Cedar

Healthcare Technology Research Centre

CALON

Cardiac Ablation: Linking Outcomes for NICE

Efficacy and Safety Outcomes of Cardiac Ablation Procedures

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Summary

CALON is a pilot study using existing routinely collected data in Wales to obtain information on outcomes of NHS cardiac ablation procedures.

The two main aims of the CALON project were to:

- find out more information about how well cardiac ablation procedures work and how safe they are.
- assess the value of using data linkage, a method of linking patient records, as a method for healthcare research in support of IP guidance.

Abnormal heart rhythms can cause unpleasant symptoms such as chest pain, headache and tiredness. Cardiac ablation is a type of procedure which treats abnormal heart rhythms by destroying sections of tissue in the heart. The National Institute for Health and Care Excellence (NICE) recommend that some cardiac ablation procedures are only used in certain circumstances, as there is currently limited evidence on how well they work and/or how safe they are. We looked at existing health records to try to address these questions. The main results indicated a reduction in utilisation of secondary care services (outpatient appointments and inpatient stays) after an ablation procedure when compared to before the ablation. This report is a summary of these and other findings.

We also assessed the method of linking patient records as a research technique. Patients were identified in a specialist register and hospital records, and then followed-up using hospital and GP records. Linkage was carried out without researchers knowing the patient's name (or other key details), so that no individual could be personally identified. The main lessons learned about data linkage as a general methodology have been collated into a separate report, which is in the form of a data linkage toolkit. This efficacy and safety report concludes with a discussion about some of the benefits and challenges of applying data linkage within the context of this particular study, and suggestions for the future.

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Abbreviations

AF	Atrial fibrillation
ALF	Anonymised linking field
ART	Atrioventricular reciprocating tachycardia
AVNRT	Atrioventricular nodal reentrant tachycardia
CALON	Cardiac Ablation: Linking Outcomes for NICE
CG	Clinical Guidance
CRM	Cardiac Rhythm Management
DAPP	Data Anonymisation Policy and Process
DVLA	Driver and Vehicle Licensing Agency
HES	Hospital Episode Statistics
HIRU	Health Information Research Unit
HQIP	Healthcare Quality Improvement Partnership
ICD-10	International Classification of Diseases, version 10
IGRP	Information Governance Review Panel
IPG	Interventional Procedure Guidance
MINAP	Myocardial Infarction National Audit Project
NICE	National Institute for Health and Care Excellence
NICOR	National Institute for Cardiovascular Outcomes Research
NRES	National Research Ethics Service
NWIS	NHS Wales Informatics Service
OPCS	OPCS Classification of Interventions and Procedures
PEDW	Patient Episode Database for Wales
PROMs	Patient Reported Outcome Measures
SAIL	Secure Anonymised Information Linkage
SPSS	Statistical Package for the Social Sciences
SQL	Structured Query Language, a programming language
SVT	Supraventricular tachycardia
VT	Ventricular tachycardia
WDS	Welsh Demographic Service

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CALON - Cardiac Ablation: Linking Outcomes for NICE

1 Introduction

1.1 Aims

CALON is a pilot study using existing routinely collected data in Wales to obtain additional information on outcomes of NHS cardiac ablation procedures.

The two main aims of the CALON project were to:

- find out more information about how well cardiac ablation procedures work and how safe they are.
- assess the value of using data linkage, a method of linking patient records, as a method for healthcare research in support of IP guidance.

This document reports our findings on the safety and efficacy of cardiac ablation, and our experience of using data linkage within this specific context. It is anticipated that subsequent publications will focus in more detail on some of the efficacy and safety results being introduced in this report, with a greater emphasis on the wider implications for patients, clinicians, health services and policy makers. The accompanying data linkage toolkit reports the main lessons learned about data linkage more generally; it includes information about the methodology using in this project as well as broader considerations that might apply to future projects.

1.2 Cardiac arrhythmias

Cardiac arrhythmias are abnormal heart rhythms; the heart may beat too fast (tachycardia), too slowly (bradycardia) or irregularly (fibrillation). Arrhythmias happen when there is abnormal electrical activity within the heart, and can have a wide range of causes including genetic and acquired conditions.

The frequency and duration of arrhythmias varies between different people. They can be very infrequent or occur on a regular basis; they may last only a few seconds or each episode may last for several days. Similarly, the symptoms are variable; some patients do not report any symptoms, but for those patients who do, they can be debilitating and profoundly reduce quality of life. Symptoms may include breathlessness, nausea, fainting, blurred vision and chest pain. Cardiac arrhythmias that occur in episodes are termed paroxysmal, continuous arrhythmia is called persistent.

Cardiac arrhythmias affect more than one million people each year, and are among the top ten reasons for hospital admissions (NHS Choices). Cardiac arrhythmias can also lead to serious illness, and in extreme cases some arrhythmias may lead to sudden cardiac death.

Withers et al. (2014) interviewed 25 patients with symptomatic arrhythmias, and found that the arrhythmia had a severe influence on their lives and their families. Impacts included the need to

change their work, give up driving, stop caring for grandchildren, or have someone accompany them when they went out. Comments included:

> *"The fear never goes away. Worry is not a strong enough word…I feel panic stricken ALL of the time"*
>
> *"I retired although I didn't want to, but going to work became too hard".*

1.2.1 Supraventricular tachycardia

Supraventricular tachycardias (SVT) are fast heart rhythms that originate from above the ventricles, the lower chambers of the heart. They include atrioventricular nodal re-entrant tachycardia (AVNRT), atrioventricular reciprocating tachycardia (ART), atrial tachycardia, inappropriate sinus tachycardia, atrial flutter and atrial fibrillation (Woods et al. 2007). Although technically atrial fibrillation is part of the SVT group, in practical terms it is usually considered separately since it has different characteristics. In this report AF is considered separately from SVT; more information can be found in the methods section 2.6.2.

SVT is characterised by a fast, but regular heartbeat (NHS Choices), and the duration and frequency of episodes are very variable.

Treatments for stopping an episode of supraventricular tachycardia include a technique known as the vagal manoeuvre, medication or if these are not successful, cardioversion. The risk of future episodes of supraventricular tachycardia can be reduced by avoiding known triggers, such as caffeine. Other preventative measures include medication and also catheter ablation. For some patients with SVT, catheter ablation will be the preferred first line treatment (Blomstrom-Lundqvist et al. 2003).

1.2.2 Atrial fibrillation

Atrial fibrillation is a rapid and irregular beating of the upper chambers of the heart (NICE IPG 168 2005), and is the most common form of arrhythmia, affecting up to 2% of the population (National Clinical Guideline Centre (CG180 2014). The proportion affected increases in older people, and affects more men than women (Camm et al. 2010).

Atrial fibrillation leads to an increased risk of stroke (NHS Choices). The European Society of Cardiology reports that one in five strokes is associated with atrial fibrillation, and that an ischaemic stroke related to atrial fibrillation is more likely to be fatal, or incur a greater disability, than other forms of stroke (Camm et al. 2010).

Initial treatments include treating an underlying cause, using anti-arrhythmic drugs to restore an appropriate heart rhythm or rate, and anticoagulant medication to reduce the risk of other cardiovascular events such as stroke. Subsequent options are cardioversion to restore the normal rhythm, implanting a pacemaker, or cardiac ablation. NICE CG180 Atrial fibrillation: the management of atrial fibrillation and the European Society of Cardiology give guidance on when different options might be appropriate.

1.3 Cardiac ablation

Cardiac ablation can be carried out as a percutaneous procedure, or during open cardiac surgery if other cardiac procedures are taking place at the same time. For percutaneous cardiac ablation, a catheter is inserted into a vein in the upper leg and moved up into the heart, using X-ray to make sure it is in the right place. An attachment at the tip of the catheter produces energy (usually in the form of heat) that damages the nerves in the area where the abnormal electrical impulses are. Figure 1.1 shows the route of the catheter from the upper leg and through the heart to reach the left atrium and the ablation site. This procedure normally takes place using a local anaesthetic and sedation with patients being discharged either the same day or after an overnight stay.

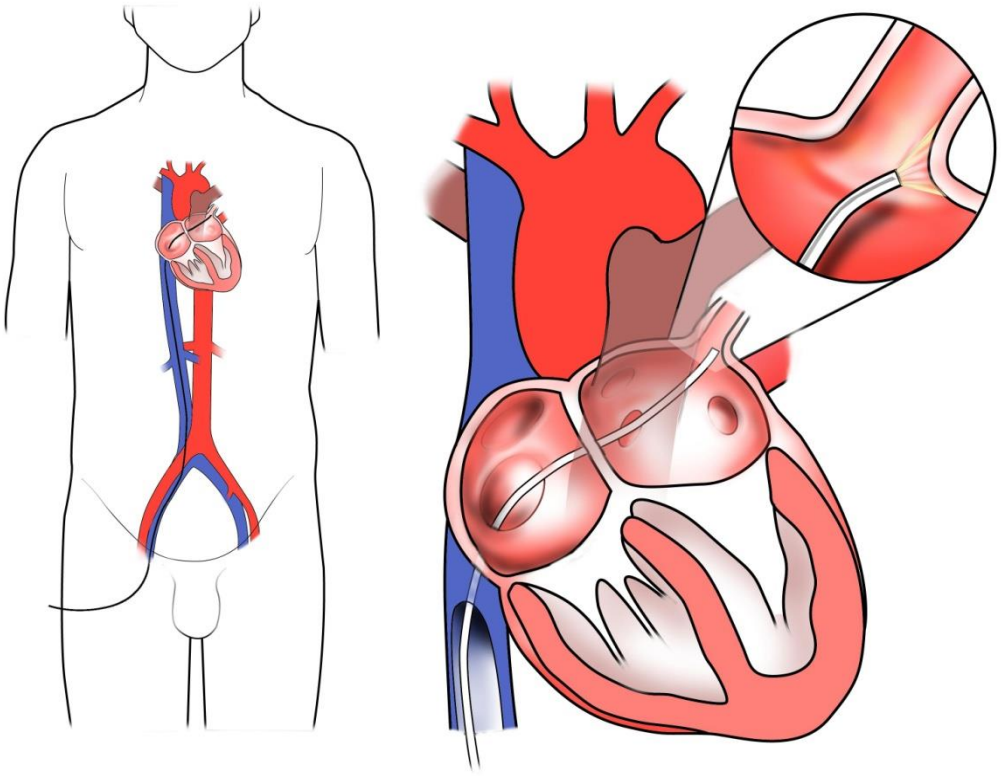


Figure 1.1. Percutaneous cardiac ablation (Cardiff University Media Resources)

It is common for some recurrence of symptoms during the months following the procedure, and it is expected to take up to three months to be able to evaluate the success of the procedure. It is also common for several repeat procedures to be required to manage symptoms.

The Atrial Fibrillation Association published an informative report “Complications of atrial fibrillation ablation” in 2009, which gives a description of the most common complications, and summarises the complication rates from seven large surveys or studies for almost 34,000 procedures. Complications may include (AFA 2009):

- Stroke or transient ischaemic attack, usually due to a blood clot blocking the supply of blood to the brain. Stroke may cause long lasting effects or death.

- Pericardial effusion: a collection of fluid (usually blood) around the heart. This may lead to cardiac tamponade, and may require a pericardial drain to be inserted to remove the fluid.
- Cardiac tamponade: fluid around the heart compresses it, reducing its ability to function effectively, resulting in a fall in blood pressure.
- Pulmonary vein (PV) stenosis: narrowing of pulmonary veins, if several are affected this can cause breathlessness, coughing or coughing up blood. Current ablation techniques have reduced the incidence of PV stenosis.

More information from the literature about complications of cardiac ablation procedures can be found in Appendix A.

1.4 Current guidelines

1.4.1 NICE guidance

NICE has published clinical guidelines for management of atrial fibrillation. The current guideline CG180 Atrial Fibrillation: the management of atrial fibrillation (2014) was published in June 2014, replacing CG36 (2006). The guidelines provide recommendations for the management of atrial fibrillation including diagnostic criterion and pathways to facilitate appropriate treatment choices. Cardiac ablation of the left atrium is recommended for some patient groups with paroxysmal atrial fibrillation, where drug treatment for rate and/or rhythm correction has not proved suitable. It may also be considered for some patients with permanent atrial fibrillation. CG180 does not contain guidance on the ablation technique that should be used.

In addition NICE has published nine Interventional Procedure Guidance (IPG) documents considering different types and methods of cardiac ablation. Table 1.1 briefly summarises the arrhythmia type and procedure covered by each relevant IPG and the conditions placed on their use. The full IPG documents are available on the NICE website , and a detailed summary can be found in Appendix B of this report. One IPG is for ventricular tachycardia, the remaining eight are related to atrial fibrillation, with four described as being performed at the same time as surgical procedures, and four using catheter ablation.

The Interventional Procedures programme considers the available evidence as to whether a procedure is safe and effective. Where the available evidence is insufficient to reach a firm conclusion, it may be recommended that the procedure should only be used where special arrangements are put into place. These can include additional arrangements for clinical governance and consent, and may also require the procedure to be carried out within audit or research programmes. If additional information becomes available at a later date, the IPG can be revised to state that the procedure is sufficiently safe and effective for normal use.

Table 1.1. NICE Interventional Procedure Guidance for cardiac ablation.

IPG	Arrhythmia type	Technology (ablation energy)	Surgical route	Conditions
IPG184	AF	High Intensity focused ultrasound	Open	*special arrangements for consent and for audit or research*

IPG	Arrhythmia type	Technology (ablation energy)	Surgical route	Conditions
IPG 121	AF	Radiofrequency	Open	Normal
IPG122	AF	Microwave	Open	Normal
IPG168	AF	Radiofrequency	Percutaneous	Normal, for selected patients
IPG294	AF	Radiofrequency	Percutaneous, epicardial	*special arrangements for clinical governance and consent*
IPG295	VT	Radiofrequency	Percutaneous, epicardial	*normal arrangements for clinical governance, but with special arrangements for consent*
IPG286	AF	Radiofrequency	Thoracoscopic, epicardial	*special arrangements for clinical governance, consent and audit or research*
IPG123	AF	Cryoablation	Open	Normal
IPG427	AF	Balloon cryoablation (for pulmonary vein isolation)	Percutaneous	Normal

1.4.2 Other guidance

The European Society of Cardiology (ESC) published guidelines for the management of atrial fibrillation in 2010 (Camm et al. 2010). This states that "For the individual patient with symptomatic AF, there must be sufficient potential benefit to justify a complex ablation procedure associated with possibly severe complications".

ESC guidelines considering catheter and surgical ablation of atrial fibrillation were published in 2007 (Calkins et al. 2007).

Guidelines for the management of patients with supraventricular arrhythmias (excluding atrial fibrillation) are published jointly by the American College of Cardiology, American Heart Association and the European Society of Cardiology (Blomstrom-Lundqvist et al. 2003).

1.5 Data linkage

As people interact with organisations on a day to day basis, data are often collected about them and stored by those organisations. These records, containing routinely collected data about individuals, are kept by many organisations including hospitals, GPs, social services, and even supermarket loyalty schemes. Another example might be driving licence information for a particular individual being held by the DVLA.

Usually, most of these routinely collected data remain 'in-house', being used by the same organisation for its own purposes. Using data linkage, data from different organisations may be joined together, so that information thought to relate to the same person is connected for analysis. For example, hospital data could be linked to school results to examine the impact of an illness on education.

There is an increasing recognition of the value of linking records from different sources, as the combined data can provide useful information about a particular population that would not otherwise be available. The associations that are made can reveal relationships, patterns and trends that may not have been previously recognised or verified. Methods have been developed that connect the records that relate to individual people, whilst maintaining privacy and confidentiality.

This opens up a wide range of opportunities for research and statistical analysis, with the potential to eventually improve the health and wellbeing of the population.

1.5.1 Advantages and limitations of routinely collected data

An important advantage of routinely collected data is that enormous sets of data have already been compiled, spanning several years and in some cases decades. These datasets potentially cover large geographical areas, and can provide relatively complete coverage of the population. To intentionally create such a resource for a specific project would be a very expensive and lengthy process, particularly where a long follow up is desirable. Data linkage offers the opportunity to explore relationships between sets of data that were never envisaged when they were initially created.

A key limitation of this method is that the databases have been created for their own purposes, and may not contain all of the data that would ideally be collected to answer a new specific question. Therefore the questions that can be answered by these data are limited at the outset by the information that has been retrospectively collected. Linking additional datasets can expand the available content, however there are often still significant limitations.

There are also limitations particular to each data source, relating to the accuracy of input and completeness of the population covered, as well as the extent of data that are missing within each variable. For secondary care provided through the NHS, there is theoretically complete geographic coverage of England and Wales in Hospital Episode Statistics (HES) and Patient Episode Database for Wales (PEDW) respectively. Some fields come from data that are mandatory for hospital payments; these tend to be completed particularly well. For primary care data, over 60% of GP practices in Wales have agreed to provide data into a single collection within the SAIL (Secure Anonymised Information Linkage) Databank; to date approximately 41% have already contributed their historic electronic patient records (in an anonymised form). In England coverage is much lower and data collection systems are hosted by several different organisations. Each of the English datasets includes fewer than 10% of English GP practices, and there is considerable overlap between the records held by the different organisations.

In addition to geographical coverage, the completion of the fields within each dataset is variable. Fields may be incomplete, inconsistently defined or contain data of varying quality. Differences in data quality might be observed between providers and datasets. There may also be fluctuations in quality over time, or due to differences in data collection methods at a local level.

There is a more detailed description of available data resources and limitations of routine data in the accompanying Data Linkage Toolkit, which has also been produced by Cedar (Poole et al. 2014).

1.5.2 Overview of data linkage methods, anonymisation and data security

A typical data linkage process, as used in this project, has the following stages:

- The trusted third party receives only the demographic data (such as NHS number, name and date of birth), with the clinical data removed, from each data provider.
- The trusted third party then links the records from the two datasets based on the demographic data (such as NHS number and name), and assigns a unique project ID code to each patient record. The project ID codes are returned to the data provider.

- The data providers send the clinical data with the associated project ID code, but with the demographic data removed.
- These are combined into one dataset of clinical data, with no personal identifiers attached.

At no point in the process is there a complete dataset of linked records containing both demographic and clinical data, and no single group has the ability to create this. This is important to protect the anonymity of the individuals whose data is included, and normally a condition of accessing the data.

There will be variations in these processes and additional steps required for some data providers. There is a more detailed description of data linkage methods specific to this CALON project in the methods section, and general information about data linkage methods in the accompanying Data Linkage Toolkit (Poole et al. 2014).

Although the data are anonymised, they still contain large amounts of detail about individual patients and must be stored and used with high levels of security. Jones et al. (2014) describe how the SAIL Databank team have established a remote access environment (the SAIL Gateway) that allows trusted researchers to work on the data that they have permission for, from their normal location. Researchers do not have access to any other data within the SAIL Databank and cannot transfer any data or documents from the SAIL remote access environment to their own computers or memory sticks without specific authorisation. Any information that is exported from the SAIL environment is checked by a senior analyst prior to release, and complies with normal confidentiality principles. These include not publishing any information that may unintentionally permit patient identification through statistical disclosure, such as data where there are groups containing fewer than six patients.

1.6 Related Cedar projects

In November 2010, Cedar was commissioned by NICE to conduct a retrospective audit to assess the feasibility of using of Patient Reported Outcome Measures (PROMs) in patients treated with ablation for symptomatic cardiac arrhythmias, and to conduct initial stages of development and testing of a disease specific tool. Almost 800 patients from three sites were subsequently invited to participate and analysable responses were received from 596 patients (71.9%). Responses were logged onto the Cardiac Rhythm Management (CRM) database, a clinical audit facility collecting information on cardiac arrhythmias within the UK. PROMs data were linked with clinical data held on the CRM database and, after anonymisation, sent to Cedar. These linked data were analysed to determine changes in patient health following ablation and differences in subgroups. The results of the audit suggested that the use of PROMs in this patient group was feasible and also illustrated the improvements in patient health following ablation (Withers et al. 2014).

Following the success of this audit Cedar was commissioned by NICE to plan and carry out a prospective study to further develop and validate the PROMs tool used in the audit. The study started recruiting patients in October 2012: Phase 1 consisted of qualitative interviews with 25 patients to gather feedback on the draft questionnaires to allow improvements to be made and gain insight into how arrhythmias affect this patient group. Phase 2 of the study has enrolled 561 patients from three clinical sites onto a postal study. These patients have all completed pre-procedure questionnaires, and post-procedure questionnaires have been sent out to all patients at 8-16 weeks post ablation. Further post-procedure questionnaires are also being sent out at one and

five years post ablation to identify changes over time, and over 1400 questionnaires have been received to date. Two manuscripts detailing this work are currently under review and more are anticipated.

