAL MEDICAL SCIENCES NIGMS	1	BOEHRINGER INGELHEIM	27	***EUROPEAN UNION EU***	***78***
NIH NATIONAL INSTITUTE OF MENTAL HEALTH NIMH	1	NIH NAT. INST. OF NEUROL. DISORD. STROKE NINDS	27	**MSD**	**75**
NIH NAT. INST. ON ALCOHOL ABUSE ALCOHOLISM NIAAA	1	NOVO NORDISK	27	**REGENERON**	**75**
NORTHWICK PARK INST. FOR MEDICAL RES. NPIMR	1	GERMAN RESEARCH FOUNDATION DFG	24	**SANOFI**	**75**
ODCDC CDC HHS	1	BAYER AG	21	**AMERICAN HEART ASSOCIATION**	**72**
PAPWORTH HOSPITAL NHS TRUST	1	NATIONAL INSTITUTE FOR HEALTH RESEARCH NIHR	21	**MIN. OF EDU. CULT. SPORTS SC. AND TECH. JAPAN**	**69**
Average31 sponsors:	***10.8***	**Average 1572 sponsors:**	**3.13**	**Average 4688 sponsors:**	**2.98**
STDEV 31 sponsors:	**23.9**	**STDEV 1572 sponsors:**	**16.71**	**STDEV 4688 sponsors:**	**18.49**

Legend: *****: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV

The five same organizations, two *US health agencies* and three pharmaceutical companies including the patent owner *Merck Company*, stand out as actual top sponsors of research on statin drugs related to cardiovascular events 2005-2018 (≥ av. + 5 x STDV). A huge gap exists between the two US agencies and again after *NHLBI* (2005-2011) and *AMGEN* (2012-2018). The spread of individual sponsors increases dramatically from the second to the third analysis period, almost tripling – from N=1,576 to N=4,688, Table 3, mainly owing to the indexing policy of WoS. 3,760 sponsors are single article sponsors constituting a very long distribution tail, hence the lower STDV compared to the 2005-2011 period. This phenomenon can be explained by the fact that many articles are sponsored by more than one organization. AMGEN constitutes a new player in the research. Large cohort, clinical and meta-analysis studies are published and often highly cited during this recent period.

Statin-positive publications and sponsors

Table 4 shows that *Circulation* and *American Journal of Cardiology* acted as top-journals for station-positive publications, 1998-2011, only partly corresponding to the overall top-pattern for the same periods, Table 2. *Circulation* and *Journal of the American College of Cardiology* served as top-journals 2005-2018 with *European Heart Journal* and *Atherosclerosis* also entering as top-journals during the third period, Table 4. This pattern at the top was quite different from that shown in Table 2 for the identical periods. Note that *PLOS One*, listed three 2012-2018, Table 2, did not appear on the top-30 list of statin-positive journals during this period, Table 4. Hence, during the period 2005-2018 the *Journal of the American College of Cardiology*, and *European Heart Journal* 2012-2018, were regarded specific to statin-positive research. Owing to their high frequencies it is highly improbable that the three top-journals 2005-2018, located in the 4 x STDV+ zone, might be replaced by lower frequency journals, given the fairly low statistical uncertainties for the two periods (p = .02 and .056, Table 4).

Table 5 shows the distributions of sponsors 2005-2018. Due to the high degree of statistical uncertainty (2005-2011: p = .40 and 2012-2018: p = .31) *and* the low WoS coverage of sponsorships until 2012, the top-10 sponsors might indeed change positions on the distributions. Consequently, Table 5 only serves as *clues* to or *indications* of the top-sponsors. The low rank positions of the top mainstream research supporters, Table 3, i.e., the two national *US health agencies*, and the apparent competition between several commercial players, with *Merck Company* only ranked 3 during 2012-2018, constituted the most interesting observations. Note also the emergence of *Amgen* as a statin- positive major sponsor during the most recent period – in line with its sudden appearance, Table 3.

Table 4. Top-30 journals publishing statin-positive articles 1998-2018. WoS, August 1, 2020.

