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This House believes that the UK healthcare system may be failing as many as 50% of patients with hyperlipidaemia by not reducing their cholesterol to effective levels: a debate

A panel of experts, sponsored by Merck Sharp & Dohme Ltd and Schering-Plough Ltd and made up of cardiologists, lipidologists, general practitioners and nurses with a special interest in coronary heart disease and lipid management, met recently to debate whether individuals with hyperlipidaemia are being treated to effective levels and, if not, how current and future treatment options could be better employed to reduce cardiovascular risk.

The panel

Dr Clive Weston	*Consultant Cardiologist, Singleton Hospital, Swansea (Chair)*
Dr Nigel Capps	*Consultant Chemical Pathologist, Princess Royal Hospital, Telford*
Dr Stewart Findlay	*General Practitioner and Chairman of Durham Dales PCT, Bishop Auckland*
Ms Julie Foxton	*Senior Nurse Advisor, H·E·A·R·T UK*
Professor Richard Hobbs	*Professor of Primary Care and General Practice, University of Birmingham, and General Practitioner, Birmingham*
Dr Terry McCormack	*General Practitioner, Whitby*
Dr Jim McMorran	*General Practitioner with a Special Interest (CHD and diabetes), Coventry*
Dr John Pittard	*GP and Hospital Practitioner in Cardiology, Staines*
Ms Jan Procter-King	*CHD Specialist Nurse and Primary Care CHD Prevention Trainer, Bradford*

Background

Most recently published data show that up to 50% of patients with raised cholesterol are not receiving lipid-lowering therapy,[1] and that of those who are being treated, around 50% are not achieving guideline targets.[1-3] This under-treated sector of the population – described as the 'Forgotten 50' in a recent report sponsored by Merck Sharp & Dohme Ltd and Schering-Plough Ltd – may be at significant risk of suffering preventable cardiovascular events, excess morbidity and premature mortality.

Although a number of initiatives, especially the National Service Framework (NSF) for Coronary Heart Disease,[4] have almost certainly contributed to the observed decline in cardiovascular mortality over the past decade, coronary heart disease (CHD) remains the most common cause of premature death in the UK.[5] Currently, almost half of all CHD deaths (46%)[6] can be linked to raised cholesterol, and about two thirds of adults in the UK have blood cholesterol levels higher than the government target level of 5.0 mmol/L.[5]

The priority attached to tackling this significant public health problem is demonstrated by the number of quality and outcome indicators relating to CHD in the new General Medical Services (GMS) contract, which came into effect in April 2004.[7] No fewer than 121 quality points relate to CHD: this is the largest proportion for any disease area, and represents a substantial financial incentive for GPs to attain the quality indicators listed. For cholesterol, the indicators are that 90% of patients with CHD should have a record of total cholesterol (TC) in the past 15 months (7 points) and that 60% of patients with CHD should have a TC level below 5.0 mmol/L (16 points).[7]

Among the concerns facing members of the panel were whether the new contract (GMS2) would have enough impact to end the under-treatment of patients with hyperlipidaemia and, indeed, whether the <5.0 mmol/L target is sufficiently low to be considered 'effective'.

Dr Clive Weston, Consultant Cardiologist at the Singleton Hospital, Swansea, and Chair, said: "We all agree that higher levels of cholesterol increase an individual's risk of dying of CHD, and that by reducing cholesterol in the population, by whatever means, we would see substantial reductions in morbidity and mortality.

"November (2004) was the seventh anniversary of the Standing Medical Advisory Committee recommendation that all patients diagnosed with CHD should be having statin therapy – and we have come a long way since 1997.

"Have we come far enough to ensure, though, that no patient can be categorised as part of the Forgotten 50'?"

'…half have the measurement, half are prescribed a statin and half have reached their goal'

