AMALFI

Active **M**onitoring for **A**tria**L** **Fi**brillation

...an invitation to join a new medical research study

FUNDED BY
NIHR | National Institute for Health Research

UNIVERSITY OF OXFORD

Study overview

- Atrial fibrillation is a common condition where the heart beats irregularly. It affects 10% of people aged over 65 years old but not everyone has symptoms.

- People with atrial fibrillation are around 5 times more likely to have a stroke than those without. Effective treatment is available to reduce this stroke risk once atrial fibrillation is diagnosed.

- This study will use a new Zio Patch monitor to detect atrial fibrillation. The patch is worn continuously for two weeks. It has been approved for use in Europe and America and is safe to use for everyone except people with a history of skin allergy, where it may cause a local reaction.

- Between 2,500 and 5,000 people will take part, half will wear the patch and half will not. Which group you are in will be decided at random by a computer. Only using the patch in half of people allows us to compare what happens between those wearing the patch and those who continue with usual medical care.

- You will be posted any study materials – the only extra visit you may need to make would be to your GP to discuss treatment if you wear the Zio Patch and are found to have atrial fibrillation.

- Although the patch is worn just once, we would like everyone to agree for the study team to access their healthcare records for up to 25 years. This allows us to see whether diagnosing atrial fibrillation makes any difference to your future health.

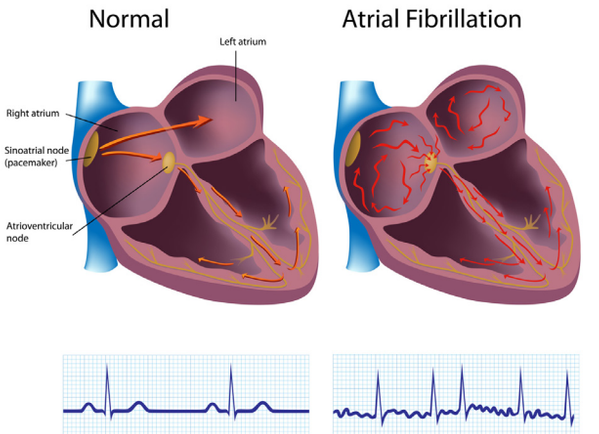
- AMALFI has been designed by the University of Oxford, who will run the study independently of any funders. The funding itself comes through the NHS funded Biomedical Research Centre & National Institute for Health Research with additional support from iRhythm, who are donating the Zio Patches free of charge.

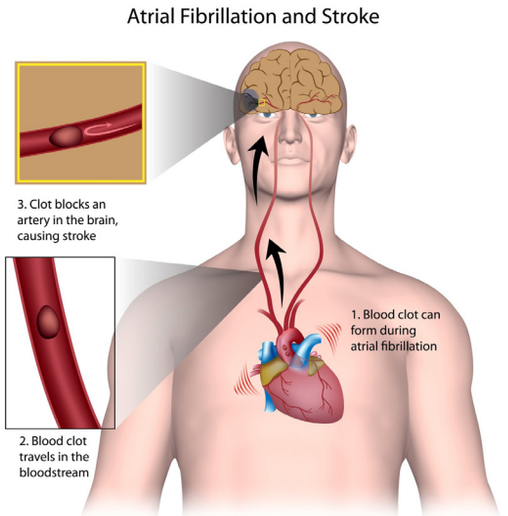
An invitation to join a new medical research study

We would like to invite you to take part in our research study. Before you decide whether or not to take part it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

Atrial fibrillation and why it matters

Atrial fibrillation is an irregular heart rhythm. Instead of the heart beating regularly like normal, the heartbeat is irregular and may also be faster than normal. Sometimes the irregular heartbeat of atrial fibrillation will cause symptoms such as palpitations, light-headedness or shortness of breath. Other people may not have any symptoms at all. The irregular heartbeat may also come and go, something that is more common when the atrial fibrillation has only recently started.





