Patient safety in English general practice: the role of routinely collected data in detecting adverse events

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Declaration of originality

I declare that the contents of this thesis are my own original work. Where content is not my own, this is indicated and referenced appropriately.

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Copyright declaration

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Abstract

The use of routinely collected, or administrative, data for measuring and monitoring patient safety in primary care is a relatively new phenomenon. With increasing availability of data from different sources and care settings, their application for adverse event surveillance needs evaluation. In this thesis, I demonstrated that data routinely collected from primary care and secondary care can be applied for internal monitoring of adverse events at the general practice-level in England, but these data currently have limited use for safety benchmarking in primary care. To support this statement, multiple approaches were adopted.

In the first part of the thesis, the nature and scope of patient safety issues in general practice were defined by evidence from a literature review and informal consultations with general practitioners (GPs). Secondly, using these two methods, measures of adverse events based on routinely collected healthcare data were identified. Thirdly, clinical consensus guided the selection of three candidate patient safety indicators for investigation; the safety issues explored in this thesis were recorded incidents with designated adverse event diagnostic codes and complications associated with two common diseases, emergency admissions for diabetic hyperglycaemic emergencies (diabetic ketoacidosis, DKA and hyperglycaemic hyperosmolar state, HHS) and cancer.

In the second part of the thesis, the contributions of routinely collected data to new knowledge about potentially preventable adverse events in England were considered. Data from a primary care trust (NHS Brent), national primary care data (from the General Practice Research Database, GPRD) and secondary care data (Hospital Episode Statistics, HES) were used to explore the epidemiology of, and patient characteristics associated with, coded adverse events and emergency admissions for diabetic hyperglycaemic emergencies and cancer. Low rates of adverse events were found, with variation by individual patient factors. Finally, recommendations were made on extending the uses of routinely collected data for patient safety monitoring in general practice.

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List of abbreviations

Abbreviation	Term
A&E	Accident and Emergency department
ADE	Adverse drug event
ADR	Adverse drug reaction
AHRQ	Agency for Healthcare Research and Quality
ACS condition	Ambulatory Care Sensitive condition
ATC	Anatomical Therapeutic Chemical Classification System
ACE inhibitor	Angiotensin-converting enzyme inhibitor
BNF	British National Formulary
COPD	Chronic pulmonary disease
CHM	Commission on Human Medicines
CI	Confidence interval
CPRD	Clinical Practice Research Datalink
dl	Decilitre
df	Degrees of freedom
DM	Diabetes mellitus
DKA	Diabetic ketoacidosis
Dx	Diagnosis
DFI	Dr Foster Intelligence
RTM	Dr Foster Intelligence Real Time Monitoring tool
DFU	Dr Foster Unit at Imperial College London
EMIS	Egton Medical Information Systems Ltd
EPR	Electronic patient record
Embase	Excerpta Medica Database
FY	Financial year
FTE	Full Time Equivalent
GDM	Gestational diabetes mellitus
GMC	General Medical Council
GMS	General Medical Services
GP	General Practitioner
GPES	General Practice Extraction Service
GPSoC	GP Systems of Choice
GPRD	General Practice Research Database
HSE	Health Survey for England

HES	Hospital Episode Statistics
IT	Information Technology
ICO	Integrated Care Organisation
ICPS	International Classification for Patient Safety
ICD-10	International Classification of Diseases 10th Revision
ICD-9	International Classification of Diseases 9th Revision
LOS	Length of stay
l	Litre
LSOA	Lower Super Output Areas
MLE	Maximum Likelihood Estimate
Medline	Medical Literature Analysis and Retrieval System Online
MeSH	Medical subject headings
MHRA	Medicines and Healthcare products Regulatory Agency
MDT	Multidisciplinary team
NDA	National Diabetes Audit
NHS	National Health Service
NHSLA	National Health Service Litigation Authority
NIGB	National Information Governance Board for Health and Social Care
NICE	National Institute for Clinical Excellence
NPSA	National Patient Safety Agency
NRLS	National Reporting and Learning System
NSF	National Service Framework
NegBin	Negative binomial regression
NPfIT	NHS National Programme for IT
NSAIDs	Non-steroidal anti-inflammatory drugs
NOS	Not otherwise specified
ONS	Office of National Statistics
OPCS-4	Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (4th revision)
OGTT	Oral glucose tolerance test
OECD	Organisation for Economic Co-operation and Development
PSIs	Patient safety indicators
PfP	Pay for performance
PACT data	Prescribing Analysis and Cost data
PCT	Primary care trust
QOF	Quality and Outcomes Framework
QIPP (Project)	Quality, Innovation, Productivity and Prevention (Project)
RAND	Research and Development Corporation