Top-30 positive journals 1998-2004; N=51	Freq.	Top-30 Positive Journals 2005-2011; N=109	Freq.	Top-30 positive Journals 2012-2018; N= 123	Freq.
**** CIRCULATION***	***16***	**** AMERICAN JOURNAL OF CARDIOLOGY***	***28***	****CIRCULATION***	***41***
AMERICAN JOURNAL OF CARDIOLOGY	5	**** CIRCULATION***	***27***	**** JOURN. OF THE AM. COLLEGE OF CARDIOLOGY***	***34***
CURRENT OPINION IN LIPIDOLOGY	5	***JOURN. OF THE AM. COLLEGE OF CARDIOLOGY***	***21***	***EUROPEAN HEART JOURNAL***	***32***
LANCET	5	***AMERICAN HEART JOURNAL***	***13***	**ATHEROSCLEROSIS**	**22**
EUROPEAN HEART JOURNAL	4	***NEW ENGLAND JOURNAL OF MEDICINE***	***13***	AMERICAN HEART JOURNAL	15
AMERICAN HEART JOURNAL	3	**LANCET**	**12**	JOURNAL OF CLINICAL LIPIDOLOGY	13
ARTERIOSCLEROSIS THROMB. AND VASC. BIOL.	3	EUROPEAN HEART JOURNAL	11	LANCET	13
EUROPEAN HEART JOURNAL SUPPLEMENTS	3	ATHEROSCLEROSIS	10	AMERICAN JOURNAL OF CARDIOLOGY	10
MEDIZINISCHE KLINIK	3	AMERICAN JOURNAL OF KIDNEY DISEASES	7	CLINICAL CARDIOLOGY	9
CURRENT OPINION IN CARDIOLOGY	2	STROKE	7	JAMA CARDIOLOGY	9
DIABETIC MEDICINE	2	ATHEROSCLEROSIS SUPPLEMENTS	5	JOURN. OF THE AM. HEART ASSOCIATION	9
JAMA JOURN. OF THE AM. MEDICAL ASS.	2	DIABETES CARE	5	EUROPEAN JOURN. OF PREVENTIVE CARDIOL.	7
KIDNEY INTERNATIONAL	2	DIABETOLOGIA	5	JAMA JOURN. OF THE AM. MEDICAL ASS.	7
NEW ENGLAND JOURNAL OF MEDICINE	2	CIRCULATION CARDIOV. QUAL. AND OUTCOMES	4	INTERNATIONAL JOURNAL OF CARDIOLOGY	6
PRESSE MEDICALE	2	CLINICAL JOURN. OF THE AM. SOC. OF NEPHRO.	4	AMERICAN JOURNAL OF MEDICINE	5
STROKE	2	CURRENT OPINION IN LIPIDOLOGY	4	DIABETOLOGIA	5
AMERICAN JOURNAL OF MEDICINE	1	JAMA JOURN. OF THE AM. MEDICAL ASS.	4	KIDNEY INTERNATIONAL	5
ANNALES DE CARDIOL. ET D ANGEIOLOGIE	1	ARTERIOSCLEROSIS THROMB. AND VASC. BIOL.	3	LANCET DIABETES ENDOCRINOLOGY	5
ANNALES DE MEDECINE INTERNE	1	BMJ BRITISH MEDICAL JOURNAL	3	ANNALS OF INTERNAL MEDICINE	4
ARCHIVES OF INTERNAL MEDICINE	1	CLINICAL RESEARCH IN CARDIOLOGY	3	ATHEROSCLEROSIS SUPPLEMENTS	4
ATHEROSCLEROSIS	1	CLINICAL THERAPEUTICS	3	CIRCULATION CARDIOVASCULAR GENETICS	4
ATHEROSCLEROSIS SUPPLEMENTS	1	DIABETES	3	CURRENT CARDIOLOGY REPORTS	4
BULLETIN DE L ACADEMIE NAT. DE MEDECINE	1	EUROPEAN HEART JOURNAL SUPPLEMENTS	3	JOURN. OF CARDIOVASC. PHARMA. AND THERAP.	4
CARDIOLOGY	1	EUROPEAN JOURNAL OF HEART FAILURE	3	JOURNAL OF THE AM. SOC. OF NEPHROLOGY	4
CEREBROVASCULAR DISEASES	1	HEART	3	CIRCULATION CARDIOV. QUAL. AND OUTCOMES	3
CLINICAL CARDIOLOGY	1	INT. JOURNAL OF CLINICAL PRACTICE	3	CLINICAL PHARMACOLOGY THERAPEUTICS	3
CLINICAL THERAPEUTICS	1	JOURNAL OF THE AM. SOC. OF NEPHROLOGY	3	CURRENT ATHEROSCLEROSIS REPORTS	3
CURRENT OPINION IN NEPHRO. AND HYPERT.	1	KIDNEY INTERNATIONAL	3	CURRENT OPINION IN LIPIDOLOGY	3
DIABETES CARE	1	ARCHIVES OF INTERNAL MEDICINE	2	DIABETES OBESITY METABOLISM	3
DRUGS	1	ARCHIVES OF MEDICAL SCIENCE	2	EUROPEAN JOURN. OF CLIN. INVESTIGATION	3
Average all 51 journals:	**1.86**	**Average all 109 journals:**	**2.86**	**Average all 123 journals:**	**3.33**
Standard deviation (STDV) all 51 journals:	**2.18**	**Standard deviation (STDV) all 109 journals::**	**4.55**	**Standard deviation (STDV) all 123 journals:**	**6.04**
		Z test vs. Table 2: z= -2.01363; p = .02222;		Z test vs. Table 2: z =-1.59486; p = .05592;	

Legend: *****: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV

Table 5. Top-30 sponsors of statin-positive articles 1998-2018. WoS, August 1, 2020.