Clive Weston

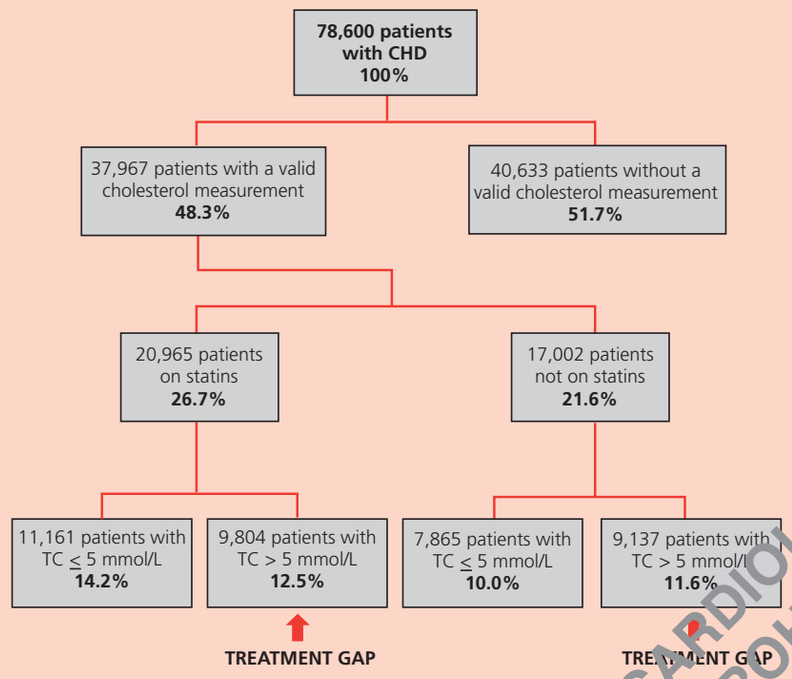
'Currently almost half of all CHD deaths (46%) can be linked to raised cholesterol, and about two thirds of adults in the UK have blood cholesterol levels higher than the government target level of 5.0 mmol/L'

The 'Forgotten 50' – the evidence

Reviewing the evidence supporting the concept of a 'Forgotten 50', Dr Weston highlighted the EUROASPIRE II study, published in 2001, which found that of more than 8,000 medical records of patients identified with manifestations of heart disease and discharged from hospital, fewer than half had a cholesterol measurement recorded in their discharge letters.[2] The study, which took place across 15 countries in Europe, including the UK, found that of those patients receiving statin therapy, about one half had not reached the TC goal of ≤ 5.0 mmol/L.

A further study, by de Lusignan and colleagues,[1] examined pooled data from the Primary Care Data Quality Programme, covering

Figure 1. Characterisation of lipid treatment gap in ischaemic heart disease patients. All percentage figures relate to the total number of CHD patients included (78,600)



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Key: CHD = coronary heart disease; TC = total cholesterol

2.4 million patients in England in 24 localities. This found a similar picture: of the 78,600 patients with CHD for whom analysable data were obtained, only 48% had a valid cholesterol reading (figure 1). Slightly over half, 55%, were taking a statin, and only 42% of these had a total cholesterol level ≤ 5.0 mmol/L.

"This study lends credence to the idea that we might be good at identifying people at risk but we may not be as good as we think at starting them on lipid-lowering therapy nor, when we have done that, at achieving targets we have all signed up to," Dr Weston said. "Essentially this is revisiting the 'rule of halves' – half have the measurement, half are prescribed a statin and half have reached their goal," he added.

de Lusignan and colleagues speculated that if this 'rule of halves' did not apply and if the treatment gap were closed, approximately 7,150 fatal and non-fatal myocardial infarctions could be prevented each year in the UK.[1]

Further evidence that patients with hypercholesterolaemia are not being treated effectively comes from a study by Brady and colleagues[3] that was presented at the Primary Care Cardiology Society meeting in October 2003.

'Have we come far enough to ensure that no patient can be categorised as part of the Forgotten 50?'

The study showed that fewer than half of the patients on statins reached target: of those patients who failed at the first dose, only one third were up-titrated or switched to a different statin.[3] Of these patients, just over half achieved a 25% reduction in TC.[3] Yet, in a postal survey (n=221), GPs believed they would achieve cholesterol targets in 80% of their patients.[3]

Dr Weston commented: "We have faith in the weapons (lipid-lowering drugs), but perhaps we are not using them correctly and perhaps we are not aware of all of the weapons at our disposal."

A similar picture emerged from a primary care-based study among 110 patients with CHD who attended screening:[8] 73% were being treated with a statin, but only 58% had TC ≥ 5.0 mmol/L and only 39% had achieved the 25% reduction in TC or TC ≥ 5.0 mmol/L set out in the NSF for CHD.[8]

Dr Weston said: "Statins are widely used, and have the largest evidence base (of drugs used in cholesterol management), with many good outcome trials. All-cause mortality is reduced for the duration of the studies, and statins appear beneficial in a wide range of patients and conditions, including diabetes and the glucose-intolerant/insulin-resistant patient. Their limitations are partly due to the way we use them."