RCA	Root cause analysis
RCGP	Royal College of General Practitioners
SUS	Secondary User Services
SEA	Significant event analysis/audit
SD	Standard deviation
SE	Standard error
SHA	Strategic health authority
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
SNOMED-CT	Systematised Nomenclature of Medicine Clinical Terms
T1DM	Type 1 diabetes (also known as insulin-dependent diabetes mellitus)
T2DM	Type 2 diabetes (also known as non-insulin-dependent diabetes mellitus)
UK	United Kingdom
US	United States of America
USA	United States of America
WTE	Whole time equivalent
WHO	World Health Organization
ZINB	Zero-inflated negative-binomial (regression)
ZIP	Zero-inflated Poisson (regression)

Chapter 1: Introduction

1.1 Chapter overview

This chapter outlines the current climate of safety and quality measurement in healthcare, with particular focus on primary care. The main sources of patient safety data are then critiqued. In the last section of this chapter, the value of safety metrics derived from data collected routinely during patient care is considered in the context of the research questions that are proposed and answered in this thesis.

1.2 Introduction

There is evidence that, despite potential under-reporting in primary care, the proportion of reported adverse events (AEs) resulting in the most severe harm or patient death in this setting is higher than reported in all other healthcare settings. Estimates of patient harm, including their preventability, in non-acute care vary considerably within countries and internationally. Much of the research in this area has been conducted in the United States of America (US). Studies show that many of the AEs occurring in this setting are associated with medication or diagnosis errors.

Routinely collected data have been used to develop screens for AEs occurring in hospital. These indicators are applied for early detection of sentinel and other serious iatrogenic events. Such flags are usually generated from electronic hospital discharge records collected for billing and insurance-related reimbursements. Arguably, the most well-known set of AE screens is the Patient Safety Indicators (PSIs), developed by the Agency for Healthcare Research and Quality (AHRQ) in the US.[1] As clinical and non-clinical patient data are collected in primary care in England, there is scope to develop similar indicators for this care setting. In this first chapter, I present an overview of patient safety in English primary care

and define the key terms used throughout the thesis. I then describe the data sources and measurement techniques that are available for quality and safety monitoring. I end this chapter by contextualising the research questions that will be addressed in the remaining chapters.

1.2.1 Estimates of harm in primary care

Research on primary care safety has focused heavily on medical errors,[2,3] and less so on actual AEs. Particular attention has been paid to drug-related events and diagnostic errors.[4-6] Few incidents of patient harm in primary care are reported, with approximately 0.36% of all reported events in England between July 2008 to June 2009 attributed to care in general practice (n=945,518).[7] In spite of low levels of reporting, the proportion of reported incidents resulting in severe harm or death is relatively high in this care setting, with 1.7% of incidents associated with severe harm and 1.1% of incidents resulting in death.[7] Estimates of preventable AEs from ambulatory care in the US suggest that nearly 10% of events lead to permanent injuries or death.[8] An estimated 0.5% of all hospital admissions in the US are due to AEs outside of acute care, with 44% of these events deemed to be preventable.[8] Medication (31.7 %) and diagnosis-related problems (17.9%) are two main causes of AEs in non-acute care.[8] Little is known about the epidemiology of patient safety incidents in primary care in the UK.[2,3,9,10]

1.2.2 Quality and safety in primary care

While patient safety is now firmly established within the main framework of healthcare research and practice across the world, momentum has tended to be behind improvements to the safety of hospital care.[11] As mentioned in the previous section, the evidence base for medical errors and patient harm in primary care is limited, especially in areas such as the interface between care settings and in community care.[3] However, knowledge and experience gained in secondary care of safety and risk management from other industries can provide a solid foundation to develop safety awareness and improvement in the non-acute setting.