Positive Sponsors 2005-2011 (N=246; 39 % of publ.)	Freq.	Positive Sponsors 2012-2018 (N=666 = 79% of publ.)	Freq.
**** MERCK COMPANY***	***42***	**** ASTRAZENECA***	***107***
**** ASTRAZENECA***	***41***	**** PFIZER***	***100***
**** PFIZER***	***40***	**** MERCK COMPANY***	***79***
BRISTOL MYERS SQUIBB	***27***	**** AMGEN***	***66***
SANOFI AVENTIS	**23**	**** SANOFI AVENTIS***	***56***
NATIONAL INSTITUTES OF HEALTH NIH USA	**22**	**** BRISTOL MYERS SQUIBB***	***50***
UNITED STATES DEP. OF HEALTH HUMAN SERVICES	**22**	***NATIONAL INSTITUTES OF HEALTH NIH USA***	***48***
NOVARTIS	**21**	***UNITED STATES DEP. OF HEALTH HUMAN SERVICES***	***48***
ROCHE HOLDING	20	**NIH NATIONAL HEART LUNG BLOOD INSTITUTE NHLBI**	**39**
GLAXOSMITHKLINE	18	**NOVARTIS**	**38**
SCHERING PLOUGH CORPORATION	17	**ELI LILLY**	**37**
NIH NATIONAL HEART LUNG BLOOD INSTITUTE NHLBI	14	**MEDICAL RESEARCH COUNCIL UK MRC**	**33**
ABBOTT LABORATORIES	12	**ROCHE HOLDING**	**32**
TAKEDA PHARMACEUTICAL COMPANY LTD	12	GLAXOSMITHKLINE	29
BRITISH HEART FOUNDATION	9	GENZYME CORPORATION	28
ELI LILLY	9	BOEHRINGER INGELHEIM	27
MEDICAL RESEARCH COUNCIL UK MRC	9	BRITISH HEART FOUNDATION	27
ISIS	8	ABBOTT LABORATORIES	25
NIH NATIONAL CANCER INSTITUTE NCI	8	SANOFI	25
BOEHRINGER INGELHEIM	7	AMARIN	23
DAIICHI SANKYO COMPANY LIMITED	7	DAIICHI SANKYO COMPANY LIMITED	22
GENZYME CORPORATION	7	REGENERON	22
NATIONAL INSTITUTE FOR HEALTH RESEARCH NIHR	7	TAKEDA PHARMACEUTICAL COMPANY LTD	21
ACCUMETRICS	6	NATIONAL INSTITUTE FOR HEALTH RESEARCH NIHR	20
BAYER AG	6	KOWA	19
GERMAN RESEARCH FOUNDATION DFG	6	NAT. HEALTH AND MED. RES. COUNCIL OF AUS.	17
NAT. HEALTH AND MED. RES. COUNCIL OF AUS.	6	EISAI CO LTD	16
DONALD W REYNOLDS FOUNDATION	5	JOHNSON JOHNSON USA	15
INTEKRIN THERAPEUTICS	5	REGENERON PHARMACEUTICALS INC	15
LEDUCQ FOUNDATION	5	AEGERION	14
Average 246 sponsors:	**2.85**	**Average 666 sponsors:**	**3.34**
STDEV 246 sponsors:	**5.85**	**STDEV 666 sponsors:**	**9.01**
Z test vs. Table 3: z = -0.26222; p = .39743		Z test vs. Table 3: z = 0.50311; p = .30854	

Legend: *****: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV

Statin-critical publications and sponsors

Table 6 demonstrates that *American Journal of Cardiology* and *Atherosclerosis* served as the most important journals publishing statin-critical research articles 2005-2018, with *European Journal of Preventive Cardiology* ranked three 2012-2018. The two latter journals covered 36% of the total statin-critical output during the third analysis period and the statistical uncertainty is quite small: $p = .015$. Thus, it is most likely that the top-journals 2012-2018 do not shift rank positions. Compared to the journals publishing mainstream statin research, Table 2, *European Journal of Preventive Cardiology* stands out as the most specific statin-critical journal in the recent period, followed by *International Journal of Cardiology*.

Table 6. Top-30 journals publishing statin-critical articles 1998-2018. WoS, August 2, 2020.

