PARTICIPANT INFORMATION SHEET

1. *Title of Study*

Brain Natriuretic Peptide (BNP) for Personalised Primary Prevention in Diabetes (4P study)

Chief Investigator: Professor Allan Struthers

2. Invitation

You are being invited to take part in a research study. This study will form part of a doctorate in medicine degree for Dr Chong. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask if there is anything that is not clear or if you would like further information. Take time to decide whether you wish to take part.

3. What is the purpose of the study?

Diabetes mellitus is known to affect various organs in the body including the heart and this happens over years despite good control of diabetes mellitus. This may also occur without the presence of any underlying symptoms.

The purpose of this study is to identify if there are accurate markers in your blood, such as BNP, that might help early identification of any underlying heart disease without you being aware of it. This would be correlated with echocardiography (scan of your heart) test.

4. Why have I been invited?

You have been invited because you have type 2 diabetes. There are two main types of diabetes – type 1 and type 2. Type 2 diabetes occurs when the body doesn't produce enough insulin, or the body's cells don't react to insulin.

5. Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form, and will be given this information sheet and a signed consent form to keep. If you decide to take part you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive from the NHS.

6. What will happen to me if I take part?

If you agree to take part, a member of the research team will obtain informed consent from you and you will get an opportunity to ask any questions to the researchers. If you consent to taking part in the study,

a date will be arranged as per your convenience, for you to come to Ninewells Hospital for 2-3 hours, where the research team will conduct some tests. A number of tests outlined below will be conducted; however if your clinic blood pressure (BP) is elevated we may require you to wear a small portable device to monitor BP for 24 hours and return the next day for the rest of the tests. If you are unable to tolerate 24 hour BP monitoring you will be given a home BP monitor and instructions on how to record this information by the doctor. We will take 20 millilitres (4 teaspoons) of blood which we will test for some routine and some research blood tests for your heart. You will undergo an electrocardiogram (ECG) that records the electrical activity of the heart. You will be also asked to hand in a urine sample.

The research bloods that will be taken will be stored for analysis after the trial has ended. Following completion of the trial we may test for additional markers of interest on any left-over blood which will be stored anonymously in the secure Dundee University laboratory in the Division of Cardiovascular and Diabetes Medicine, which is under the governance of the Tayside Tissue Bank. Should any of the left over blood be used for future genetic analysis that sample will be fully anonymised and will be subject to approval of a Research Ethics Committee prior to this DNA analysis. The results of any future genetic tests would not be linked to your records and you would not receive any information about the results. You can opt not to have this done without affecting your participation in the study.

Following this, Dr Chong will do a scan of your heart or Echocardiogram. To assess whether the blood flow in your heart is optimal, we will gradually inject a medicine called Dobutamine through a cannula in your arm and then repeat the echocardiogram. Multiple ECG leads will be placed on your chest to monitor the heart rhythm; excess chest hair may sometimes have to be removed to facilitate this. Your blood pressure and ECG will be monitored throughout the test. Dobutamine causes the heart to beat faster and will mimic the effects of exercise on the heart. This procedure will cause your heart to race a little, but it should not be uncomfortable. Dr Chong is trained and qualified to perform these procedures. You will then be allowed to go home in around an hour's time. We would recommend that you be taken home by a taxi that we will pay for. Before you leave you will be given a 24 hour BP monitor or a home BP monitor (as detailed above) if not already done. The BP monitor can either be dropped off at Ninewells Hospital or the study team will arrange for it to be collected at your home.

In a few cases the above test may not give us definite technical information about the heart function. In that case we will arrange for you to attend Ninewells Hospital to get a further specialised scan of your heart either by a nuclear Myocardial Perfusion Scan (MPS) or a Computed Tomography Coronary Angiogram on another day. Images of your heart will be taken after injecting a special dye via a cannula in your arm. In a minority of patients, the MPS scan will need to be repeated on the next day.

7. Will my GP be notified?

With your permission only we will inform your GP of your participation in this study and let him or her know if there is any significant new abnormality in your blood tests or scan results.

8. What are the possible disadvantages of taking part?

You will be asked to fast (from midnight for a morning study and from 9am for an afternoon study visit) but may drink water freely in that time. However if you are unable to fast for these visits it will not prevent you from taking part in this study. In case you are on anti-asthma medicines like theophylline and heart rate slowing medicines like beta blockers, they would need to be withheld as they interfere with interpretation of your scan. If needed your diabetes medication will be adjusted for that part of the day. Discomfort associated with venepuncture will be minimised, as much as possible.

Echocardiogram is an ultrasound scan of heart which is very safe and has no known risks. As mentioned earlier, we will use a medicine called Dobutamine for this scan. Some patients may feel minor adverse effects of Dobutamine including palpitations, chest pain, shortness of breath, nausea, vomiting, dizziness and flushing. These are transient and will disappear within minutes after the test is completed. Leakage of the drug at the infusion site may cause temporary local pain.

Another medicine Atropine that is occasionally used in this test to augment the effect of Dobutamine may temporarily cause symptoms like dry mouth, blurring of vision and occasionally retention of urine. Because atropine persists for longer in the body than Dobutamine, these symptoms may last up to few hours after the test. Major complications are very rare (1 in 5000 chance of experiencing it).

Dr Chong and his team including a trained research nurse would be present all through your tests who are well experienced to deal with all these potential complications. Various medications are available to counter these problems in the unlikely event of their occurrence.

