

Review

Statin wars: have we been misled about the evidence? A narrative review

Maryanne Demasi PhD

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<http://bjsm.bmj.com/content/bjsports/early/2018/01/16/bjsports-2017-098497.full.pdf?ijkey=Rsap0XafIjfcOCR&keytype=ref>

EXPERT REACTIONS

Prof Peter Gotzsche*Nordic Cochrane Collaboration*

“When drug industry sponsored trials cannot be examined and questioned by independent researchers, science ceases to exist and becomes nothing more than marketing. Harms of drug are very often left out of published trial reports, e.g. in psychiatric drug trials, half of the suicides and half of the deaths are missing. Dr Maryanne Demasi has described many of the unresolved questions related to the statin trials. There is, for example, a large discrepancy between the occurrence of muscular problems in the trials and what patients report in clinical practice. A recent systematic review found that only one trial had specifically queried about muscle problems.

The whole issue is shrouded in secrecy and riddled with huge financial conflicts of interest, which does not instil public confidence. The CTT collaboration, led by Sir Prof Rory Collins, published a review in the Lancet that, although it took up 30 pages, did not impress me. It was not even a systematic review, and the authors were not interested in the harms of statins, which violates the basic principles for doing systematic reviews. The CTT refuses to share its data with other researchers, including the authors of the Cochrane review on statins. On top of this, they did not even ask the companies and academic researchers for harms data; they were only interested in mortality, as if this is the only thing that matters.

Demasi describes the inappropriate statistical tricks used by the CTT researchers in their Lancet paper to arrive at their paternalistic conclusions. It is most unfortunate that their dogmatic views are rewarded with a publication in a high profile medical journal while they aggressively dismiss

dissenting views on statins to the point of calling their opponents responsible for many killings. This is not how a scientific debate should be.

I have seen Demasi's two ABC TV programmes about cholesterol/statins and found them to be very good. Unfortunately, the subsequent unjustified attacks against Demasi led the ABC to cowardly censoring a much needed debate about the over-prescription of statins by banning her programmes. I can see absolutely no justification for this decision, which I find disgraceful and shameful for Australia and against the public's interest.

The statins war will continue for as long as independent researchers have not got access to the full clinical study reports of statins; to all the individual anonymised patient data; and to all the case report forms in order to find out if muscular problems and other common harms were never investigated, or were simply omitted from the publicly available reports."

Dr Aseem Malhotra

Consultant cardiologist, London, UK

Member of the Academy of Medical Royal Colleges' Choosing Wisely steering group.

"This thorough review paper legitimately highlights all the major outstanding concerns regarding a systemic lack of transparency in the prescription of statins. In fact, it was Dr Demasi's brilliant journalism in an ABC Catalyst programme 'Heart Of The Matter' that inspired a number of eminent doctors in the UK to challenge the UK health watchdog, NICE when they announced they were going to lower the risk threshold for prescription of statins. Subsequently in an unprecedented move NICE made a U-turn and millions of people at low risk of heart disease were spared from being recommended to take the drug. Sadly despite no factual error the ABC caving in to establishment and industry pressure were forced to retract the documentary for fear it may cost lives, despite no evidence of a single heart attack or death from alleged fear mongering because of the programme.

In my view this was not only a deliberate attempt to destroy Dr Demasi's credibility and threaten her career but to scare off other journalists who might ask legitimate questions on statins and over-medication; Specifically in relation to the collusion of academics, institutions and medical journals with industry for financial gain to the detriment of scientific integrity and patient care. I have no doubt that history will judge Dr Demasi's incredible journalism as, not just courageous, but game changing to improve the health of Australians for the better."

Dr Rita Redberg

Cardiologist, Director of Women's Cardiovascular Services, University of California, San Francisco Medical Center

Editor-In-Chief, JAMA International Medicine

"In this carefully researched and documented paper, Dr Demasi details the history of how the use of cholesterol lowering drugs – statins – has far exceeded any evidence of benefit. She describes the lack of transparency of the data, the persistent conflict of interest issues in the cholesterol guidelines, and how the industry funded Cholesterol Treatment Trialists group have refused any other researchers access to the cholesterol trial data. Furthermore, she notes how the data on risks of statins have not been collected or have been minimized. Unfortunately, until all data is available and discussed with patients, millions of people taking these drugs will continue to have far greater chance of harm than benefit."

Prof Sherif Sultan,

President of the International Society for Vascular Surgery
University Hospital Galway

“Dr Demasi manuscript is a Joan of Arc move to remove the old aristocracy out of main stream Medicine. In her manuscript she showed strong evidence that statins are, what I believe, to be the biggest fraud in the history of medicine.

Dr Demasi has outlined how the data was manipulated and presented with a PR campaign from the multinational, which is akin to organized crime. The paper highlights that statin adverse effects have been under-reported and concealed from the public which, in my view, is a scientific farce and a crime that must go to the high court in order to punish the collaborators. This includes the regulators who approved the guidelines and the members of the guidelines committees who are mostly sponsored by multinationals.”