Unfortunately the irregular heartbeat can cause problems even when it is not causing any symptoms or is only happening some of the time. The most serious is that clots can form in the heart due to the irregular beating and these may then travel in the blood supply to the brain, where they can cause blockages in the small blood vessels resulting in a stroke. Any stroke can result in permanent disability, such as paralysis, loss of speech or even death. People with atrial fibrillation are thought to be around five times more likely to have a stroke. Reassuringly, treatment is available in the form of blood thinning medication which can significantly reduce the risk of having a stroke in those who are suitable to take it. This makes identifying atrial fibrillation and treating people early extremely important.

Why are we doing the AMALFI study?

Diagnosing atrial fibrillation is normally done using an electrocardiogram (ECG) which catches the heart rate at a single point in time. However, as atrial fibrillation may only be happening some of the time, this test might not always detect a problem if, by chance, the heart is beating regularly when the ECG is done. Also people who do not have symptoms from their atrial fibrillation are unlikely to see their doctor to have their pulse checked or to have an ECG done.

The purpose of the AMALFI study is to see whether wearing a new home monitor called a Zio Patch, which can give a continuous heart trace reading for 2 weeks, will increase the number of people we can detect with atrial fibrillation. The hope is that this would allow more people to be put on the right treatment at an earlier stage and so bring down their risk of having a stroke. To do this we will recruit between 2,500 and 5,000 people from across the UK.

Why should I take part?

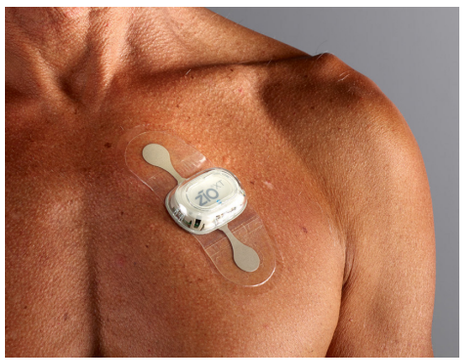
For some people taking part will mean having an irregular heartbeat detected that they did not know they had. This may lead to them starting new treatment and potentially bringing down their chances of having a stroke in the future. Everyone who does take part will be contributing towards answering an important research question, even if you are not in the group that wears the Zio Patch. We hope this information may lead to better medical care for millions of people in the future and possibly even a new national screening programme.

Do I have to take part?

No. Participation in the study is entirely voluntary. Choosing not to take part will not affect your future medical care or your statutory rights in any way. If you do choose to take part in the AMALFI study you will be free to withdraw at any stage. If you decide you no longer wish to continue, you can contact the study team by telephone, email or post using the contact details given on the back cover. Just let us know you have changed your mind and we will remove your details from our contact list. You do not have to tell us the reason for your decision if you do not wish to do so.

What is the Zio Patch?

The Zio Patch is a new piece of medical equipment, made by iRhythm Technologies Inc. based in San Francisco, USA. The Zio Patch has been created to monitor the rhythm of the heart for 2 weeks at a time. The patch simply sticks to your chest, over your heart, and can be easily peeled off once you've finished using it. People who have worn the patches have found them discrete and comfortable to wear. They are waterproof so can be worn in the shower or bath, although swimming should be avoided. All the information is analysed by iRhythm's computer systems and a report is sent back to your GP. The Zio Patch has already been put through thorough testing in America and the UK. It has been approved by the USA Food and Drug Administration Department and awarded a CE mark in Europe for diagnosing atrial fibrillation.

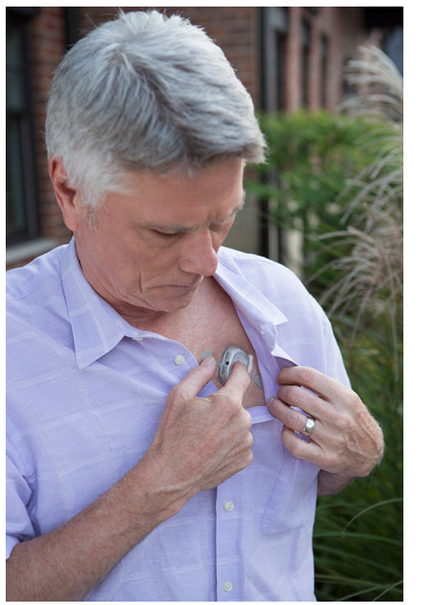


What would be involved?

