Heart Function in patients assessed for Sleep Disordered Breathing (SDB)

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'A Study of Heart Function in patients assessed for Sleep Disordered Breathing (SDB)'

Prevalence and Prognosis of Heart Failure with Preserved Ejection Fraction (HFpEF) in patients assessed for Sleep Disordered Breathing (SDB)

Version 3.1 20/11/2017

MAIN SPONSOR: Imperial College London
STUDY COORDINATION CENTRE: Royal Brompton Hospital
NRES reference: 17/SC/0320

Protocol authorised by:

Name & Role	**Date**	**Signature**

Study Management Group

Chief Investigator:	Professor Martin Cowie
Co-investigators:	Professor Anita Simonds Dr Angela Gallagher
Statistician:	Mr Winston Banyan

Study Coordination Centre

For general queries, supply of study documentation, and collection of data, please contact:

Study Coordinator:	Dr A Gallagher
Address:	Royal Brompton Hospital, Sydney Street, London SW3 6NP
Tel:	020 7352 8121 ext. 2003
Fax:	02073518148
E-mail:	angela.gallagher02@imperial.ac.uk

Clinical Queries

Clinical queries should be directed to Dr A Gallagher who will direct the query to the appropriate person.

Sponsor

Imperial College London is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

Joint Research Compliance Office
Imperial College London & Imperial College Healthcare NHS Trust
2nd Floor Medical School Building
St Mary's Hospital
Praed Street
London
W2 1NY
Tel: 020 7594 1862

This protocol describes the 'Prevalence and Prognosis of Heart Failure with Preserved Ejection Fraction (HFpEF) in patients assessed for Sleep Disordered Breathing (SDB)' study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the NHS Research Governance Framework for Health and Social Care (2nd edition). It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

Table of Contents

GLOSSARY OF ABBREVIATIONS

SDB	Sleep Disordered Breathing
OSA	Obstructive sleep apnoea
CSA	Central sleep apnoea
HFpEF	Heart Failure with preserved ejection fraction
HFrEF	Heart Failure with reduced ejection fraction
AHI	Apnoea-hypopnoea index
LVEF	Left ventricular ejection fraction

STUDY SUMMARY

TITLE Prevalence and Prognosis of Heart Failure with Preserved Ejection Fraction (HFpEF) in patients assessed for Sleep Disordered Breathing (SDB)

DESIGN Prospective observational study

AIMS

1. To establish the prevalence of HFpEF among patients being investigated for SDB.
2. To examine the type and severity of SDB in patients identified with HFpEF.
3. To characterise the phenotype of the patients that are identified with HFpEF
4. To determine the prognosis of patients with HFpEF based on hospitalisation and mortality data.

OUTCOME MEASURES Primary Outcome measure:

1) Number of patients with diagnostic criteria for HFpEF

Secondary outcome measures:

1) The number of patients with SDB and the proportion of OSA and CSA.
2) Apnoea-hypopnoea index (AHI) as an indicator of SBD severity.
3) The frequency of cardiac co-morbidities including hypertension, coronary artery disease, diabetes and atrial fibrillation.
4) Rate of hospitalisation and mortality over 12 months.

POPULATION Patients referred for respiratory polygraphy at the Royal Brompton Hospital

ELIGIBILITY Patients ≥40 years without pre-existing treated SDB or heart failure

DURATION 20 months

1. INTRODUCTION

1.1 BACKGROUND

Daytime somnolence, fatigue and feeling unrefreshed on waking are typical symptoms of sleep disordered breathing (SDB). Respiratory polygraphy, performed either in hospital or at home, readily allows confirmation of the diagnosis. Obstructive sleep apnoea (OSA) and central sleep apnoea (CSA) are two types of SDB. In OSA there is collapse of the pharynx leading to partial or complete airway obstruction, whilst in CSA there is abnormality in the neural brainstem control of breathing. Although the mechanisms of obstructive and central apnoea differ, they both result in in repetitive reduction (hypopnoea) or cessation of breathing (apnoea). This in turn can cause sleep fragmentation, exaggerated negative intra-thoracic pressure swings, intermittent hypoxia and sympathetic nervous system activation, which can have detrimental effects on the cardiovascular system [1].