However, Dr Weston suggested that failure to up-titrate statin dosage may not be because clinicians forget to do so, but because "we know that doubling the dose of the statin does not halve LDL (low-density lipoprotein) cholesterol but might only reduce LDL by a further 6%."

He added: "We are aware of the worry of increased risk of side effects at the higher doses, and the possibility of building up a group of people who are statin-intolerant."

The 'Forgotten 50' – why is there a treatment gap?

Members of the panel agreed that clearly there were gaps between the proportion of the population eligible for lipid-lowering therapy under current guidelines, and those receiving treatment. They also accepted that there was plenty of evidence that not everyone receiving statin therapy was achieving the treatment goals that health professionals had agreed.

However, there was a perception that some of the published data may already be unrepresentative of current practice, simply because of the inevitable delays between data collection, analysis and publication. Dr Weston said: "We might decide that the rate of change in practice is such that already this is not our experience."

CHD nurse specialist Jan Procter-King predicted that when primary care records were examined

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Jan Procter-King

next year as part of the review of the GP contract, 'considerable polarisation' between practices would be observed, with some practices still needing to do a great deal of work to identify candidates eligible for treatment, to initiate therapy and to achieve target cholesterol goals. "It may be that the 'Forgotten 50' are becoming the 'difficult 30' but in some practices it may be the 'forgotten 90'," she said.

Consultant Chemical Pathologist Dr Nigel Capps concurred, pointing out that it was not only patients with, or at risk of, CHD who might be under-treated. "Recent data from the National Stroke Audit primary care database on 1.5 million patients, including 11,000 patients with stroke, found that only half were on a lipid-lowering drug, and only 35% had a cholesterol level of below 5.0 mmol/L," he said.

Patients with peripheral vascular disease should also be considered for treatment, Dr Capps said. "It is very important that a large group of patients who are at very high risk of coronary disease are not excluded. With those it could be the 'forgotten 70', if we are not careful. If you include all these groups who deserve treatment – high-risk, primary prevention and familial hyperlipidaemia – I am sure that it would be at least 50%."

Another group of people who are at risk of under-treatment are the 50 to 65 year olds, according to Professor Richard Hobbs. "Most primary prevention is aimed at people over the age of 65, and there are many middle-risk, middle-aged people who are being under-treated," he said.

Statins – are we using them effectively?

Statin therapy has been the mainstay of treatment for hyperlipidaemia for more than a decade, but there is some evidence that patients receiving treatment with statins are not always receiving an adequate dose[3] – and this class of drugs is not the only treatment option.

There are limitations to statin treatment.[9] In clinical practice a significant number of people are statin-intolerant due to adverse effects and, for many, the statin doses that they can tolerate are not enough for them to reach their target cholesterol levels.[9] Statins are also less effective in patients with familial hypercholesterolaemia who lack the LDL receptor gene or carry a defective LDL receptor gene.[9]

Dr Terry McCormack, a GP in Whitby, said: "We would all like a pill to get patients to their cholesterol target straightaway, but it is not always possible. The UK has always been very conservative – we were all taught at medical school to start with the very smallest dose and build it up – but we may have failed to do the building up."

'Most primary prevention is aimed at people over the age of 65, and there are many middle-risk, middle-aged people who are being under-treated'

Richard Hobbs

'In my experience, GPs are now prescribing statins in much higher doses'

John Pittard

A further consideration is that increasing the dose of statins does not produce a proportionate increase in response. Professor Hobbs explained: "There will always be a proportion of people who respond less well to statins, and there may be people who are relatively statin-resistant. There are also practical considerations of diminishing returns."

Dr Capps said: "We need to explain to patients that we are not going to double the effect by increasing the dose. From the patients' perspective, having a low dose of two drugs is better than a very high dose of one (drug). There is the cohort of patients who are fully compliant, responding to lifestyle advice, but who don't drop their cholesterol levels. We know now there are genetic differences in HMG (hydroxy-methylglutaryl) CoA reductase which affect response to statins."

When statins first came into general use, GPs were encouraged to prescribe cheaply rather than to achieve patients' target cholesterol levels, according to Dr John Pittard, a GP in Staines and hospital practitioner in cardiovascular medicine. In his experience, GPs are now prescribing statins in much higher doses.