Models of quality and safety in healthcare have evolved over the last decade. **Quality** spans multiple dimensions related to the functional purpose of an organisation to achieve

favourable outcomes for both the patient and itself (Figure 1.1). One internationally applied definition is "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge".[12] Distinctions between quality and safety are generally deemed unnecessary and may even be potentially counter-productive to improvements in healthcare. **Patient safety**, being typically concerned with the reduction and prevention of potential or actual harm to service users, is commonly perceived to be one element of the quality paradigm, which also includes efficiency and patient experience (Figure 1.1).[10,13,14] Assessments of quality and performance have been established in the healthcare sector since the late 1980s. A commonly measured dimension of quality is performance, where measurement is made against explicit standards or criteria.[15]

Figure 1.1 Dimensions of quality in healthcare

Source: Kelley & Hurst 2006.[16]

There is growing recognition of the need to address patient safety issues in primary care, partly due to practice-based payment for performance (PfP) and quality targets as part of service improvement initiatives.[14] One example is the national auditing of cancer diagnoses

carried out on behalf of the Royal College of General Practitioners (RCGP), as part of cancer service reforms.[17] Without precise identification and accurate measurement of errors and harm occurring in primary care, the true burden of AEs in this care setting and on the overall health system cannot be determined.[18] Better measurement techniques along with more reliable data will support practice improvements, allow for economic evaluations of the costs of patient harm, and will improve the effectiveness of quality and safety improvement interventions. As well as the financial incentives for General Practitioners (GPs) and their practices, the use of safety measurements is of interest to other stakeholders such as patients, commissioners and policy makers.

1.2.3 Importance of measuring patient safety

A lack of standardised mechanisms to define, identify, record or investigate poor quality of care has plagued the National Health Service (NHS).[19] The increasing complexity of changes to working practice, patient populations, and technological improvements make patient safety monitoring all the more important.[20-22] In light of inadequate and ambiguous terminology in primary care and in safety research, primary care-oriented terminology and several patient safety taxonomies have been developed, such as the World Health Organization's (WHO) International Classification for Patient Safety (ICPS).[23] It is perhaps too early to tell whether the WHO ICPS will succeed where the majority of other classification systems have failed; the compendium of patient safety concepts requires widespread adoption if it is to be of benefit to researchers, healthcare professionals and patients.

In the WHO ICPS, **adverse events** are defined as *injuries caused by medical management and that are not due to the underlying disease, but that may increase length of hospital stay, result in temporary or permanent disability at the time of discharge, or both.*[23] Adverse events may or may not be due to **medical errors**, which can be defined as *actions or omissions by staff at a general practice that were unanticipated, should not have happened, should not reoccur, and that may have or did result in harm to a patient, and may be preventable.*[9] **Patient harm** can be perceived as *physical, psychological injury of temporary or permanent effect.*[23,24]

1.3 Defining primary care

Before examining patient safety in general practice, we must be able to define the care setting of interest. As mentioned in section 1.2.3, terminology used in primary care is often ambiguous. This lack of clarity can be partly explained by the structural variation in health systems, within and between countries, which has obstructed the creation of an universal definition of primary care. Development of a common description is also hindered by the unclear delineation between services offered in this setting and those offered in ambulatory care and secondary care. As a result of such organisational differences, comparison and generalisation of research methodologies or findings are not always possible.[25]

In the international context, the terms "primary care" and "ambulatory care" are sometimes used interchangeably. This use is misleading as the "ambulatory care" setting encompasses a wider catchment of services than primary care, including services that may fall within secondary and tertiary settings. Ambulatory care may include community health centres, day surgery clinics, doctors' offices and specialist treatment.[26,27] Primary care is typically the first point of contact with health services, with treatment and continuity of care usually provided within the local community.[28-30]

Non-acute care is commonly referred to as primary health care, primary care, primary medical care, general practice or family medicine.[25,31] It is questionable whether these terms should be used interchangeably when they refer to different elements of the primary care infrastructure; some terms describe the type of care provided, the care system in operation or the types of clinicians involved.[28] The term "primary medical care" is used synonymously with "primary care", as "family medicine" is with "general practice".[29] The distinction between the former two and latter set of terms is that the latter set refers to one component of primary care or primary medical care.[25]

1.3.1 Primary care in England

Now that the care setting has been defined, I describe the setting in England. A strong primary care sector is crucial to support the rest of the UK's health system.[32,33] In England, elsewhere in the UK and countries with similar health systems, the majority of patient contact occurs in primary care. There are approximately 8,230 GP practices in England, with

the number of practices decreasing as the number of GPs per practice increases.[34] Demand for consultations is rising, with an estimated 5.4 visits per patient every year.[34-36] High priority is assigned to the diagnosis and management of chronic conditions, health promotion and disease prevention within primary care.[13] Primary care professionals are also responsible for referrals to specialist care.