Whilst performing a respiratory polygraphy allows accurate diagnosis of SDB it does not address potential underlying cardiovascular disease in the same patient. It is well – established that SDB is common among patients with heart failure, both with reduced (HFrEF) and preserved ejection fraction (HFpEF) [2]. SDB may occur as a consequence of heart failure, but has also been implicated in its progression. Bitter et al studied SDB in patients with heart failure with normal ejection fraction identifying its prevalence in 69% of individuals [3]. Central sleep apnoea, which is principally linked with heart failure, is independently associated with a worse prognosis, including mortality.

Heart failure with preserved ejection fraction (HFpEF) accounts for up to half of all heart failure cases and is associated with significant morbidity and mortality [4]. It can be challenging to diagnose as it can present with non-specific symptoms, be obscured by concomitant diseases and there is a lack of a simplified diagnostic test. Unrecognised heart failure, predominately with preserved ejection fraction, was shown to be present in 1 in 6 primary care patients with breathlessness on exertion [5]. In 2016 the European Society of Cardiology (ESC) set out updated diagnostic criteria for HFpEF. This combined the signs and symptoms of heart failure, left ventricular ejection fraction (LVEF) ≥50%, elevated natriuretic peptide levels, and relevant structural disease or diastolic dysfunction [6].

The phenotype of patients with SDB and those with heart failure with preserved ejection fraction (HFpEF) share similar characteristics [7]. Increasing age, hypertension, obesity, diabetes mellitus and atrial fibrillation are well recognised links in both groups. It has been shown that in patients with similar co-existent diseases, the added presence of heart failure with preserved ejection fraction results in higher morbidity and mortality rates [8].

1.2 RATIONALE FOR CURRENT STUDY

Previous studies have evaluated the prevalence of SDB in patients known to have HFpEF, but not vice versa. Given the relationship between the two conditions and their similar phenotypes, we hypothesise that a subset of patients with unrecognised HFpEF can be identified in the population being investigated for SDB. We aim to determine the prevalence of patients with diagnostic criteria for HFpEF and examine the relationship with SDB. We will also collect prognostic data on hospitalisations and mortality over a 12 month period. This will allow inferences to be made as to whether this population should be targeted for screening for HFpEF.

2. STUDY OBJECTIVES

2.1 PRIMARY OBJECTIVE

- To identify patients with diagnostic criteria for HFpEF and establish the prevalence.

2.2 SECONDARY OBJECTIVES

- To examine the type and severity of SDB in patients identified with HFpEF.
- To characterise the phenotype of the patients that are identified with HFpEF.
- To determine the prognosis of patients with HFpEF based on hospitalisation and mortality data.

3. STUDY DESIGN

This is a prospective, observational study. The aim will be to recruit 155 patients and to collect prognostic data over a 12 month period from the participant's enrolment.

We will recruit patients referred for respiratory polygraphy, as part of their standard clinical care, at the Royal Brompton Hospital Sleep Centre. These patients would be symptomatic or be at moderate or high risk for SDB. Patients eligible will be ≥ 40 years with no history of pre-existing heart failure with reduced ejection fraction or treated sleep disordered breathing.

The patients will have a respiratory polygraphy (Embletta MPR) performed either in-hospital or at home as part of their usual care. The respiratory polygraphy involves recording nasal air flow, snore sensor, pulse oximetry, chest and abdominal movement. It is a validated for screening for sleep disordered breathing, distinguishing between obstructive sleep apnoea (OSA) and central sleep apnoea (CSA). Hypopnoea will be defined as a 30% reduction in airflow in combination with at least 3% oxygen desaturation. Apnoea will be defined as a cessation of airflow for >10 s, and in case of CSA without any thoracic or abdominal breathing effort. The apnoea-hypopnoea index (AHI) will be used to assess the severity of SDB with the following classification: Mild 5-14/h, moderate 15-30/h and severe >30/h. Patients will be classified as OSA or CSA depending on the majority of events.

