THRIVE
WORKING TO REDUCE HEART ATTACKS AND STROKES

....an invitation to join a health research study.
Questions about the study should be directed to the coordinating centre in Oxford

By phone:
24-hour Freephone service:
0800 585323

By post:
HPS2-THRIVE, CTSU,
Richard Doll Building,
Old Road Campus, Roosevelt Drive,
Oxford, OX3 7LF

By email:
thrive@ctsu.ox.ac.uk

Or visit our website:
www.thrivestudy.org
Did you know there is such a thing as **good** cholesterol (and we don’t just mean low levels of bad cholesterol)? And the more you have, the better it is for you?
Cholesterol, heart attacks and strokes

If you have had a heart attack or stroke, you will know about cholesterol and the need to keep its level low. It can be a struggle, but a good diet, plenty of exercise and statins can help.

But did you know that there is a good type of cholesterol? And the more good cholesterol you have, the better – because it may help to prevent further heart attacks and strokes?

THRIVE: what is the purpose?

THRIVE is a study to see if boosting levels of good cholesterol can save more lives. THRIVE is doing this by testing a treatment called niacin, which raises levels of good cholesterol in your blood. Everyone taking part in THRIVE will also receive tablets, called statins, to lower their bad cholesterol. If you are taking statins already you can still join this study.

Why me?

You are being invited to take part in this study with the knowledge of your hospital consultant. Your hospital records suggest you may be suitable. We have also written to your GP to tell them that some of their patients are being asked to take part. If you agree to participate your GP will be informed.

You can take part whether or not you are already taking a statin to reduce your bad cholesterol. This is because this study is not looking at statins. Statins have been tried and tested successfully in similar studies over many years – to provide the evidence that they are safe and help protect people from heart attacks and strokes.
Who is running the study?

THRIVE is being led by medical scientists at Oxford University who carried out the important Heart Protection Study (HPS). This study showed conclusively how effective statins were at saving lives. That is why THRIVE is sometimes known as HPS2-THRIVE.

Do I need to take part?

You do not have to take part in this study. It is entirely your decision. But if you did help, many millions of people from around the world might benefit from this research in years to come.

Travel expenses

A contribution towards the cost of travelling to your THRIVE appointment can be provided. Make sure you ask at the clinic.

What happens to me if I take part?

Getting started

Your continued good health is the prime concern of the trained medical staff involved with the THRIVE study. They will monitor your health at regular intervals throughout the study. Your GP will be informed if you decide to join the study.

At your first visit to the THRIVE clinic a trained researcher (usually a nurse) will ask you about your medical history. The researcher will take your blood pressure and a sample of blood. They will explain the study to you. If you are interested you will be asked to sign a form agreeing to take part. Over the course of the next few weeks you will have the chance to try out the tablets. You will also be measured and weighed. You will then be asked to make a commitment to the study long-term. You can withdraw from the study at any time. If you do stop taking the tablets after committing to the study long-term, we would still like to keep in touch with you, if possible. Ideally this means still coming to the study clinic, if this is not possible then by phone.
Further information about the study is available from the THRIVE clinic nurses.

For the first few visits it is helpful if you avoid any food and drink – other than water and any usual tablets – for at least 4 hours before your appointment. If you have diabetes and would like advice about fasting please call Freephone 0800 585323.

**Increasing good cholesterol**

The tablets being tested contain niacin and a compound called laropiprant. It is known that niacin increases levels of good cholesterol in the blood. Doctors hope that this will reduce the number of heart attacks and strokes, but they do not know this for certain. The laropiprant will reduce the side effects that people taking niacin have had before. People have experienced flushing (reddening) of the skin, which laropiprant is designed to prevent.

*‘It is known that niacin can increase levels of good cholesterol’.*

In the first few weeks you will be asked to take one of these tablets each day. After 4 weeks, this will increase to two tablets a day.

**Lowering bad cholesterol**

Everyone taking part in THRIVE will also be given a statin to reduce their bad cholesterol. You will be asked to take a statin called simvastatin. This may mean that you have to change from your current treatment. However, all statins work in very much the same way, and this should not cause you any problems.

The amount of statin-based treatment you receive on the THRIVE trial will be at least as strong as your current treatment.
Usually, this is just 40mg of simvastatin daily. In the first few months, trained specialist THRIVE researchers will monitor your levels of bad cholesterol to ensure that the statin treatment works satisfactorily. After that your doctor can keep an eye on your levels if they wish to.

This treatment aims to get your cholesterol to the current recommended target (below about 4.0 mmol/l).