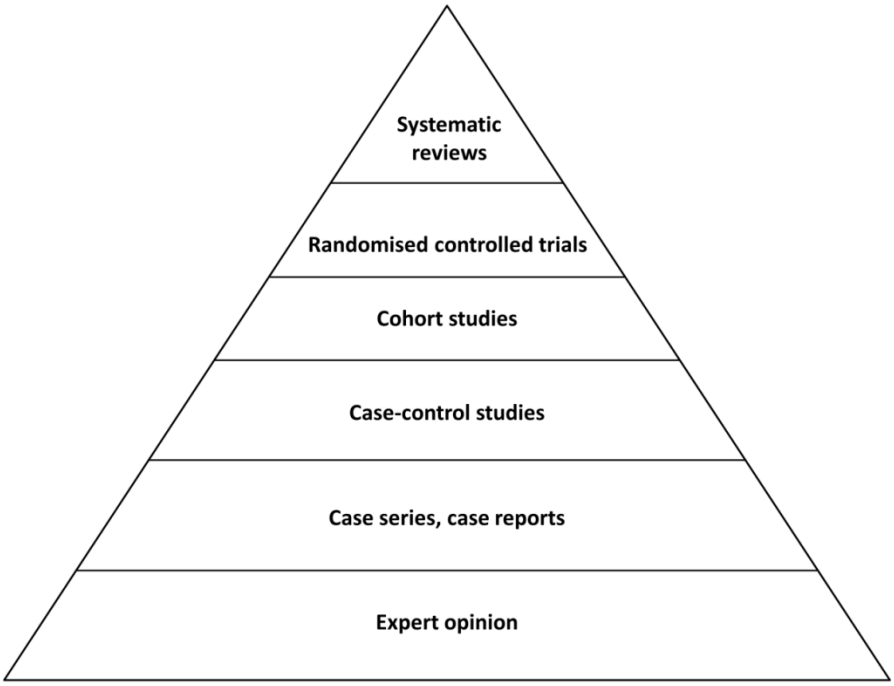
Healthcare in the UK is undergoing unprecedented operational reforms, not least is the pressure on the NHS to save £15 to £20 billion by 2013/14.[37] In the 2009/10 financial year, £8,321 million was invested in general practice in England, an increase of 4.57% from the previous financial year.[38] Historically, approximately 80% of the NHS budget was allocated to Primary Care Trusts (PCTs) which commission primary and secondary care services in the local area.[39] In one of the most radical and unpopular changes to the NHS, Strategic Health Authorities (SHAs) and PCTs will be fully dissolved during 2013 and services will then be commissioned by GP-led consortia.[14] In the midst of these organisational changes, there have been attempts to improve efficiency by wider integration of information technology (IT) across health services. These efforts have been criticised for high costs, poor functionality and concerns about the privacy and security of patient information.[40,41] The most ambitious of these projects is the partly-cancelled NHS National Programme for IT (NPfIT), one of the largest-scale healthcare information technology projects in the world.[40-42]

Despite the ongoing structural flux, the role of primary care, and that of GPs in particular, as the gatekeeper of the health system has not changed. One transitional element of service delivery has been the relationship between the health professional and patient, with patients becoming increasingly more proactive in their care decisions. A report from the Picker Institute drawing from 26 national patient surveys reflects some of the main changes in patient opinions of UK health care since 2002.[43] For example, patient trust in GPs remained consistent between 2004 and 2006 but 42% of patients felt that they had received inadequate information about side effects of new medications in primary care.[43] At the national level, the health system has also been criticised for fragmented approaches to evaluation, failure to optimise resource use, delays in communication and in translating recommendations into changes in practice.[44,45]

1.4 Measurement methods

In sections 1.2.2 and 1.2.3, I argued for the importance of using appropriate terms in translational research for healthcare policy and practice. Now I consider the collection of evidence (Figure 1.2). When measuring patient safety, the evidence must meet the explicit criteria of being technically sound, clinically relevant and fit for purpose. The hierarchical grading system shown in Figure 1.2 is one method of evaluating and categorising research evidence, based on the merits of study design and other study components of clinical interest (prevention, diagnosis, prognosis, therapy and harm).[46]

Figure 1.2 Hierarchy of evidence-based research



Source: Oxford Centre for Evidence-based Medicine.[46]

The classic measurement method is to consider quality and safety in terms of structure, process and outcome (the Donabedian approach).[47] Errors that occur during processes of care may be attributable to elements of the organisational structure. Expanding on the definitions from WHO ICPS (section 1.2.3), medical errors can be defined as failures in the course of planned medical treatment and may be associated with adverse patient outcomes, but errors do not always result in patient injury.[48,49] Where physical or other injuries to

patients occur as a result of health treatment and are not caused by disease or illness, then these events are deemed adverse (iatrogenic) events.[48,50] For instance, a GP may erroneously co-prescribe a potassium-sparing diuretic and an angiotensin-converting enzyme (ACE) inhibitor without valid indication.[51] In this example, the active failure to prescribe appropriately resulted in the patient developing hyperkalaemia (medical error) and consequently admitted to hospital for the drug event (adverse outcome).[51] This incident may have occurred at a GP practice where GPs ignore computer drug contraindication alerts, where there is a culture of non-adherence to drug prescribing guidelines or where staff are over-burdened and lack the resources or support to ensure appropriate and safe care.