On attendance for respiratory polygraphy the following investigations will be performed:

1. Each patient will have documentation of their symptoms, medical diagnoses, medications and social history. A clinical cardiovascular examination will be performed.

2. Two symptom questionnaires will be completed. The Epworth Sleepiness questionnaire will assess daytime somnolence and is standard practice in SDB assessment. The SF-36 Questionnaire will assess indices of quality of life.

3. Biomarker assessment of heart failure will be performed by taking a single venous blood sample for plasma N-terminal-pro BNP (NT-proBNP) level and Growth Differentiation Factor-15 (GDF-15).

4. An electrocardiogram (ECG) will be carried out for documentation of cardiac rhythm.

5. Echocardiography will be performed for assessment of structural heart disease and diastolic function in accordance to standard techniques. Parameters assessed will include: Left ventricular ejection fraction (LVEF), left ventricular diastolic function (E/A, DT, E' septal. E' lateral, E/E'), left ventricular wall thickness/mass, left atrial size and right ventricular (RV) function.

The criteria for heart failure with preserved ejection fraction will be in accordance to European Society of Cardiology guidelines as set out: Presence of symptoms and/or signs of heart failure, LVEF ≥50%, elevated levels of natriuretic peptides, and relevant structural disease or diastolic dysfunction.

All recruited patients will be contacted by telephone at 3 monthly intervals over the next 12 months. Information recorded will include symptoms, new diagnoses, medication changes and hospitalisations. Additional data from hospital records and GP records will be used to verify the number of hospitalisations, the reason for admission and the outcome. This method will also be used to collect mortality data and if required certification information will be sought from the General Register Office.

4. PARTICIPANT ENTRY

4.1 INCLUSION CRITERIA

Patients aged ≥ 40 years referred for a respiratory polygraphy at the Sleep Centre at the Royal Brompton Hospital.

4.2 EXCLUSION CRITERIA

Patients with known heart failure and those receiving treatment for pre-existing sleep disordered breathing.

5. ADVERSE EVENTS

5.1 DEFINITIONS

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): any untoward and unexpected medical occurrence or effect that:

- Results in death
- Is life-threatening – *refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe*
- Requires hospitalisation, or prolongation of existing inpatients' hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital anomaly or birth defect

Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, will also be considered serious.

5.3 REPORTING PROCEDURES

All adverse events should be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

5.3.1 Non serious AEs

All such events, whether expected or not, should be recorded.

5.3.2 Serious AEs

An SAE form should be completed and faxed to the Chief Investigator within 24 hours. However, relapse and death due to pre-existing conditions, and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

All SAEs should be reported to the South Central-Oxford B REC where in the opinion of the Chief Investigator, the event was:

- 'related', i.e. resulted from the administration of any of the research procedures; and
- 'unexpected', i.e. an event that is not listed in the protocol as an expected occurrence

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify the Sponsor of all SAEs.

Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Contact details for reporting SAEs

Please send SAE forms to:

Professor Cowie
Imperial College London
National Heart & Lung Institute
Dovehouse Street
London
SW3 6LY

Fax: 020 7351 8148, F.A.O. Professor Cowie

Tel: 020 73518856 (Mon to Fri 09.00 – 17.00)

6. ASSESSMENT AND FOLLOW-UP

We will be conducting telephone calls at 3 monthly intervals following the patient's enrolment to collect information related to the patient's health and hospitalisation history. The patient's involvement in the study will be concluded following the final telephone contact at month 12.

Any cardiovascular findings requiring follow-up will be reported to the patient's usual clinical care team and General Practitioner.