In case your Dobutamine stress echocardiography test is inconclusive you would have to come for a second time for another special nuclear scan of your heart either a Myocardial Perfusion Scan (MPS) or a CT Coronary angiography on a pre-appointed date and time. The choice of which test will be done will be down to availability of these in the NHS clinics concerned, the discussion you have with Dr Chong as to which may be more suitable for you, and off course which you would prefer if you have a strong preference for either and they are both available. Dr Chong will explain the procedures to you and offer you the opportunity to ask any questions that you might have about the procedures. The MPS will be done by NHS staff at Nuclear Medicine department at Ninewells Hospital as per arrangement by medical physicist Dr John Davidson and the CT coronary angiography will be done in the X-Ray department at Ninewells by radiology staff there.

The MPS scan will be done the same way it is done as a standard test in NHS and uses a radioactive dye and a medicine Dipyridamole that dilates the blood vessels of heart. The injectable radioactive dye is used as a "tracer," which means it travels through the blood stream and is taken up or absorbed by the heart muscle tissue. This test consists of two phases – the stress phase and the rest phase. The stress phase is usually performed first. If your scan shows straightforward pictures of your heart then the test ends there. This part of the test will usually take 2 to 4 hours. In some patients we may require additional information not available from the first scan on its own, so you will be asked to return for a second scan. This second scan will give extra information. On the scan (MPS), the areas where this tracer has been absorbed will

show up differently than the areas that do not absorb it (due to possible damage to the tissue, or from decreased or blocked blood flow).

The radioactive tracer given during the scan is low risk and is the same amount used for this scan when used in the NHS; the amount of associated radioactivity is moderate and the lifetime risk of developing cancer due to MPS is approximately 1 in 1700 people. This is much smaller than the lifetime risk of developing cancer in the UK, which is 4 in 10 people. Dipyridamole medicine is safe and tolerable. Some may experience minor side effects such as dizziness, headache, nausea and chest discomfort. These symptoms usually last only a few minutes. Major complications are very rare.

The CT Coronary Angiography test uses an x-ray machine to give a detailed 3D picture of your heart and blood vessels. To get the best pictures of your heart and how it is working, the radiologist may need to give you medication to slow your heart rate down (beta blockers) and medication to relax the arteries. In order for the scanner to get a clear picture of the heart, you are given a contrast agent through a small cannula in your vein in your arm. It is common to feel a warm sensation as this contrast agent passes through your body. Some patients may also experience a metallic taste in their mouth which lasts for less than a minute. During the test you will lie on a bed, in a well-lit spacious room. The bed will pass into a wide 'doughnut' shaped part of the scanner. You simply lie, take a deep breath and the images are taken.

A CT coronary angiogram is a routine medical procedure. The scan itself is associated with very few side effects. The most important potential side effect, as with any x-ray scan, is the use of radiation. The amount of radiation used during the scan varies but it is about 3 to 4 times the amount that you would normally receive in a year from background natural sources of radiation such as cosmic rays and rocks in the Earth's crust. On rare occasions, for example if you have a faster heart rate, a slightly larger amount of radiation may be used. The lifetime risk of developing cancer due to a CT scan would be approximately 1 in 1400 people. Again, this is much smaller than the lifetime risk of developing cancer in the UK, which is 4 in 10 people. There is also a small risk of developing a reaction to the contrast agent. This usually involves an itchy rash that settles down by itself. Occasionally people require additional medications for this. If you are known to be allergic to the contrast agent you will not be referred for this test. Some patients experience a transient headache after taking the medication (GTN) to relax the arteries.

If there is a significant finding during the procedure, the research team will discuss with you the further management plan.

If you develop any complications after you have left the hospital, please contact the research team on (01382) 383346 (Mon- Fri; 9am to 5pm and NHS-24 on 111 for out of hours emergencies).

9. What are the possible benefits of taking part?

This is a pilot study, which means that if we do get data suggesting that there are specific tests and markers that may predict heart disease in type 2 diabetes patients who have no symptoms suggestive of heart disease- we can then start them on medication to prevent them from developing life threatening events arising from the heart, if this is appropriate.

10. Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. The result of the study will in part be recorded in your medical notes. . A study identifier will be allocated to each participant. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised from it.

11. What will happen to the results of the research study?

The average results over 200 people will be presented at scientific meetings and published in scientific journals. You will not be identified in any journal articles or presentations.

12. Expenses

Taxi transport, or reasonable costs to cover your travel costs, will be provided for any visits to the hospital for the purposes of this study.

13. Who is funding and organising this research?

The study has been sponsored by the University of Dundee and NHS Tayside and is funded by the Scottish Government.

14. Who has reviewed this study?

The East of Scotland Research Ethics Service (REC 1), which has responsibility for scrutinising all proposals for medical research on humans in Tayside, has examined the proposal and has raised no objections from the point of view of medical ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from NHS Tayside, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

15. What if there is a problem?

Complaints, insurance and indemnity:

a. Right to raise concerns.

If you have any concerns about your participation in the study you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care.

b. Right to make a complaint

If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However you have the right to raise a formal complaint. You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Fife:

Patient Relations Department
Fife NHS Board
Room 104
Hayfield House
Hayfield Road
Kirckaldy
KY2 5AH
Phone: 01592 643355
Ext: 28153
Email: **patientrelations.fife@nhs.net**

c. Right to make a claim

In the event that you think you have suffered harm as a result of your participation in the study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation against the University of Dundee or NHS Tayside. Where you wish to make a claim, you should consider seeking independent legal advice but you may have to pay for your legal costs.

d. Insurance

The University of Dundee maintains a policy of professional negligence clinical trials insurance which provides both legal liability cover and no fault compensation in respect of accidental injury. Tayside Health Board is a member of the Clinical Negligence and Other Risks Insurance Scheme which provides legal liability cover.

16. Contact details for the study doctor

If you have any further questions about the study please contact

a) Dr Victor Chong

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Thank you for taking the time to read this information sheet.