Top-30 Critical Journals 1998-2004; N=36	**Freq.**	**Top-30 Critical Journals 2005-2011; N=62**	**Freq.**	**Top-30 Critical Journals 2012-2018; N= 89**	**Freq.**
CIRCULATION	***6***	**** AMERICAN JOURNAL OF CARDIOLOGY***	***13***	**** ATHEROSCLEROSIS***	***21***
AMERICAN JOURNAL OF CARDIOLOGY	5	CIRCULATION	8	**EUR JOURNAL OF PREVENTIVE CARDIOLOGY**	**11**
EUROPEAN HEART JOURNAL SUPPLEMENTS	5	NEW ENGLAND JOURNAL OF MEDICINE	8	INTERNATIONAL JOURNAL OF CARDIOLOGY	10
ATHEROSCLEROSIS	3	ATHEROSCLEROSIS	7	AMERICAN JOURNAL OF CARDIOLOGY	8
EUROPEAN HEART JOURNAL	3	ATHEROSCLEROSIS SUPPLEMENTS	6	CIRCULATION	8
JAMA JOURN. OF THE AM. MEDICAL ASS.	3	EUROPEAN HEART JOURNAL	6	HEART	8
LANCET	3	EUR JOURNAL OF CARDIOVASC. PREVENT. REHAB.	5	EUROPEAN HEART JOURNAL	6
CLINICAL CARDIOLOGY	2	JOURNAL OF THE AM. COLLEGE OF CARDIOLOGY	5	JOURNAL OF CLINICAL LIPIDOLOGY	6
DIABETES CARE	2	EUROPEAN HEART JOURNAL SUPPLEMENTS	4	PLOS ONE	5
DIABETIC MEDICINE	2	JOURNAL OF INTERNAL MEDICINE	3	ATHEROSCLEROSIS SUPPLEMENTS	4
JOURNAL OF THE AM. COLLEGE OF CARDIO.	2	CARDIOLOGY	2	CURRENT ATHEROSCLEROSIS REPORTS	4
NEPHROLOGY DIALYSIS TRANSPLANTATION	2	CLINICAL JOURN. OF THE AM. SOC. OF NEPHROL.	2	CURRENT MEDICAL RESEARCH AND OPINION	4
ACTA DIABETOLOGICA	1	CLINICAL THERAPEUTICS	2	LIPIDS IN HEALTH AND DISEASE	4
ACTA PHYSIOLOGICA SCANDINAVICA	1	CURRENT MEDICAL RESEARCH AND OPINION	2	ANNALS OF THE RHEUMATIC DISEASES	3
ADVANCES IN THERAPY	1	CURRENT OPINION IN LIPIDOLOGY	2	CURRENT OPINION IN LIPIDOLOGY	3
AMERICAN JOURNAL OF TRANSPLANTATION	1	DIABETIC MEDICINE	2	JOURNAL OF THE AM. COLL. OF CARDIOLOGY	3
ANNALS OF MEDICINE	1	EUROPEAN JOURNAL OF HEART FAILURE	2	JOURNAL OF THE AMERICAN HEART ASS.	3
BIOCHEMICAL SOCIETY TRANSACTIONS	1	EXPERT OPINION ON PHARMACOTHERAPY	2	NEW ENGLAND JOURNAL OF MEDICINE	3
CARDIOVASCULAR DRUG REVIEWS	1	INTERNATIONAL JOURNAL OF CLINICAL PRACTICE	2	AMERICAN HEART JOURNAL	2
CLINICAL AND EXP. PHARMAC. AND PHYSIOL.	1	JAMA JOURN. OF THE AM. MEDICAL ASS.	2	CLINICAL THERAPEUTICS	2
CLINICAL DRUG INVESTIGATION	1	JOURNAL OF HYPERTENSION	2	CURRENT CARDIOLOGY REPORTS	2
CLINICAL INFECTIOUS DISEASES	1	JOURNAL OF THE AM. SOC. OF NEPHROL.	2	DIABETES OBESITY METABOLISM	2
CLINICAL NEPHROLOGY	1	LANCET	2	DIABETES VASCULAR DISEASE RESEARCH	2
CLINICAL THERAPEUTICS	1	TRANSPLANTATION PROCEEDINGS	2	ECHOCARDIOGRAPHY	2
DIABETOLOGIA	1	ACTA NEUROLOGICA SCANDINAVICA	1	EUROPEAN HEART JOURNAL SUPPLEMENTS	2
DRUGS AGING	1	AM. JOURNAL OF CARDIOVASCULAR DRUGS	1	EUROPEAN JOURNAL OF HEART FAILURE	2
EU. JOURNAL OF CLINICAL INVESTIGATION	1	AMERICAN JOURNAL OF KIDNEY DISEASES	1	GLOBAL HEART	2
EXPERT OPINION ON PHARMACOTHERAPY	1	AMERICAN JOURNAL OF TRANSPLANTATION	1	JAMA CARDIOLOGY	2
FUNDAMENTAL CLINICAL PHARMACOLOGY	1	ANNALS OF MEDICINE	1	JAMA JOURN. OF THE AM. MEDICAL ASS.	2
INT. JOURNAL OF CLINICAL PRACTICE	1	ARTHRITIS AND RHEUMATISM	1	NATURE REVIEWS ENDOCRINOLOGY	2
Average all 36 journals:	**1.72**	**Average all 62 journals:**	**2.11**	**Average all 89 journals:**	**2.25**
Standard deviation (STDEV) all 36 journals:	**1.31**	**Standard deviation (STDEV) all 62 journals:**	**2.26**	**Standard deviation (STDEV) all 89 journals:**	**2.87**
		Z test vs. Table 2: z = -2.05809; p = .0197;		Z test vs. Table 2: z = -2.15466; p = .01578;	

Legend: *****: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV

The three pharmaceutical companies, *Merck Company*, *Pfizer* and *AstraZeneca* topped the two distributions, Table 7, as in the case of statin-positive supporting institutions, Table 5. Also like in the statin-positive case the statistical uncertainties are very high (2005-2011: $p = .44$; 2012-2018 $p = .30$) and position changes might indeed occur in the distributions. Still, compared to Tables 3 and 5, outlining mainstream and statin-positive sponsors the various *US state agencies* played an even minor role in supporting critical research.

Table 7. Top-30 sponsors of statin-critical articles 1998-2018. WoS, August 2, 2020.