Without monitoring patient progress and outcome, it would be extremely difficult to determine whether a course of treatment has been appropriate and effective. In fact, such importance is placed on definable and measurable outcomes that national outcome measures have been proposed under the NHS Outcomes Framework.[14] Hospital admissions, readmissions and death are common patient endpoints measured in healthcare. Of course these are crude measures of patient outcomes and represent small fragments of patient care. Regardless of whether they measure structure, process or outcome, indicators should be meaningful to patients and the public.[14]

One investigative approach seeks the causes of errors and AEs, with contextual information collected to identify contributory and precipitating factors (Table 1.1). Several methods are reasonably well utilised in primary care, such as root cause analysis (RCA) and significant event audit (SEA), to examine failures and errors for specific events attributable to individual staff, processes of care and organisations, which may then also be translated into future improvements in care (Table 1.1). However, all these analysis methods are retrospective in nature and are not suitable for active patient safety surveillance, especially to detect errors or AEs in large populations, such as nationally.

Table 1.1 Common methods for analysing causes of adverse events and medical errors

Type of analysis	Type of event	Description	Evaluation
Cascade analysis	Chain of events leading to error.	Retrospective creation of storyline to identify causal factors and solutions through reporting.	Goes further than RCA by identifying intermediary problems.[52]
Failure modes and effects analysis (FMEA)	Potential failure or error in system, design, process, product or service.	Prospective, step-by-step identification and prevention of all potential failures using an interdisciplinary meeting approach.[53]	Resource costly and questionable ability to affect design of existing processes.[53]
Failure reporting analysis and corrective action system (FRACAS)	All error events.	Retrospective analysis of all observed error events to identify areas for corrective action. Often combined with other tools.[54]	Unknown evidence.
Global trigger tool	Actual patient harm rather than MEs.	Random medical record review for predetermined selection of triggers for certain AEs, especially ADEs.[50]	Widely implemented in the US and are relatively quick to use.[50]
Root cause analysis (RCA)	Patient safety incidents causing serious harm or death and frequently occurring incidents.	Retrospective, structured identification of all contributory and causal factors of AEs. Uses multidisciplinary approach.	Useful for detecting system failures but may be affected by hindsight bias, resource costly and not possible to determine causality.
Significant event analysis/ audit (SEA)	Analysis of any event deemed significant to patient care by any member of the healthcare team.[55]	Retrospective structured investigation by team members, using action plans and peer review.[55]	Examines positive and negative events. Subjective interpretation of 'significant'. Needs standardisation in primary care.[56,57]

Key: ADEs – adverse drug events; AEs – adverse events; FMEA - Failure modes and effects analysis; FRACAS - Failure reporting analysis and corrective action system; MEs – medical errors; RCA – root cause analysis; SEA – significant event analysis/audit; US – United States of America

1.4.1 Theoretical models

The systematic methods to determine causes of errors and harm that were described in the previous section (section 1.4) were based on conceptual frameworks for risk analysis and management in healthcare and other industries. One of the most widely applied models is Reason's organisational framework of accident causation.[58-64] This model describes the onset of patient harm through circumstances which facilitate the occurrence of error (latent failures) and direct actions that cause patient harm (active failures).[59] This human factors approach seeks to identify the effects of organisational processes, together with patient, staff, workplace or situational factors on the subsequent actions by staff and resulting patient outcomes.[65] Organisational factors associated with latent and active errors and AEs can be measured using different methods (Figure 1.3). However, as shown in the diagram, few measurement methods capture all elements of care associated with errors and harm, and are seldom used as "one method for all purposes".