The follow-up of patients from a sleep disordered breathing perspective will be directed by their usual clinical care team.

7. STATISTICS AND DATA ANALYSIS

The prevalence of HFpEF in this population has not previously been defined. In this study if we assume the prevalence of HFpEF to be 10% and if the precision of this estimate is within 5% then for a 95% confidence interval, the required sample size will be 139 subjects. Assuming a 10% drop out, we would require a final sample size of 155.

The primary outcome will be presented as a proportion. For the prognostic data, categorical data will be presented as frequency (percentage) and the survival pattern described using the log rank test and Kaplan-Meier survival plots.

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

8. REGULATORY ISSUES

8.1 ETHICS APPROVAL

The Chief Investigator has obtained approval from the South Central Oxford B Research Ethics Committee. The study must be submitted for Site Specific Assessment (SSA) at each participating NHS Trust. The Chief Investigator will require a copy of the Trust R&D approval letter before accepting participants into the study. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

8.2 CONSENT

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration. Signed participant consent should be obtained. The right of the participant to refuse to participate without giving reasons must be respected. After the participant has entered the study the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In these cases the participants remain within the study for the purposes of follow-up and data analysis. All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

8.3 CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

8.4 INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

8.5 SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

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8.6 AUDITS

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

9. STUDY MANAGEMENT

The study will be co-ordinated by Dr Angela Gallagher, Clinical Research Fellow, Royal Brompton Hospital, Sydney Street, London, SW3 6NP. Tel: 0207 3528151 ext. 2003; Fax: 02073518148.

10. PUBLICATION POLICY

It is anticipated that the study's results will be published in peer-reviewed journals, presented at scientific meetings and submitted as part of MD (Res) thesis.

11. REFERENCES

1. Cowie, M. R. (2017) Sleep apnea: State of the art. Trends in Cardiovascular Medicine. 27 (4), 280-289

2. Pearse SG, Cowie MR. Sleep-disordered breathing in heart failure. Eur J Heart Fail. 2016;18(4):353-61

3. Bitter, T., Faber, L., Hering, D., Langer, C., Horstkotte, D. & Oldenburg, O. (2009) Sleep-disordered breathing in heart failure with normal left ventricular ejection fraction. European Journal of Heart Failure. 11 (6), 602-608.

4. Owan, T. E., Hodge, D. O., Herges, R. M., Jacobsen, S. J., Roger, V. L. & Redfield, M. M. (2006) Trends in prevalence and outcome of heart failure with preserved ejection fraction. The New England Journal of Medicine. 355 (3), 251-259.

5. van Riet, E. E., Hoes, A. W., Limburg, A., Landman, M. A., van der Hoeven, H. & Rutten, F. H. (2014) Prevalence of unrecognized heart failure in older persons with shortness of breath on exertion. European Journal of Heart Failure. 16 (7), 772-777.

6. Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G., Coats, A. J., Falk, V., Gonzalez-Juanatey, J. R., Harjola, V. P., Jankowska, E. A., Jessup, M., Linde, C., Nihoyannopoulos, P., Parissis, J. T., Pieske, B., Riley, J. P., Rosano, G. M., Ruilope, L. M., Ruschitzka, F., Rutten, F. H., van der Meer, P., Authors/Task Force Members & Document Reviewers. (2016) 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European Journal of Heart Failure. 18 (8), 891-975.

7. Triposkiadis, F., Giamouzis, G., Parissis, J., Starling, R. C., Boudoulas, H., Skoularigis, J., Butler, J. & Filippatos, G. (2016) Reframing the association and

significance of co-morbidities in heart failure. European Journal of Heart Failure. 18 (7), 744-758.

8. Campbell RT, Jhund PS, Castagno D, Hawkins NM, Petrie MC, McMurray JJ. What have we learned about patients with heart failure and preserved ejection fraction from DIG-PEF, CHARM-preserved, and I-PRESERVE? J Am Coll Cardiol. 2012;60(23):2349-56.