Top-30 Critical Sponsors 2005-2011 (N=64; 35 %)	Freq.	Critical Sponsors 2012-2018 (N = 301; 80 %)	Freq.
PFIZER	***20***	**** MERCK COMPANY***	***56***
ASTRAZENECA	**18**	**** ASTRAZENECA***	***37***
MERCK COMPANY	**17**	**** AMGEN***	***28***
NOVARTIS	9	**** PFIZER***	***25***
SCHERING PLOUGH CORPORATION	8	**NOVARTIS**	**18**
SANOFI AVENTIS	7	SANOFI AVENTIS	17
NATIONAL INSTITUTES OF HEALTH NIH USA	6	ROCHE HOLDING	15
UNITED STATES DEPARTMENT OF HEALTH HUMAN SERVIC	6	ABBOTT LABORATORIES	13
ROCHE HOLDING	5	ELI LILLY	12
BRISTOL MYERS SQUIBB	4	NOVO NORDISK	12
GENZYME CORPORATION	4	GENZYME CORPORATION	11
KOWA	4	NATIONAL INSTITUTES OF HEALTH NIH USA	11
SOLVAY	4	SCHERING PLOUGH CORPORATION	11
TAKEDA PHARMACEUTICAL COMPANY LTD	4	UNITED STATES DEPARTMENT OF HEALTH HUMAN SERVIC	11
GLAXOSMITHKLINE	3	BRISTOL MYERS SQUIBB	10
SMB	3	BOEHRINGER INGELHEIM	9
WYETH	3	GLAXOSMITHKLINE	9
ABBOTT LABORATORIES	2	MSD	9
BOEHRINGER INGELHEIM	2	KOWA	8
BRITISH HEART FOUNDATION	2	SANOFI	8
MSP SINGAPORE COMPANY LLC SINGAPORE	2	AEGERION	7
NIH NATIONAL HEART LUNG BLOOD INSTITUTE NHLBI	2	NOVO NORDISK FOUNDATION	7
NIH NATIONAL INSTITUTE OF DIABETES DIGESTIVE KIDNEY	2	SERVIER	7
RECORDATI	2	NATIONAL INSTITUTE FOR HEALTH RESEARCH NIHR	6
SERVIER	2	MEDICINES COMPANY	5
AMGEN	1	RECORDATI	5
ASTELLAS PHARMACEUTICALS	1	REGENERON	5
BAYER AG	1	REGENERON PHARMACEUTICALS INC	5
BI	1	RESVERLOGIX	5
COMMONWEALTH FUND	1	AMARIN	4
Average all 64 sponsors:	**2.81**	**Average all 301 sponsors:**	**2,43**
Standard deviation (STDEV) all 64 sponsors:	**3.91**	**Standard deviation (STDEV) all 301 sponsors:**	**4,92**
Z test vs. Table 3: z =-0.15299; p = .44038;		Z test vs. Table 2: z = -0.51613; p = .30153;	

Legend: *****: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV

Comparing statin-positive and critical distributions

We have compared the journal and sponsor distributions of statin-positive and critical nature 2005-2011 (journals) and 2012-2018 (journals and sponsors), Tables 4 vs. 6 and Tables 5 vs. 7, by means of the non-parametric Spearman´s correlation coefficient *Rho*. The displayed distributions are used in all calculations.

For *journals 2005-2011*, Spearman's *Rho = .21144* demonstrates an extremely weak association, implying that the statin-critical and statin-positive groups of journals are quite different. This variance is also emphasized by the fact that 13 top-30 statin-critical journals, mostly with low frequencies, were not found among the top-30 statin positive ones. Similarly, 12 statin-positive journals did not appear on the list of statin-critical journals. Among the top-listed statin-positive journals *American Heart Journal* (ranked 4) was not found on the top-30 distribution of statin-critical sources and may thus be regarded as a specific statin-positive journal. The *European Journal of Preventive Cardiology* served as the highest ranked source (rank 7) solely publishing statin-critical research. The top-statin mainstream journals, *Atherosclerosis, American Journal of Cardiology* and *Circulation,* published articles from both research positions, Table 4 vs. Table 6.

During the most recent period, *2012-2018*, the Spearman´s correlation coefficient is even weaker compared to the previous period, *Rho = .13254*. The two opposite distributions are very different. 11 top-30 statin-critical journals were not found among the top-30 statin-positive ones and 13 statin-positive journals did not appear on the list of statin-critical journals. During this period *Circulation, Journal of The Aerican. College of Cardiology, European Heart Journal* and *American Heart Journal* shift from neutral top-journals 2005-2011 to serve as the *dominant* statin-positive journals, with very few published statin-critical articles, Table 8. *Lancet* assists the statin-positive position, ranked six. *Heart* is the highest ranked statin-critical journal (ranked 4) not found on the positive list.

Table 8. Top-41 statin-positive journals compared to the frequency of matching statin-critical journals 2012-2018. WoS August 13, 2020.