Data analysis is underway to validate the questionnaires, and preliminary report on the initial stages of the analysis was provided to the PROMs steering group in July 2014. The current validation analysis will be followed by additional work to calculate changes in patient health and quality of life following ablation. This will be repeated with data received from responses at one and five years follow up.

The original design of the CALON project intended to make use of this expertise in the area of PROMs for cardiac ablation, by further linking patient records to evaluate the relationship between self-reported quality of life and routinely collected clinical outcomes. This is discussed further along with other study limitations in section 3.

2 Methods

Due to the nature of the project as a feasibility study, there were changes in the methods during the course of the work. The methods were complex, and to aid clarity only the final method and datasets used are described here. The changes made, reasons for them, and how they impacted on results are described, in section 3 (limitations of methods).

Six-weekly meetings of the steering group provided valuable input from different experts from the design stage through to completion of the project. Steering group members included representatives from NICE, a patient group, primary and secondary care clinicians, data providers, and technical advisors on data linkage and analysis.

Data from a cardiac register were linked with national primary and secondary care records to provide information on long-term outcomes of cardiac ablation procedures. The main comparisons were based upon 'before and after' differences in efficacy outcomes (healthcare service utilisation and prescription frequencies). Frequencies were analysed for follow-up periods up to a maximum of five years. Two years of pre-procedural data were also obtained for comparative purposes.

Additional information on data linkage methods, data sources and coding are available in the Data Linkage Toolkit (Poole et al. 2014).

2.1 Hypothesis

A priori hypotheses were:

- Records of visits to healthcare service providers decrease after cardiac ablation
- Prescriptions for anti-arrhythmic medications decrease after cardiac ablation
- Prescriptions for antidepressant and anxiolytic medications decrease after cardiac ablation
- Safety events are recorded consistently in both routine data sources and the specialist register.

Our main efficacy measure would ideally have been the cessation or reduction of symptoms, and a corresponding improvement in the quality of life. However these parameters are generally not recorded in routine datasets. The outcome measures that have been selected, therefore, are surrogate measures that should give an indication of changes in patients' general health.

2.2 Data sources

Four data sources were used, three of which were already linked within the SAIL Databank (table 2.1). A new linkage was created to incorporate data from the specialist register. The four sources were:

- A register of patients who have had cardiac ablations
- Hospital information (inpatient and outpatient data)
- GP information
- Mortality information.

The National Institute for Cardiovascular Outcomes Research (NICOR) maintain a specialist register which collects information on Cardiac Rhythm Management (CRM), including cardiac ablation

procedures. The SAIL Databank contains secondary care data inpatient and outpatient data (within the Patient Episode Database for Wales, PEDW), primary care data, and mortality records provided by the Welsh Demographic Service (WDS). Diagnoses are recorded using the International Classification of Disease (ICD-10) system, and interventions are recorded using the OPCS Classification of Interventions and Procedures codes. These are standard codes that are widely used in UK healthcare. GP information is recorded using "Read codes" which are widely used in primary care across the UK to record clinical information and events.

The Health Information Research Unit (HIRU) at Swansea University facilitated the secure transfer of anonymised clinical data from NICOR's register into the SAIL Databank, and linkage to the routine clinical records from the other sources (figure 2.1). Authorised members of the project team accessed the anonymised data through the secure SAIL Gateway.

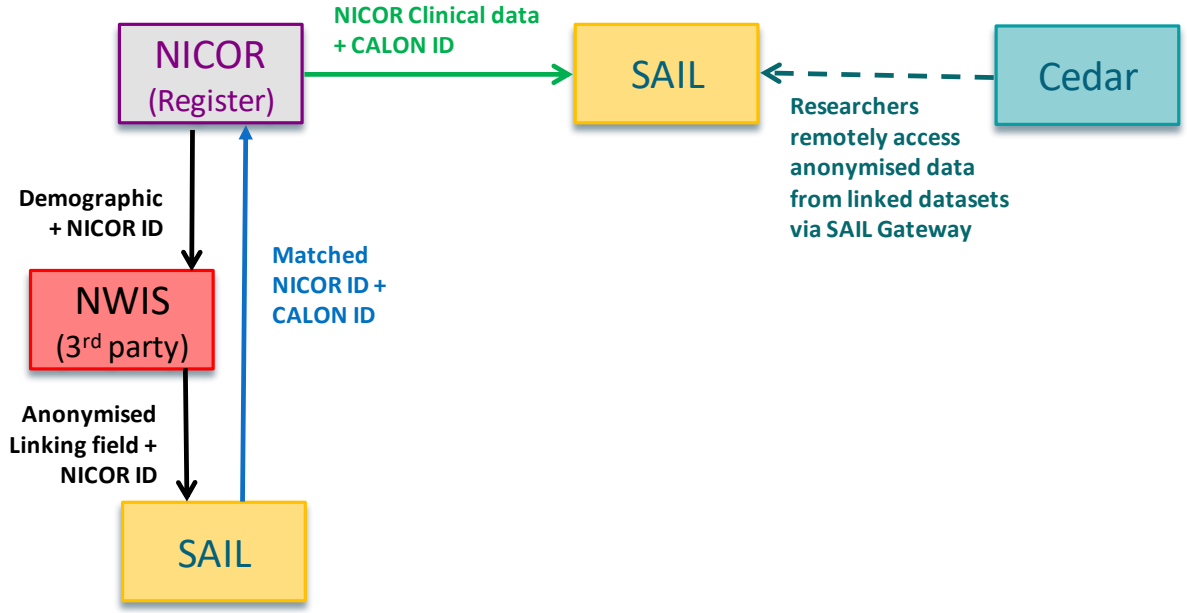


Figure 2.1. Diagram illustrating the flow of data for the CALON data linkage process.

Table 2.1. Sources of data used within the CALON project.

Dataset	Organisation(s)	Description
Cardiac Rhythm Management (CRM)	• National Institute for Cardiovascular Outcomes Research (NICOR) • Healthcare Quality Improvement Partnership (HQIP)	NICOR hosts a collection of clinical data from cardiovascular audits. Data from the Myocardial Ischaemia National Audit Project (MINAP) has been linked and used widely for research purposes. CALON has created a new link to data relating to patients with cardiac arrhythmias.
Patient Episode Database for Wales (PEDW)	NHS Wales Informatics Service (NWIS)	A database that records all episodes of inpatient and outpatient activity in NHS Wales hospitals. Data for Welsh residents treated in hospitals in England is also included. OPCS codes are used for procedure coding, and ICD-10 for diagnostic coding. The format and content of the database is very similar to the English Hospital Episode Statistics (HES).
Welsh Demographic Service (WDS)	NHS Wales Informatics Service (NWIS)	The Welsh Demographic Service maintains a register of Welsh residents' demographic details, including name, address, date of birth, General Practice and NHS Number.
Secure Anonymised Information Linkage (SAIL) Databank	• SAIL • Health Information Research Unit (HIRU) • Centre for Improvement in Population Health through E-records Research (CIPHER)	SAIL is a data linkage repository that collects data across the whole of Wales. Includes secondary care inpatient and outpatient data (from PEDW), primary care data, and death data (from WDS). Other core datasets are also available. 63% of GP practices in Wales have signed up to provide data and 41% already have data included in SAIL.

NICOR provided a dataset from the CRM audit that included:

- Records from 1 January 2008 to 31 December 2012 (inclusive)
- Patients with a record of ablation procedure according to criteria established in consultation with clinicians during the PROMS project.
- Duplicate records removed
- Scottish, Northern Irish and overseas patients removed.

The demographic portion of the dataset was provided to a trusted third party, NWIS. The records were anonymised and securely sent to SAIL to match patients that had any primary or secondary care data in the Welsh healthcare system recorded at any time. An anonymised linking field (ALF) was used, which uniquely identifies a patient throughout all SAIL data. For all patients with records in the Welsh healthcare system, anonymised project ID codes that link to the registry information were returned to NICOR, who then sent the clinical dataset to SAIL for the matched patients only.

This resulted in a dataset of patients who had a cardiac ablation procedure recorded in the CRM registry, and also had some routine Welsh healthcare data. The routine data indicated that these patients had encountered Welsh healthcare services at some point in time, but in some cases these

events had occurred outside the period of the CALON study; for these patients we were unable to access linked data and received the data from the registry entry only.

In addition, the HIRU team used procedure codes (OPCS) from PEDW hospital records to identify patients who were recorded in PEDW as having had cardiac ablations, but who had not already been captured through the NICOR CRM registry. Patients that were resident in Wales, but had ablations in England were also included in the PEDW database. The OPCS codes used to identify ablation procedures were K52.1, K57.1, K57.2, K57.4, K62.1, K62.2, K62.3 and K64.1.

The use of both methods to identify patients with cardiac ablations captured additional outcome information, and allowed a comparison of data available from each source. In comparing patient identification methods, the following definitions applied:

- **Registry group**. These were the patients initially identified through the record of an ablation procedure in the registry. Many, though not all, also had linked follow-up data available from primary and secondary care records in SAIL.

- **Routine group**. These patients had not been identified through the register, but were additional individuals who were recognised as having undergone ablation procedures through there being ablation procedure codes listed in their secondary care records within SAIL. Some also had linked primary care data.

2.3 Scope

There were some changes to the scope during the project. The reasons for these changes and the impact they had on the project are discussed in the limitations section.

2.3.1 Inclusion criteria

- 18 years or older on date of procedure
- Underwent (at least) one of the nine cardiac ablation procedures that are currently covered by NICE guidance (as recorded in NICOR's Cardiac Rhythm Management dataset *or* as indicated by secondary care records)
- Received first cardiac ablation procedure between 1 January 2008 and 31 December 2012 (inclusive)
- Underwent the procedure in the NHS, either in England or Wales
- Included within the SAIL Databank as having utilised healthcare services in Wales at some point in time.

2.3.2 Exclusion criteria

- Indication in patient records that earlier ablation procedures had been carried out
- Evidence in register that planned ablation procedure did not go ahead
- Where there was no follow up data, patients were excluded from efficacy and safety outcomes (they were only included in simple reporting of numbers, procedural safety events and the comparison of patient identification methods).

Some further information about exclusion criteria applied and the impact on patient numbers can be found in the results section.

2.4 Information governance and ethics

The Research and Development department at Cardiff and Vale University Health Board designated this project as Service Evaluation, rather than research. It was therefore deemed not necessary to obtain approval from a research ethics committee. This was confirmed by the South Wales Research Ethics Committee. Similarly, the Health Research Authority's Confidentiality Advisory Group advised that it was not necessary to apply for their approval in order to proceed with the project.

Separate applications were made to data providers for permission to use their data. Approvals were granted by NICOR (subject to certain conditions being upheld), HQIP (the Healthcare Quality Improvement Partnership, who commissioned the Cardiac Rhythm Management audit), and SAIL's Information Governance Review Panel (IGRP).

Researchers accessed all project data via the SAIL Gateway, which is a secure Remote Access System, ensuring that data users cannot copy or transfer files out of the Gateway. Individual researchers are granted access to data only after IGRP approval and receipt of a signed Data Access Agreement. The data accessed via SAIL is fully anonymised.

The SAIL Data Anonymisation Policy and Process (DAPP) describes the principles and policies that underpin HIRU's activities, and describes the anonymisation process to demonstrate that their working practices conform to, or exceed, all the relevant legal, ethical and information governance frameworks currently in place. The HIRU System Level Security Policy describes the range of security policies and procedures that are employed to secure data within the SAIL Databank: including security management, physical security, operating system security, network security and user access control. Further information is available from the SAIL website, and publications (Ford et al. 2009; Lyons et al. 2009, 2012; Jones et al. 2014)

To further protect patient identities, Cedar agreed that any outputs shared with third parties would use aggregated data where any sub-group is found to include five or fewer individuals or events. For this reason, rare outcomes are described as occurring in "fewer than six" patients.

2.5 Data preparation

Complex data processing is a feature of using routinely acquired data, particularly where several data sources are merged. Each dataset will have a unique way of recording information, and the data was not collected with the same aims as the project using it. Data preparation includes ensuring that coding is consistent throughout the whole dataset. Many data fields are only partially completed, and so the impact of any coding on records with missing data also has to be considered. As these datasets are so large, automated processes need to be written.

For each patient there may be up to seven rows of data (one for each annual period before or after the ablation), and the dataset released by SAIL had 15307 records (or rows), with 152 variables (or columns). Many of the variables were created or modified by SQL code written by the SAIL team.

Cedar completed additional data processing steps which resulted in a base dataset for analysis that contains 10543 records (rows) for a total of 2220 patients and uses 196 variables (columns).

2.5.1 Data preparation by SAIL

Linking NICOR data

The data are loaded into the SAIL Databank using the SAIL split file process and an anonymised linking field (ALF), which uniquely identifies a patient throughout SAIL data. This is a method for linking data while maintaining anonymity (Lyons et al. 2009) and is also explained in detail in the Data Linkage Toolkit (Poole et al. 2014).

Processes

NICOR registry and SAIL Databank data were merged them into one data extract. Each column in the extract was processed individually; the result was either a direct copy of what is in the data or a value derived from processing many individual pieces of data. The main processing stages were:

1. Creation of the structure for extract table.
2. Extract and process an algorithm to define procedure type based upon CCAD variables.
3. Generate a list of individuals in PEDW to be included in the data extract.
4. Populate main extract table with processed data.
5. Process data for Charlson Index values.
6. Populate annual drugs prescribed.
7. Populate events dates based on GP Events data for specific event codes.
8. Populate complications based on PEDW diagnoses data.

The Charlson Index gives a weighting according to co-morbidity scores that are then used during data analysis. It provides an indication of a patient's general health, and particularly takes into account major illnesses. The calculations used in SAIL were previously developed by Mark Atkinson, HIRU, based upon original work (Charlson et al. 1987) that has been updated and adapted for use with English data (Bottle & Aylin 2011, NHS IC 2011).

Documentation

The SAIL team created a "Data Dictionary" of variables that populated the data extract. The information in the data dictionary defines the meaning of the variable in non-technical language so that others can understand the field and where the data was derived from. Within the data dictionary there is also a record of the tests carried out on each variable by the analysts. An example is shown in table 2.2.

Table 2.2. Example of information provided by SAIL in the data dictionary.

Column name	Data type	Description and analysis methods	Test number
PERIOD	INTEGER	Period of time before or after procedure for analysis. Each period is 365 days long and is represented by one row. Periods -2 and -1 come before the procedure, while period 1 starts on the procedure date and is followed by periods 2-5. If a period starts after the end of available inpatient/outpatient data (2013-08-31), it is not included in the file.	3.10
PERIOD_ START_DATE	DATE	The start date of the analysis period (each period is inclusive of its start and end dates).	3.12-3.13

SAIL quality assurance

The SAIL quality assurance process included the following steps:

1. First developer writes code to process data.
2. Second developer reviews code compared to the requirements.
3. Third developer runs tests on data.

All code developed was accompanied by comments, so that queries about the process could be easily understood by any developer looking at the code. Code was stored using source control software, with the user's name and a history trail of changes stored against each file. Changes could be undone by loading up a previous version of the file. Version control was strictly adhered to, which was useful for comparing previous results to a later code revision.

The tests were created based on criteria for the variable defined in the data dictionary, rather than from examining the code. Each test was numbered and referenced in the data dictionary. Results were stored in a database table including a test number, description, results, tester name and date. This allowed auditing of the quality assurance process. All tests were required to pass successfully before the creation and supply of an extract.

The SPSS file was given a version number and copied into a shared folder where it could be accessed by the Cedar team. An updated version of the data dictionary was also copied into this folder with the same version number.

2.5.2 Data preparation by Cedar

Once the data was published into an SPSS version, additional coding created by Cedar researchers was used to clean and select data. Due to the nature of the planned analyses, multiple rows of data had been provided for each individual patient, with each row representing one year of data from either before or after the procedure (table 2.3). For this reason, there were between one and seven rows of data per patient. This added to the complexity of the computations for analysis, for example when calculating cumulative survival.

Table 2.3. Example of multiple rows shown for two fictional patients, and the calculation of period start and end dates. None of the information presented in this table is based on actual patient data.

CALON ID	Period	Procedure Date	Period Start Date	Period End Date	Further 191 data variables
123456	-2	12/11/2010	12/11/2008	11/11/2009	XXX
123456	-1	12/11/2010	12/11/2009	11/11/2010	XXX
123456	1	12/11/2010	12/11/2010	11/11/2011	XXX
123456	2	12/11/2010	12/11/2011	11/11/2012	XXX
123456	3	12/11/2010	12/11/2012	11/11/2013	XXX
789123	-1	06/05/2009	06/05/2008	05/05/2009	XXX
789123	1	06/05/2009	06/05/2009	05/05/2010	XXX
789123	2	06/05/2009	06/05/2010	05/05/2011	XXX

Tasks completed by Cedar included:

- Sorting records by patient and period.
- Improving data formatting and coding classifications to facilitate subsequent tasks.
- Identifying and removing records based on the inclusion and exclusion criteria.
- Censoring records where follow-up had discontinued (for example due to death).
- Recoding and labelling variables and values to improve clarity.
- Differentiating between missing data and zero values.
- Aggregation of data into groups (to prevent statistical disclosure).
- Calculating outputs to account for partial years of data.
- Accounting for 'gaps' in patient records in subsequent calculations.
- Calculating cumulative lengths of follow-up across the available periods.
- Identifying and classifying safety event codes.

These activities required a considerable amount of time, but their completion was necessary before analysis of data could be carried out.

2.5.3 Cedar quality assurance

SPSS syntax was written for the majority of the processing tasks and to facilitate the generation of results. This left a clear audit trail, and also facilitated consistent and rapid reprocessing of data when new versions of the dataset were released by SAIL. Consistent version control was used for syntax, datasets and outputs.

A second Cedar researcher tested the syntax created for processing the dataset, using alternative methods to corroborate the impact on the data or output. An audit trail was maintained to record the tests conducted and any corrective actions that were necessary.

A third researcher carried out checks on data extraction into report tables and diagrams.

2.6 Data analysis

Demographic characteristics of patients included within the linked CALON dataset used for efficacy survival analyses were calculated and presented in summary form. To prevent statistical disclosure, age and comorbidity scores were grouped into ranges to give an indication of the distributions.

Numbers of records available for efficacy and safety analyses were calculated and displayed in the form of Venn diagrams.

2.6.1 Covariates

Covariates included in statistical models that adjusted for confounding were:

- Age
- Sex
- Comorbidity score.

Comorbidity scores were determined using a version of the Charlson Index (as described in section 2.5.1). For CALON the calculation made use of ICD-10 codes from the diagnosis fields of secondary care records, taken from the year prior to the ablation procedure.

2.6.2 Subgroups

It was possible with many of the analyses to produce separate outputs for two subgroups of patients according to their arrhythmia type, namely:

- **Atrial fibrillation** (AF)
- **Supraventricular tachycardia** (SVT).

The arrhythmia type was determined primarily through assessing ICD-10 diagnosis codes from PEDW, but supplemented by information from the NICOR registry's 'EPSArrhythmia' variable. All patients who could not confidently be allocated to either of the subgroups using these methods were excluded from subgroup analyses, but would still have been included in the 'all patients' results. Although it had been possible to recognise some other patients as having a diagnosis of ventricular tachycardia, there were not sufficient numbers for them to form a subgroup and so these were also excluded from the subgroup analyses.

2.6.3 Descriptive statistics for efficacy outcomes

Before running the generalised linear mixed model analyses to determine whether 'before and after' results were statistically significant, a number of bar graphs were generated. These provided a visual indication of mean efficacy measures across the seven periods (two pre-procedural and five post-procedural years) for all patients with follow-up data. This exercise was also completed for the AF and SVT subgroups. The efficacy outcomes investigated were:

- number of outpatient appointments
- total length of stay as an inpatient
- number of GP appointments
- number of prescriptions for antiarrhythmia drugs
- number of prescriptions for antidepressant or anti-anxiety drugs.

2.6.4 Statistical analysis (generalised linear mixed model) for efficacy outcomes

One of the main aims the study was to find out whether it was possible to demonstrate that cardiac ablation procedures had an impact on efficacy outcomes. The efficacy outcomes included in the formal statistical analyses were the same as those listed above in section 2.6.3.