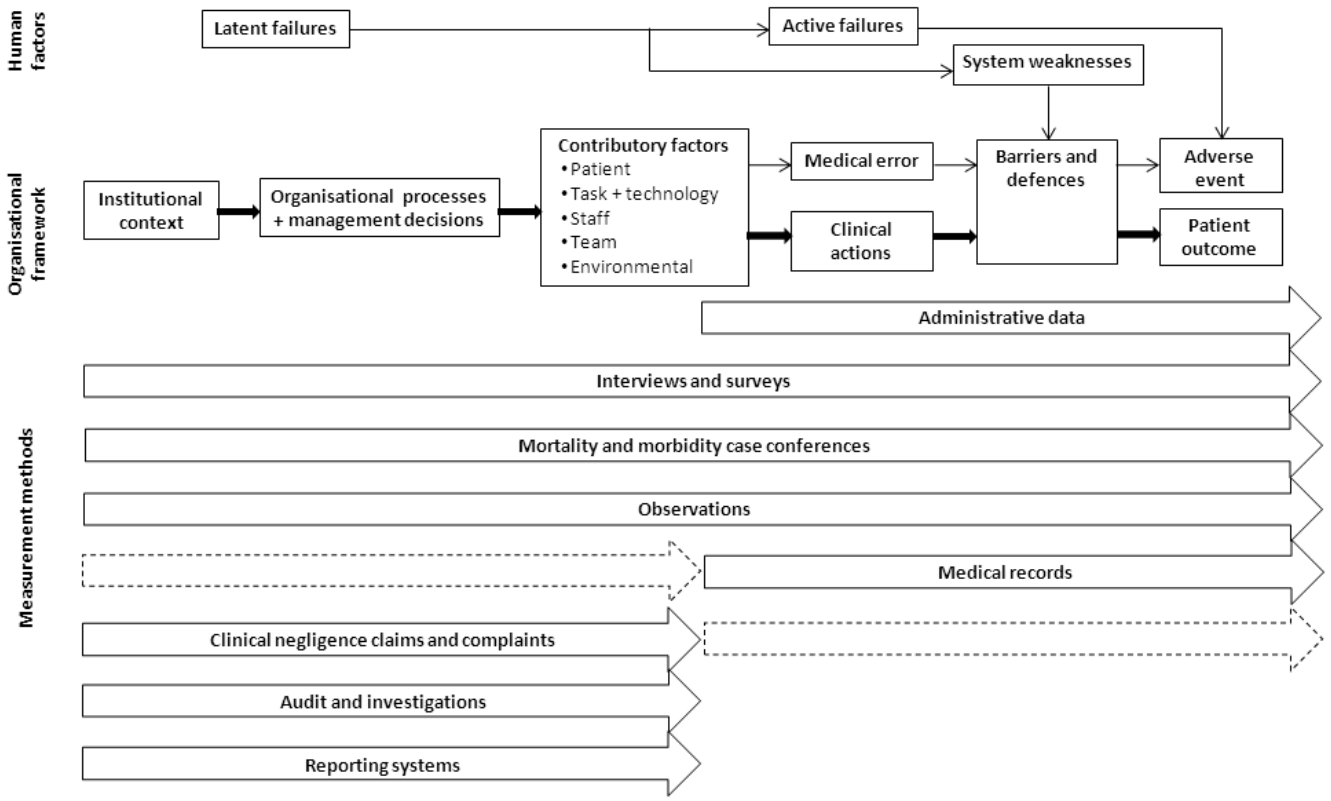
1.4.2 Multiple methods

To better understand the processes of care involved in "near misses" and AEs, data should be collected from a selection of measurement techniques.[62] As there may be little overlap in the types of errors and events detected by individual methods,[6,62,66,67] application of qualitative surveys, collection of quantitative data and analysis of metrics may provide a more complete picture of patient care than from using a single methodology (Figure 1.3).[62,63,68,69] Triangulation will also compensate for methodological limitations associated with the respective individual measurement tools, such as the retrospective nature of methods to analyse causes of harm (section 1.4 and Table 1.1).[68]

Together with medical records, which are usually resource intensive for secondary usages, administrative data can be used to detect potential medical errors, weaknesses in safety barriers and adverse patient outcomes (Figure 1.3). Although these aspects of the safety continuum can also be assessed by interviews and surveys, morbidity and mortality case conferences and observations, routinely collected data are most suited for semi- or fully-automated computerised, real time surveillance. Uniquely, a monitoring system based on

such data can undergo active improvement with the addition of new or modified data, including data contributions from patients.

