



Who needs statins?

Justin Smith argues that the NHS is wasting hundreds of millions on statins

Heart disease statistics show large reductions in the number of people with 'high' cholesterol. Despite this, the rate of heart disease continues to increase. Statins form the single greatest drug expenditure for the NHS, but the effectiveness of these drugs is routinely exaggerated and recent studies have raised questions about the cholesterol hypothesis.

1 April was more significant this year than most. It marked the start of the government's initiative to provide a 'health MoT' for everyone aged 40 to 74. These health checks include some potentially beneficial aspects – it has been reported that nutrition and lifestyle advice will be included and those at risk could be referred to relevant specialists. However, how much emphasis will be placed on exercise prescription, compared to other prescriptions?

The 'MoT' includes cholesterol checks. Last year, the government's national director for heart disease in England, Professor Boyle, said that these checks may more than double the number of people taking statins to lower their cholesterol: potentially pushing the number up to around seven million (*The Investigation*, 3 April 2008).

The cholesterol hypothesis

Unfortunately, very few experts and policy makers have noticed that reducing cholesterol does not reduce the rate of heart disease. This statement will come as a surprise to most people and it requires further explanation. I would like to start by putting cholesterol levels into perspective. Considering the level of attention cholesterol is given, it would be logical to assume that cholesterol levels have risen in the UK. However, in recent years the average cholesterol level has actually reduced slightly and there have been large reductions in the number of people with 'high' cholesterol.

For example, between 1994 and 2006 the percentage of men aged 65 to 74 with 'high' cholesterol decreased from 87% to 54% (Allender *et al*, 2008a). Despite this, the rate of coronary heart disease for this age group stayed about the same (Allender *et al*, 2008b). Other age groups have experienced an increase in the rate of heart disease as the number of people with 'high' cholesterol has decreased.

So, cholesterol has not risen. Perhaps then, cholesterol in the UK is high when compared to other countries? Information published by the British Heart Foundation shows that the average cholesterol level for women in the UK is the 12th lowest on a scale of 45 European countries. A similar pattern is found for men in the UK, who are the 15th lowest on the same scale (Allender *et al*, 2008a). Despite this, the UK has one of the highest rates of coronary events in the world (Allender *et al*, 2007).

When we compare the rate of heart disease with cholesterol levels across Europe, we find that no correlation between the two exists. For example, men in Glasgow have lower cholesterol levels than men in Switzerland, but the rate of heart attacks in Glasgow is more than two-and-a-half times greater. This is by no means an isolated case since there are more examples that contradict the idea cholesterol causes heart disease than prove it.

Causes of heart disease

Heart disease is complex – other factors certainly come into play. However, if cholesterol levels are really as dangerous as we are led to believe, then surely at least some correlation would be seen with morbidity. Perhaps then, cholesterol is somehow more specific to those who are at high risk? The ultimate way to test this idea would

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be to look at the cholesterol levels of those who already have heart disease or have had a heart attack – what we find is that these people actually have an average cholesterol level – not high cholesterol at all. In the UK, the typical person who has a heart attack tends to have the same cholesterol level that is seen for middle-aged and older people in the general population (Durrington, 2003). This phenomenon is not unique to the UK.

A study published in the *Lancet*, included 5,754 patients from Australia and New Zealand who had already had a heart attack. The average cholesterol level of this group of people was around 5.7 mmol/l (Tonkin *et al*, 2000). Data from the World Health Organization Global Infobase (2009) shows that around the same time, the average cholesterol level for the general population was between 5.5 mmol/l and 5.8 mmol/l. People who suffered a heart attack had the same average cholesterol level as the general population.

A study published in the *American Journal of Cardiology* included 8,500 men with existing heart disease (Rubins *et al*, 1995). The average cholesterol level for this group of people was around 5.5 mmol/l, which (again, according to the World Health Organization) is around the same or even slightly lower than the average cholesterol level for the general population.

Bad and good cholesterol

People take statins to reduce ‘bad’ cholesterol (LDL ‘cholesterol’), however ‘bad’ cholesterol may not be as bad as we think. A study published in January this year in the *American Heart Journal* looked at cholesterol levels for people who had been admitted to hospital in America with coronary artery disease (CAD). The study included 136,905 people – all of these people had their LDL level measured within 24 hours of arrival in hospital (Sachdeva *et al*, 2009). The average LDL level for this group of people, who were admitted across 541 hospitals, was 2.7mmol/l. But this was actually lower than the average level for the general population. The average level for the general population was around 3.2mmol/l (Carroll *et al*, 2005).

If people with CAD have lower LDL levels than the general population, then perhaps we need to rethink the policy of spending hundreds of millions on reducing LDL levels in the general population?

Relative and absolute risks and gains

The headlines promote statins as ‘wonder drugs’, however, the results of clinical trials that involve statins are routinely exaggerated. A common method used to exaggerate benefits is to report relative percentages rather than absolute percentages. Towards the end of last year the results of the JUPITER trial were published (Ridker *et al*, 2008). It was widely reported in the media that the statin used in this trial reduced the risk of serious cardiovascular events by 44%. However, this was a relative percentage reduction. If we look at what has been referred to as ‘hard cardiac events’ (heart attack, stroke, or death from cardiovascular causes), 1.8% of the people in the placebo group suffered these events compared with 0.9% in the statin group (Hlatky, 2008). This reporting of relative percentages rather than absolute percentages is ubiquitous in published statin trials. While positive results are routinely exaggerated, negative findings are often played-down or not mentioned in the summary of the report.

Big Pharma’s needs

The well-publicised problems that the pharmaceutical giants are facing may be providing the motivation for this. Innovative pharmacological breakthroughs have been in short supply in recent years; this has forced drug companies to increase their marketing efforts in order to achieve business growth. Faced with a lack of blockbuster drugs, the industry has had to convince more people to take existing drugs. Drug company marketing includes the ‘education’ of doctors and the general public about perceived risk factors for disease. The focus on

cholesterol has made us fear the suggested risk factor more than the disease itself and has also changed the practice of medicine.

One obvious example relates to the introduction of the Quality and Outcomes Framework (QOF). A significant proportion of the performance indicators in QOF are related to risk factors – cholesterol being one of them. This creates a strong financial incentive for doctors to lower the cholesterol levels of certain patients. Some doctors have highlighted the potential problems associated with performance measures being based solely on risk factors for disease (Krumholz *et al*, 2008) and there are a number of examples where focus on the risk factor has actually caused more harm. Take for instance the ILLUMINATE trial, which found that the drug torcetrapib was associated with a 40% increase in deaths from cardiovascular causes – despite reducing ‘bad’ cholesterol by 25% and increasing ‘good’ cholesterol by 72% (Nissen *et al*, 2007).

Professor Boyle has acknowledged that statins do not benefit 99% of people who take them for primary prevention (*The Investigation*, 3 April 2008). There is also concern that doctors’ awareness of statin adverse effects is low. The most common adverse effects include: muscle related problems, cognitive loss, neuropathy, pancreatic and hepatic dysfunction, and sexual dysfunction (Golomb *et al*, 2008).

The new ‘health MoTs’ have been predicted to prevent up to 1,600 heart attacks and strokes each year, however, this is a theoretical forecast. The complex nature of cardiovascular disease will make it difficult to confirm which interventions provide the most benefit. Statins, for their part, are not living up to their life-saving reputation.

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