The events or counts of each outcome for each patient were recorded for each year for a maximum of two years before the procedure took place and up to five years after the procedure. Therefore, for each patient, each outcome was reported up to a maximum of seven times and was presented as counts or events per year. For partial years (where the data was not recorded for a whole year because data was not available), the data was recalculated to provide an estimate of the number of events or counts that would have occurred that year if data had been available or the patient had survived. A dummy variable, 'after_p', was calculated to code whether the data referred to pre- or post-procedure.

A generalised linear mixed model (SPSS version 20) was used for the statistical analysis of the efficacy of cardiac ablation. This allows analysis of datasets with missing data (where the datasets are not complete), where repeated measurements are made on patients at different time points, and to allow for different covariance structures. The mixed model comprises both fixed and random

effects. Fixed effects included in the model for CALON comprised the patients' sex, age and comorbidity score and the dummy variable 'after_p'. Random effects, nested within the fixed effects, comprised the repeated measures on each patient, identified by the patient's CALON ID, and 'after_p' was also added as a random effect to account for heterogeneity. The type of covariance of the random effects was selected to be unstructured.

A log-linear function was selected on the assumption that the data would follow a Poisson distribution (a typical distribution for counts/events over a particular time period).

A separate analysis was carried out for each efficacy outcome, and for arrhythmia subgroups. A p-value less than 0.05 was taken to indicate a significant effect.

2.6.5 Safety event counts

Although it was not always possible to determine length of follow-up in all cases, numbers of safety events recorded in the records from each data source could be reported. For some of these outcomes, it was possible to count the number of events and number of patients affected (since some patients may experience an event more than once). A list of common procedural complications and later safety outcomes of cardiac ablation procedures was drawn up based upon available literature. Where possible, codes were identified that are used to describe these events in routine hospital and GP records. The CALON patient records were then searched for these specified codes in order to produce a summary of the number of events and patients, both at one year of follow-up and at the end of the five-year study period. These measures were relatively crude, as they did not account for differing lengths of follow-up within those timescales.

It was not possible to determine whether these safety outcomes were causally related to the ablation procedure. A consultant cardiologist was consulted for advice about the length of time after the procedure in which there might be an association between the procedure and the safety outcome. As well as the one- and five-year results, counts were presented where they occurred within the period in which the event might be 'expected' to be observed.

2.6.6 Statistical analysis for survival (time-to-event analysis)

Other aims of the study were to carry out survival analyses and to calculate the incidence of safety events, allowing for patients for whom a complete dataset was not available. Kaplan-Meier survival analyses were used to determine the survival rate over one and five years post-procedure. Cox regression analysis was used to determine the effect of the covariates sex, age and comorbidity on survival over five years post-procedure. These analyses were also carried out for the AF and SVT subgroups.

Available data

Once Cedar had completed preparation of the CALON dataset, the following variables were available (amongst others):

- the duration (in days) of the known records for each patient between the date of the procedure and the last known record.
- the duration (in days) between the date of the procedure and the date of death (if death occurred).

- the status of the patient (alive or dead)
- the duration (in days) between the date of the procedure and the date that each specified safety event was first recorded for:
    - Stroke/silent cerebral embolism (SCE)
    - Transient ischaemic attack (TIA)
    - Myocardial infarction (MI)
    - Cardiac tamponade.
- patient characteristics (sex, age and comorbidity).

Kaplan-Meier survival curves

Patients who were still alive at the date of the final record or were lost to follow-up were counted as censored cases. The survival rate after one or five years is the proportion of patients who are still alive at the end of that period allowing for the patients who were lost to follow-up before the end of the duration of interest.

The survival rate at one and five years was obtained from the survival analysis carried out using SPSS version 20.

Cox regression (proportional hazards)

Cox regression analysis was used to determine the effect of covariates (age, sex and comorbidity score) on survival. The Cox regression model was built using 'Forward – Likelihood Ratio (LR)'. This technique builds the model by adding covariates one at a time, starting with the one that has the most effect and continues adding covariates until no other covariates significantly improve the model. For the categorical covariate 'sex', female was used as the reference value.

An estimate of the odds ratio (or hazard ratio) for each covariate was derived from the value of 'exp(B)' from the analysis for that covariate. The 95% confidence intervals for the odds ratios were calculated in the same way.

In all analyses, a p-value less than 0.05 was taken to indicate a significant effect.

Cumulative incidence of safety events and repeat ablation procedures

The methods used to calculate cumulative incidence of repeat ablation procedures and of four safety outcomes (Stroke/SCE, TIA, MI and tamponade) were identical to those used to calculate the results for the mortality analyses described above. The only difference was that rather than report the proportion of patients yet to experience an event (such as 98% survival), we reported the proportion that had experienced an event (for example, 2% cumulative incidence).

In calculating the time between the procedure and the first record of a safety event, both GP and hospital data were searched; where date discrepancies occurred, the earliest of the dates was used for the analysis. A similar method was used for repeat ablation procedures, but instead referred to hospital and registry data to identify the earliest recorded evidence of a second procedure.

It was not possible to use this method for those safety events with very low numbers. Similarly, as numbers of some safety events were relatively small, subgroup analyses for arrhythmia types (AF and SVT) were not conducted. The numbers reported were calculated based upon the time to the

first record of each event per patient; incidence therefore refers to number of patients affected rather than number of occurrences.

Furthermore, it was decided that this method was not appropriate to use for other safety outcomes with codes that were particularly non-specific. For example, codes relating to 'infection' were detected up to five years after the procedure, but it was not clear which were likely to be associated with the cardiac ablation procedures and which were not. On the other hand stroke, MI and cardiac tamponade are more closely related to ablation and so calculation of their incidence rates was considered to be of potential value.

2.6.7 Common post-procedural codes

The study design included in the project protocol made provision for searching for some undefined safety outcomes. A list of all diagnosis codes found in CALON patient records in the five-year post-procedural period was drawn up, and arranged in order of descending frequency. The list was then limited to the 'top 20' most common codes, and patient numbers were calculated. These steps were repeated with a restriction placed on the search to extract only those recorded within the first year, as these were thought most likely to be related to the ablation procedure.

This highlighted events or conditions that are commonly encountered by patients after an ablation procedure. It was thought that this exercise might reveal an association that would not otherwise have been detected if searching for pre-specified outcomes.

2.6.8 Comparison of patient identification methods

To determine whether the method of identifying patients (through the registry or through routine data) had affected the demographic composition of the dataset, a series of comparisons were conducted. As well as calculating numbers and proportions of patients represented within each category, the following statistical tests were used to determine whether patient identification methods differed significantly in terms of:

- Sex - Chi-squared test
- Age - Independent samples t-test
- Comorbidity score – Mann-Whitney U test.

Counts of numbers of procedures recorded in each group for each calendar year in which the procedure occurred were calculated. This gave an indication of how many procedures were being recorded over time in the register and in routine data.

2.6.9 Recording of safety events

An attempt was made to compare the consistency of recording of safety events from different data sources. Mortality data from the NICOR registry and from routine (WDS) records were examined.

3 Limitations of methods

There were a number of limitations to the methods used in the CALON project, some of which were known from the outset and others discovered over time, including some that subsequently impacted on the final outcomes.

3.1 Outcome measures

The most obvious limitation of using routinely recorded data is that we did not have any influence over the types of data being collected or how they were recorded. The data sources were originally designed for other purposes, such as to document the clinical care of individual patients. When initially deciding upon outcome measures for CALON, we were aware that we may not be able to access the exact information that we would ideally wish to see. For example, cardiac arrhythmias are known to have an impact upon quality of life for patients, affecting the activities of daily living and emotional wellbeing (Withers et al. 2014). However this type of information is not well recorded in routine clinical records. As we were solely reliant upon pre-existing data, alternative outcome measures were sought. Utilisation of healthcare services and usage of prescriptions were selected on the basis that they might act as a proxy for patient wellbeing. The assumption was that if patients feel well, they will not access healthcare services as often as they would if they were feeling unwell. We also investigated the possibility of obtaining employment data, which might indicate whether patients were unable to work due to illness, but these data were not available in a suitable form for data linkage and processes were not in place to permit their release.

3.2 Geographical population and statistical power

Whilst the original project plan had been to obtain data from both England and Wales, unforeseen external circumstances at a national level obstructed our access to data from England. This was related to the launch of the care.data initiative; the subsequent heightened awareness of data sharing and public concerns about privacy led to a suspension of data linkage activities for several months. In contrast, once the NICOR dataset had been provided to us, the SAIL team were able to proceed immediately with linkage and data preparation processes for Welsh records. As a consequence, this report does not include data from England.

Although the English population is larger than the Welsh, the extent of primary care data available for analysis from England is limited. Collections of primary care data in England contain fewer than 10% of the population, whereas the SAIL Databank contains data for over 40% of the Welsh population. We were also able to demonstrate that the number of records available in Wales was easily sufficient to power the primary outcomes for CALON. This can be illustrated with an example of a calculation based on the assumption that the outcome data (such as number of outpatient appointments) has a Poisson distribution, as follows.

> If the mean number of outpatient appointments was five per year before the procedure, and we wanted to detect a post-procedural difference of +/-1 appointment per year, the sample size required to detect a reduction to four appointments per year is given by:
>
> $4/(5^{0.5} - 4^{0.5})^2 = 72$ patients

The CALON dataset included many times this number of patients, and so would have sufficient power to detect even smaller differences in efficacy measures.

The lower number of patients might have had a more important effect on secondary safety outcomes, which in some cases were rare events. For these outcomes obtaining data from a larger population would have improved the accuracy of the results, as patient numbers fewer than six could not be precisely reported due to privacy protection rules.

3.3 Data extract provided

3.3.1 PROMs data

It had been our intention to compare self-reported changes in health and social outcomes from earlier PROMs studies (see section 1.6) with linked clinical records from the same group of patients. Unfortunately the relevant PROMs questionnaire results were not made available for linkage and analysis within the project timescale. It was therefore not possible to evaluate the differences in quality of life alongside other efficacy measures, though this remains a potentially valuable direction for future research.

3.3.2 Other inconsistencies with extract and matching process

There were some issues with a number of English and Welsh patients being accidentally excluded from the initial dataset released by NICOR, due to geographical changes in mapping to clinical commissioning groups; these problems were never fully resolved. Further investigation was hampered by the fact that patient records had been anonymised and could not be traced back to determine which were missing. The result is that the final CALON dataset used was known to be missing some Welsh records and PROMs data, although we could not be certain of the exact numbers affected. An exercise is described in the results of this report, presenting the demographic characteristics of patients identified through the NICOR registry as compared to a separate group of patients identified through routine data (section 4.5). This provides assurance that, despite the likelihood of some missing patient records, those that were included in CALON from the registry were probably representative of the entire group.

When analysing the final matched and cleaned dataset, there were 289 patients who had an ablation recorded in the NICOR register, but did not have corresponding PEDW or GP records within the CALON dataset. The PEDW database contains records from English hospitals if the patients are Welsh residents, so treatment in England is not a likely reason for the missing follow-up data. It seems likely that these patients were not resident in Wales at the time of ablation but underwent treatment in Wales at a point in time beyond the study period. They might possibly have been resident in Wales at some other period of time either before or after their ablation. Had both English and Welsh datasets been available for the study then we assume that all the available data for that patient would have been recorded, regardless of the location of their treatment or place of residence.

3.4 Procedure classification

Our original intention for the project was to be able to report comparative data, differentiated by the types of ablation procedures described in NICE IP guidance (Appendix B). This was not possible for several reasons relating to how procedures are defined in the registry and in routine data.

We had hoped that the detailed information in the registry would be sufficient to allow us to distinguish between the procedures. We later discovered that some types of procedures would not be entered into the cardiac rhythm dataset at all. For example, there are a number of IP guidance documents relating to ablation procedures "in association with other cardiac surgery". These ablations would have been carried out by surgeons rather than cardiologists, and the procedure details would not have been recorded in the registry. Likewise, the registry data contained little information about the procedural approach (such as percutaneous/non-thoracoscopic).

In an attempt to classify other procedures, an algorithm was produced by the project team in discussion with one of the Consultant Cardiologists who works closely with the NICOR registry (Appendix C). It was designed to differentiate between procedure types, largely based upon the ablation energy source used. Once we had received the dataset, we realised that we would not be able to use the algorithm due to the limited variety of energy sources used. The vast majority of procedures were carried using radiofrequency energy, but in some cases this was also in combination with other types of energy, which could have confused the analyses. There were a few procedures where cryoablation was used, but numbers were too small to enable their use as a comparator group. Other types of energy described in IP guidance (such as high-intensity focused ultrasound or microwave) were not recorded.

Similarly, an attempt was made to classify procedure type using the OPCS and ICD-10 codes recorded in PEDW. The NICE website provides guidance to clinicians on code combinations that should be added to clinical records to describe each ablation procedure. When we searched for these codes in routine data, we found that the recommended code combinations were not widely used.

Eventually, after attempts to use both of these methods to classify procedure types, we unfortunately concluded that it was not possible to categorise the procedures in accordance with the NICE IP descriptions. If changes are made to the codes that are recorded in the future, this may become a possibility.

3.5 Routine data coding/classification limitations

There were other limitations of the ways in which data are recorded in routine healthcare datasets. Recognising an outpatient appointment or an inpatient admission in secondary care records was relatively straightforward. In contrast, there is no reliably-recorded code that is used to indicate that a patient has had an appointment with their primary care GP. This is a challenge that many health informaticians are seeking ways to address. For the purposes of CALON, which compares records of the same patients before and after an ablation procedure, the exact definition of a GP 'encounter' was less important than making sure that a consistent rule was applied. The most pragmatic approach was therefore to count any day in which a Read code was recorded as one GP 'event'.

Whilst this may not always have been an actual appointment (for example, it might relate to a letter being received about that patient or laboratory result), it still provides an indication of service usage.

When designing our search for specified safety events that were known to be associated with cardiac ablation, we sought advice from experts in clinical coding. In their field of work, they provide guidance on the codes that should be documented in patients' clinical records to indicate that a particular diagnosis was made, or that a particular intervention was undertaken. We received a list of these recommended codes. However, when we tried to use these codes to identify safety events, we realised that some of the high-level codes were not specific enough to select the intended events. For example, we requested a code for atrio-oesophageal fistula, but it was allocated T81.7 "Other complications of procedures, not elsewhere classified". Also there were some overlapping categories, such as the code I63- initially being proposed for both stroke and silent cerebral embolism; had this issue not been recognised it might have led to over-reporting of some safety events. In eventuality we were able to re-categorise these events as appropriate to some extent, though we were unable to report some (such as a potential atrio-oesophageal fistula) as anything except 'other complications'.

There were many occasions like those described above on which the codes and classifications used within CALON required some refinement. Clinicians were consulted when categorisations were not clear, or to confirm allocations. We are aware of other research groups developing complex algorithms over many months simply to define one diagnosis (such as atrial fibrillation) with confidence. The limited time and resources available for the CALON project required a more pragmatic approach to be taken for this feasibility study.

3.6 Study design and analytical limitations

Since we were unable to compare outcomes for different cardiac ablation procedures, our main analyses were not conducted as a comparative exercise, other than the use of patients as their own historical controls. An alternative approach could have been to select a control group of patients from SAIL, matched by demographics (such as age, sex and comorbidity score) but having not undergone ablation procedures. Such an exercise would allow results to be adjusted for any effects that might occur over time. This is possible with large datasets, where numbers of controls could even be included at a higher ratio (such as one case to every five controls), and might be considered for similar projects in the future.

Due to the complexities of determining follow-up lengths and differences in definitions of events between datasets, calculating incidence was not possible for all of the safety outcomes described. In the absence of definite denominators, simple counts of events observed in the dataset have been reported. Fortunately it was possible to calculate cumulative incidence for a few of the key safety outcomes.

Similarly, cumulative survival data are presented to show the mortality rate of patients within the dataset. It should be noted that we could not be confident that the denominator was accurate. Where there was no record of a death occurring according to the Welsh Demographic Service, it was assumed that the patient was still living.

4 Results

4.1 Excluded patients

After a final linked dataset (version 12) had been provided to Cedar by HIRU, further amendments were required to present these data in a suitable format for subsequent analysis. One of the aims was to exclude records relating to patients that would not be included in the analyses, according to criteria previously developed in discussion with clinicians. The main objective of this exercise was to identify patients who had undergone their *first* ablation procedure. The flow diagram below shows the criteria for exclusion, and the effect that each subsequent stage had on total patient numbers (figure 4.1).

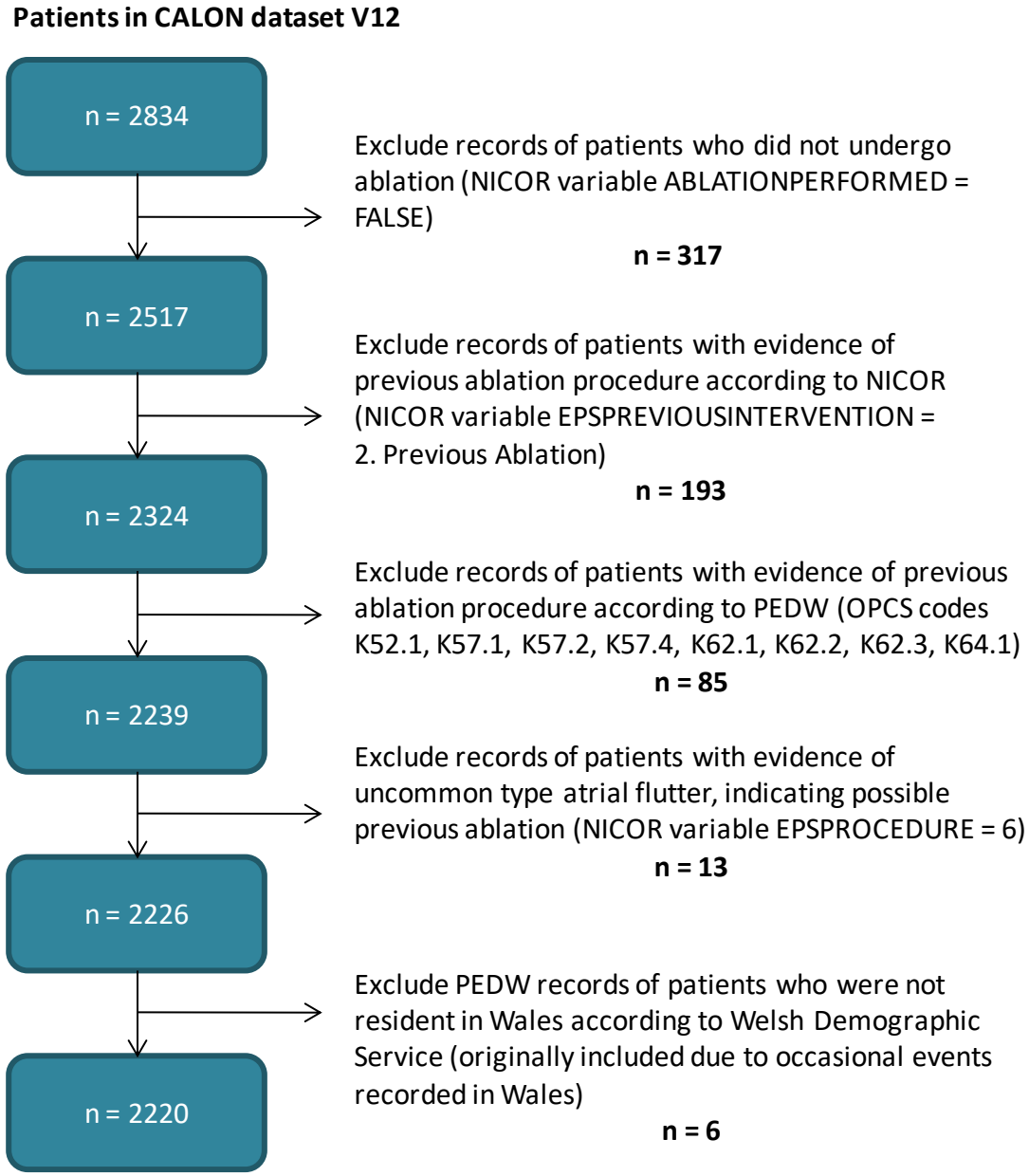


Figure 4.1. Flow diagram to show exclusion criteria and numbers of patient records affected.