Figure 1.3 Factors and measurement methods associated with patient harm



Adapted from: Reason 1995;[64] Vincent et al 1998;[59] Michel 2003;[62] Thomas & Petersen 2003.[68]

1.4.3 Patient involvement

As mentioned in section 1.3.1, patients are increasingly involved in all elements of care and service improvement. Learning from patient experiences is pivotal in raising standards of care and improving patient experiences. Indeed, patients may provide expert input as shown in Figure 1.2 (section 1.4). There are numerous established methods of data collection in healthcare, including many where patent input has an important role in alerting healthcare professionals to potential and actual adverse events, and in guiding investigations into patient harm (Figure 1.3). For example, patients' observations of their healthcare experiences form the basis of clinical negligence claims and complaints, which can also precipitate, and most certainly feature in, audits and investigations into the quality and safety of care. Patients' views are often sought by interviews and surveys, but they are also able to report safety concerns directly to health regulatory organisations such as the NHS Commissioning Board (formerly reported to the National Patient Safety Agency, NPSA[*]).

1.5 Data sources

I will now summarise individual data sources and methods used to measure medical errors and AEs, with evaluation of their applications in patient safety.

1.5.1 Clinical negligence claims and complaints

Historically, data from financial compensation claims for iatrogenic harm have played a central role in safety investigations.[70,71] During the 2010/11 financial year, 8,655 clinical negligence claims were received by the NHS Litigation Authority (NHSLA) and £729 million was paid out.[72] The advantages of using claims data for safety research include evidence from multiple perspectives gained during the claim process and the potential identification of errors in the course of the detailed cross-examination that may be missed by other methods.[68,73] On the other hand, these data usually contain small numbers and results may

[*]As part of the NHS reforms, the NPSA's function was transferred to NHS Commissioning Board Special Health Authority in June 2012.

not be generalisable due to the specific nature of the circumstances under which the claims are made. The data are also affected by uncertain reliability and validity of reviewer assessments, reporting bias and hindsight bias.[68,74,75]

1.5.2 Morbidity and Mortality case conferences

Case conferences play a key role in medical education despite inconclusive evidence of learning derived from studying errors and AEs using these sources.[62] The application of this data type in medicine extends to peer-reviewed journals dedicated solely to publishing case reports.[76] The effectiveness of case conferences on learning is dependent on the motivation of the participants,[77] and the method is subject to hindsight and reporting biases,[68] with no standardised structure for conferences.[62] The application of case conferences is much less well documented in non-acute care settings but may be comparable with SEAs (Table 1.1) performed within the NHS's Quality and Outcomes Framework (QOF).[57,78,79]

1.5.3 Audit and investigations

In the UK, independent external assessments of the quality of healthcare have been carried out by three National Confidential Enquiries, commissioned by the NPSA.[80] Additionally, there have been over 60 independent public and private inquiries since the 1970s.[45] National and local clinical audits also take place within NHS trusts and other areas of healthcare. These investigations may consider aspects of quality assessment beyond effectiveness, such as safety and service evaluation and improvement.[81] Even though there is an established clinical governance infrastructure in primary care in England, there are also numerous barriers that prevent quality improvement.[82,83] Audits and investigations require extensive resources, and there may be considerable delays from the event in question, assessments of the event, to the publication of findings and recommendations from the investigations.[45]

1.5.4 Observation

Direct observation is useful to identify active errors and to examine interactions between healthcare staff and patients.[68,84] More AEs may be detected through observation than by other methods.[85,86] Observation, whether by ethnographers physically in the environment or through filming, is seldom possible in healthcare due to confidentiality issues.[68]

Nevertheless, there are examples of its successful application in secondary care to identify errors and AEs related to medication and surgery.[87,88] Interpretation and analysis of data collected by observation can be problematic because of the large amount of information collected, as well as there being reliability issues with observer training and potential hindsight bias.[68]

1.5.5 Interviews and surveys

Incorporating the views of patients on their health services experiences in monitoring of service quality is recommended.[82] Interviews and surveys have typically been used for patient safety research in secondary care and primary care to gauge clinician and patient attitudes about safety culture and reporting,[89,90] to measure prescription-related AEs[63,69,91] and to assess the effectiveness of computerised systems.[92,93] These measurement methods are often used in conjunction with other measures.[63,66,69,94] Recall and reporting biases are associated with interview studies, which are resource costly compared to other techniques.[62,95] However, evidence from secondary care suggests that interviews can be used to reliably detect preventable AEs.[96]

1.5.6 Reporting systems

Voluntary reporting of errors, "near misses" and incidents of patient harm is widely used in healthcare.[97-102] England has a national data collection system in the form of the National Reporting and Learning System (NRLS), launched by the NPSA in 2004. Like other measurement methods, reporting systems are only able to detect a limited range of safety incidents and it is often not possible to determine the causality of events.[103] Difficulties in implementing and maintaining electronic reporting systems have been documented,[104,105] including under-reporting[98,106] and inconsistent detection of certain errors and events in primary and secondary care.[107,108] Yet there is evidence that NRLS data can be successfully translated into improvements to patient safety at the local level.[109] Medication-related incidents are the most common type of AE occurring in primary care reported to the NRLS.[110]