If you choose to participate in the AMALFI study you will be assigned to one of two study groups – one group who will wear the patch and the other who will not. This is because sometimes, when we don't know which way of treating patients is best, we need to compare different treatments to find out. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly). This means you would have an equal chance of being put in either the group who wears the patch or the group who doesn't. Everyone who takes part will receive a letter informing them which group they have been assigned to. We will also write to your GP letting them know you are taking part; including a copy of your consent form signature page for their information.

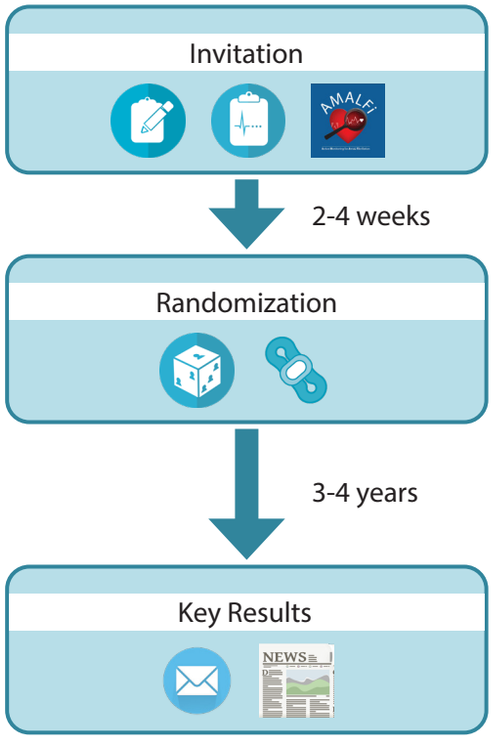
The first group will also be sent a Zio Patch monitor by post. If you are in this group you will then need to stick the Zio Patch on to your chest over your heart. Instructions will come with the patch explaining how to apply it - it is quick and easy to do. If required, a video is also available on the study website www.amalfitrial.org showing what the patch looks like and how it can be put on.

The patch should be worn all the time for 2 complete weeks. This may seem a long time but it will provide the most information possible about what your heart is doing in that time. If you have any difficulty with this process or need advice on putting the patch on please contact the study team.



After 2 weeks, the patch should be removed and returned using the packaging provided. This is postage-paid, so there is no need for a stamp. The patch will be processed in the UK but the heart rhythm information that the patch contains will be sent to iRhythm's laboratory in America for analysis. This information does not contain your name, address or personal data other than your heart rhythm and a number that the AMALFI team back at Oxford can use to link you to your results. The results should normally be analysed within 6 weeks of receipt and sent to your GP. We will send your GP any information related to the presence and duration of atrial fibrillation episodes, including additional information to assist in the interpretation of the results, such as the time the monitor was worn, and how much of that time was possible to analyse. You will receive a copy of this letter and your GP may ask you to come in for an appointment to discuss the findings.

AMALFI Timeline



What might happen in the trial?			
	Consent form		Randomization to Zio Patch or control group
	Questions about your health		Zio Patch
	Patient information leaflet		Study results letter
	Study results published in medical journal		

For most people we expect the results to be normal and so no treatment would be required. Some, however, will be diagnosed with atrial fibrillation and your GP will be able to decide on your best treatment. There is a range of treatments available for atrial fibrillation, including blood thinning medication (anticoagulation) or medication to control the heart rate or rhythm. GPs are experienced in managing atrial fibrillation and there are clear national treatment guidelines in place. Sometimes further investigations or referral to a specialist will be needed but this will be decided in consultation with your GP.