Top-41 positive Journals 2012-2018; N= 123	Freq.	Corresponding critical journal	Freq.
**** CIRCULATION***	***41***		8
**** JOURN. OF THE AM. COLLEGE OF CARDIOLOGY***	***34***		3
EUROPEAN HEART JOURNAL	***32***		6
ATHEROSCLEROSIS	**22**		21
AMERICAN HEART JOURNAL	15		2
JOURNAL OF CLINICAL LIPIDOLOGY	13		6
LANCET**	13		0
AMERICAN JOURNAL OF CARDIOLOGY	10		8
CLINICAL CARDIOLOGY**	9		0
JAMA CARDIOLOGY	9		2
JOURN. OF THE AM. HEART ASSOCIATION	9		3
EUROPEAN JOURN. OF PREVENTIVE CARDIOL.	7		11
JAMA JOURN. OF THE AM. MEDICAL ASS.	7		2
INTERNATIONAL JOURNAL OF CARDIOLOGY	6		10
AMERICAN JOURNAL OF MEDICINE**	5		0
DIABETOLOGIA**	5		0
KIDNEY INTERNATIONAL**	5		0
LANCET DIABETES ENDOCRINOLOGY**	5		0
ANNALS OF INTERNAL MEDICINE**	4		0
ATHEROSCLEROSIS SUPPLEMENTS	4		4
CIRCULATION CARDIOVASCULAR GENETICS**	4		0
CURRENT CARDIOLOGY REPORTS	4		2
JOURN. OF CARDIOVASC. PHARMA. AND THERAP.**	4		0
JOURNAL OF THE AM. SOC. OF NEPHROLOGY	4		0
CIRCULATION CARDIOV. QUAL. AND OUTCOMES**	3		0
CLINICAL PHARMACOLOGY THERAPEUTICS**	3		0
CURRENT ATHEROSCLEROSIS REPORTS	3		4
CURRENT OPINION IN LIPIDOLOGY	3		3
DIABETES OBESITY METABOLISM	3		2
EUROPEAN JOURN. OF CLIN. INVESTIGATION**	3		0
ANNALS OF THE RHEUMATIC DISEASES***	0		3
CLINICAL THERAPEUTICS***	0		2
CURRENT MEDICAL RESEARCH AND OPINION***	0		4
DIABETES VASCULAR DISEASE RESEARCH***	0		2
EUROPEAN HEART JOURNAL SUPPLEMENTS***	0		2
EUROPEAN JOURNAL OF HEART FAILURE***	0		2
GLOBAL HEART***	0		2
HEART***	0		8
NATURE REVIEWS ENDOCRINOLOGY***	0		2
NEW ENGLAND JOURNAL OF MEDICINE***	0		3
PLOS ONE***	0		5

Legend: *: ≥ av.+ 5 x STDV; ***BOLD + Italics*** rows = av.+ 4 x STDV; **BOLD** rows = av. + 3 x STDV
: journals NOT on critical list; *: journals NOT on positive list.

For Sponsors 2012-2018, Tables 5 vs.7, *Rho = 0.52403*. By normal standards, this association between the two variables is considered quite weak and not significant. Compared to the much lower *Rho* coefficients for journals more sponsor units overlapped the two distributions. An additional reason for a higher sponsor *Rho* was the fact that the same group of identical pharmaceutical companies topped both distributions. However, it is interesting to observe, Table 7, that the *Merck Company* ranked far ahead as statin-critical sponsor 2012-2018, compared to its third position as a statin-positive supporter after *AstraZeneca* and *Pfizer*, Table 5. Further, *Novo Nordisk* (ranked 9, Table 7) and *Shering Plough Corporation* (ranked 11) exclusively supported statin-critical research, 2012-2018, not being ranked among top-30 in the Table 5 distribution for the same period. The highest ranked unique statin-positive sponsors were *NIH National Heart Lung Blood Institute, NHLBI* (ranked 9, Table 5) and *Medical Research Council, UK* (ranked 12). 7 top-30 statin-critical sponsors were not found among the top-30 statin-positive ones and 8 statin-positive sponsors did not appear on the list of statin-critical journals.

Concluding discussion

Our methodology contains some possible biases of subjective nature. We applied four kinds of sources in order to collect data in our study.

1) The main data source in the study consisted of articles extracted by common information retrieval. In our case the retrieval profile contained the terms ((‘simvastatin’ OR atorvastatin OR statin(s)) AND ‘cardiovascular’). The profile was searched in WoS, that is, Science Citation Index limited to 1998-2018 and to articles only. The reasons for using WoS are twofold: The database coverage is high in the health sciences (Ingwersen & Lynge, 2004) and powerful analytic tools are available (Clarivate Analytics, 2020). This retrieval mode was objective and exhaustive, covering a variety of associated health problems without these being mentioned directly in the profile, e.g. diabetes, heart failure, renin issues, adverse events, etc. The initial set on the statin topic was then divided into three sets covering 1998-2004; 2005-2011; and 2012-2018. This data capture mode contains no biases.