Sir Richard Thompson

Immediate Past President of The Royal College of Physicians
Her Majesty The Queen’s personal physician 1984-2005

“This formidable review adds to the voices that are questioning the cholesterol/statin/cardiovascular disease hypothesis, and are criticizing the presentation of many of the trial data. Some observers question whether statins promote *any* absolute benefit on cardiovascular mortality, even for secondary prevention, and certainly that side effects from these drugs are common, ignored by trialists, and lead to poor adherence to the treatment. There are also ethical issues, such as missing data, while the Oxford group benefited from a genetic test in the USA that was promoted to predict statin side effects, which were emphasized in the patent at the same time as the authors were denying their importance!

Dr Demasi’s paper on the statin controversy is another example of murky conflicts, misleading statistics and abuse of contrarian views that are sadly so frequent in clinical trials, a problem that the Review from the Academy of Medical Sciences failed adequately to address. Aegean stables?

I propose, first, a full independent review with judicial input into all the evidence, including the release of all the data; secondly, that physicians should carefully follow up their patients after prescribing statins to enquire for their side effects; and thirdly, that physicians should emphasise the benefits on cardiovascular disease of physical activity and a Mediterranean diet, both of which are effective, and safer and cheaper than drugs.

The public will continue to distrust the value of their doctor’s advice if these uncertainties are not quickly resolved.”

Dr John Mandrola

Cardiac electrophysiologist, Baptist Health in Louisville, KY.

Fellow of the American College of Cardiology, Columnist at theHeart.org / Medscape

"I think the CTT Collaboration should share their database with independent scientists. That they refuse fosters suspicion. If you have a great result, wouldn't confirmation make it even greater?"

Prof Vikas Saini

Cardiologist, President of Lown Institute

I believe that the patient-level data ought to be released because the CTT analysis published in The Lancet has some contradictory results that raise doubts about the robustness of the findings — specifically the authors were notably selective in their handling of subgroup analyses, prominently reporting that low risk patients with no vascular disease appear to show a mortality benefit in the statin group. However, there was an absence of effect on coronary mortality, stroke mortality, other cardiac mortality, vascular mortality, nonvascular mortality, or all cause mortality. The selected subgroup is therefore potentially quite anomalous.

Dr Mikael Rabaeus

Cardiologist, Internal Medicine, CIC Groupe Santé,

Clarens, Switzerland

"An excellent review of the many flaws having led to the acceptance of cholesterol as a major indicator of disease risk and to statins becoming a widely overprescribed "medication", in particular in primary prevention i.e. healthy people. Importantly, prescribing a medication to a healthy individual is an efficient means of making him/her sick. Soon all statins will have lost their patent. There is therefore strictly no reason to continue to withhold the raw data from public examination. If these data do not become public, it can only mean that they do not support the results that were published. This has to be established once and for all and I strongly support Dr Demasi's standpoint."

Dr Scott Murray

Consultant Cardiologist and Clinical lead for preventative cardiology and rehabilitation,
Royal Liverpool Hospital

President, British Association For Cardiovascular Prevention & Rehabilitation (BACPR)

"Dr Maryanne Demasi cleverly dissects the established consensus and demands to be heard. There is broad agreement that statins have some benefit to offer individuals with confirmed heart disease, even if this may not all be due to the lowering of "cholesterol". However, the argument is still ongoing about the role of statins for healthy people and the potential for side effects. The simple fact that the raw data on statin side effects has not been made available yet, sounds alarm bells and breeds mistrust - something we can do without when heart disease is increasing now in the most statinized populations ever. Dissenting, alternative views do have a place in Cardiology and should be countered with unbiased, independent evidence and raw data"

Dr Alan Cassels

Drug Policy researcher, University of Victoria, Canada

Co-Author, *Selling Sickness*

“Dr Demasi highlights that science cannot advance without a lack of transparency. As much as we'd like to, we cannot trust the conclusions of research derived through a scheme that doesn't allow us to independently examine the evidence for ourselves. That is the main thing at stake. The "trust us, we're experts" approach to the statin hypothesis has probably been more damaging to science and humanity than many other controversies in medicine.

Over the last 20 years, global billions have been spent on these drugs in the absence of independent validation of statin research. It is possible that those billions have contributed very little to advances in population health and reductions in cardiovascular disease. We know that rates of cardiovascular morbidity and mortality have decreased over the last few decades, but quite likely a negligible portion of that is related to the overall amount of statins consumed by the population.

As for the adverse effects of statins, this is, quite frankly, a whole additional controversy where the proponents and researchers of statins have [probably] so profoundly downplayed statin adverse effects that I believe it is likely the population-level of muscle weakness experienced by many older people is probably, more than any single other cause, due to statins.”

Ass Prof Robert DuBroff

Cardiologist and lipidologist

Division of Cardiology at the University of New Mexico, Albuquerque, NM

“Despite the protestations of some lipid experts, the statin wars are unlikely to go away any time soon. Severely outnumbered and without financial backing, the statin skeptics continue to emphasize the limitations of statin clinical trials and the inconsistency of results. Many believe that this failure to acknowledge anomalies in the cholesterol hypothesis (lower is better) has led to an overtreatment of healthy individuals. Not only are financial conflicts of interest at play, but the behavior of many statin proponents exemplifies the concept of confirmation bias – seeing what you want to see and ignoring what you do not. Reputations and big money are at stake, but ultimately the complete empirical record must prevail.”