4.2 Linked dataset results

The following summaries of demographic characteristics are based on the CALON linked dataset that was used for efficacy analyses. Additional patients were excluded from this section if they had no follow-up data (GP or hospital records) available beyond the time of the procedure itself (n=289). The number of patients included in this current section and the efficacy analyses was therefore n=1931.

Section 4.5 examines differences in the way that patients were initially identified (as having undergone an ablation procedure), and compares demographic characteristics of these two groups. This exercise includes some patient records that were not linked and have no follow-up data; no eligible patients were excluded for the purpose of comparing patient identification methods (n=2220).

4.2.1 Demographic profiles

There were 1138 males (58.9%) and 793 females (41.1%). The mean age on the date of procedure was 55.3 years. Age group distributions are shown in table 4.1.

Table 4.1. Number and proportion of patients within each age group.

Age group (years)	Count	Percentage
18 to 30	202	10.5%
31 to 45	342	17.7%
46 to 60	528	27.3%
61 to 75	671	34.7%
Over 75	188	9.7%
Total	1931	100.0%

Charlson comorbidity scores were available for 1919 patients (99.4%) (table 4.2). These data were highly skewed, with 60% of the patients having a score of 0 or -1.

Table 4.2. Number and proportion of patients within each comorbidity score group.

Comorbidity score	Count	Percentage
-1 or 0	1168	60.9%
1 to 10	423	22.0%
11 to 20	248	12.9%
21 to 30	62	3.2%
Over 30	18	0.9%
Missing	12	0.6%
Total	1931	100.0%

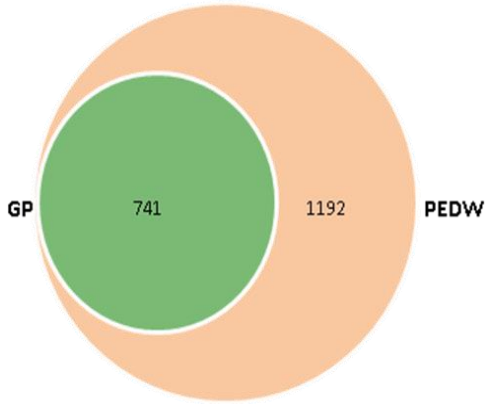
According to NICOR data, 82.8% (875/1057) of procedures were elective, 5.8% (61/1057) were urgent, and fewer than six were recorded as an emergency. The remainder had no record of urgency.

4.2.2 Data availability

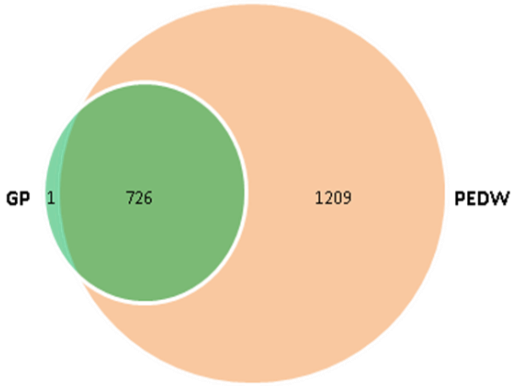
The following Venn diagrams illustrate how many records contributed to the analyses from each of the periods; sizes of circles are only approximately in proportion to numbers (figure 4.2). Numbers of records available for each period of follow-up vary. Note that there are two versions of the diagram for Period 1. This is because the NICOR data did not contribute to efficacy analyses, but have been used for some safety analyses. NICOR data were only available for Period 1 (around the time of the procedure itself). Efficacy analyses were based on pre- and post-procedural data from hospital and GP records only. Safety analyses were based on post-procedural records (periods +1 to +5).

Five complete years of follow-up data was available for a quarter of the total patients included in the efficacy analyses (530/1931 = 27.4%).

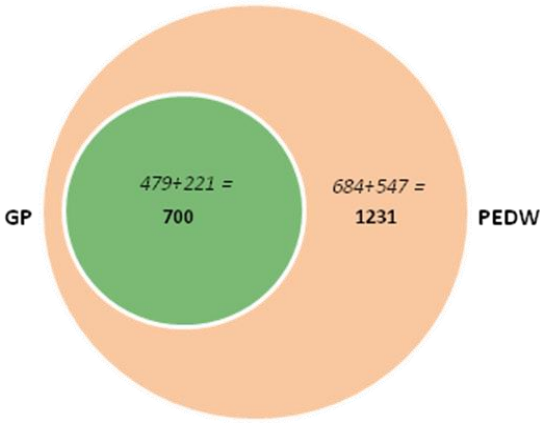
Pre-procedure period -2



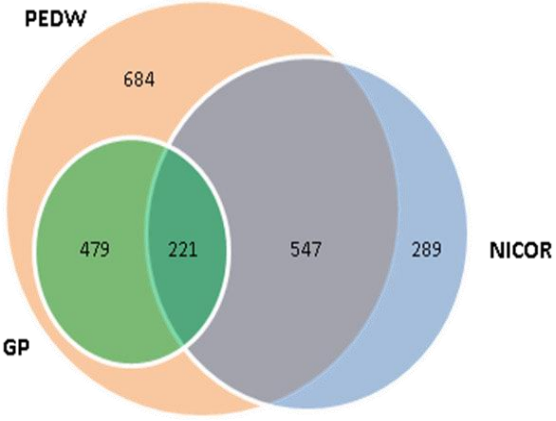
Pre-procedure period -1



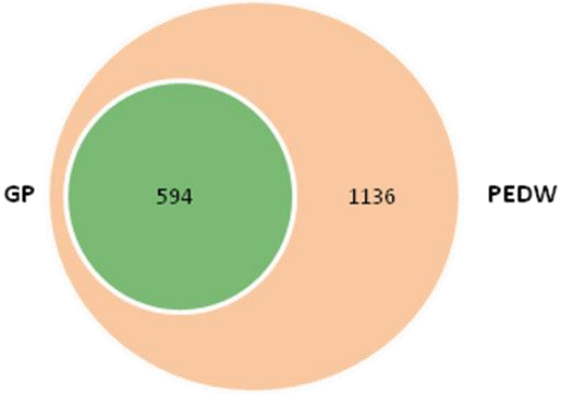
Post-procedure period +1 (Efficacy)



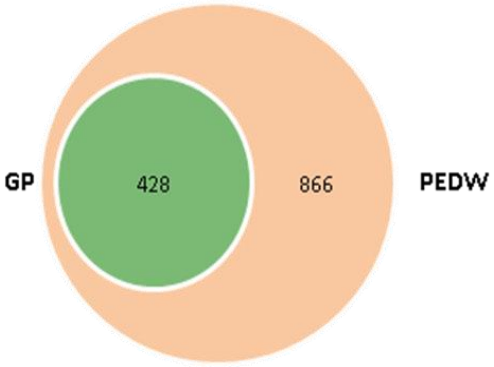
Post-procedure period +1 (Safety)



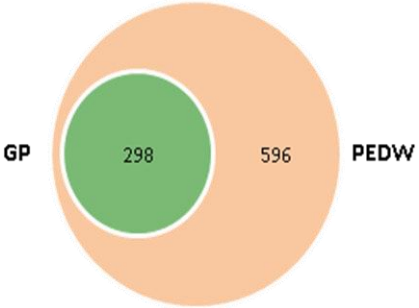
Post-procedure period +2



Post-procedure period +3



Post-procedure period +4



Post-procedure period +5

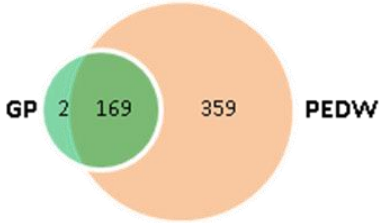


Figure 4.2. Venn diagrams to illustrate numbers of patient records available in each period from different data sources. Sizes of circles are only approximately in proportion to numbers.

4.3 Efficacy outcomes

According to the NICOR data, procedural success was recorded as 87.9% (929/1057) complete, 3.1% (33/1057) partial, and 2.8% (30/1057) failed. The result was unknown or not recorded for 6.1% (65/1057) procedures.

Other efficacy results are presented as a series of bar graphs summarising the pre- and post-ablation frequencies of:

- Outpatient appointments
- Days spent as an inpatient (length of stay)
- GP service encounters
- Antiarrhythmia drug prescriptions
- Antidepressant/anxiolytic drug prescriptions.

Bar graphs have also been provided to show the same results but for two subgroups of patients – those with codes indicating a diagnosis of either atrial fibrillation (AF) or of supraventricular tachycardia (SVT).

The results of the generalised mixed model analyses indicated whether or not differences between pre- and post-ablation frequencies were significant, having adjusted for covariates. These results were used to evaluate the primary outcome measure for this study, and can be found below in section 4.3.2. Again, results are also shown for the arrhythmia subgroups.

4.3.1 Efficacy graphs

Outpatient appointments and inpatient length of stay

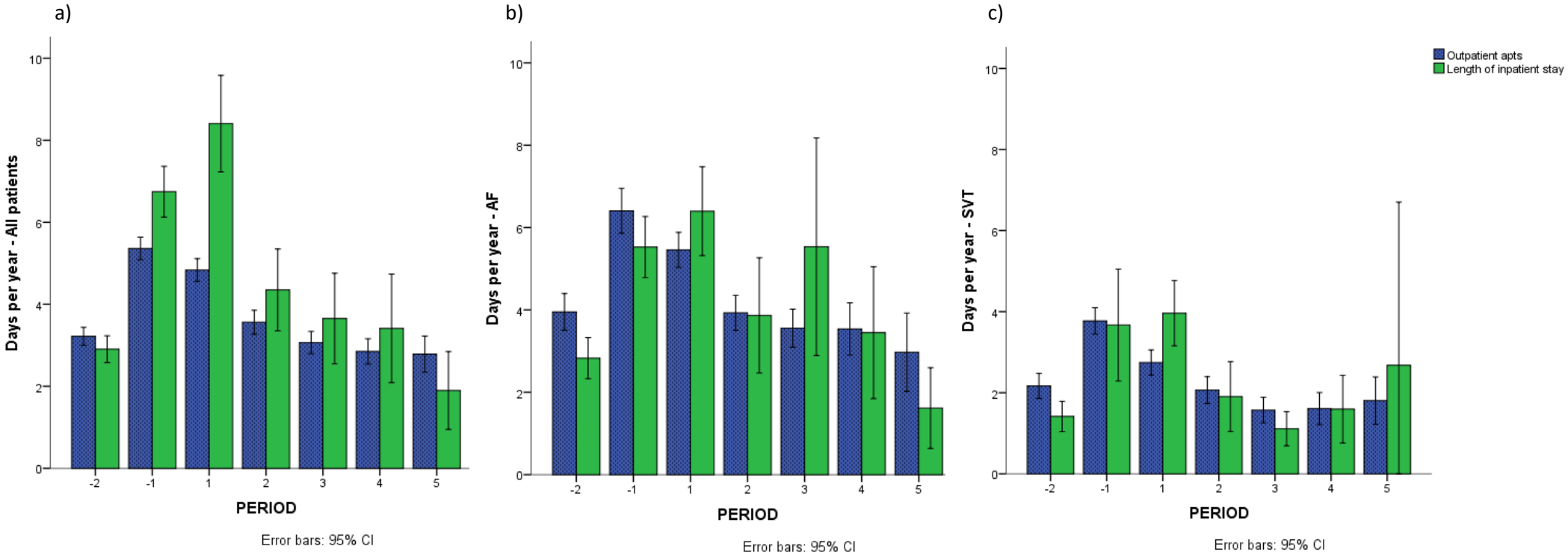


Figure 4.3. Mean (95% confidence interval) days per year of outpatient appointments (blue) and days spent as an inpatient (green) for a) All patients b) Patients with code for atrial fibrillation c) Patients with code for supraventricular tachycardia. Periods -2 and -1 indicate pre-procedure years and periods 1 to 5 show the post-procedural follow-up outcomes.

The mean number of outpatient appointments was highest in the year preceding the ablation procedure (at 5.4 appointments per year) (figure 4.3). The frequency reduced throughout the follow-up period, reaching a mean of 2.8 appointments per year in the final year. Days spent as an inpatient was

greatest in the first year of follow-up (8.4 days), although this would have included the time admitted for the ablation procedure itself. This measure decreased substantially in the second and subsequent periods, with a final mean of 1.9 days in the last year.

Results were more variable for the subgroup analyses, which may be attributed in part to the lower numbers of patients included. Average healthcare service use was generally lower in the SVT group than in the AF group.

GP events

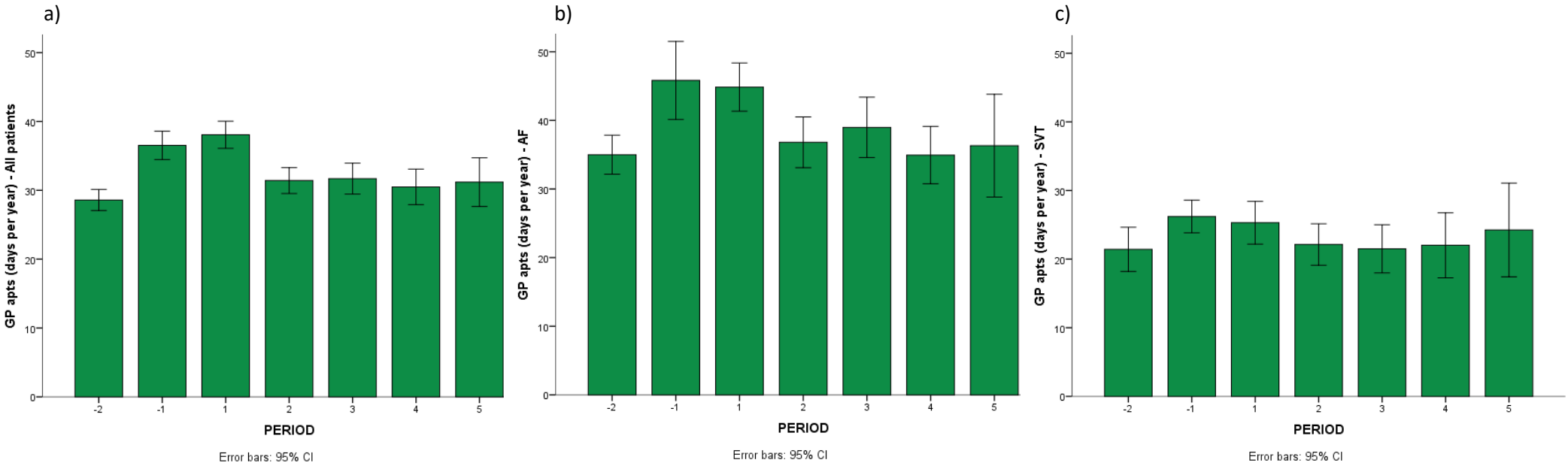


Figure 4.4. Mean (95% confidence interval) GP events (days on which Read codes were recorded) per year for a) All patients b) Patients with code for atrial fibrillation c) Patients with code for supraventricular tachycardia. Periods -2 and -1 indicate pre-procedure years and periods 1 to 5 show the post-procedural follow-up outcomes.

The frequency of entries in GP records (measured by number of days on which a Read code was recorded) remained fairly consistent throughout the study at approximately 30 events per year (figure 4.4). Higher frequencies were observed in the years immediately before and after the ablation procedure, with a mean of 38.1 events in the first year of follow-up.

Whilst a similar pattern is observed when focusing on arrhythmia subgroups, mean numbers of GP events were higher in patients diagnosed with AF when compared to those with SVT.

Antiarrhythmia and antidepressant/anxiolytic drug prescriptions

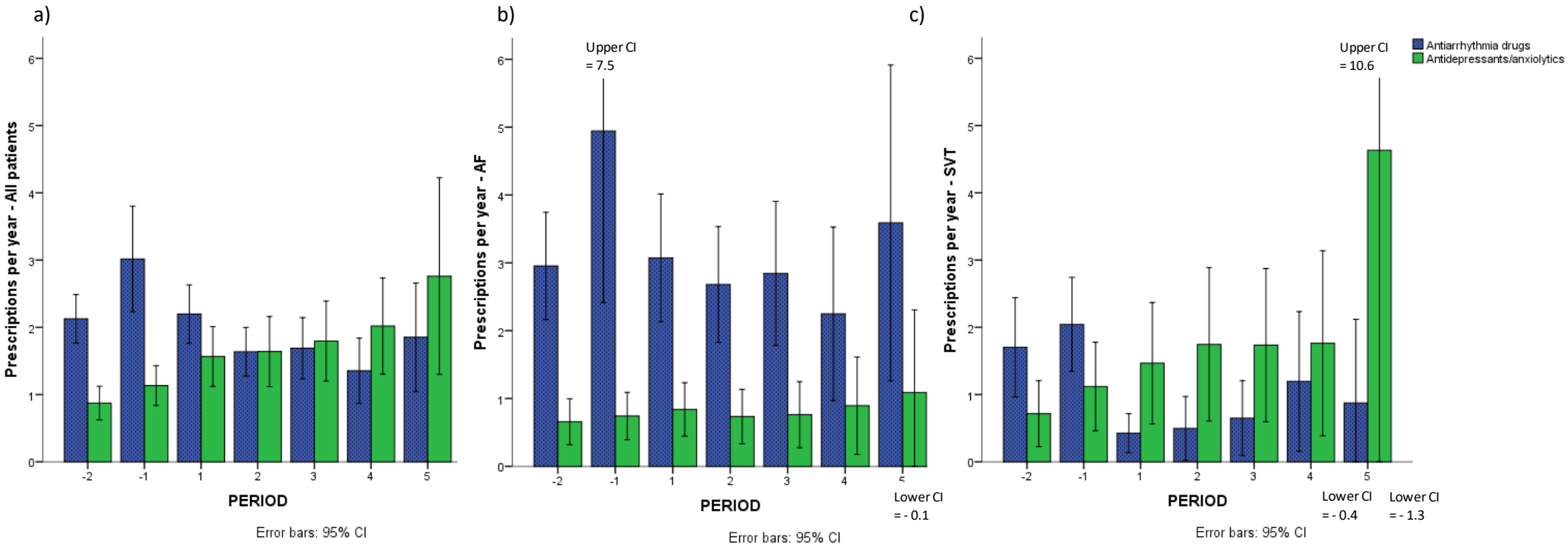


Figure 4.5. Mean (95% confidence interval) number of antiarrhythmia (blue) and antidepressant/anxiolytic (green) prescriptions per year for a) All patients b) Patients with code for atrial fibrillation c) Patients with code for supraventricular tachycardia. Periods -2 and -1 indicate pre-procedure years and periods 1 to 5 show the post-procedural follow-up outcomes.

The mean number of prescriptions issued for antiarrhythmia drugs fluctuated between 1.4 and 3.0 prescriptions per year (figure 4.5). The greatest numbers were issued in the one-year period immediately preceding the ablation period. Lower numbers were seen in follow-up periods 2 to 5, although there was no clear pattern observed after the first year of follow-up. On the other hand, prescribing of antidepressants/anxiolytics showed a consistent increase over time, from a mean of 0.9 prescriptions per year to a mean of 2.8 prescriptions per year in the fifth year of follow-up. From the generalised linear mixed

model analysis, the number of prescriptions for antidepressants and/or anxiolytic drugs increased by 30.7% after the procedure (p=0.016). Although an increase might be expected as patients become older, the model showed that age only had a modest effect of 1.4%, meaning that a patient who is one year older is likely to increase their number of prescriptions by 1.4%. The change of 30.7% observed here is therefore not primarily accounted for by the aging population.

Whilst patients with AF were issued with antiarrhythmia drugs averaging 3.3 prescriptions per year, the equivalent mean was 1.1 per year for patients diagnosed with SVT. Antidepressant/anxiolytic prescriptions on the other hand were higher in the SVT group than in the AF group, with respective means of 1.5 and 0.8. There is a wide variation in the number of antidepressants/anxiolytics prescribed for patients with SVT in the fifth year of follow-up. This is due to a relatively low number of patients (n=32) in this subgroup with follow-up GP data extending this far. Only seven of these patients (21.9%) were issued with prescriptions for antidepressant/anxiolytic drugs, but some of these had a relatively high number of prescriptions per year.

4.3.2 Efficacy analyses (generalised linear mixed model)

Results obtained for the analysis of procedural efficacy are displayed in table 4.3. In addition to whether each covariate, *i*, had an effect on the outcome, its coefficient *Bi* was also calculated. From the value of the coefficient, the percentage change in the outcome (such as the number of outpatient appointments) was calculated from $100 \times (1 - e^{Bi})$, where the percentage change is expressed in units appropriate to the covariate, such as per year for age. A negative value indicates a reduction in the outcome measure; a positive value indicates an increase in the outcome measure. For sex, the reference level was female.