2) Finding known protagonists of statin-positive and critical/doubtful research positions, named Key-Researchers. This kind of initial known-person or known-item searching is well-known in the information retrieval discipline as a starting point (Ingwersen & Jarvelin, 2005). Typically, such researchers may indeed be retrieved from the classic media, such as TV documentaries or newspapers/magazines, to where scientific debates have penetrated because they are seen to be of public interest. Such areas might concern climate change, energy issues, immigration, etc. Among health issues the pro et contra of the application of face masks or vaccine reliability in relation to Covid-19 constitute actual topics that might be investigated scientometrically in the near future. In the actual study concerning the topic ´statins used to prevent cardiovascular events’ BBC and other news media as well as national medical magazines/journals were used. Searching the ‘key-researchers’ in WoS provided sets of articles and consequently also the co-authors of Key-Researchers. The co-author names were

put aside to be added later in search mode 3). As stated above in the Methodological section the assumption behind applying co-authorship analysis is that co-authors commonly share scientific views on a published issue (Bates, 1979).

3) For each seven-year analysis window WoS analytics made it possible to sort the retrieved article records according to citations. Logically, the most interesting articles to check are the most used (=cited) articles (Rousseau & Egghe, 2018). By going through the highly cited abstract titles and conclusions (≥ 50 citations, 1998-2011; ≥ 20 citations, 2012-2018) it was possible (subjectively) to assess if articles belonged to mainstream, statin-positive or critical positions. We carried out double-checking. Only if the assessments agreed an article was extracted as positive or critical. If in doubt the article belonged to mainstream research. For each article deemed statin-positive or critical all authors were extracted and added to the Key-Researcher co-author sets from search mode 2) into extended author-dependent search profiles. Previously selected authors were monitored for appearance in the highly cited abstracts. The extended author profiles were then combined logically (by Boolean AND) with the three period-dependent topical sets, providing statin-positive and critical author-derived sets of articles for each period. Due to its interpretative nature subjectivity biases exist in this search mode. To an extent they were controlled by means of inter-assessor agreement but, like for inter-indexer agreement, cannot completely be avoided (Tell, 1969; Jones, 1983).

Search mode 3) constituted a first round of co-author retrieval, resulting in 2 x 3 novel and larger sets than retrieved from the Key-researchers and their co-authors alone in mode 2). These sets were again analyzed for additional co-authors by means of WoS analytic tools. Not previously observed authors were added to the search. However, to be certain that statin-critical Key-researchers and direct co-authors did not form part of the statin-positive sets as false-positive, such researcher names were excluded from the final sets. The same treatment was done with respect to the statin-critical sets. The twice repeated co-author searching, and the exclusion, served as instruments for enlargement of the sets in a controlled manner. It was possible that some of the new co-author names might lead to other scientific positions than intended. However, their number would be small. The final sets to be analyzed in terms of journal and sponsor distributions constituted approximately 10% of the total retrieval output associated with statins and cardiovascular events (1,210 / 12,563 articles).

4) At this point we experimented with searching the three original period sets by means of specific keywords considered to signal positive or critical positions. However, this retrieval mode did only supply a few additional articles published in each period compared to the outcomes from other search modes. Typically, the new articles were opinion papers below the citation thresholds applied. In addition, this retrieval mode might introduce a new subjective bias owing to the interpretation of the keywords in context. Consequently, this retrieval mode is not to be recommended.

Table 9. Minimum sample size and maximum sample mean at p=.05; with actual p values of samples.

Journals, Table 2	**Min. # units**	**Max. Mean**	**Sponsors, Table 3**	**Min. # units**	**Max. Mean**
1998-2004	≥ 36	≤ 1.75	1998-2004	….	….
2005-2011	≥ 89	≤ 2.20	2005-2011	≥ 230	≤ 1.3
2012-2018	≥ 270	≤ 3.31	2012-2018	≥ 400	≤ 1.4
Pos. Journ, Table 4	**Real # units**	**Real Mean**	**Pos. Spons., Table 5**	**Real # units**	**Real Mean**
1998-2004*	51	*1.86 p=.02*	1998-2004	….	….
2005-2011*	109	*2.86 p=.02*	2005-2011	246	2.86 p=.39
2012-2018	123	3.3 p=.06	2012-2018	666	3.34 p=.30
Crit. Journ., Table 6	**Real # units**	**Real Mean**	**Crit. Spons., Table 7**	**Real # units**	**Real Mean**
1998-2004*	36	*1.72 p=.03*	1998-2004	….	….
2005-2011*	62	*2.11 p=.02*	2005-2011	64	2.81 p=.44
2012-2018*	89	*2.25 p=.02*	2012-2018	301	2.43 p=.30

Legend: * and *values in Italics* siginify *p values below .05.*

The z-tests served to demonstrate the degree of uncertainty or probability of error associated with the data sets containing statin-positive or critical journals as well as sponsors. According to Amrhein, Greenland & McShane (2019) if applying null-hypothesis and significance testing, one should define the alpha value and assess the sample parameters prior to a study with a given population. We did not apply null-hypothesis and statistical significance testing. However, we performed such additional calculations. We regarded each of the two statin-positive and critical sets of articles retrieved per period as samples of the three original sets. Table 9 shows the sample parameters in a z-test at $p=.05$, i.e., the minimum number of units and maximum mean values necessary in samples from each original period set of journals and sponsors (the given populations), Tables 2-3. Alpha was set to .05 since all distributions in the samples had steep start frequencies. A probability of error at 5% might not replace the top-ranked units in a distribution by lower ranked units due to the high frequencies of the former. However, their mutual order might indeed change.