Many formularies recommend starting on simvastatin 40 mg, based on the evidence from the Heart Protection Study that this dose reduces the rates of myocardial infarction,

'It isn't just statins that lower lipids. They will remain the number one choice but there are other options and we may be able to do better for the majority of patients'

Nigel Capps

stroke and revascularisation by about a third.[10]

Side effects of treatment were a concern among the panel. The most common adverse effects of statins are gastrointestinal upset, muscle aches and hepatitis.[11] To distinguish genuine statin-related muscle pain from the normal aches and pains of everyday life, Dr Capps suggested a therapeutic challenge: only if pain recurred on resumption of treatment would it be reasonable to assume it might be related to statin use, and to stop treatment.

Dr Capps said: "Although intolerance to statins is low in percentage terms, now that so many people are being treated it only needs 1% or 2% of patients to start becoming intolerant for it to have a big impact. We are seeing more patients who are intolerant to statins – we can try two or three, and the patient may still be intolerant to treatment at any dose. But some patients have been started on a high dose and have never had a lower dose. If you explain that the drug level will be much less, there are some patients who can manage fine on the lowest dose though they could not on the higher dose.

"It isn't just statins that lower lipids. They will remain the number one choice but there are other options and we may be able to do better for the majority of patients," Dr Capps said.

Statins are the most widely prescribed lipid-lowering drugs and represent the biggest drug spend in the NHS budget, costing £694 million in England.[12] However, one alternative to prescribing ever-increasing doses of statins to achieve a treatment goal is to use a different lipid-lowering therapy. Other commonly used agents in addition to statins are fibrates, a cholesterol absorption inhibitor, bile acid resins, and further cholesterol-lowering alternatives such as niacin and omega 3 fish oils.

Fibrates are effective primarily in lowering triglyceride levels, and to a certain extent in increasing high-density lipoprotein (HDL) cholesterol levels. Bile acid resins reduce cholesterol levels by binding to bile in the small intestine and preventing it from being absorbed into the circulation. The selective cholesterol absorption inhibitor, ezetimibe, works by treating cholesterol absorption in the intestine. When co-administered with a statin, ezetimibe can be particularly effective at lowering cholesterol levels.[13] Dr Capps said he was now seeing use of the combination of low-dose statin plus ezetimibe, rather than up-titrating with statins to high doses, at a much earlier stage.

'Nurses will take the lead, not only in identifying people but prescribing statins and other drugs. That is the way forward'

Terry McCormack

'The new pharmacy contract will incentivise pharmacists to do more, and delivering CHD targets is an ideal area for them to get involved in'

Stewart Findlay

Targets – are they tough enough?

Stringent targets for total cholesterol and LDL cholesterol levels have been set by the British Hypertension Society (BHS) (TC 4.0 mmol/L, LDL-C 2.0 mmol/L).[14] It is anticipated that they will be echoed in the Joint British Societies Guidelines.[15] Targets also feature in the quality and outcomes framework of the GP contract, GMS2.[7]

The panel considered whether a simple numerical target, such as the total cholesterol ≤ 5.0 mmol/L set in GMS2, was in patients' best interests.

Dr Capps said: "We know that the closer you get to biologically normal, which is about 3.0 mmol/L, the better you are going to be in terms of vascular disease. The GMS contract is a big step forward but the other driver, the NSF for CHD, has not gone away. The concepts of the 25% reduction in TC and 30% reduction in LDL-C are still there. People should be working towards this."

Professor Hobbs argued that a 25% reduction was a more complicated calculation than a numerical target, derived from the outcomes recorded in the major intervention trials. "You would have to find out what the baseline was

'If you could empower the patients and give them information and education, I think you could bring the 'Forgotten 50' into line'

Julie Foxton

and work the reduction out prospectively." Professor Hobbs did not think this was likely to occur in busy surgeries, but he added: "The main justification for the revised lower target levels is a pragmatic consideration. If we aim for TC 4.0 mmol/L and LDL 2.0 mmol/L, we will bring a higher proportion of the population to below 5.0 mmol/L and 3.0 mmol/L," he said.

The GMS2 contract requires GPs to record cholesterol measurements, and to reduce TC to ≤ 5.0 mmol/L for 60% of their patients with established CHD.[7] When asked what stops GPs from trying to reduce cholesterol levels, and therefore risk, further, "it was a question of resources", said Dr Jim McMorran, a GP in Coventry with a special interest in CHD and diabetes. "It is not just CHD: it is all the other disease areas we have to look at. For the practice population we will look at our points, but the individual patient still receives proper clinical care," he said.