The results of subgroup analyses are included for those patients with diagnosis codes indicating atrial fibrillation (AF) or supraventricular tachycardia (SVT).

Table 4.3. Results from Generalised Linear Mixed Model analyses. †Change calculation based on 100 x (1 – e^{Bi}) For age and comorbidity, the change is expressed per year and per unit increase in comorbidity score, respectively. For sex, the reference level is 'female'.

	All CALON patients (*max. n=1931*)			Atrial Fibrillation (AF) (*max. n=700*)			Supraventricular Tachycardia (SVT) *(max. n=514*)		
Covariate	**Change†**	**95% CI**	**p-value**	**Change†**	**95% CI**	**p-value**	**Change†**	**95% CI**	**p-value**
Number of outpatient appointments									
After_p (before vs after procedure)	-26.7%	-29.8% to -23.4%	< 0.001	-22.0%	-27.4% to -16.1%	< 0.001	-46.3%	-51.4% to -40.6%	< 0.001
Sex	-8.5%	-15.3% to -1.1%	0.025	-22.5%	-32.6% to -11.0%	< 0.001	-13.8%	-25.5% to 0.0%	0.049
Age	1.6%	1.4% to 1.9%	< 0.001	1.0%	0.5% to 1.6%	< 0.001	1.1%	0.7% to 1.6%	< 0.001
Comorbidity	2.7%	2.1% to 3.3%	< 0.001	2.0%	1.1% to 2.9%	< 0.001	2.9%	1.0% to 4.9%	0.003
Length of stay for inpatients (total days admitted)									
After_p (before vs after procedure)	-21.5%	-26.9% to -15.7%	<0.001	-16.6%	-26.4% to -5.6%	0.004	8.2%	-9.0% to 28.7%	0.368 (NS)
Sex	-3.2%	-11.6% to 6.0%	0.482 (NS)	-32.2%	-41.9% to -20.8%	< 0.001	0.4%	-17.0% to 21.5%	0.964 (NS)
Age	1.9%	1.6% to 2.2%	<0.001	0.7%	0.0% to 1.3%	0.035	1.1%	0.5% to 1.7%	< 0.001
Comorbidity	7.3%	6.5% to 7.9%	<0.001	5.7%	4.7% to 6.7%	< 0.001	10.2%	7.6% to 12.9%	< 0.001
Number of GP 'appointments' (days with Read code recorded)									
After_p (before vs after procedure)	-0.2%	-4.3% to 4.0%	0.910 (NS)	-5.8%	-11.9% to 0.6%	0.075 (NS)	-12.0%	-20.1% to -3.2%	0.009
Sex	-17.0%	-23.8% to -9.4%	<0.001	-19.9%	-30.6% to -7.5%	0.002	-34.2%	-48.2% to -16.3%	0.001
Age	2.2%	2.0% to 2.5%	<0.001	1.2%	0.6% to 1.7%	< 0.001	2.1%	1.3% to 2.9%	< 0.001
Comorbidity	1.6%	0.9% to 2.3%	<0.001	1.4%	0.3% to 2.4%	0.011	0.0%	-2.9% to 3.0%	0.981 (NS)
Number of prescriptions for antiarrhythmia drugs									
After_p (before vs after procedure)	-65.1%	-72.4% to -55.9%	<0.001	-72.5%	-80.8% to -60.5%	< 0.001	-92.5%	-96.3% to -84.5%	< 0.001
Sex	32.6%	-4.9% to 85.0%	0.096 (NS)	-9.5%	-51.1% to 67.7%	0.751 (NS)	8.9%	-52.5% to 149.2%	0.841 (NS)
Age	1.8%	0.8% to 2.9%	0.001	-3.7%	-6.0% to -1.4%	0.002	3.3%	0.5% to 6.2%	0.022
Comorbidity	-0.1%	-2.6% to 2.4%	0.951 (NS)	1.9%	-2.5% to 6.5%	0.391 (NS)	0.5%	-8.7% to 10.7%	0.913 (NS)
Number of prescriptions for antidepressants and/or anti-anxiety drugs									

	All CALON patients (*max. n=1931*)			Atrial Fibrillation (AF) (*max. n=700*)			Supraventricular Tachycardia (SVT) (*max. n=514*)		
Covariate	**Change†**	**95% CI**	**p-value**	**Change†**	**95% CI**	**p-value**	**Change†**	**95% CI**	**p-value**
After_p (before vs after procedure)	30.7%	5.0% to 62.9%	0.016	-20.5%	-46.0% to 17.0%	0.244 (NS)	34.0%	-16.3% to 114.9%	0.222 (NS)
Sex	-49.0%	-66.1% to -23.3%	0.001	-24.4%	-67.5% to 75.4%	0.514 (NS)	-38.6%	-74.5% to 47.6	0.275 (NS)
Age	1.4%	0.1% to 2.7%	0.033	2.3%	-1.3% to 6.1%	0.213 (NS)	2.9%	0.0% to 5.9%	0.047
Comorbidity	3.1%	0.0% to 6.4%	0.046	7.4%	1.8% to 13.3%	0.009	-3.3%	-13.5% to 8.0%	0.544 (NS)

An example of interpretation of the results is as follows. The primary outcome was whether the cardiac ablation procedure reduced the number of secondary care appointments allowing for the sex, age and comorbidity of the patients. For outpatient appointments for all CALON patients, there was a statistically significant reduction of 26.7% in the number of appointments per year after the procedure had been carried out compared to before. From the analysis of the covariates (sex, age and comorbidity), men had 8.5% fewer appointments than women; there was a 1.6% increase in the number of appointments per year increase in age of the patient; and there was a 2.7% increase in the number of appointments per unit increase in the comorbidity score. From these results, the following can be calculated as examples. For a patient who is ten years older, the increase in the number of appointments would be 17%. A patient with a comorbidity score five points higher than another patient would expect to have a 14% increase in the number of appointments.

Key points that can be interpreted from these statistical analyses for efficacy across the patient group as a whole are as follows:

- There was a statistically significant ($p<0.001$) reduction in both the number of outpatient appointments and days spent as an inpatient, after the ablation procedure. This was the primary outcome measure for the study.
- The number of GP events (days on which a Read code had been recorded) did not differ significantly before and after an ablation procedure ($p=0.910$)
- Whilst the number of prescriptions for antiarrhythmia drugs decreased after the ablation procedure ($p<0.001$), there was an increase in the number of prescriptions for antidepressants/anxiolytics ($p=0.016$).
- Sex did not have a significant influence on either length of inpatient stay or antiarrhythmia prescriptions for the dataset as a whole. For the other efficacy measures, significantly higher numbers were seen in women compared to men ($p<0.05$). This difference was particularly marked in the number of prescriptions for antidepressants/anxiolytics, where women were almost twice as likely to have been issued with a prescription ($p=0.001$).
- An increase in age was associated with higher numbers across all efficacy measures ($p<0.05$).
- Patients with a higher comorbidity score had more healthcare service encounters as outpatients, inpatients and in primary care ($p<0.001$). Comorbidity score was not significantly related to numbers of antiarrhythmia drugs prescribed. However patients with higher comorbidity scores had a slightly greater number of antidepressant/anxiolytic prescriptions; an increase by one point of the Charlson index resulted in a 3.1% increase in the number of prescriptions issued ($p=0.046$).

Other observations relating to subgroup analyses for patients diagnosed with AF or SVT were:

- Whilst the whole dataset had not seen a change in the number of GP events before and after the procedure, a 12% reduction was seen in the SVT subgroup ($p=0.009$).
- In the analysis of inpatient data for the AF group, results indicated that women spent more days admitted to hospital than men ($p<0.001$). This only applied to the AF group (results were not significant across the dataset as a whole).
- Whilst there was a substantial fall in antiarrhythmia drugs prescribed after an ablation across all patients, this was particularly true for patients with SVT, who saw a reduction of 92.5% ($p<0.001$).
- Changes in prescribing of antidepressants/anxiolytics varied considerably between patient groups. In the CALON dataset as a whole, there was a 30.7% increase in prescriptions after the procedure ($p=0.016$). The AF group saw a 20.5% reduction, although this result was not statistically significant ($p=0.244$).
- Some broad ranges were seen between confidence intervals for prescriptions in the SVT group; this is likely to be due to there being relatively low numbers of patients with GP data for this subgroup.

4.4 Safety outcomes

4.4.1 Safety event counts

A description of which data sources contributed to safety outcomes can be found in section 4.2.2. The maximum number of patients for this section of the results was n=2220. Counts of pre-specified safety events are presented in table 4.4. As there were different lengths of follow-up for each patient, the

numbers in table 4.4 should not be used to calculate incidence rates. Results of an alternative method of calculating incidence rates can be found later in section 4.4.2 under the heading "Time-to-event for other safety outcomes".

Table 4.4. Counts of safety events from different data sources. The ICD-10 codes and GP Read codes used to identify these events are listed in Appendix D. Differing lengths of follow-up have not been accounted for, and safety outcomes listed may not be causally related to the ablation procedures.

Safety event	Data source	Patient records available (max.)	Up to 5 year follow-up		Up to 1 year follow-up		First event within 'expected' period	'Expected' period
			Patients	Events	Patients	Events	Patients	
Ablation complications: First degree heart block, Pneumothorax, Haematoma, Pericardial effusion, Respiratory arrest, VF, Pulmonary embolus, Cerebral embolus, Peripheral embolus, Coronary artery complications, Unintended complete AV block, Haemodynamic collapse, DC cardioversion, or Unlisted	NICOR	1057	<6	n/a	<6	n/a	n/a	n/a
Bleeding	PEDW	1931	120	126	98	99	86	12 weeks
Other vascular complications/air embolism	PEDW	1931	6	7	<6	<6	<6	12 weeks
Bleeding or other vascular complications	GP data	700	18	19	12	12	8	12 weeks
Arterial repair	NICOR	1057	<6	n/a	<6	n/a	n/a	n/a
Infection, cellulitis, mediastinitis	PEDW	1931	18	22	8	11	<6	12 weeks
Mediastinitis or Infection	GP data	700	41	63	23	30	6	12 weeks
Pericarditis	GP data	700	<6	<6	<6	<6	<6	12 weeks
Pericardial effusion	GP data	700	7	9	<6	7	<6	12 weeks
Cardiac tamponade	PEDW	1931	31	37	25	31	22	12 weeks
Chest drain	NICOR	1057	<6	n/a	<6	n/a	n/a	n/a
Pericardial tap	NICOR	1057	<6	n/a	<6	n/a	n/a	n/a
Myocardial infarction	PEDW	1931	25	29	13	15	<6	6 weeks
Acute coronary artery occlusion	PEDW	1931	<6	<6	<6	<6	<6	6 weeks
Myocardial infarction or acute coronary artery occlusion	GP data	700	12	20	9	15	<6	6 weeks
Oesophageal injury	PEDW	1931	7	7	<6	<6	<6	6 months
Oesophageal injury	GP data	700	<6	<6	<6	<6	<6	6 months
Pulmonary embolism	PEDW	1931	11	14	<6	6	<6	12 weeks
Pulmonary embolism	GP data	700	<6	<6	<6	<6	<6	12 weeks
Stroke & Silent Cerebral Embolism	PEDW	1931	24	43	10	18	<6	6 weeks
Stroke or silent cerebral embolism	GP data	700	11	21	<6	11	<6	6 weeks

Safety event	Data source	Patient records available (max.)	Up to 5 year follow-up		Up to 1 year follow-up		First event within 'expected' period	'Expected' period
			Patients	Events	Patients	Events	Patients	
Transient ischaemic attack (TIA)	PEDW	1931	11	11	<6	<6	<6	6 weeks
Transient ischaemic attack (TIA)	GP data	700	10	16	<6	<6	<6	6 weeks
Pulmonary vein stenosis	PEDW	1931	<6	<6	<6	<6	<6	3 years
Cardioversion	GP data	700	30	38	17	20	8	12 weeks
Heart Block	GP data	700	13	16	8	9	<6	12 weeks
Heart Failure	GP data	700	23	29	13	17	<6	12 weeks
Pacemaker insertion	GP data	700	23	26	13	15	7	12 weeks
Gastric motility/pyloric spasm disorders	PEDW	1931	7	9	<6	<6	<6	6 months
Gastric motility/pyloric spasm disorders	GP data	700	<6	<6	<6	<6	<6	6 months
Nerve injury/paralysis	GP data	700	<6	<6	<6	<6	<6	12 weeks
Other complications	PEDW	1931	7	7	<6	<6	<6	12 weeks
Other complications, not elsewhere classified	GP data	700	<6	<6	<6	<6	<6	12 weeks
Other significant complications	NICOR	1057	<6	n/a	<6	n/a	n/a	n/a

4.4.2 Survival outcomes

Survival analysis was used to calculate the incidence of safety events and repeat ablation procedures whilst accounting for patients for whom a full five years of follow-up was not available. When viewing survival/incidence curves, please note that the scale of the y-axes has been adjusted to best show the shape of each curve; minimum/maximum values do not cover the whole range of 0-100%.

Mortality

Table 4.5. Results from the Kaplan-Meier for the whole dataset, then for subgroups of patients with diagnosis codes for atrial fibrillation (AF) and supraventricular tachycardia (SVT). Patients with no follow-up were excluded from the analysis. One-year survival for SVT is not reported due to low numbers (<6 patients died within the first year).

Arrhythmia	No. of patients	Five-year survival	One-year survival
All patients	1946	91.0%	98.2%
AF	633	88.6%	98.4%
SVT	440	97.0%	-

Patients with no follow-up in either PEDW or GP data were excluded from these analyses (n=274).

From the remaining 1946 patients, 106 were identified as having died according to the Welsh Demographic Service. A Kaplan-Meier survival analysis indicated that the five-year survival rate was 91.0% (table 4.5). The survival rate at one year was 98.2%.

The five-year survival rate for patients diagnosed with SVT (97.0%) was substantially greater than that of patients diagnosed with AF (88.6%).

Table 4.6. Results from the Cox Regression Analysis for the whole dataset, then for subgroups of patients with diagnosis codes for atrial fibrillation (AF) and supraventricular tachycardia (SVT). Patients with no follow-up were excluded from the analysis. Sex was not found to have an effect on any of the outcomes and was not included in the final model. For AF and SVT, age was also excluded from the final model.

Arrhythmia	Covariates in final model	Estimate of odds ratio (95% confidence interval)	p-value
All patients	Age	1.054 (1.036 to 1.073)	<0.001
	Comorbidity	1.079 (1.060 to 1.098)	<0.001
AF	Comorbidity	1.082 (1.049 to 1.116)	<0.001
SVT	Comorbidity	1.219 (1.124 to 1.323)	<0.001

The Cox regression analysis indicated that younger patients and patients with a lower comorbidity score were more likely to survive (table 4.6). Sex did not have an effect on outcome and was not included in the final model. Data were missing from 25 patients, as they had no pre-procedural hospital records on which to calculate a comorbidity score. There were 1815 patients who either survived or were lost to follow-up.

In the subgroup analyses, data were missing for five cases from the AF group, and for eight cases from the SVT group. Age was not found to have an effect and was excluded from the model for the subgroup analyses. Lower comorbidity scores were particularly influential in improving survival for patients with SVT, but also showed a significant effect for patients with AF.

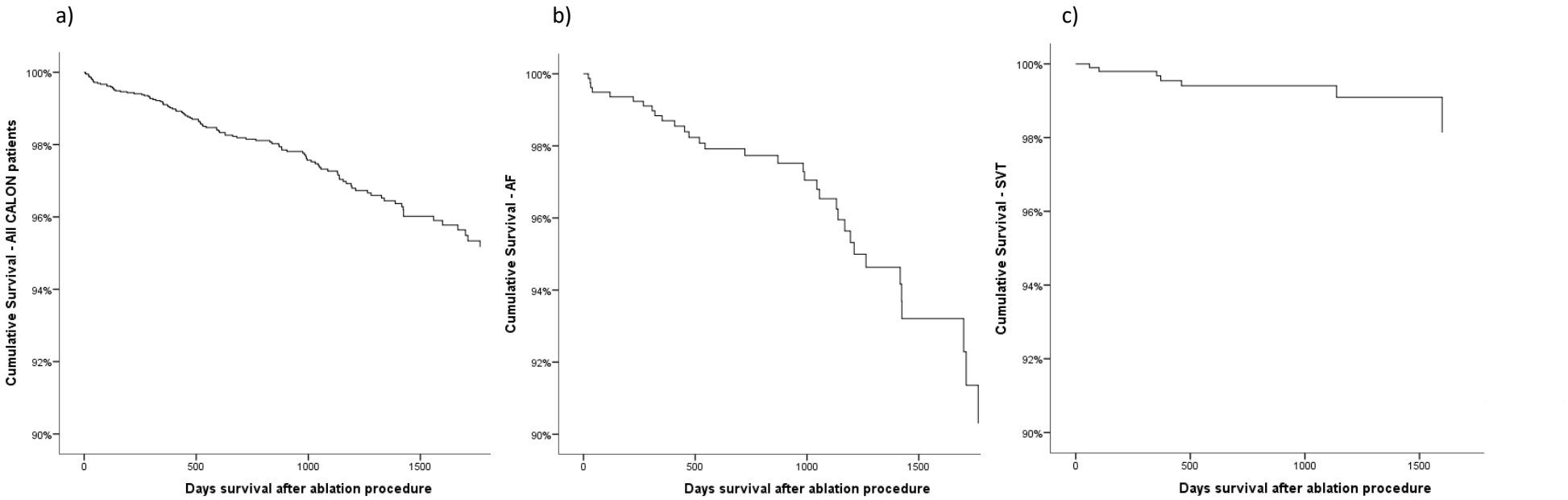


Figure 4.6. Survival curve for an 'average' patient based on the mean of the covariates from the Cox Regression Analysis. From left to right a) All patients b) Patients with code for atrial fibrillation c) Patients with code for supraventricular tachycardia. Note that the y-axis scale is from 90 to 100%.

The Cox Regression cumulative survival curve that included all patients with known lengths of follow-up (n=1921) showed a negative linear relationship over time, indicating that the rate of death after the procedure remained fairly constant (figure 4.6). As previously highlighted by the Kaplan-Meier analysis, it is estimated that over 90% of patients were still alive after five years (having adjusted for variable lengths of follow-up) (table 4.5).

The survival curves for AF and SVT show some clear differences. Due to lower total numbers (n=700 and n=514 respectively) compared to the results from the whole dataset, granularity is reduced and therefore the line is less smooth. However some obvious patterns can still be observed. The steeper slope of the line for AF indicates a higher death rate than can be seen in the SVT patients. This is consistent with the findings of the Kaplan-Meier analysis, which concluded that 5-year survival rates for AF and SVT were 88.6% and 97.0% respectively (table 4.5).

Time-to-event for repeat ablation procedures

Table 4.7. Results from the Kaplan-Meier based on cumulative incidence of repeat procedures for the whole dataset, then for subgroups of patients with diagnosis codes for atrial fibrillation (AF) and supraventricular tachycardia (SVT). Patients with no follow-up were excluded from the analysis.