With respect to statin-positive and critical journals, Tables 4 and 6, Table 9 demonstrates that in most cases the conditions for $p \leq .05$ became satisfied, mainly due to a higher number of units which compensated for too high mean values. During the period 2012-2018 the statin-positive journals provided a p value on the borderline ($p = .06$). For sponsors the conditions were far from being satisfied, with p values ≥ .30. The implication was that the probability of error became very high (from 30% upwards) and the top-10 sponsors in each distribution might very well change rank order or in some cases be replaced by middle-range frequency units. However, the overall finding that the commercial sponsors backed the two opposite statin positions holds. Albeit, the largest bias in the study derives from the low sponsor coverage 1998-2011 in WoS (< 30%), which influences both conditions in non-parametric tests negatively, given known populations. A test of WoS coverage of the topic ‘statin use

in cardiovascular events' 2012-2019 shows an annual coverage of approx. *60%* of the records that contains sponsor data. This consistency leads to the conclusion that approx. 40% of the research on this topic has no external sponsors, but in reality is supported by internal funding.In other topics this percentage might be different.

At the *general topical analysis level*, the findings showed a huge gap between two central US state funding agencies and the remaining sponsors, in addition to a gap between three commercial companies as top sponsors and other supporting organizations during the two recent periods. All five sponsors were located above the quadruple STDEV zone. From normalization and display points of view the application of STDV was shown to be valuable. The spread of individual journals publishing statin drugs applied to cardiovascular cases increased dramatically, more than tripling during the analysis period 1998-2018. With respect to sponsors during the period 2011-2018 a long tail of frequency-one institutions indicated that many research projects were sponsored by more than one supportive agent.

Our hypothesis stated that statin-positive and statin-critical scientists primarily published in and were sponsored by one or a few committed major journals and supporting actors. The idea was that such dedicated journals and sponsors back a position and could be observed consistently across two to three analysis windows. Commercial or public health reasons were hypothesized to be the motivation for the involved actors.

At *general journal level* the findings were consistent, showing that *Atherosclerosis* and *Circulation* were the most important mainstream journals in the overall topic across all three analysis windows. They were consistently located in the triple-quadruple+ STDEV zones. *American Journal of Cardiology* acted as top-journal 1998-2011 but dropped to rank 7 during the third period, replaced at the top by *PLOS One*. The latter journal did not appear in the top STDV zones, of its position on the use of statins. Interestingly, *Atherosclerosis* appeared outside the top STDV zones in the statin-positive journal distributions and did only appear as top-statin-critical journal during the 2012-2018 period. *Journal of American College of Cardiology* entered the quadruple+ STDV zone among the statin-positive sources but was hardly detected at the general topical level and in the statin-critical distributions.

Circulation and *American Journal of Cardiology* served to a large extent both the statin-critical as well as statin-positive research over the period. The findings indicated that *Journal of the American College of Cardiology* and *European Heart Journal*, with *American Heart Journal* as runner up 2012-2018, can be regarded as specific to statin-positive research 2005-2018. *PLOS One*, listed three 2012-2018 in mainstream research did not appear on the top-30 list of statin-positive journals and very low on the statin-critical distribution during this period. The *European Journal of Preventive Cardiology* and *International Journal of Cardiology* served as the highest ranked sources 2012-2018 publishing statin-critical research. However, no journals were located consistently among the top statin-critical journals across two consecutive periods. The assumption about position-dedicated journals consistently

observed across two or more periods only held for statin-positive journals. In the statin-critical case the assumption was true only for single periods. Notwithstanding, the correlations between the statin-positive/critical journal distributions decreased dramatically over the three analysis windows 1998-2018, as demonstrated by means of Spearman's *Rho*. Thus, the statin-positive and critical journal distributions were increasingly very different.

At the general topical level, the statin research was consistently backed by two major US health funding agencies, *United States Department of Health Human Services* and *National Institutes of Health*, USA, (NIH), followed by central pharmaceutical companies. However, the two US state agencies played minor roles in supporting statin-positive or critical research. During recent periods 2005-2018 *Medical Research Council, UK*, appeared in the distributions. All the commercial top companies sponsored both statin-positions, but to different degrees. The assumption of sponsors uniquely dedicated a scientific position consistently over time could not be verified by the study, perhaps owing to lack of sponsor coverage in WoS 1998-2011. However, the study showed that approx. 80% of the research 2012-2018 was sponsored by external actors, regardless of statin research position, Tables 5 and 7, that is, a figure *20 percentage points higher* than the average sponsor coverage for that period.

In conclusion our hypothesis was entirely substantiated at the general topical mainstream level for journals and supporting organizations. It was partly verified in relation to the disagreeing positions. Some distinct journals central to the two disagreeing positions were uncovered, but that was not the case for sponsors. Observations showed that many top-journals and top-commercial sponsors backed both positions, in the case of sponsors often in an asymmetric way. The major limitation of the study was associated with the sporadic sponsor coverage until 2012. In terms of generalization we claim that the study's research question and methodology are transferrable to other topics demonstrating scientific disagreements. However, with the sponsor limitation in mind, we recommend making 2012 as the analysis starting point in further investigations using WoS as data resource.

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