Dr McMorran added: "The (contract) target of ≤ 5.0 mmol/L will take over from any other, such as the NSF. In terms of the individual, TC ≤ 5.0 mmol/L is a very good start, but there is always something more to be done – a 1% increase in HDL will reduce risk of coronary heart disease by 2% to 3%."

The panel noted that when the contract is reviewed in 2006, targets will also be revised, possibly by increasing the percentage of the relevant practice population from 60% to 75% or by changing cholesterol targets in line with BHS – and the eagerly anticipated new Joint British Societies – recommendations.

Dr McCormack suggested that if health professionals wanted to reduce patients' cardiovascular risk, they should aim for 'the lowest target' possible – "that's the way to succeed," he said.

The future – how can we improve management of hyperlipidaemia?

Discussing how to achieve more effective treatment for the population identified as the 'Forgotten 50', the panel agreed that a number of approaches needed to be adopted. Among these were making better use of all the members of the healthcare team, employing more systematic methods for recalling and reviewing patients, reinforcing lifestyle advice and, most importantly, tailoring pharmacotherapy to meet the needs of individuals.

Ms Procter-King predicted that within three to four years, nurses would carry out the majority of lipid management systematically, in primary care – a view also held by other members of the panel.

Dr McCormack commented: "Nurses will take the lead, not only in identifying people to assess them, but prescribing statins and other drugs. That is the way forward."

Pharmacists were also predicted to have a bigger role to play in managing cardiovascular risk. County Durham GP, Dr Stewart Findlay, said: "The new pharmacy contract will incentivise pharmacists to do more, and delivering CHD targets is an ideal area for them to get involved in."

The emphasis would change from reliance on statins for lipid lowering to an 'ABCD of lipid management for the individual', Ms Procter-King said.

Ms Foxton added: "As with blood pressure management, we will say (to the patient) we are likely to have to introduce two or three tablets. We will watch if they work, and whether they work enough – but what we are aiming for is control. It is about involving the patient. If you could empower the patients and give them information and education, I think you could bring this cohort into line."

Now that there is a greater awareness in primary care of the importance of HDL and LDL cholesterol, laboratories have to provide not just

'We will be using a combination of agents to achieve a satisfactory profile'

Jim McMorran

TC and triglyceride (TG) results, but full lipid profiles, Dr McMorran proposed. Nonetheless, reducing LDL cholesterol levels is still seen to be the most important factor in influencing cardiovascular risk, based on evidence from trials such as Cholesterol And Recurrent Events (CARE) and the Scandinavian Simvastatin Survival Study (4S), he added.[16,17] GPs would rely less on a single lipid-lowering agent. "We will be using a combination of agents to achieve a satisfactory profile," he said.

Hypertension management has shown us other ways of achieving treatment goals, Dr Weston said – "not just fixed-dose, combination therapies but logical combinations of therapies." This approach is well established in the management of hypertension, and in the US it is already being used for hyperlipidaemia management.

Conclusions and the vote

It is reported in some studies[1] that only half of patients with established CHD have a valid cholesterol measurement, and only half of those are receiving statin therapy.[1,2] The focus of this debate, however, was those patients who are being treated with statins but who are not reducing their cholesterol to effective levels and who therefore remain at unnecessary risk of cardiovascular events and premature death. The 'Forgotten 50' is one

term used to describe this group. Although one solution to this problem is to increase the dose of statin therapy, there are issues concerning the potential for side effects (particularly at higher doses), statin intolerance and the emergence of statin resistance. An alternative solution may be to use a fibrate, bile acid resin, a selective cholesterol absorption inhibitor and/or a combination of drugs in order to secure effective treatment.

Having considered the arguments for and against the motion, "*This House believes that the UK healthcare system may be failing as many as 50% of patients with hyperlipidaemia by not reducing their cholesterol*", the panel voted overwhelmingly in favour of the motion, with a majority of 70% to 30%.

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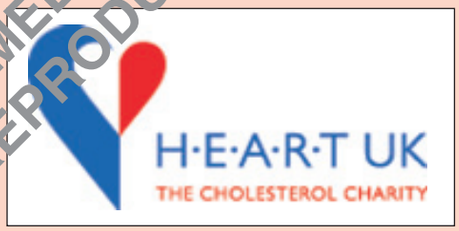

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