		Cumulative incidence		
Arrhythmia	**No. of patients**	**Five years**	**One year**	**90-days**
All patients	1945	8.1%	4.5%	0.8%
AF	632	10.6%	4.2%	<6 patients
SVT	440	5.3%	4.0%	<6 patients

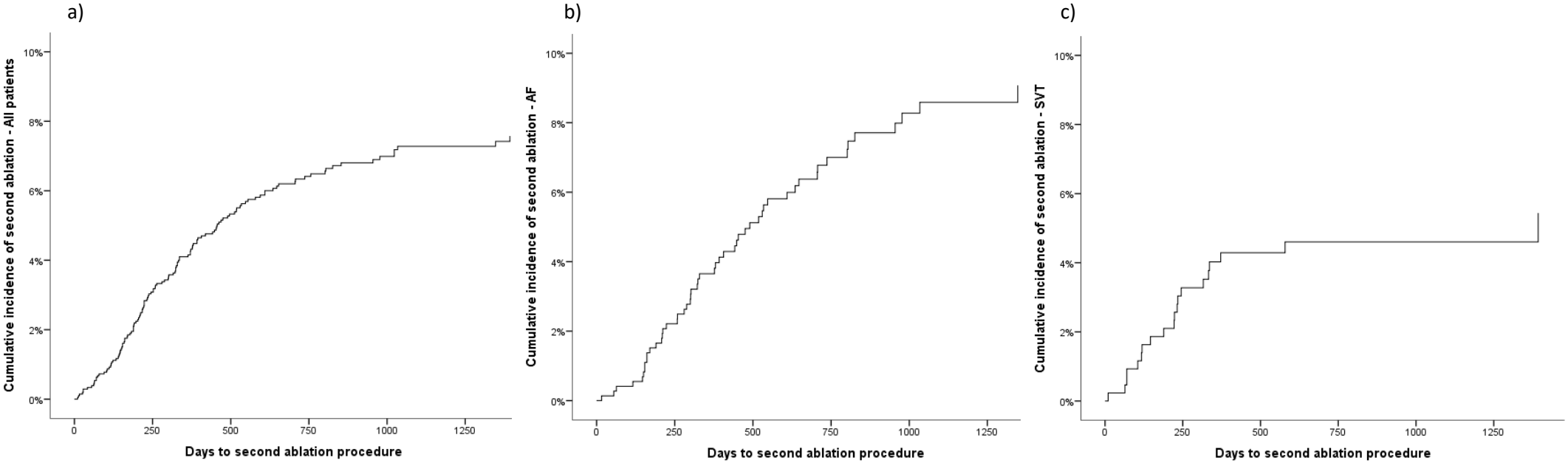


Figure 4.7. Cumulative incidence of second ablation procedure for an 'average' patient based on the mean of the covariates from the Cox Regression Analysis for a) All patients b) Patients with code for atrial fibrillation c) Patients with code for supraventricular tachycardia.

Results of time-to-event analyses showed that 8.1% patients underwent a repeat ablation procedure within five years (table 4.7 and figure 4.7). The rate was higher for patients with AF when compared to the dataset as a whole. Fewer patients with SVT underwent repeat procedures within five years; where a repeat procedure was carried out, it was typically within one year of the first procedure.

Time-to-event for other safety outcomes

Kaplan-Meier analyses (table 4.8) allowed more reliable estimates of the incidence of some safety outcomes than were possible using the simple counts reported in table 4.4.

Table 4.8. Estimated incidence of patients with specified safety event codes recorded based on Kaplan-Meier analysis.

Safety event	Data source(s)	Incidence within 5 years follow-up	Incidence within 1 year follow-up
Stroke or Silent Cerebral Embolism	PEDW & GP	1.7%	0.5%
Transient Ischaemic Attack (TIA)	PEDW & GP	1.3%	<6 patients
Myocardial Infarction (MI)	PEDW & GP	2.1%	1.1%
Cardiac Tamponade	PEDW	1.8%	1.3%

Graphs showing cumulative incidence of these four safety events give an illustration of any changes in rate of incidence over the five years of follow-up (figure 4.8). Incidence of stroke/silent cerebral embolism remains relatively constant throughout the period of follow-up. There appears to be a short delay before the first few transient ischaemic attacks were recorded, and then a gradual increase over time whilst remaining at a slightly lower incidence than stroke. The rate of occurrence of myocardial infarction is initially high, with a 90-day cumulative incidence of 0.6% (according to the Kaplan-Meier analysis). Similarly, but to a greater extent, the incidence rate of cardiac tamponade is highest within the initial post-procedural period. The 90-day cumulative incidence of cardiac tamponade was 1.1%; after this the incidence rate drops considerably, as can be seen by the levelling off of the graph.

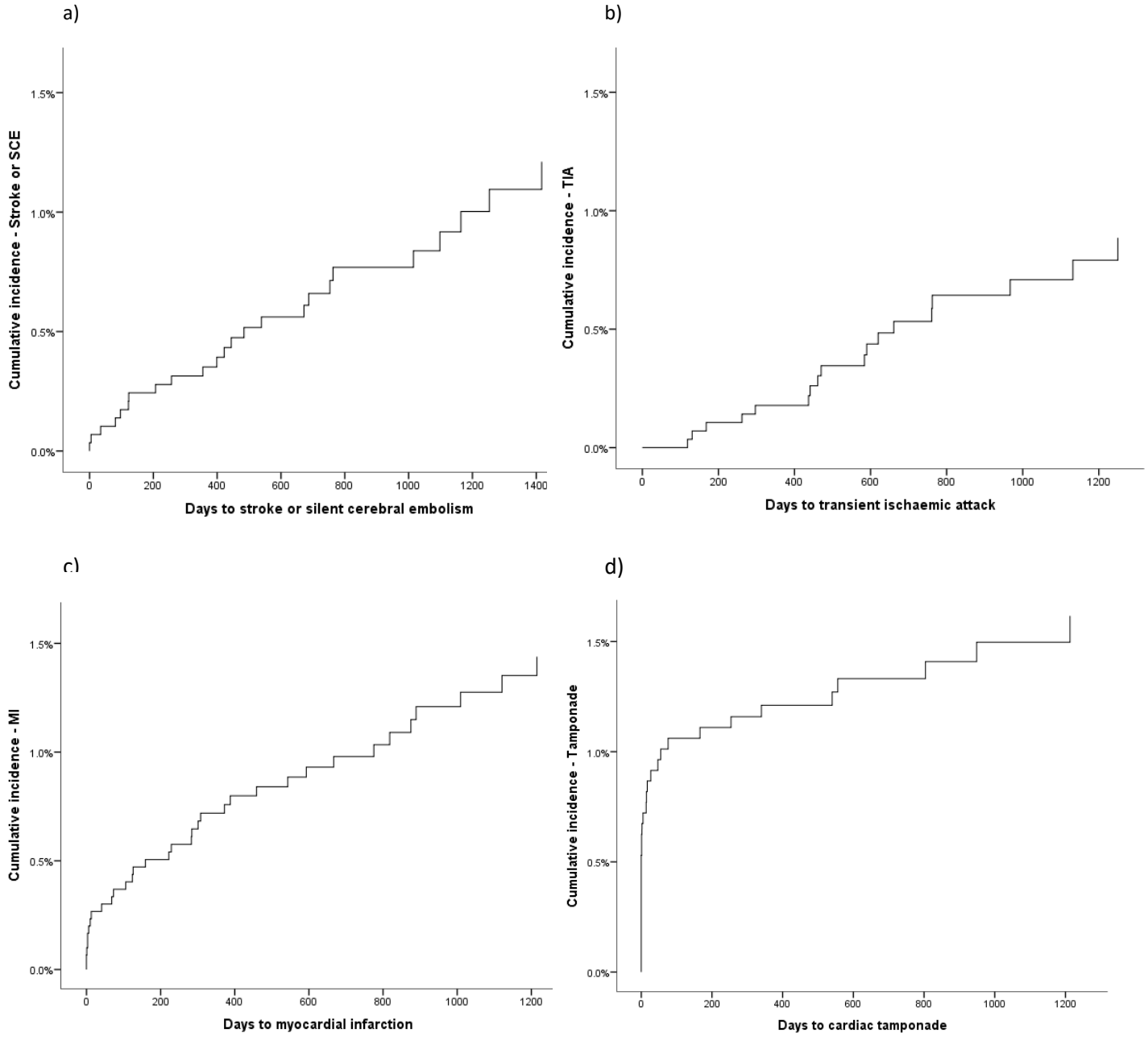


Figure 4.8. Time to first record of specified safety event based on Cox Regression Analysis. a) Stroke or Silent Cerebral Embolism b) Transient Ischaemic Attack c) Myocardial Infarction d) Cardiac Tamponade.

4.4.3 Common post-procedural codes

As described in the protocol, all diagnosis codes recorded after the procedure were sorted in order of descending frequency to look for common safety events. Table 4.9 shows the results of this exercise across five years of follow-up. A total number of 1931 patients had follow-up data from PEDW available during Period 1; the most common diagnosis codes recorded during that first year of follow-up are presented in table 4.10.

Table 4.9. Commonly recorded diagnosis codes observed across five years of follow-up.

Code	Description	Count	No. of Patients
I48.X	Atrial fibrillation and flutter	2362	964
Z92.1	Personal history long -term (current) use of anticoagulants	1562	678
I10.X	Essential (primary) hypertension	1363	668
I47.1	Supraventricular tachycardia	689	539
Z95.0	Presence of cardiac pacemaker	641	248
Z82.4	Family history of ischaemic heart disease and other diseases of the circulatory system	578	484
E11.9	Type 2 diabetes mellitus without complications	577	189
Z86.4	Personal history of psychoactive substance abuse	575	385
E78.0	Pure hypercholesterolaemia	435	296
J45.9	Other and unspecified asthma	413	207
Z86.7	Personal history of diseases of the circulatory system	406	254
Z95.1	Presence of aortocoronary bypass graft	392	135
Z92.2	Personal history long -term (current) use of other medicaments	362	277
I25.8	Other forms of chronic ischaemic heart disease	361	162
I25.1	Atherosclerotic heart disease	337	191
E78.5	Hyperlipidaemia, unspecified	261	229
E03.9	Hypothyroidism, unspecified	248	112
Z72.0	Tobacco use	242	200
I45.6	Pre-excitation syndrome	233	153
I50.1	Left ventricular failure	231	136

Table 4.10. Commonly recorded diagnosis codes observed in the first year of follow-up.

Code	Description	Count	No. of Patients	% of 1931
I48.X	Atrial fibrillation and flutter	1394	841	43.5
Z92.1	Personal history long -term (current) use of anticoagulants	858	558	28.9
I10.X	Essential (primary) hypertension	798	520	26.9
I47.1	Supraventricular tachycardia	586	506	26.2
Z82.4	Family history of ischaemic heart disease and other diseases of the circulatory system	494	445	23.0
Z86.4	Personal history of psychoactive substance abuse	400	316	16.4
Z95.0	Presence of cardiac pacemaker	359	193	10.0
E11.9	Type 2 diabetes mellitus without complications	290	147	7.6
E78.0	Pure hypercholesterolaemia	290	225	11.7
Z92.2	Personal history long -term (current) use of other medicaments	268	225	11.7
J45.9	Other and unspecified asthma	238	161	8.3
E78.5	Hyperlipidaemia, unspecified	226	206	10.7
Z86.7	Personal history of diseases of the circulatory system	217	159	8.2
Z95.1	Presence of aortocoronary bypass graft	205	103	5.3
I25.8	Other forms of chronic ischaemic heart disease	190	116	6.0
Z72.0	Tobacco use	189	145	7.5

Code	Description	Count	No. of Patients	% of 1931
I25.1	Atherosclerotic heart disease	188	128	6.6
I45.6	Pre-excitation syndrome	182	136	7.0
E66.9	Obesity, unspecified	141	117	6.1
I47.2	Ventricular tachycardia	126	104	5.4

The records of commonly-recorded diagnosis codes (tables 4.9 and 4.10) are arranged in order of descending frequency of events as this was the way in which they were detected; the numbers of patients associated with these events may in fact be more informative, as each patient may have the same code recorded multiple times. This method is only possible using large datasets of routinely-recorded data, as it was not necessary in this case to pre-specify the exact codes to be recorded or searched.

As the search included all ICD-10 diagnosis codes for patients who have undergone cardiac ablation procedures, it is unsurprising that many of those codes listed are related to cardiovascular conditions. A corresponding 'control' group of patients matched for age, sex and comorbidity (without having undergone ablation) would highlight the different risks faced by this particular population; any future similar studies may wish to consider this design. These tables have been made available to clinicians with cardiology expertise; any unexpected results may form the basis of discussions for the project steering group, and potential inclusion in a publication if considered to be of sufficient interest.

4.5 Comparison of patient identification methods

The earlier section 4.2.1 did not report demographic data for patients who did not have sufficient follow-up data available (and who were not therefore included in efficacy analyses). This section (4.5) includes all patients from the complete CALON dataset, after excluding only those records which met the criteria described in figure 4.1. A total of 47.6% (1057/2220) patients from the CALON dataset were identified through the NICOR registry. The remaining 52.4% (1163/2220) were identified using OPCS ablation procedure codes from routine PEDW data.

These analyses were carried out to check whether there were any significant differences in demographic characteristics between the group of patients identified as having had an ablation using registry data when compared to the group identified using routine data.

4.5.1 Sex

Table 4.11. Proportion of male and female patients detected through both patient identification methods.

	Patient identification method					
	Registry group		Routine group		All patients	
Sex	Count	Percentage	Count	Percentage	Count	Percentage
Male	638	60.4%	671	57.7%	1309	59.0%
Female	419	39.6%	492	42.3%	911	41.0%
Total	1057	100.0%	1163	100.0%	2220	100.0%

The proportion of men was approximately 60% across both groups (table 4.11). A Chi-square test confirmed that there was no significant difference in the proportion of men and women when the two methods of identifying patients were compared (p=0.218).

4.5.2 Age

Table 4.12. Age groups reported separately by patient identification method.

	Patient identification method					
	Registry group		Routine group		All patients	
Age group (years)	**Count**	**Percentage**	**Count**	**Percentage**	**Count**	**Percentage**
18 to 30	114	10.8%	142	12.2%	256	11.5%
31 to 45	180	17.0%	219	18.8%	399	18.0%
46 to 60	270	25.5%	323	27.8%	593	26.7%
61 to 75	384	36.3%	371	31.9%	755	34.0%
Over 75	109	10.3%	108	9.3%	217	9.8%
Total	1057	100.0%	1163	100.0%	2220	100.0

The mean age on the date of first ablation procedure for registry and routine groups was 55.7 years and 54.1 years respectively, and a wide range of ages were represented in both groups (table 4.12). Whilst a t-test indicated that ages differed significantly between the two groups (p=0.022), the mean difference of 1.6 years and narrow confidence intervals of 0.23-3.04 years may not be considered a clinically important difference.

4.5.3 Comorbidity score

Table 4.13. Frequencies of comorbidity scores for patients detected using registry and routine data. To facilitate comparison of patient identification method, patient records with no comorbidity score calculated due to lack of pre-procedural data (n=277) were excluded.

	Patient identification method					
	Registry group		Routine group		All patients	
Comorbidity score	**Count**	**Percentage**	**Count**	**Percentage**	**Count**	**Percentage**
-1 or 0	470	60.1%	721	62.1%	1191	61.3%
1 to 10	190	24.3%	234	20.2%	424	21.8%
11 to 20	90	11.5%	158	13.6%	248	12.8%
21 to 30	24	3.1%	38	3.3%	62	3.2%
Over 30	8	1.0%	10	0.9%	18	0.9%
Total	782	100.0%	1161	100.0%	2220	100.0%

The distribution of comorbidity scores was very similar for the two methods of identifying patients (table 4.13). A Mann-Whitney U test indicated that there was no significant difference in comorbidity scores between registry and routine identification methods (p=0.389).

4.5.4 Calendar year of procedure

The number of procedures recorded in each calendar year was summarised for those patients identified through the registry and those detected using procedure codes from hospital data (figure 4.9).

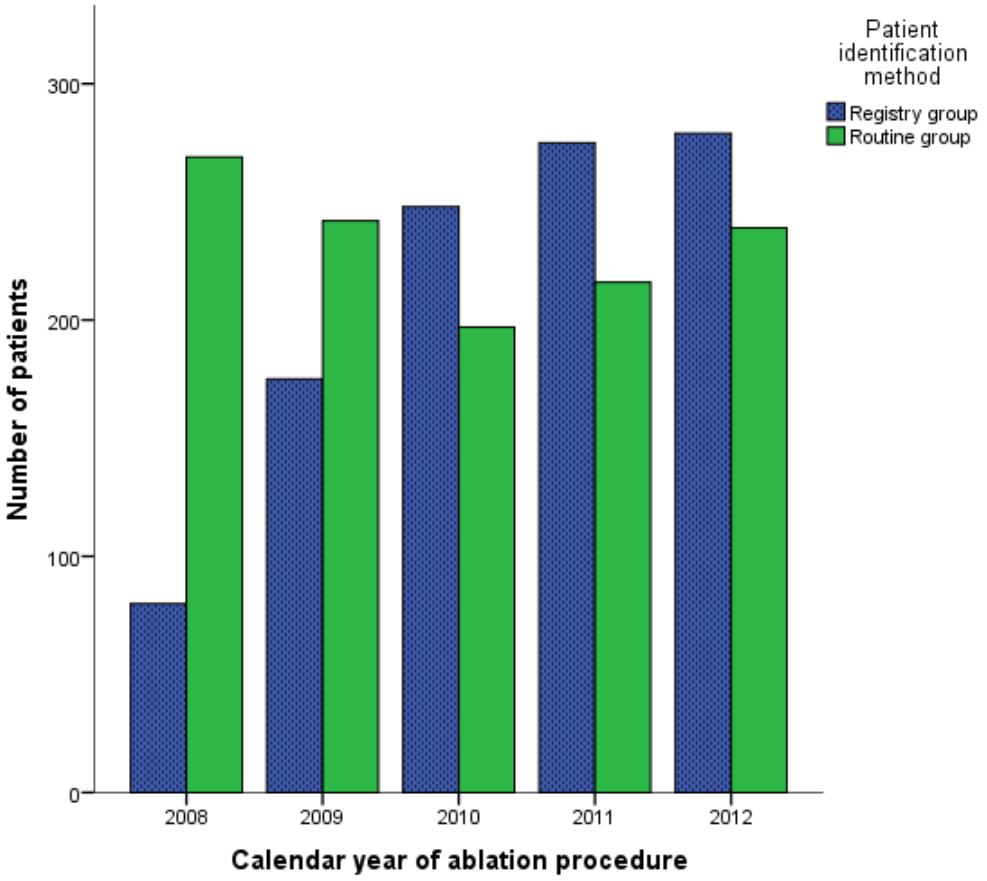


Figure 4.9. Numbers of patients recorded as undergoing first ablation procedures per calendar year, according to patient identification method.

The registry data shows that an increasing number of procedures were recorded in the ablation dataset every year, with 2012 having 3.5 times as many procedures recorded as in 2008. In contrast procedures detected in routine data showed no clear frequency pattern over time, with a range of 197 to 269 patients undergoing first ablation procedures per year throughout the study period. This suggests that while actual numbers of procedures stays relatively constant over time, the recording of data by clinicians into the registry has substantially improved.

4.6 Recording of safety events

4.6.1 Mortality

Entries in the NICOR 'Death' field were either 'Yes', 'No', or 'Unknown', and a further 13.6% were missing (144/1057 patient records). According to the registry group, fewer than six (of 1057) patients died during their admission for the ablation procedure. For those patients recorded as

having died according to NICOR, we were unable to verify their deaths using WDS data. Either there was no record of the death within the WDS data, or the appropriate WDS data were not available.

There was one record within the NICOR dataset which indicated that a patient had died, but evidence of clinical appointments was found in linked records for the same patient more than a year later. It was not clear how this data discrepancy had occurred.

4.6.2 Other safety events

Numbers of safety codes identified from hospital, GP and registry data sources are listed in table 4.4. The quality and completeness of these records was not evaluated due to differences in classification definitions as well as variable (and sometimes unknown) lengths of follow-up.

5 Discussion and conclusions

The aims of the CALON project were to find out more information about how well cardiac ablation procedures work and how safe they are, and to assess the value of using data linkage as a method for healthcare research. This report presents the results of the efficacy and safety analyses, and provides insight into the value of data linkage as a methodology.

There is a wealth of information presented within the results section, and it is anticipated that a number of publications will be produced following further discussions with the project steering group and with NICE. Some of the main observations could be summarised as follows:

- The number of days of secondary care service use (outpatients and inpatients) reduced after the ablation procedure. The number of GP events did not differ significantly before and after the procedure.
- Prescriptions of antiarrhythmia medications reduced after ablation.
- Prescriptions of antidepressant/anxiolytic medications increased after ablation, particularly in the subgroup of patients with a diagnosis of supraventricular tachycardia.
- Direct comparison of the recording of safety events between data sources was not attempted due to differences in classifications and length of follow-up. It was however possible to estimate the incidence of some key safety outcomes up to five years of follow-up based on routine data.
- Key differences were observed between subgroups of patients diagnosed with atrial fibrillation and supraventricular tachycardia, particularly in relation to:
    - Antiarrhythmia prescriptions
    - Antidepressant/anxiolytic prescriptions
    - Survival to five years
    - Repeat ablation procedures.

It is likely that these results will raise interesting ideas for further analysis, some of which may be permissible within the existing project providing they are consistent with the original protocol plans and/or are approved by relevant data providers.

Rather than further scrutinising individual results within this report, the authors felt that it would be more appropriate at this stage to comment on the benefits and challenges of applying data linkage methodology within the context of this particular study. We have therefore provided limited commentary on the clinical outcomes.

