The case for statins: has it really been made?

Journal of the Royal Society of Medicine

October 2004; Volume 97, Number 10, pp. 461-464

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FROM ABSTRACT

Statin drugs are a modern success story. They are the medical treatment for coronary disease and the star of the pharmaceutical industry. Worldwide, sales of statins are running at about $19 billion a year and growing quickly.

This success profits not only the pharmaceutical industry but also all those whose finances and careers are furthered by the research and the sales. But to what extent is it also a success for the general public?

To answer this we will look at the major long-term (five to six year) clinical trials of statins. We start with the treatment offered to the participants, then look at the endpoints that were selected, and continue with a look at how the results have been reported.

We conclude with a discussion of the cost-effectiveness of statins for people at different levels of risk of coronary heart disease (CHD).

THESE AUTHORS ALSO NOTE:

In 1988, the US National Cholesterol Education Program stated:

“Drug therapy is likely to continue for many years, or for a lifetime. Hence, the decision to add drug therapy to the regimen should be made only after vigorous efforts at dietary treatment have not proven sufficient.”

“Vigorous” dietary efforts are defined as a minimum of 6 months of intensive dietary counseling before starting statin drug therapy.

Although all of the statin drug cholesterol trials were initiated after the publication of these guidelines, none of the trials adhered to the 6 month dietary protocols prior to putting subjects on statin drugs.

“Why were these guidelines not followed?” If all statin drug trial participants had been given dietary intervention before starting statins, “it would have much reduced the differences in deaths from CHD and all-cause mortality in the trials.” In other words, the statins would have appeared to be less effective in reducing deaths from CHD and other causes of mortality.
In performing a clinical trial of a drug, “all-cause mortality” is the only endpoint measure not prone to diagnostic variance, and is therefore not popular with the drug company studies. Most statin drug trials do not even look at all-cause mortality because of the probability that taking the drugs do not alter all-cause mortality.

Drug company study designers search for endpoints that are most apt to yield a positive result. “This would not be the scientific approach but would make sense if the aim was to make the study appear highly successful.”

“With respect to data on deaths the most important endpoint is all-cause mortality. This can be manipulated only by fraud and is the one primary concern to the recipients of the treatment—are they less likely to die soon, whatever the reason, if they take this drug?”

“If a drug or other intervention neither extends life nor improves its overall quality, then it is of no value.”

“There is no rigorous reporting of all-cause morbidity, nor of measurement of changes in overall quality of life, in any of the [statin drug] studies.”

Statin drug trials show absolute differences of less than 1% to a maximum of 3.3% in all-cause mortality between the control and treatment groups. “These are not impressive results.”

However, drug companies make statin drug results look impressive “by expressing the results as relative difference rather than as absolute difference.” In a statin drug trial of patients with existing CHD, the difference in deaths between the statin group and the placebo group was 3.1% (14.1% of the placebo group died and 11% of the statin group). The benefit of such results can appear to be magnified by expressing them as relative differences, which would be 11/14.1 = 22%: “The statin drug lowered the risk of death by 22% (11 is 22% lower than 14.1).”

Another serious problem is that the study does not state the number needed to treat (NNT) for one patient to benefit, which is over 100 in primary prevention trials. This means that more than 100 patients would have to take the drugs for one patient to actually receive any benefit.

In a study where 100 patients take statins drugs, 2 will have a fatal heart attack. In 100 patients taking a placebo, 3 will have a fatal heart attack. The absolute risk reduction of a fatal heart attach is 1%. Yet the drug company spins the pathetic results by dividing 2/3 and publish the relative risk, which is a 33% reduction of a fatal heart attack. This is dishonest. These authors claim an honest disclosure would be to state “if you take statins, then in seven years’ time there is a one chance in about 120 that your death will have been prevented.”
Using current available NNT data and assuming the cost of a year of statin drugs is $500, the cost of postponing one death by using statin drugs is $85,500 for patients with the highest risk, to more than $300,000 for those with the lowest risk.

“It is arguable that statins are cost-effective for the small minority of people at especially high risk of CHD.”

CONCLUSIONS

The design of the statin drug trials has not involved the testing of the value of statin drugs relative to that of guideline-recommended promotion of lifestyle changes.

The small differences favouring statin drugs in published studies “have been magnified by the manner of presentation of results, most notably by the use of relative differences between statins and placebo groups rather than absolute differences.”

“Lowering the threshold to make much larger numbers of people eligible for drug therapy has the effect of making statins an extremely expensive means of preventing heart disease. The case for statin drugs, especially for primary prevention, has not been made.”

KEY POINTS FROM DAN MURPHY

1) Because statin drug therapy is likely to continue for many years, or for a lifetime, the official written position of the National Cholesterol Education Program of the National Institutes of Health state “the decision to add drug therapy to the regimen should be made only after vigorous efforts at dietary treatment have not proven sufficient.” “Vigorous” dietary efforts are defined as a minimum of 6 months of intensive dietary counseling before starting statin drug therapy.

2) Statin drug trials are not preceded by vigorous dietary efforts because to do so would help people and render statin drug therapy less effective in reducing deaths from CHD and other causes of mortality.

3) In performing a clinical trial of a drug, “all-cause mortality” is the only endpoint measure not prone to diagnostic variance, and is therefore not popular with the drug company studies. Most statin drug trials do not even look at all-cause mortality because of the probability that taking the drugs do not alter all-cause mortality.

4) Drug company study designers search for endpoints that are most apt to yield a positive result. “This would not be the scientific approach but would make sense if the aim was to make the study appear highly successful.”

5) “If a drug or other intervention neither extends life nor improves its overall quality, then it is of no value.”
6) “There is no rigorous reporting of all-cause morbidity, nor of measurement of changes in overall quality of life, in any of the [statin drug] studies.”

7) Statin drug trials show absolute differences of less than 1% to a maximum of 3.3% in all-cause mortality between the control and treatment groups. “These are not impressive results.”

8) However, drug companies make statin drug results look impressive “by expressing the results as relative difference rather than as absolute difference.” In a statin drug trial of patients with existing CHD, the difference in deaths between the statin group and the placebo group was 3.1% (14.1% of the placebo group died and 11% of the statin group). The benefit of such results can appear to be magnified by expressing them as relative differences, which would be 11/14.1 = 22%: “The statin drug lowered the risk of death by 22% (11 is 22% lower than 14.1).”

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10) Another serious problem is that the study does not state the number needed to treat (NNT) for one patient to benefit, which is over 100 in primary prevention trials. This means that more than 100 patients would have to take the drugs for one patient to actually receive any benefit.

11) In a study where 100 patients take statins drugs, 2 will have a fatal heart attack. In 100 patients taking a placebo, 3 will have a fatal heart attack. The absolute risk reduction of a fatal heart attack is 1%. Yet the drug company spins the pathetic results by dividing 2/3 and publish the relative risk, which is a 33% reduction of a fatal heart attack. This is dishonest. These authors claim an honest disclosure would be to state “if you take statins, then in seven years’ time there is a one chance in about 120 that your death will have been prevented.”

12) Using current available number needed to treat (NNT) data and assuming the cost of a year of statin drugs is $500, the cost of postponing one death by using statin drugs is $85,500 for patients with the highest risk, to more than $300,000 for those with the lowest risk.

13) “It is arguable that statins are cost-effective for the small minority of people at especially high risk of CHD.”

14) “Lowering the threshold to make much larger numbers of people eligible for drug therapy has the effect of making statins an extremely expensive means of preventing heart disease. The case for statin drugs, especially for primary prevention, has not been made.”