As well as detecting atrial fibrillation, the Zio Patch can also identify other heart rhythm changes. Many of these are very common and do not indicate serious heart problems. We will not routinely report any changes other than atrial fibrillation to your GP. However, if there are any additional serious findings on the monitor report we will tell your GP. We will also seek specialist advice from a cardiologist if there is uncertainty about any findings. Please note that the ECG monitoring that you will be having is not part of your clinical care. Therefore, if you develop any symptoms such as chest pain, palpitations, dizziness or breathlessness, you should consult your GP in the same way as you would normally do.

Half of the people who take part in the study will not have to wear the patch. If you are in this group your medical care will not be affected in any way compared to if you choose not to take part in the study. You will still be able to have all the usual medical care available on the National Health Service. If you do develop symptoms we encourage you to discuss these with your GP or access medical care in the usual way. We understand some people may be disappointed having volunteered to take part if they do not receive the Zio Patch. However, the only way we can know if this approach to screening is worthwhile is by having an even mix of people wearing and not wearing the patch. The information you are providing will be just as important to the study and the wider community as for those who do wear the patch.

What happens after that?

The only difference between the two groups is the patch, which will only be worn in the early stages of the trial. After this, everyone's medical care in both groups will be as normal. We do ask that you give us permission to access your medical records (from your GP surgery and NHS Digital) so we can see what happens to you over the next few years. We will ask your GP for information 3 times in the next 5 years. We will also request information about any hospital admissions, other serious medical conditions, and medications from NHS Digital both during this time and for up to a further 20 years. To do this, identifiable data (NHS number and date-of-birth) will be supplied by the AMALFI team to NHS Digital, and used to trace and link to Hospital Episode Statistics, Office of National Statistics mortality data, and other sources of health information held by NHS Digital (such as medications and primary care records) for each person taking part. This is so that we can see if there are longer-term benefits of screening for atrial fibrillation.

Besides collecting information on new diagnoses of atrial fibrillation and other health conditions, we would also like to investigate the potential impact of this screening intervention on quality of life and use of the healthcare system. This information will help us understand the potential economic implications and benefits of screening. In order to do this, we will ask you to complete a brief questionnaire (called EQ-5D) approximately 2.5 and 5 years after your inclusion in the study. This may be done by post or using the internet.

We would like to know if you move address or change GP so we can continue to be in contact with you - if you have an email address this would be a very good way for us to stay in touch. However, if you change your mind and would like not to be contacted again, just let us know using the contact details at the back of this leaflet.

What are the risks?

The Zio Patch can cause an allergic reaction in those with known skin allergies e.g. to latex. If you know you have a skin allergy you should not take part in the study. The Zio Patch can also cause minor irritation to the skin. Patients with skin conditions such as psoriasis may want to consider not taking part as it is possible that the patch will make any existing skin conditions worse. Most mild skin conditions should be unaffected. If you are unsure about the effect on your skin or are worried about this you can always check with the study team.

Some people who want to take part in the study but are then included in the group who do not wear the Zio Patch may wonder about their chance of having an irregular heartbeat that is not detected. Overall, about 1 in 10 people over the age of 65 will develop atrial fibrillation over their lifetime. If you feel your pulse may be irregular or have any of the symptoms mentioned above you are still able to see your GP in just the same way you would do if you were not taking part in the study.

How do I take part?

If you would like to take part in the AMALFI study, the first step is to complete the consent form and questionnaire that provides us with some background information on your health. You will find these included in this pack. These need to be returned in the postage-paid envelope.

If you choose to join the study, we will contact you to let you know which group you have been assigned to.

If you have any questions about the process at any time or need help with any of the information you can find more details on the study website or can contact the study team (see back page of this booklet for all our contact details).

What happens at the end?

After the main 5-year follow-up phase of the study, we will inform you and your GP of the results. We plan to publish the results of the study in professional medical journals and also to present them to international healthcare audiences. No personal identifiable information will be published or presented at any time.

If the study shows this approach to screening appears to be successful and cost-effective, we will consider how to implement screening on a larger scale across the United Kingdom including the feasibility of a national screening programme.