Our experience in applying for and working with data from different providers has taught us some valuable lessons. The SAIL Databank is a secure anonymised linked data linkage system containing hospital and primary care data, as well as a number of other datasets such as those listed in table 5.1. As it stands, it has considerable value and may be used to answer NICE's research questions. Access to SAIL is relatively quick and straightforward. The Health Informatics Research Unit (HIRU) at Swansea University hosts the SAIL Databank and is part of Cedar's consortium. Cedar has privileged access to the Databank through this relationship, and a process for expediting Cedar's requests to their Information Governance Review Panel (IGRP) is due to be implemented shortly.

Linked resources such as the SAIL Databank provide longitudinal data, and in this pilot project we were able to interrogate up to seven years worth of data in a project lasting less than two years.

Table 5.1. Other core SAIL datasets.

Annual District Birth Extract
Bowel Screening Wales (BSW)
Breast Test Wales (BTW)
Cervical Screening Wales (CSW)
Congenital Anomaly Register and Information Service (CARIS)
Emergency Department Data Set (EDDS)
National Community Child Health Database (NCCHD)
Welsh Cancer Intelligence and Surveillance Unit (WCISU)

To supplement the 1057 records of patients initially identified by NICOR for the CALON project, a further 1163 patients were identified using procedure codes from PEDW data within the SAIL Databank. Our analysis included statistical comparisons of demographic characteristics of patients identified through these two patient identification methods (registry and routine). The only variation found was a minor difference in mean age (of 1.6 years); otherwise the patients were comparable in levels of comorbidity and proportions of men and women. Many of the patients identified through the registry also had routine records in PEDW. If patients had been identified through hospital records alone, the CALON dataset would have totalled 1931 patients. The patient records found only within the registry did not contain sufficient long-term follow-up data to enable their use within the majority of the analyses, but they were used to identify early procedural complications.

The registry contains details of ablation procedures that cannot be found within routine sources. When designing CALON, it had been anticipated that these details would enable the classification of the procedures according to the criteria described by NICE's Interventional Procedures guidance documents. Appendix C shows a procedure definition algorithm that was developed to facilitate classification based upon some of the registry variables. Once the data was received, it became apparent that the granularity and consistency of data recorded within key variables was not sufficient for this purpose. Similarly, HES/PEDW data is based on coding and available codes do not always match the procedures in IP guidance. Therefore in this study it was not possible to conduct sub-group analysis of the different ablation procedures. This is a limitation of the use of routinely held data, since the data was not collected for the purpose of research, and the nature of the intervention is not necessarily of great interest to the data owner.

There were also concerns about the completeness of the registry extract when it was found that PROMs data were missing, indicating that data from Cardiff had not been provided; a later extract (not used for analysis) was also found to have over 8,000 missing records. Whilst the reasons for these omissions were never fully elucidated (with investigations being hampered by the fact that patient details had been anonymised), the similarity of the registry-identified patients to those found in routine data alleviated these concerns.

Obtaining the registry data was very time consuming. The application process took five months from initial enquiry to approval, and the clinical data extract was provided after an additional four

months. Given that it was not possible to use the registry data to distinguish between the ablation procedures of interest, and that a large number of patients could alternatively be successfully detected through routine data sources, the time, effort and financial cost of obtaining the registry data for should be balanced with the additional information gained from the data. It would be advantageous to view a sample of the registry data at the design stage to assess feasibility. If the registry were to prospectively collect appropriate data within a mandatory field, there is potential that future analyses could allow comparison of the efficacy and safety outcomes of each type of ablation procedure.

Since the SAIL Databank contained sufficient patient numbers to answer important questions relating to cardiac ablation procedures, it is suggested that Cedar's preferential access to the Databank could be utilised by NICE to conduct preliminary analyses prior to commissioning a bespoke linkage.

The news coverage of care.data and subsequent review of governance in HSCIC impacted on the project and we were unable to include English data within a reasonable timescale. These events at a national level could not have been predicted at the outset of the CALON project. Considerable time and effort was spent on working towards linking English data. Without this added complexity the project could have been completed in a shorter duration.

The population of England is much greater than that of Wales, and for rare events this might be an advantage. However the coverage of GP data is less than 10%, whereas over 60% of Welsh GP practices have agreed to provide data to the SAIL Databank. In the four countries of the UK there are differences in the NHS. For example in Wales prescriptions are free of charge for all patients, whereas in England some patients but not all are exempted from charges. These differences may impact on the results of data linkage studies, for example we do not know if the numbers of prescriptions issued by GPs in England would show the same changes as we have seen in the Welsh data. In the context of our research questions, this is not a consideration as we were using prescription and other data as a surrogate to show improved general health. If we were interested in resource usage, we may have to consider the different administrations independently.

Whilst access to HES/PEDW is relatively straightforward our results are greatly enhanced by having GP data, linked at an individual patient level. We can see that the reduction in secondary care episodes is not simply a case of transfer of workload to primary care. Power calculations have demonstrated that numbers of CALON patients provided through Welsh records were easily sufficient to power the primary outcome measures for the study.

Data providers conduct their own data cleaning processes prior to releasing data, and the team at HIRU also carried out a substantial amount of data preparation before releasing the anonymised linked data to Cedar. Even after these processes, it was necessary for Cedar to perform additional cleaning steps and to run automated calculations to compute new variables in a suitable form for analysis. Through these exercises Cedar has gained proficiency in writing syntax to prepare and analyse large datasets of linked data.

The creation of this linkage between the NICOR dataset and the SAIL Databank is temporary. At the end of this project the data must be destroyed. Creating permanent linkages is more realistically the

territory of specialist teams such as HIRU, rather than EACs such as Cedar. However, we do have an opportunity to influence HIRU and to request that HIRU seek to link with particular datasets that may be of interest to NICE for the future.

In conclusion, the CALON project has demonstrated that linked secondary and primary care data can be useful in elucidating the outcomes of interventional procedures. Lessons have been learned that will be of great value to any further data linkage work at both strategic and operational levels.

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Appendix A – Complications related to cardiac ablation

Cedar has not completed a formal literature search for complications of cardiac ablation, or a complete critical analysis of the papers presented.

The European Society of Cardiology list complications of cardiac ablation in their published Guidelines for the management of Atrial Fibrilation (Camm et al. 2010). They cite as references papers by Cappato et al (2005), Cappato et al (2009) and Calkins et al (2009). Information on their methods, and a summary of selected results is presented below, however Cedar have not undertaken a critical analysis of these papers. Both papers by Cappato report on a very large survey, where voluntary responses may result in a selected group of patients that do not have a representative complication rate. Controlled trials may result in higher levels of complications, although some are rare and may not occur within the study population. A Health Technology Assessement (Rodgers et al. 2008) gives an example of this.

Cappato et al. 2005) sent a questionnaire to 777 centres worldwide with 43 questions looking at their cardiac ablation programme, the number of ablations annually, techniques used, patient characteristics, success rate with and without antiarrhythmia drugs, and incidence of complications. Data was requested from 1995 to 2002. Of the 181 responses (response rate 23%), 100 centres had commenced cardiac ablation programmes between 1995 and 2002. Data was received for 11762 procedures, and 9370 patients, with an average length of follow up of 11.6±7.7 months (median 12, range 1 to 98). Complications were reported for all types of procedures (n=8745) and for procedures involving left atrial ablation (n=7154). There is no explanation given of the difference between total data reported (9370 patients) and complication reporting (8745 patients). The paper calculates percentage incidence rates for complications, however this does not account for missing data on patients, data from centres that did not respond, or for the varying length of follow-up for patients included.

This survey was updated (Cappato et al. 2010) with data from 2003 to 2006, receiving data for 20825 catheter ablations on 16309 patients, and 182 centres worldwide. As with the previous survey (Cappato et al. 2005), percentage complication incidence rates are reported, but should be treated with caution.

Calkins et al (2009) a systematic literature review and meta-analysis on radiofrequency ablation as treatment for atrial fibrillation that selected 63 studies, with 8789 patients (plus 25 papers on the same studies and patients but with additional information) published between 1990 and 2007. In reporting safety outcomes, the total number of patients in the studies that included those outcomes were used as the denominator. Studies will have excluded some groups of patients, who may have had different incidence of safety outcomes. Studies with fewer than seven days follow-up were excluded, the mean follow-up was 14 months (range 2-30 months). Of the included studies, nine were RCTs, 11 were prospective comparative studies, 31 were prospective single arm studies, and 12 were retrospective.

Although there is information on the mean length of follow up in these papers there is no attempt to adjust the reporting for follow up length.

Complications of cardiac ablation (ESC Guidelines)

Complications investigated in CALON	Calkins 2009	Cappato 2005	Cappato 2010
Follow up length, months: Mean (range)	14 (2-30)	11.6±7.7 (1 - 98)	18 (3-24)
All complications	97/1964 (4.94%) [a]	524/8745 (5.99%)	741/16309 (4.54%)
Bleeding	1/2960 0.03%[c]	n/r	n/r
Other vascular complications/ air embolism	n/r	n/r	n/r
Arterial repair	Arteriovenous fistula 1/2885 (0.03%) [b]	Arteriovenous fistulae 37/8745 (0.42%)	Total arteriovenous fistulae 88/16309 (0.54%)
Infection	n/r	Sepsis, abscesses or endocaditis 1/8745 (0.01%)	Sepsis, abscesses or endocaditis 2/16309 (0.01%)
Pericarditis	n/r	n/r	n/r
Pericardial effusion	36/5719 (0.63%) [a]	n/r	n/r
Tamponade	45/5723 (0.79%) [a]	107/8745 (1.22%)	213/16309 (1.31%)
Chest drain	n/r	Haemothorax 14/8745 (0.16%)	Haemothorax 4/16309 (0.02%)
Pericardial tap	n/r	n/r	n/r
Myocardial infarction	n/r	n/r	n/r
Acute coronary artery occlusion	n/r	n/r	n/r
Oesophageal injury	Left atrial-oesophageal fistula 0/5496 (0%) [a]	n/r	Atrium –oesophageal fistula 6/16309 (0.04%)
Pulmonary embolism	3/5496 (0.05%) [a]	n/r	n/r
Stroke and silent cerebral embolism	17/5665 (0.30%)[a]	20/7154[c] (0.28%)	37/16309 (0.23%)
Transient ischaemic attack (TIA)	13/5467 (0.24%) [a]	47/7154[c] (0.66%)	115/16309 (0.71%)
Pulmonary vein stenosis	Stenosis >70% 91/5831 (1.56%) [a]	Stenosis >50% 117/7154[c] (1.64%)	requiring intervention 48/16309 (0.29%)
Cardioversion	n/r	n/r	n/r
Heart block	AV block 1/5496 (0.02%) [a]	n/r	n/r
Heart Failure	n/r	n/r	n/r
Pacemaker insertion	Need for a pacemaker 4/3902 (0.10%) [a]	n/r	n/r
Gastric motility / pyloric spasm	n/r	n/r	n/r
Nerve injury / paralysis	n/r	Permanent diaphragmatic paralysis 10/8745 (0.11%)	Permanent diaphragmatic paralysis 28/16309 (0.17%)

Complications investigated in CALON	Calkins 2009	Cappato 2005	Cappato 2010
Other complications	Death overall 42/5781 (0.7%) Procedure related death 0/51921 (0%) Haematoma 17/3719 (0.46%) Femoral artery pseudoaneurysm 15/3032 (0.49%) Deep vein thrombosis 1/4758 (0.02%) [a] Other embolism 10/5347 (0.19%) [a] Other fistula 3/5407 (0.06%)[a] CHF exacerbation 0/5496 (0%) [a]	Periprocedural death 4/8745 (0.05%) Pneumothorax 2/8745 (0.02%) Femoral pseudoaneurysm 47/8745 (0.54%) Valve damage 1/8745 (0.01%) Aortic dissection 3/8745 (0.03%)	Death 25/16309 (0.15%) Pneumothorax 15/16309 (0.09%) Total femoral pseudoaneurysm 152/16309 (0.93%) Valve damage requiring surgery 11/16309 (0.07%)

n/r = Not reported, [a] Periprocedure, [b] Vascular access site, [c] Results reported for procedures involving left atrial ablation, n=7154 patients

Appendix B – Related NICE Interventional Procedure Guidelines

Procedures combined with open cardiac surgery

See also IPG 123 (under 'cryoablation procedures').

- **IPG 184 High-intensity focused ultrasound for atrial fibrillation in association with other cardiac surgery**.

  In HIFU an ultrasound device is placed outside the left atrium of the beating heart. This sends a focused beam of ultrasound energy across the wall of the heart. The heart absorbs the energy, causing the temperature to rise. The heat destroys the chosen area of cardiac tissue and disrupts the transmission of the abnormal electrical impulses.

  NICE guidance (2006): "*Current evidence on the safety and efficacy of high-intensity focused ultrasound (HIFU) for atrial fibrillation in association with other cardiac surgery is insufficient for this procedure to be used without special arrangements for consent and for audit or research*".

- **IPG 121 Radiofrequency ablation for atrial fibrillation in association with other cardiac surgery**.

  In radiofrequency ablation, heat is used to make scars through heart tissue in the atria. The scars may then interrupt the electrical signals and stop them from spreading and causing the problems. The heat is produced from a source of radiofrequency energy. Scars may be formed on both the atria or on only the left-hand atrium. The surgeon may get to the tissue from inside the atrium or from the outside. Radiofrequency ablation is usually carried out at the same time the person is having other heart surgery, and the NICE guidance described here has only looked at radiofrequency ablation when it is used in these circumstances. The most common type of surgery a person would be having is mitral valve surgery.

  NICE guidance (2006): "*Current evidence on the safety and efficacy of radiofrequency ablation (RFA) for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance".*

- **IPG 122 Microwave ablation for atrial fibrillation in association with other cardiac surgery**.

  In microwave ablation, heat is used to make scars through heart tissue in the atria. The scars may then interrupt the electrical signals and stop them from spreading and causing the problems. The heat is produced by microwave energy, produced from a flexible probe. Scars may be formed on both the atria or on only the left-hand atrium. The surgeon may get to the tissue from inside the atrium or from the outside. Microwave ablation is usually carried out at the same time the person is having other heart surgery, and the NICE guidance described here has only looked at microwave ablation when it is used in these circumstances. The most common type of surgery a person would be having is mitral valve surgery to replace or repair the mitral valve.

  NICE guidance (2005): "*Current evidence on the safety and efficacy of microwave ablation for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance*".

Percutaneous ablation

- **IPG 168 Percutaneous radiofrequency catheter ablation for atrial fibrillation**.

  Percutaneous radiofrequency ablation can be carried out without open heart surgery. In this procedure, a catheter is inserted into a vein in the upper leg and moved up into the heart, using X-ray to make sure it's in the right place. An attachment at the tip of the catheter produces heat that damages the nerves in the area where the abnormal electrical impulses are.

  NICE guidance (2006): "*Current evidence on the safety and efficacy of percutaneous radiofrequency ablation for atrial fibrillation appears adequate to support the use of this procedure in appropriately selected patients provided that normal arrangements are in place for audit and clinical governance*".

- **IPG 294 Percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation**.

  'Epicardial' refers to the outermost membrane of the heart and 'radiofrequency ablation' means using heat energy to remove tissue. A special thin tube is inserted through the skin in the lower chest area and positioned next to the epicardium. X-rays are used to make sure it is positioned properly. Heat is passed to the tip of the tube to break down the parts of the heart muscle where the abnormal electrical impulses are. Ablation from the inside and outside of the heart may be combined. This procedure can be carried out for patients with different types of arrhythmias – this particular guidance refers to treatment of atrial fibrillation.

  NICE guidance (2009): "*Current evidence on the safety and efficacy of percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation (AF) is inadequate in quantity. Therefore this procedure should only be used with special arrangements for clinical governance and consent*".

- **IPG 295 Percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for ventricular tachycardia**.

  'Epicardial' refers to the outermost membrane of the heart and 'radiofrequency ablation' means using heat energy to remove tissue. A special thin tube is inserted through the skin in the lower chest area and positioned next to the epicardium. X-rays are used to make sure it is positioned properly. Heat is passed to the tip of the tube to break down the parts of the heart muscle where the abnormal electrical impulses are. Ablation from the inside and outside of the heart may be combined. This procedure can be carried out for patients with different types of arrhythmias – this particular guidance refers to treatment of ventricular tachycardia.

  NICE guidance (2009): "*The evidence on percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for ventricular tachycardia (VT) is limited to a small number of patients, but it shows that the procedure is efficacious in carefully selected individuals and raises no major safety issues, in the context of a condition which is potentially life-threatening. Therefore, the procedure may be used with normal arrangements for clinical governance, but with special arrangements for consent*".

Thoracoscopic procedures

- **IPG 286 Thoracoscopic epicardial radiofrequency ablation for atrial fibrillation**.

  'Thoracoscopic' means keyhole surgery through the chest wall. 'Epicardial' refers to the

outer surface of the heart and 'radiofrequency ablation' means using heat energy to destroy tissue. Small incisions are made in the chest wall, through which a camera and instruments are inserted. The right lung is deflated to gain access. Selected areas of the heart are destroyed using an instrument that delivers heat energy.

NICE guidance (2009): "*There is evidence of efficacy for thoracoscopic epicardial radiofrequency ablation for atrial fibrillation (AF) in the short term and in small numbers of patients. The assessment of cardiac rhythm during follow-up varied between studies, and some patients were concomitantly treated with anti-arrhythmic medication. Evidence on safety shows a low incidence of serious complications but this is also based on a limited number of patients. Therefore the procedure should only be used with special arrangements for clinical governance, consent and audit or research*".

Cryoablation procedures

- **IPG 123 Cryoablation for atrial fibrillation in association with other cardiac surgery**.

  In cryoablation, a probe that produces very cold temperatures is used to freeze tissue. This process makes scars through heart tissue in the atria. The scars may then interrupt the electrical signals and stop them from spreading and causing the problems. Scars may be formed on both the atria or on only the lefthand atrium. The surgeon may get to the tissue from inside the atrium or from the outside. Cryoablation is usually carried out at the same time the person is having other heart surgery, and the NICE guidance described here has only looked at cryoablation when it is used in these circumstances. The most common type of surgery a person would be having is mitral valve surgery to replace or repair the mitral valve. Cryoablation of the atria can also be performed via a catheter introduced through a femoral vein in the leg.

  NICE guidance (2005): "*Current evidence on the safety and efficacy of cryoablation for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance*".

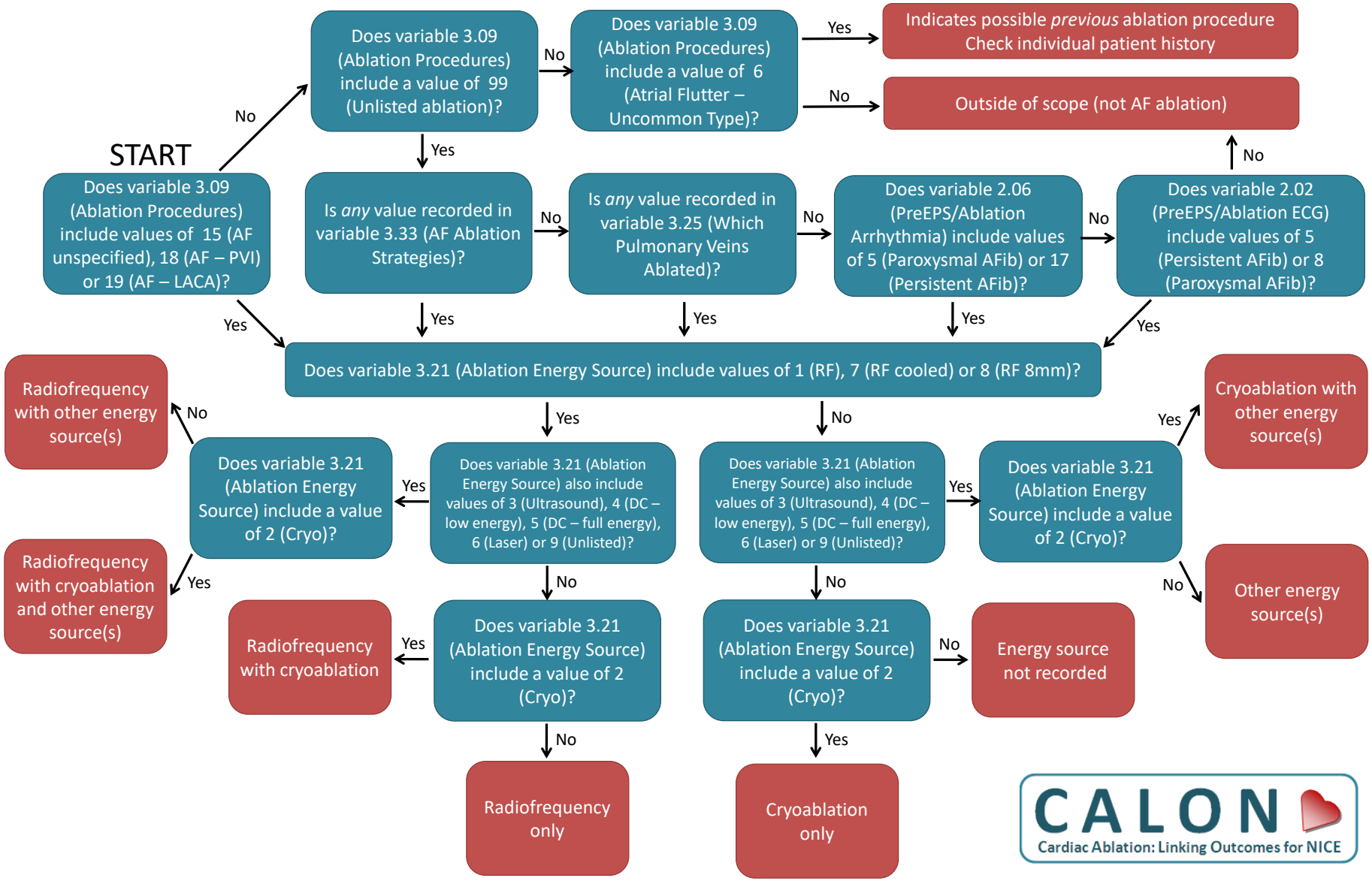
- **IPG 427 Percutaneous balloon cryoablation for pulmonary vein isolation in atrial fibrillation**.