Appendix 1. Schedule of events table

		Month			
	Baseline Visit	3	6	9	12
Informed consent	X				
History & Examination	X				
Symptom Questionnaires	X				
Blood test (NT-proBNP & GDF-15)	X				
ECG	X				
Echocardiogram	X				
Sleep Study Test	X				
Telephone Call		X	X	X	X

Appendix 2. Patient Information Sheet (PIS)

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

IRAS ID Number: 228728

Participant Information Sheet (PIS)

A study of Heart Function in patients assessed for Sleep Disordered Breathing (SDB)

Invitation to participate in the above study:

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it will involve for you. Please take time to read the following carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?

The purpose of this study is to find out about the heart function of patients who have been referred for a sleep study test as part of their normal clinical care.

Sleep disordered breathing (SDB), also known as sleep apnoea, causes typical symptoms of daytime sleepiness, fatigue and feeling unrefreshed on waking. SDB results in brief pauses or reduced airflow during breathing. This can have potential negative effects on the heart and the body's blood supply. Sleep study tests performed either in hospital or at home readily allow the diagnosis of SDB to be made. However, they do not provide information on the heart function.

In this study we would like to screen the heart function of patients referred for a sleep study test. In particular this will focus on a condition called heart failure. This is a common heart condition in the older population and can cause symptoms of breathless, tiredness and sometimes disturbed sleep. The aim will be to find out if this condition is present in patients being investigated for SDB. The goal will be to find out how often it occurs, investigate its relationship with SDB and to collect information on the outcomes of patients.

This study will be part of an educational project linked to an MD research programme.

What will happen if I am diagnosed with abnormal Heart Function?

If any abnormality of your heart function is detected, or diagnostic criteria for heart failure is met, your usual doctor or GP will be informed. This will allow appropriate follow-up and management for your heart function to be put in place.

Why have I been invited?

You are being asked to take part as you have been referred for a sleep study test and are aged 40 years or older. This study will involve 155 participants.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form to show you have agreed to take part. You may choose not to participate in this study or you may leave the study at any time without giving a reason. This would not affect the standard of care you receive.

What will happen to me if I take part?

You have been referred for a sleep study test by your doctor to investigate sleep-disordered breathing. Taking part in the study will not affect the management of this.

In addition to your sleep study test we will organise the following when you attend for your appointments:

1. Meet a member of the research team to discuss the study and consent form in more detail. If you chose to participate you will be asked to sign the consent form.

2. Discuss your medical history, medications and perform a routine medical examination which will take around 20 minutes.

3. You will be asked to complete two symptom questionnaires, one of which is standard when having a sleep study test. Together these will take about 15 minutes.

4. You will be requested to have a blood test to look for two protein markers of heart failure. Only a small sample will be required.

5. You will be requested to have an electrocardiogram (ECG), which is a painless, non-invasive test to check your heart rhythm, taking about 5 minutes.

6. You will be requested to have an echocardiogram, which is a non-invasive ultrasound scan of the heart taking about 40 minutes

After your sleep study test we will phone you every 3 months over the next year to find out how you are. We would like to record if you started any new medications, had any new diagnoses or admissions to hospital. In total this will be 4 phone calls, each taking about 10 minutes. We may also need to contact your GP, access your hospital records or seek

information from the General Register Office to gain a complete picture of how you have been over the year.

Expenses and payments

You will not receive any payment for taking part in this study.

What do I have to do?

Involvement in this study should not impose any restrictions to your current lifestyle. There are no specific dietary restrictions. You can drive, drink, take part in sport or indeed do anything that follows the advice given to you by your doctor, taking into consideration any medical conditions. Your treatment will not be altered.

What are the alternatives for diagnosis or treatment?

You do not have to participate in this study for diagnosis and treatment of sleep apnoea.