You may be given a statin booster to help get your bad cholesterol down further, if necessary. This is a tablet combining simvastatin 40mg with ezetimibe 10mg. It is known as ezetimibe/simvastatin 10/40mg.

Simvastatin is provided free to you by the study team. Even if you decide eventually not to carry on with the study tablets, you can still keep taking these statins.

THRIVE researchers ask all participants to use the same statin so that the ‘background’ treatment to reduce bad cholesterol in all participants is the same. This helps the research scientists to know that any results they get from the trial to increase good cholesterol are ‘real’.

Simvastatin and ezetimibe have been shown in large trials to be safe. They are effective treatments for lowering levels of bad cholesterol.

‘People already taking statins can take part in this study’.
After two months

During the early part of the study you are provided with niacin, the treatment under examination, to check if it suits you. You also receive simvastatin, to reduce your bad cholesterol. The tablets are taken with food in the evening, or at bedtime.

You will be monitored so that the THRIVE nurses can be sure the niacin agrees with you, and that your bad cholesterol is under control.

The detail

After 8 weeks of trying the study tablets you will then be asked if you would like to continue with the study. If you agree, you will be asked to commit to the study for the next four years.

Everyone on the trial will continue with their statin treatment. However, only half of the participants will receive the tablet containing niacin. The other half will be given a dummy drug, called a placebo. Scientists do not know which treatment is best, but this study should give the answer.

Whether or not you receive niacin is done randomly. This means that you have as much chance of receiving it, as you do in not receiving it (like the toss of a coin). You will not know which treatment you receive, nor will your GP or the THRIVE staff. However, this information would be made available to your doctor if this was medically necessary.

After 6 months

After the first 6 months, you will attend a 20-30 minute appointment every six months. A sample of blood will be taken and you will be provided with more treatment for the
First Appointment

When you provisionally agree to take part

Duration: up to 8 weeks

During the early months, study nurses will check that your statin treatment is adequate and you can try out the niacin tablets. Participants already on statins used in the trial may be able to miss out this stage.

Duration: 4 weeks:
Statin + one niacin tablet

Duration: 4 weeks:
Statin + two niacin tablets

Duration: About 8 - 16 weeks, depending on the individual
Confirm long-term commitment to the study
Participants are selected randomly (by chance) to receive one of these treatments. Doctors do not know which one is best.
Half of all participants receive a statin and niacin.
Half of all participants receive a statin and a dummy tablet called a placebo.
Study finishes
Results are published

Duration: About 4 years
One visit to the THRIVE clinic after 3 months and then an appointment every 6 months

Study Timetable

THRIVE Patient Information Leaflet (UK) V7.1 2009-10-05
next six months. You will not need to fast beforehand. With regular check ups from the THRIVE specialist nursing team, you can be assured of the best possible follow up care and attention.

If you do choose to withdraw, it would be helpful if you would allow the study scientists to stay in touch with you, to see how you get on. If any problems emerge for you while you are on the study, your GP will be informed.

At each visit the THRIVE nurse will take a blood sample. This will be tested to check the liver. If you have muscle problems, a muscle blood test will be done. Sometimes the blood samples will be sent to the laboratory in Oxford for extra tests.

What will I have to do?

For THRIVE to produce the best results, it is important that people stay in the study for as long as possible. We will ask you to commit to the study for at least four years. You will need to attend the THRIVE clinic several times in the first few months and then once every six months.

You will be asked to take a statin called simvastatin and either a treatment to raise your good cholesterol, or a dummy treatment called a placebo. Scientists do not know which treatment is best.

You will also be asked to allow your blood and urine to be stored for future analysis.

You can withdraw from the study at any time.
What is the treatment being tested?
A treatment to raise good cholesterol with a combination of niacin and laropiprant is being tested. Before this study about 3,000 people received this treatment. About 25,000 people in the UK, Scandinavia and China will take part in THRIVE. Already over 20,000 people have joined the study.

What are the benefits of taking part in this study?
You may be helping yourself, but you will most certainly be helping doctors and scientists improve treatment for people who have had heart attacks or strokes, or who may be at risk of having one. We hope that being on the study may help you by reducing the risk of having a heart attack or stroke. If successful, results from this study will help to prevent many thousands of heart attacks and strokes and bypass procedures around the world.

Are there any risks?
Most treatments have side effects which some people may experience and others do not. If you do experience any side effects while on the THRIVE study they will be noted, so that scientists can learn from you. You can withdraw from the study if you wish.