Prof Timothy Noakes

Emeritus Professor, Exercise Science and Sports Medicine

University of Cape Town

“One of the greatest paradoxes of modern medicine is that a drug class, the statins, which make almost no difference to the health of the vast majority of users, became the most profitable drugs of all time. How has this been allowed to happen?”

Dr Nadir Ali Mir

Cardiologist, Clear Lake Regional Medical Center
Webster, Texas, USA

There is an army of pharma funded organizations like the AHA, ACC, CTT who are intent to drown an honest education of “Lipoprotein and specifically LDL metabolism” because of financial and intellectual bias. They have the bully pulpit and the authority to spread their dogma and deception through media coverage and prestigious medical journals while the dissenters are not well-funded or organized and relegated to anonymity. A few like Dr Maryanne Demasi who gain public attention are severely and unfairly prosecuted by prominent physicians who are leaders of medical societies but whose role is to function as paid goons of the pharmaceutical mafia.

This review by Dr Demasi raises important questions about the role of LDL, the importance of bias, the need for transparency in making raw data available to third parties who do not have conflict of interest, designing clinical trials with equal importance given to assessing adverse effects, and preventing statistical deception of “relative risk reduction” rather than “absolute risk reduction” that is clearly being done to increase the profits of the pharmaceutical industry.

As a practicing cardiologist for over 25 years, I have had a front row seat in listening to my patients complains of the adverse side effects of statins therapy like mental fatigue and dullness, myopathy, cognitive and memory decline, diabetes and erectile dysfunction.

The above list is of course incomplete. They are also not rare and uncommon like the pharmaceutical industry would like us to believe. The mainstream healthcare providers are complicit in relinquishing our critical thinking abilities to the key opinion leaders who are paid spokesmen of the drug and food industry. The practice guidelines and education that is disseminated by a well-orchestrated collusion between prestigious medical societies and Big Pharma promotes deception about LDL, diabetes medications and proton pump inhibitors for treatment of GERD. This distracts from finding real solutions to the major health concerns of western societies. The medical community is thus at risk of being exposed as the major cause of death and disability in developed countries. A critical evaluation of questions posed by Dr Demasi can start us on the path or intellectual honesty about LDL and statins. This is the least we can do, because as medical professionals our main duty is to protect the health of our patients.

Prof Klim McPherson

Em Prof Public Health Epidemiology
New England Oxford, UK

" Dr Demasi’s paper demonstrates the lack of balance between reliably and transparently measuring the therapeutic effects and the measuring of side effects of drugs. The Chief Medical Officer has recently determined that we need an authoritative independent report looking at how society should judge the safety and efficacy of drugs as an intervention. This paper is therefore timely and what is described is outrageous.

Typically efficacy has to be demonstrated by law with transparent rigorous double blind trials, conducted with declared absence of conflicts of interest, among highly eligible

patients. If found efficacious a clinical euphoria tends to set in which often puts pressure to massively enlarge the indications to patients with much lower risk thresholds. Thus sales are maximized.

But the evidence for the necessarily much smaller absolute effect among low risk patient is perforce weaker, less well studied and more speculative. Among such patients therefore the likely rate of side effects is much more important to their choice, these will be just as pronounced as for high-risk individuals. In this particular case rigorous data on side effects is kept secret because of confidentiality agreements. So even among high risk patients their rigorous assessment is compromised and secret; few validated methods of measurement, no double blind randomization, strong vested interests in finding none, etc .

Thus low risk patients are asked to believe that Statins will work for them (they will, but not much), that side effects amount to little (we do not know that since most of the data is locked up and scandalously unavailable to independent review). Many front line clinicians tend not to believe that.

Is there is a definite trend emerging for inadequate assessment of drugs which aim to maximize sales by playing down side effects for low risk patients and playing up efficacy among high risk individuals, to maximize sales? It happens already for HRT with CVD and breast cancer risk, Transvaginal mesh, etc. Clearly the long-term health interest of patients is not important enough for proper assessment. Its high time it was and the proper evaluation of harms is enforced to provide reliable data as soon as possible.

Dr Joe Kosterich

General Practitioner, Perth, Australia

"Our views on cholesterol and heart disease are based on the flawed work of Ancel Keyes. A perfect storm of industry drivers, complicit doctors and ideology has conspired to drive the cholesterol theory, at a cost of tens of billions spent on statin medications. Those questioning the dogma have been ridiculed and threatened. Yet it is vital that our assumptions in medicine are questioned. This paper by Dr Demasi exposes the conflicts of interest and questionable research underpinning the cholesterol and statin theory. Time for policy makers to sit up and listen"

Dr Eric M Thorn

Cardiologist & Obesity Medicine Specialist,
Virginia Hospital, VA, USA

"The negative effect of the obfuscation of the data by pharmaceutical companies and certain researchers absolutely degrades public confidence in our profession; I deal with this daily and it makes my job harder with regard to all my medication, diagnostic testing, and overall therapy recommendations, not just with use of statins.