What are the possible disadvantages and risks of taking part?

There are no disadvantages of taking part. The ECG and echocardiogram are both non-invasive and safe tests. The blood test will be taken by a trained professional using standard safety precautions.

What are the possible benefits of taking part?

You will have an assessment of your heart function. As mentioned before, if this shows any significant abnormalities your doctor will be informed. This will allow any appropriate follow-up appointments to be put in place.

What happens when the research study stops?

At the end of the research, your care will continue as usual.

What if relevant new information becomes available?

Sometimes during the course of a research study, new information becomes available about the condition that is being studied. If this happens, we will tell you about it and discuss with you whether you want to continue in the study. If you decide not to carry on we will make arrangements for your care to continue. If you decide to continue in the study you may be asked to sign an updated consent form. Also, on receiving new information we might consider it to be in your best interests to withdraw you from the study. We will explain the reasons and arrange for your care to continue.

What will happen if I don't want to carry on with this study?

If you do not want to take part in this study, you will receive standard care as determined by your doctor. Your participation in this study is voluntary and you may withdraw from the study at any time without prejudice to your future medical care. Should you decide to withdraw from the study for any reason, you are asked to contact Dr Angela Gallagher

immediately. Should your participation in the study be terminated, regardless of the reason, you will not suffer any penalties or loss of benefits to which you are otherwise entitled.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (Dr Angela Gallagher 0207 352 8121 ext. 2003). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure (and also by speaking with the Patient Advice and Liaison Service (PALS) at the Royal Brompton Hospital on 0207 349 7715).

Harm:

Imperial College holds Public Liability ("negligent harm") and Clinical Trial ("non-negligent harm") insurance policies which apply to this trial. If you can demonstrate that you experienced harm or injury as a result of your participation in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. If the injury resulted from any procedure which is not part of the trial, Imperial College will not be required to compensate you in this way. Your legal rights to claim compensation for injury where you can prove negligence are not affected

Will my taking part in the study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name, address and personal details removed so that you cannot be recognised from it. The data collected and analysed will be anonymised meaning that no names will be used. Any documents with personal details will be destroyed after 12 months i.e. following your final contact with the research team.

Will my General Practitioner (GP) / Family Doctor be informed of my involvement?

Provided you consent to this, your GP will be informed that you are participating in the study and will be updated of your medical progress. We will also request information from your GP about any hospital admissions or other health problems that you have had.

What will happen to any samples I give?

A blood sample will be taken to look for two markers of heart failure. The sample will be processed at the Royal Brompton & Harefield NHS Trust laboratory. The sample will not be kept for future research and will be destroyed as per the usual Royal Brompton & Harefield Laboratory procedure.

Will any genetic tests be done?

No

What will happen to the results of the research study?

Your medical records will be made available for review by the study investigators and regulatory authorities (who periodically check that the studies are being carried out correctly). This information will be kept confidential. At the end of the project all the research results are gathered together and analysed. The researchers have a professional responsibility to publish their findings, however your identity will not be revealed. Most research is published in the medical press – if you are interested in knowing the overall results of the study, ask the researchers about this. You are entitled to see any results or information about you under the Freedom of Information Act.

Who is organising and funding the research?

Imperial College London is sponsoring the research. The doctors conducting the research are not being paid for including you in the study.

Who has reviewed the study?

All research in the NHS is looked at by an Independent group of people, called a Research Ethics Committee (REC) to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favorable opinion by the South Central Oxford B Research Ethics Committee. In addition approval has been gained from local Research & Development (R&D) Offices.

Further Information and Contact Details

If you would like any further information about the study, either now or at time during the course of the study, please ask a member of the Research Team: Dr. Angela Gallagher, Clinical Research Fellow, Department of Cardiology, Royal Brompton Hospital, Sydney Street, London, SW3 6NP. 0207 3528151 ext. 2003.