- **Laropiprant** is not known to have any side-effects. It may be that some emerge in this study, but doctors think this is unlikely. If common side-effects did emerge, you would be told about them;

- **Niacin** use has been limited because it can cause a feeling of warmth, redness and itching of the skin (flushing) in some people. Laropiprant ought to reduce this side-effect.
However, some people may still experience flushing in the first few weeks of taking the treatment. Though unpleasant, flushing episodes are not dangerous. Some people experience tummy upset, nausea, diarrhoea and rashes and rarely allergic reactions. Blood tests are used to monitor for a rare liver problem (that usually resolves when niacin is stopped). Niacin can also increase blood sugar levels, particularly in people with diabetes. However, researchers running THRIVE hope that people with diabetes will take part. Steps can be taken to control their blood sugar levels. The study may help to explain why niacin raises blood sugar in this way.

**Statins** are generally very well tolerated. A rare side-effect is muscle pain and weakness.

There is nothing to suggest that stopping the tablets will cause you harm. If you do experience side-effects, you may choose, or be advised by your doctor, to stop the tablets provided by the study but you can usually continue to take your statins.

If you do experience unexpected symptoms after joining the study you can contact your THRIVE nurse, or a study doctor on Freephone 0800 585323.

**Will my taking part be kept confidential?**

Yes, absolutely. Information about you is entered on to a computer and stored securely. Oxford University is a world-leader in developing systems to ensure that information is stored safely for studies such as THRIVE.

The coordinating centre will ask for information from your doctors and from NHS and other central registries about any serious illnesses that you have. All information received is used in confidence only for medical research purposes and for routine regulatory and audit purposes.

Blood samples are sent to a laboratory at Oxford University for analysis. They are identified by a unique number linked in
the computer to other study information. In the laboratory they are not linked to your name.

The information used for scientific analysis will not include any details that identify you.

**What will happen at the end of the study?**

The results will be published widely in health or scientific journals and be discussed at major conferences. Others will learn from the results which we hope will show that more lives can be saved by increasing good cholesterol. No individual participant will be identified in any report or publication. We will endeavour to inform participants and their GPs of the results, and any ensuing publicity.

‘**Results from the study will be published and help doctors improve the treatment of heart attacks and strokes’.**

**How is this study organised?**

Scientists and doctors consider the questions being asked by THRIVE to be important, because they could improve treatment for people who have had, or may be at high risk of, a heart attack or stroke. THRIVE is built on the success of the Heart Protection Study which showed how useful statins are in saving lives.

Scientists at Oxford University, who are carrying out the project, have had to get permission from ethics committees to do so. These committees check whether the health question being asked is important enough to
warrant a study, and that the study is being carried out in an independent, honest and professional manner.

An independent committee also watches over the study and keeps an eye on results. This committee could halt the study early if important new evidence emerged that had an impact on the need for the study to continue.

THRIVE has been designed and is coordinated by Oxford University’s Clinical Trial Service Unit (CTSU), one of the world’s leading centres for this type of work. The study involves many heart doctors and nurses around the country and in Scandinavia and China.

THRIVE is lead by Professor Jane Armitage at CTSU, a qualified and practising doctor at an Oxford hospital. She has played an important role in previous studies that have shown the health benefits of statins.

Independent studies such as THRIVE are costly to run. Treatment for the study is provided free by Merck & Co., Inc. which also contributes to the cost of running the study, by a grant to Oxford University. Merck also provided some of the funding for the Heart Protection Study that provided clear evidence of the benefit of statin treatment to reduce heart attacks and strokes.

However, THRIVE is conducted independently of Merck, which has no say in the running of the project.

‘THRIVE is testing niacin, not statins, to see if we can improve health further’. 
What if there is a problem?

You retain all the usual rights of an NHS patient.

In the unlikely event of your being harmed by taking part insurance cover is provided by Merck & Co., Inc. Any compensation would be paid in accordance with the guidelines of the Association of British Pharmaceutical Industry (ABPI). Any payment would be without legal commitment.

If you have a concern about any aspect of the study you can speak with the researchers. They can be contacted on a 24-hour Freefone number: 0800 585323.

Thank you

Thank you for your interest in this study. More information is available from the THRIVE clinic nurses, by calling the telephone number above, or from the THRIVE web site: www.thrivestudy.org

If you would like to take part, travel expenses to and from the THRIVE clinic can be claimed. Our aim is to make your participation an interesting and worthwhile experience while helping us and others to improve the treatment of people who have had, or who may have, a heart attack or stroke.