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# Heart Protection Study

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**Invitation to Join  
a Large Medical  
Research Project**

**Heart Protection Study  
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## Invitation to join a large medical research project

You are being invited to join a nationwide Medical Research Council and British Heart Foundation study of the overall effects on survival of long-term treatment to prevent heart attacks. Big differences in survival are not likely, so the study is designed to look for small — but worthwhile — differences (and to look for any serious side-effects of long-term treatment). In order not to overlook such effects, more than 20,000 people in Britain who may be at above-average risk of having a heart attack are being invited to participate.

The invitation to you was made with the agreement of your own doctor. You are, of course, free to choose not to join the study (or, if you do decide to take part, to withdraw from the study treatment at any time) without affecting the medical care you can expect from your own doctors. If, after reading this leaflet, you have any questions then please discuss them either with the study clinic staff or with your own doctor.

### Cholesterol and heart disease

Heart attacks (“coronaries”) are the leading cause of death in Britain. One of the main things that makes a heart attack more likely is having too much cholesterol (a fatty substance) in the blood. Some cholesterol in the bloodstream is necessary for normal body processes, but too much of it can narrow the vessels supplying blood to the heart and so increase the chances of having a heart attack. Blood cholesterol levels may be too high in most British men and women.

Cholesterol levels in the blood can be reduced by reducing the amount of animal fat in the diet, and you will have been given information about how to do this (for example, by eating much less butter, cheese and fatty meat). In addition, blood cholesterol levels can be further reduced by special cholesterol-lowering drugs, although until recently the drugs that were available produced only small cholesterol reductions.

## New treatment for lowering cholesterol

A newer type of cholesterol-lowering drug (called the “statins” or “reductase inhibitors”) is now available. These produce much larger reductions in cholesterol than can be achieved with the older drugs, and so the statins are now widely used for lowering very high levels of cholesterol. In preparation for this study, one of the statins (simvastatin) has been carefully studied for over 4 years in more than 600 patients: it has proved effective at lowering cholesterol, with very few side-effects. Lowering cholesterol does reduce the chances of having a heart attack, but taking drugs regularly for several years might have some unsuspected adverse effects that counterbalance a reduction in heart attacks. In a 5-year study of over 4,000 patients with heart disease — most of whom were middle-aged men with raised cholesterol levels who had already had a heart attack — simvastatin reduced the number of deaths (as well as heart attacks and heart operations) by about one-third, again with very few side-effects. The purpose of the Heart Protection Study is to find out whether these drugs also save lives when given to other types of people who, like you, may be at above-average risk of having a heart attack.

### Vitamins and heart disease

Although your level of cholesterol affects your chances of having a heart attack, other factors (particularly cigarette smoking and high blood pressure) also play a part. There have been suggestions that certain vitamins (in particular, vitamins E, C and beta-carotene) can help protect against heart attacks, but this is unproven. Moreover, taking regular supplements of these vitamins may have little or no beneficial effect among people living in a country, such as Britain, where most get adequate amounts in their diet. It has also been suggested that long-term use of some of these vitamins could, on balance, be slightly harmful, but this too is unproven. It is not yet known whether

these vitamins are of any importance at all in reducing the risk of heart attacks and in saving lives. The Heart Protection Study will also help to answer this question.

### **What the Heart Protection Study involves**

The Heart Protection Study will involve many thousands of men and women from around Britain. Like you, these men and women are being invited to take part because their past medical history suggests that they may be at above-average risk of having a heart attack. Everyone taking part will have agreed to do so voluntarily, knowing that it may involve them in taking study treatment for at least 5 years.

The daily study treatment consists of one tablet and two capsules. The tablet contains either the active cholesterol-lowering drug (simvastatin) or a similar-looking inactive substance (called a "placebo"). The capsules contain either active vitamins E, C and beta-carotene or similar-looking "placebo". So, you could receive two, one or no active study treatments (with all your other medical care left unchanged). The type of study treatment being taken — whether active or inactive — will not generally be known by you, or by the research clinic nurse, or by your doctor. This information will be known only by the staff at the central administration, but it would be made available to your own doctor if this was ever medically necessary. This design ensures that reliable information will be obtained about the effects of these potentially important treatments.

### **If you decide to join the study**

If you do choose to participate in the Heart Protection Study, you will be given a box of conveniently packaged study treatments and asked to take one tablet and two capsules every evening for the next two months. After completing these first two months of the study you will be seen again in this clinic, and can decide whether or not you would be willing to continue taking

study treatment long-term. If so, you would be given further supplies of the study treatment and would be seen every 4 months in the first year and then every 6 months for about 5 years more. In general, these visits to the study clinic should involve very little waiting and should take no more than 15 minutes.

Simvastatin lowers blood cholesterol substantially, and this should be associated with a lower risk of a heart attack. In a small proportion of patients taking simvastatin or other statins, changes in blood measurements related to the liver (which have only very rarely been associated with any liver problems) or muscles (which are occasionally associated with muscle pain or weakness) have also been observed. Consequently, patients who have serious liver or muscle disease should not enter the study (and nor should women who are likely to become pregnant). As a safety check in the study, a small blood sample will be collected each time we see you (but cholesterol will not be re-measured routinely). Side-effects with the statins are very uncommon, and usually are not serious and disappear on stopping treatment. So, if you do develop some unexpected symptoms — in particular soreness or weakness of your muscles which is not the result of exercise — you should contact one of the staff in the study clinic or in the coordinating centre (**0800-585323: 24-hour Freephone service**).

The doses of vitamins being used in this study are somewhat higher than are commonly taken. Such doses are not known to cause any particular problems, but again we shall monitor their effects carefully. Patients who join the study would be asked to avoid taking non-study vitamin E supplements in daily doses of over 100 mg, but could take other vitamin supplements. (N.B. If you are taking an oral anticoagulant, like warfarin, then the dose will need to be checked by your doctor when either of the study treatments is started or stopped.)

## Long-term collaboration

Participation in the study will require a commitment to take the study treatment for at least 5 years, with regular visits to the clinic. **If you do not think that you would be willing or able to do this then it would be better not to join in the first place.** (Unfortunately, we are not able to reimburse travel expenses.) If you do decide to take part, you would, of course, be free to withdraw from the study treatment at any time without necessarily giving any reason (and without adversely affecting the medical care you can expect from your own doctors). In particular, you will be encouraged to withdraw after the first two months if you have any second thoughts or problems with study treatment or clinic attendance. If you do stop during the first two months then no further enquiries will be made of you. But, if you decide to continue, then we would like to see you regularly for the next 5-6 years to check on your health – even if you stop taking the study treatment during this period. **Throughout the study, your own doctors would remain fully responsible for all your other medical care, as usual.**

The important details of your progress will be sent to the study coordinating centre in Oxford. The coordinating centre will seek information about any serious illnesses (such as heart attacks, strokes, cancers, etc) that occur from participating patients' own doctors and from central registries. All such information will be used, **in confidence**, only for medical research purposes and for regulatory purposes by government agencies in Britain or elsewhere.

**N.B.** The MRC/BHF Heart Protection Study involves the collaboration of several dozen British hospitals and is organised centrally by the University of Oxford. It is funded jointly by the UK Medical Research Council, the British Heart Foundation and by the manufacturers of the treatments it is studying (Merck Sharp & Dohme and Hoffmann-La Roche). The study is, however, conducted independently of the pharmaceutical companies.

**If you have any questions about  
the study then please feel  
free to ask the clinic staff**

**— Thank you for your help —**