Thank you for taking the time to consider this study. If you do choose to participate, you will be given a copy of this information sheet to keep and also a copy of the consent form that you will be asked to sign.

Appendix 3. Patient Invitation Letter

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

IRAS ID Number: 228728

PATIENT LETTER

Dr <name>
<address>
<address>
<address>

<date>

Dear <name>,

A study of Heart Function in patients assessed for Sleep Disordered Breathing (SDB)

We are writing to invite you to consider taking part in the above research study at the Royal Brompton & Harefield NHS Foundation Trust. You have been identified as a possible participant for this study as you have been referred by your doctor for a sleep study test. Taking part in the study is completely voluntary. If you do not wish to be involved, this will have no effect on your medical care.

The purpose of this study is to find about the heart function of patients who have been referred a sleep study test as part of their normal clinical care.

I have enclosed an information leaflet that explains the study in more depth. If you are interested in participating or would like to be contacted with more details please complete the tear-off form below and return the letter in the stamped addressed envelope provided or contact the research fellow Angela Gallagher on tel. no: 0207 352 8121 ext. 2003. On receipt of this form, one of the study team will contact you and provide you with further information.

Completion and return of this form does not oblige you in any way to take part in the study if you decide you do not wish to.

Yours sincerely,

Dr Angela Gallagher
Clinical Research Fellow

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I………………………………, am interested and would like member of the study team to contact me.

My phone number is…………………………

I understand that this expression of interest places me under no obligation to take part in the trial.

Appendix 4. GP Letter

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

Royal Brompton Hospital
Sydney Street
London
SW3 6NP

IRAS ID Number: 228728

GP LETTER

Dr <name>
<address>
<address>
<address>

<date>

Dear Dr <name>,

Re: Patient Forename SURNAME, DOB, Address

A study of Heart Function in patients assessed for Sleep Disordered Breathing (SDB)

We are writing to inform you that your patient has kindly agreed to participate in the above research study at the Royal Brompton & Harefield NHS Foundation Trust. Your patient was enrolled into the study on **<date>**. We plan to recruit 155 patients into the study and collect data over a 12 month period. Ethical approval for this study has been granted by South Central Oxford B Research Ethics Committee.

The aim of this study is to determine the prevalence of heart failure with preserved ejection fraction (HFpEF) in the cohort of patients being investigated for sleep disordered breathing. The patients will be assessed with symptom questionnaires, an ECG, echocardiogram and N-Terminal Pro-BNP (NT-proBNP) and Growth Differentiation Factor-15 (GDF-15) level when attending for their sleep study test. You will be informed of any significant diagnostic findings from these tests. We would also like to collect prognostic data on hospitalisation and mortality. We will arrange telephone consultations with the patients at 3 monthly intervals and may contact you to ask for information about significant medical events that may occur during the course of the study.

We shall inform you of any relevant medical changes in the patients' status that may occur during the course of the study.

If you want any further details about the study, the involvement of your patient, or you wish to see a more detailed description of the study, please contact a member of the Research team.

Enclosed with this letter is the study Participant Information Sheet (PIS) for your reference.

Yours sincerely,

Dr Angela Gallagher
Clinical Research Fellow

Appendix 5. Consent Form

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

IRAS ID Number: 228728

REC Reference Number: 17/SC/0320

Patient Identification Number for this trial: _____

INFORMED CONSENT FORM

Study Title: A study of Heart Function in patients assessed for Sleep Disordered Breathing (SDB)

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated Day Month Year (Version x.x) for the above study and have had the opportunity to consider the information, ask questions and have these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from Royal Brompton & Harefield NHS Foundation Trust, Imperial College London or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
4. I agree to my GP being informed of my participation in the study. ☐
5. I agree to take part in the above study. ☐

_____	_____	_____
Name of Patient		Date Signature
_____	_____	_____
Name of person taking consent	Date	Signature

When completed 1 copy for patient; 1 copy for researcher; 1 (original) copy to be kept with hospital