What if new information becomes available?

Sometimes during long-term studies new information comes to light that might affect the current treatment you are receiving. If this does happen we will tell you and your GP and let you know how it might impact on your involvement in the study.

What if something goes wrong?

You retain all your usual rights as an NHS patient. The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of any clinical treatment provided by your GP as a result of taking part in this study.

If you do have any concern about taking part or if you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the AMALFI research team, by calling Freephone 0808 164 5080 or by email using amalfi@ndph.ox.ac.uk. Alternatively you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480, or the head of CTRG, email ctrg@admin.ox.ac.uk.

Will my taking part be kept confidential?

Yes, protecting your personal data is very important to us. Personal information will only be shared with your GP and NHS Digital so that we can ensure you receive the best possible healthcare as a result of the information we collect. We will also need to access your medical data from your GP and from NHS Digital for Hospital Episode statistics and Office of National Statistics mortality data. For this we will need to share identifiable data (NHS number and date-of-birth). All information collected will be held securely in a database by the study team on computer servers managed by the University of Oxford and used only for the medical research purposes outlined in this study. The data will be analysed by appropriately qualified clinicians and statisticians and will only be used for the AMALFI study. We plan to keep the data we collected about you for least 25 years after the end of the study, but this will not be identifiable. By signing the consent form to take part you are giving our team permission to use your data in this way. If you decide that you do not want any more information to be collected about you, the University of Oxford may be obliged by law to keep the information already gathered about you to ensure consistency and reproducibility of the study results.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is *a task in the public interest*. The University of Oxford is the data controller and is responsible for looking after your information and using it properly.

We will be using information from you, your medical records and NHS Digital, and will use the minimum personally-identifiable information possible. We will keep identifiable information about you for up to 12 months after the study has finished. However, we will store the de-identified research data and any research documents with personal information, such as consent forms, securely at the University of Oxford for 25 years after the end of the study as part of the research record. Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights

You can find out more about how we use your information by contacting amalfi@ndph.ox.ac.uk

Study organisation

The AMALFI study has been designed and is run by researchers at the University of Oxford's Clinical Trial Service Unit and the Division of Cardiovascular Medicine, which are world-leading centres for this type of work. The study is led by Professor Louise Bowman and Professor Barbara Casadei and involves local cardiology and General Practice specialists as well as partnership work with many other local doctors, nurses and healthcare professionals.

The study has been approved by London - Bromley Research Ethics Committee (Ref. No 19/LO/0220), an independent committee, which includes medical professionals and members of the general public. The Ethics Committee has reviewed all the study documentation as well as checking that the question the study is hoping to answer is important enough to warrant the research being undertaken.

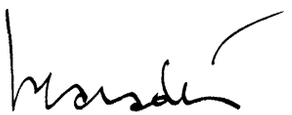
AMALFI is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre, Oxford. Government funding is provided to the NIHR with the aim of supporting new research and making sure the results of research studies go towards improving the healthcare received on a day-to-day basis in the United Kingdom. The study was designed and is run completely independent of iRhythm, the company who make the Zio Patch, however they are donating the Zio Patches free of charge.

Thank you

Our aim is to make your participation an interesting and worthwhile experience, while helping us work out ways of reducing the chance of you and other people having a stroke or other vascular problems.

Thank you for your interest in this study,

Professor Louise Bowman



Professor Barbara Casadei

"We hope this information may lead to better medical care for millions of people in the future and possibly even a new national screening programme"

Professor Louise Bowman and Professor Barbara Casadei

More information is available from the AMALFI research team:

	Freephone 0808 164 5080
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	www.amalfitrial.org

Questions about the study should be directed to the coordinating centre in Oxford

By phone:
24-hour Freephone service:
0808 164 5080

By post:
AMALFI
Clinical Trial Service Unit (CTSU)
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University of Oxford
Roosevelt Drive
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OX3 7LF

By email:
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Or visit our website:
www.amalfitrial.org