  The abnormal electrical impulses in atrial fibrillation usually start where the large blood vessels carrying blood from the lungs (the pulmonary veins) enter the heart. Balloon cryoablation uses a balloon catheter to freeze tissue in one of the chambers on the left side of the heart. The aim is to produce scarring, which may interrupt the electrical signals that come from the pulmonary veins, and so help to maintain a normal heartbeat. Catheters (thin tubes), one with a small balloon attached, are inserted into one or both of the veins at the top of the legs (the femoral veins) and guided into the heart. The freezing balloon and a device used to record electrical signals are passed into the left side of the heart and the balloon is inflated to fix it in the correct position at the entrance to the pulmonary vein. The freezing balloon is cooled in several-minute bursts until the abnormal electrical signals are stopped. This is repeated for each of the pulmonary veins.

  NICE guidance (2012): "*Current evidence on the efficacy and safety of percutaneous balloon cryoablation for pulmonary vein isolation in atrial fibrillation is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit"*.

Appendix C

Algorithm to define procedure type based upon CCAD variables



CALON
Cardiac Ablation: Linking Outcomes for NICE

Appendix D – ICD-10 and Read codes related to safety events

ICD-10 codes used for complications related to cardiac ablations, for PEDW data	
Complication	**ICD-10 code**
Other vascular complications/air embolism	I72.4, I77.0, T81.7
Infection, cellulitis, mediastinitis	J98.5, L03.0, L03.1, T81.4
Cardiac tamponade	I31.9, I30.9, I30.1, I31.3
Myocardial infarction	I21.0, I21.1, I21.4, I21.9, I22.0, I22.8, I22.9
Acute coronary artery occlusion	I24.0
Oesophageal injury	K22.1, K22.3, K22.8
Pulmonary embolism	I26.0, I26.9
Stroke & Silent Cerebral Embolism	I63.4, I63.5, I63.8, I63.9, I64.X, I66.3, 65.2
Transient ischaemic attack (TIA)	G45.9
Pulmonary vein stenosis	I28.8
Gastric motility/pyloric spasm disorders	K31.3, K31.8
Other complications	T81.2, T81.8

Read codes used for complications related to cardiac ablations, for GP data	
Bleeding or other vascular complications	
16R..00	Bleeding symptom
172..00	Blood in sputum - haemoptysis
172..12	Haemoptysis - symptom
G728.00	Dissection of artery of lower extremity
G760.00	Acquired arteriovenous fistula
G8y0.00	Haemorrhage NOS
R063.00	[D]Haemoptysis
R063z00	[D]Haemoptysis NOS
SE45.11	Haematoma of leg
SE4z.11	Haematoma NOS
SK02.00	Secondary and recurrent haemorrhage
SK02.12	Secondary and recurrent haemorrhage
SP01000	Mechanical complication of vascular device unspecified
SP12.00	Peripheral vascular complications of care
SP12z00	Peripheral vascular complications of care NOS
SP21.00	Peri-operative haemorrhage or haematoma
SP21.11	Haematoma - postoperative
SP21.12	Haemorrhage - postoperative
SP21100	Post-operative haemorrhage
SyuK411	[X] Mechanical complication of vascular catheter
TA0..11	Accidental haemorrhage during medical care
TB02000	Arteriovenous anastomosis with complication without blame
Cardioversion	
793F.00	Cardioverter defibrillator introduced through the vein

793F000	Implantat cardioverter defibrillator us one electrode lead
793F100	Implant cardioverter defibrillator using two electrode leads
793F500	Implantat cardiovert defibrillator us three electrode leads
793Fy00	Other specified cardioverter defibrillator intro thr vein
793Fz00	Cardioverter defibrillator introduced through the vein NOS
793M200	Percutaneous transluminal internal cardioversion NEC
7L1H.11	Cardioversion and stimulation
7L1H000	Direct current cardioversion
7L1H100	External cardioversion NEC
7L1H111	External electrode cardioversion
7L1H200	Internal electrode cardioversion
Gastric motility/pyloric spasm disorders	
761..00	Stomach and pylorus operations
761..11	Gastric and pylorus operations
761z.00	Stomach and pylorus operations NOS
J16y700	Gastric spasm
J16y800	Gastric dysmotility
J16y900	Delayed gastric emptying
J17y000	Pylorospasm
J529.00	Generalised intestinal dysmotility
SP14.00	Gastrointestinal complications of care
SP14z00	Gastrointestinal complication of care NOS
Heart block	
3297.11	Electrocardiogram: Mobitz type 1 second degree AV block
329..00	ECG: heart block
3292.00	ECG: partial sinu-atrial block
3293.00	ECG:complete sinu-atrial block
3294.00	ECG:partial A-V block-long P-R
3295.00	ECG: partial A-V block - 2:1
3296.00	ECG: partial A-V block - 3:1
3298.00	ECG: complete A-V block
3299.00	ECG: right bundle branch block
329A.00	ECG: left bundle branch block
329B.00	ECG: trifascicular block
329C.00	ECG: bifascicular block
329D.00	ECG: left anterior fascicular block
329E.00	ECG: left posterior fascicular block
329F.00	ECG: right bundle branch and left anterior fascicular block
329G.00	ECG: right bundle branch and left posterior fascicular block
329H.00	Electrocardiogram: Mobitz type 2 second degree AV block
329Z.00	ECG: heart block NOS
G56..12	Heart block
G560.00	Complete atrioventricular block
G560.11	Third degree atrioventricular block

G561.00	Partial atrioventricular block
G561000	Atrioventricular block unspecified
G561100	First degree atrioventricular block
G561200	Mobitz type II atrioventricular block
G561300	Mobitz type I (Wenckebach) atrioventricular block
G561311	Mobitz type 1 second degree atrioventricular block
G561400	Second degree atrioventricular block
G561z00	Atrioventricular block NOS
G562.00	Left bundle branch hemiblock
G562.11	Left bundle branch block
G562000	Left anterior fascicular block
G562100	Left posterior fascicular block
G562z00	Left bundle branch hemiblock NOS
G563.00	Left main stem bundle branch block
G564.00	Right bundle branch block
G565.00	Other bundle branch block
G565000	Bundle branch block unspecified
G565100	Right BBB with left posterior fascicular block
G565200	Right BBB with left anterior fascicular block
G565300	Other bilateral bundle branch block
G565400	Trifascicular block
G565500	Bifascicular block
G565z00	Other bundle branch block NOS
G566.00	Other heart block
G566000	Sinoatrial block
G566100	Interventricular block NOS
G566200	Right fascicular block
G566z00	Other heart block NOS
G56y400	Right fascicular block
Gyu5U00	[X]Other and unspecified atrioventricular block
Gyu5V00	[X]Other and unspecified fascicular block
Gyu5W00	[X]Other and unspecified right bundle-branch block
Gyu5X00	[X]Other specified heart block
Heart failure	
1J60.00	Suspected heart failure
1O1..00	Heart failure confirmed
8H2S.00	Admit heart failure emergency
G58..00	Heart failure
G580.00	Congestive heart failure
G580.12	Right heart failure
G580000	Acute congestive heart failure
G582.00	Acute heart failure
G583.00	Heart failure with normal ejection fraction
G583.11	HFNEF - heart failure with normal ejection fraction

G58z.00	Heart failure NOS
G5y4z00	Post cardiac operation heart failure NOS
SP11111	Heart failure as a complication of care
Mediastinitis or infection	
H531.00	Abscess of mediastinum
H5y2.00	Mediastinitis
M03..00	Other cellulitis and abscess
M032600	Cellulitis and abscess of groin
M036.00	Cellulitis and abscess of leg excluding foot
M036.11	Cellulitis and abscess of leg
M036100	Cellulitis and abscess of thigh
M036z00	Cellulitis and abscess of leg NOS
M03y.00	Other specified cellulitis and abscess
M03z.00	Cellulitis and abscess NOS
M03z000	Cellulitis NOS
M03z100	Abscess NOS
M03zz00	Cellulitis and abscess NOS
M08..00	Cutaneous cellulitis
M081.00	[X]Cellulitis of other parts of limb
M085.00	Cellulitis of leg
M09..00	Cutaneous abscess
M094.00	[X]Abscess of limb
M095.00	Skin abscess
SP25.00	Postoperative infection
SP25000	Postoperative stitch abscess
SP25100	Postoperative wound abscess
SP25500	Postoperative wound infection unspecified
SP25600	Postoperative wound infection-deep
SP25700	Postoperative wound infection-superficial
SP25800	MRSA infection of postoperative wound
SP25z00	Postoperative infection NOS
Myocardial infarction or acute coronary artery occlusion	
323..00	ECG: myocardial infarction
323Z.00	ECG: myocardial infarct NOS
G30..00	Acute myocardial infarction
G30..15	MI - acute myocardial infarction
G30..17	Silent myocardial infarction
G301.00	Other specified anterior myocardial infarction
G301z00	Anterior myocardial infarction NOS
G304.00	Posterior myocardial infarction NOS
G305.00	Lateral myocardial infarction NOS
G306.00	True posterior myocardial infarction
G307100	Acute non-ST segment elevation myocardial infarction
G308.00	Inferior myocardial infarction NOS

G30B.00	Acute posterolateral myocardial infarction
G30X000	Acute ST segment elevation myocardial infarction
G30y.00	Other acute myocardial infarction
G30yz00	Other acute myocardial infarction NOS
G30z.00	Acute myocardial infarction NOS
G311500	Acute coronary syndrome
G31y000	Acute coronary insufficiency
G35..00	Subsequent myocardial infarction
G350.00	Subsequent myocardial infarction of anterior wall
G351.00	Subsequent myocardial infarction of inferior wall
G353.00	Subsequent myocardial infarction of other sites
G35X.00	Subsequent myocardial infarction of unspecified site
G38..00	Postoperative myocardial infarction
G380.00	Postoperative transmural myocardial infarction anterior wall
G383.00	Postoperative transmural myocardial infarction unspec site
G384.00	Postoperative subendocardial myocardial infarction
G38z.00	Postoperative myocardial infarction unspecified
Gyu3400	[X]Acute transmural myocardial infarction of unspecif site
Gyu3600	[X]Subsequent myocardial infarction of unspecified site
SP11000	Cardiac arrest as a complication of care
Nerve injury/paralysis	
7051700	Crushing of phrenic nerve
SJ1y200	Vagus (10th) nerve injury
SJ7..00	Injury to other nerves
SJ7x.00	Other specified nerve injury
SJ7z.00	Injury to other nerve NOS
SJ81.00	Crush injury of phrenic nerve
SP22100	Injury to nerve during surgery
Oesophageal injury	
J102z00	Ulcer of oesophagus NOS
J104.00	Perforation of oesophagus
J10y800	Rupture of oesophagus
S722100	Closed injury of oesophagus
S723100	Open injury of oesophagus
Other complications, not elsewhere classified	
S895300	Open wound of inguinal region with complication
S895311	Open wound of groin with complication
SA01100	Open wound of thigh with complication
SC43.00	Late effect of medical and surgical care complication
SC43.12	Late effect of surgical care complication
SK...00	Traumatic complications and unspecified injuries
SN5..00	Adverse effects NEC
SN5y.00	Other adverse effects NEC
SN5yz00	Other adverse effects NEC NOS

SN5z.00	Adverse effects NOS
SP...00	Surgical and medical care complications NEC
SP...13	Catheter complications
SP...16	Medical care complications NEC
SP0..00	Complications of certain procedures
SP00.00	Mechanical complication of cardiac device implant and graft
SP00000	Mechanical complication of cardiac device unspecified
SP00z00	Mechanical complication of cardiac device/implant/graft NOS
SP01.00	Mechanical complication other vascular device/implant/graft
SP01700	Mechanical complication of arterio-venous surgical fistula
SP01z00	Mechanical complication of vascular device/implant/graft NOS
SP0z.00	Certain procedure complications NOS
SP11.00	Cardiac complications of care
SP11.11	Post operative cardiac complication
SP11100	Cardiac insufficiency as a complication of care
SP11200	Cardiorespiratory failure as a complication of care
SP11z00	Cardiac complication of care NOS
SP2..00	Other procedure complication NEC
SP2..11	Operation complication NEC
SP2..12	Surgical complication NEC
SP26.00	Persistent postoperative fistula
SP2y.00	Other procedure complication NEC
SP2yz00	Other procedure complication NEC NOS
SP2z.00	Postoperative complication NOS
SP3..00	Medical care complication NEC
SP31.00	Air embolism as a complication of medical care
SP31.11	Air embolus as a complication of medical care
SP32.00	Other medical care vascular complications
SP32z00	Medical care vascular complication NOS
SP3y.00	Other medical care complication NEC
SP3yz00	Other medical care complication NOS
SPz..00	Medical and surgical care complications NOS
SyuK.00	[X]Complications of surgical and medical care NEC
SyuK200	[X]Other complications of procedures NEC
SyuK400	[X]Mechan complic of oth cardiac & vasc devices & implants
SyuK500	[X]Infect/inflam react due oth card/vasc device/impl/grafts
TB...00	Medical + surgical procedures causing complications no blame
TB0..00	Surgical procedures causing complications without blame
TB0y.00	Other surgical operations/procedures+complication no blame
TB0z.00	Surgical operations/procedures + complication no blame NOS
TB1..00	Other medical procedures with complication no blame
TB10.00	Cardiac catheterisation with complication without blame
TB1y.00	Other procedure with complication without blame
TB1yz00	Other procedure with complication no blame NOS

TB1z.00	Other medical procedure with complication
U6...00	[X]Complications of medical and surgical care
U621.00	[X]Cardiovascular devices associated with adverse incidents
U624.00	[X]Gener hosp+person use device assoc with adverse incident
U62y.00	[X]Other + unspec medical devs assoc with adverse incidents
Pacemaker implantation	
7936.11	Introduction of intravenous cardiac pacemaker system
7936000	Implantation of intravenous cardiac pacemaker system
7936500	Implantation of emergency intravenous cardiac pacemaker
7936511	Implantation of temporary intravenous cardiac pacemaker
7936600	Implantation of permanent intravenous cardiac pacemaker
7936700	Implantation of intravenous fixed-rate cardiac pacemaker
7936800	Implantation of intravenous triggered cardiac pacemaker
7936900	Implantation of intravenous atrial overdrive pacemaker
7937000	Implantation of cardiac pacemaker system NEC
7937700	Implantation of single chamber cardiac pacemaker system
7937800	Implantation of dual chamber cardiac pacemaker system
7937900	Implantation of biventricular cardiac pacemaker system
7936.00	Introduction of cardiac pacemaker system via vein
7936A00	Implant intravenous pacemaker for atrial fibrillation
7936B00	Implantation simple one wire intravenous cardiac pacemaker
7936C00	Implantation of complex 1 wire intravenous cardiac pacemaker
7936D00	Implantation complex two wire intravenous cardiac pacemaker
7936E00	Implantation of intravenous dual chamber permanent pacemaker
7936G00	Implantat intraven single chamber cardiac pacemaker system
7936H00	Implantat intravenous dual chamber cardiac pacemaker system
7936J00	Implantat intravenous biventricular cardiac pacemaker system
7936K00	Implantation of intravenous cardiac pacemaker system NEC
7936y00	Other specified cardiac pacemaker system introduced via vein
7936z00	Cardiac pacemaker system introduced via vein NOS
7937.00	Other cardiac pacemaker system
7937y00	Other specified other cardiac pacemaker system
7937z00	Other cardiac pacemaker system NOS
TB01000	Implant of cardiac pacemaker with complication no blame
ZV53300	[V]Fitting or adjustment of cardiac pacemaker
Pericardial effusion	
G50..11	Pericardial effusion - acute
G50z511	Pyopericardium
G530.00	Haemopericardium
G533.00	Pericardial effusion - noninflammatory
G534.00	Pericardial effusion - acute
G536.00	Pericardial effusion
S714.00	Injury of heart with haemopericardium
Pericarditis	

85C7.00	Inj.pericard.sac-local action
85C7.11	Pericardial sac inj.
G50..00	Acute pericarditis
G501.00	Post infarction pericarditis
G50z.00	Other and unspecified acute pericarditis
G50z000	Acute pericarditis - unspecified
G50z100	Acute idiopathic pericarditis
G50z500	Acute purulent pericarditis unspecified
G50zz00	Acute pericarditis NOS
G531.00	Adhesive pericarditis
G531z00	Adhesive pericarditis NOS
G532.00	Constrictive pericarditis
G532z00	Constrictive pericarditis NOS
G53yz11	Chronic pericarditis
Gyu5000	[X]Other forms of acute pericarditis
Pulmonary embolism	
1JC..00	Suspected pulmonary embolism
G401.00	Pulmonary embolism
G401.12	Pulmonary embolus
G401000	Post operative pulmonary embolus
Stroke or Silent cerebral embolism	
1JA1000	Suspected cerebrovascular accident
1JA1011	Suspected stroke
7A25200	Embolisation of cerebral artery NEC
G312.00	Coronary thrombosis not resulting in myocardial infarction
G61..11	CVA - cerebrovascular accid due to intracerebral haemorrhage
G61..12	Stroke due to intracerebral haemorrhage
G63..11	Infarction - precerebral
G63y000	Cerebral infarct due to thrombosis of precerebral arteries
G63y100	Cerebral infarction due to embolism of precerebral arteries
G64..00	Cerebral arterial occlusion
G64..11	CVA - cerebral artery occlusion
G64..12	Infarction - cerebral
G64..13	Stroke due to cerebral arterial occlusion
G640.00	Cerebral thrombosis
G640000	Cerebral infarction due to thrombosis of cerebral arteries
G641.00	Cerebral embolism
G641.11	Cerebral embolus
G641000	Cerebral infarction due to embolism of cerebral arteries
G64z.00	Cerebral infarction NOS
G64z200	Left sided cerebral infarction
G64z300	Right sided cerebral infarction
G66..00	Stroke and cerebrovascular accident unspecified
G66..12	Stroke unspecified

G66..13	CVA - Cerebrovascular accident unspecified
G676000	Cereb infarct due cerebral venous thrombosis nonpyogenic
G677100	Occlusion and stenosis of anterior cerebral artery
Gyu6400	[X]Other cerebral infarction
Transient Ischaemic Attack	
1JK..00	Suspected transient ischaemic attack
G537.00	Carotid territory transient ischaemic attack
G65..00	Transient cerebral ischaemia
G65..12	Transient ischaemic attack
G65y.00	Other transient cerebral ischaemia
G65z.00	Transient cerebral ischaemia NOS
G65z100	Intermittent cerebral ischaemia
G65zz00	Transient cerebral ischaemia NOS