Adverse drug reactions or undesired effects suspected to have been caused by medications are also monitored through the Yellow Card Scheme by healthcare professionals and

patients. This national voluntary reporting initiative is run by the Medicines and Healthcare products Regulatory Agency (MHRA) and the Commission on Human Medicines (CHM), with the aim of assessing drugs' side effects and their roles within the pharmaceutical market.[111] Comparisons of AEs detected by reporting, medical record review and patient survey suggest that reporting may under-detect AEs, especially preventable drug events.[69] In spite of these disadvantages, the National Audit Office has recommended that PCTs should encourage all primary care service providers to have reporting systems in place.[82]

1.5.7 Routinely collected data

Given the limitations of the data sources described so far in this section, it is worthwhile considering how the wealth of data collected routinely as part of patient care can be used for measuring patient safety. Information is recorded every time a patient has contact with any element of the health system. I now describe the two main sources of data; medical (clinical) data and administrative (clinical and non-clinical) data.

1.5.7.1 Medical records

Medical record (or case note or chart) review is frequently used in research on AEs, to the extent that it is considered the 'gold standard' measure in comparative studies.[96] One of the attractions of these data for secondary research purposes is that they are often available in electronic format, with electronic patient records (EPRs) being standard in many countries, including England. Computer-based flags for medical mistakes, such as diagnostic errors, have been developed as an ambulatory care safety tool in the US.[112] Medical records have been used in global trigger tools and RCA methods (Table 1.1). Compared to paper care records, electronic patient information may contain richer clinical detail for identifying precipitating events or process errors associated with patient harm.[113] The validity of investigations using medical records can be affected by inaccurate and incomplete records and variable reviewer reliability.[114-116] There is also potential to under-estimate the number of preventable AEs, especially those that are medication-related.[62]

1.5.7.2 Administrative data

Information technology is driving changes in the delivery of healthcare. Patient-level data are routinely collected throughout the course of patient care for administrative purposes,

including reimbursement. Data from these systems are useful to indicate the processes of care associated with AEs which require more detailed examination.[117,118] These data can also be used to track treatment across different levels of care.[119] Examples of clinical-administrative databases in the UK include Hospital Episode Statistics in England (HES), the Clinical Practice Research Datalink (CPRD) which has succeeded the General Practice Research Database (GPRD), and cancer registries. As the GPRD was still in operation at the time of analyses in this project, references will be made to this organisation rather than the CPRD. I will return to HES and GPRD in Chapter 3.

1.6 Indicators and metrics

Indicators, also referred to as screens and flags, are an integral component of quality improvement strategies in many health systems. Yet the term has been applied loosely and the structure of quality and safety indicators can be quite different from each other.[15,120] Indicators may be used to help prioritise care, facilitate accountability and transparency, and also aid monitoring and evaluation within and across service providers.[15,120,121] These quantitative measures can be considered as markers of explicitly defined healthcare structures, processes or patient outcomes.[120,121] Patient safety indicators typically identify cases or rates of patient harm (temporary or permanent physical or other disabilities, or death) that may be due to medical error and are amenable to organisational changes.[120,122] Good indicators should be reliable, valid, sensitive to change, comparable with other markers, measure clinically useful processes or outcomes, and not be affected by bias or random variation.[120-122]

1.6.1 Indicators based on routinely collected data

There are approximately 270 healthcare databases in active use in the UK.[118] By making use of these available data, patient safety research would benefit from expertise gained from clinical and administrative applications of these data and also contribute to improving the quality of the data sources.[123] In fact, the WHO has identified the development of better indicators as a priority in patient safety research.[124] The following sections describe some of the reasons why routinely collected data are particularly suited for developing patient safety measures.

1.6.2 Computer systems and databases

In recent years, a plural approach to IT has been adopted by the NHS following the failure of the centralised NpfIT project.[42] In English primary care, there has been a history of using computerised clinical systems that spans circa three decades. Since 2007, GP practices have been able to select their preferred clinical information system from a selection of approved suppliers, under the GP Systems of Choice (GPSoC) scheme.[125] The options include the LV, PCS and Web systems from Egton Medical Information Systems Ltd (EMIS), SystmOne from Computer Sciences Corporation Alliance, Vision from In Practice Systems Ltd (INPS) and Synergy and Premiere from iSOFT.[126-129]

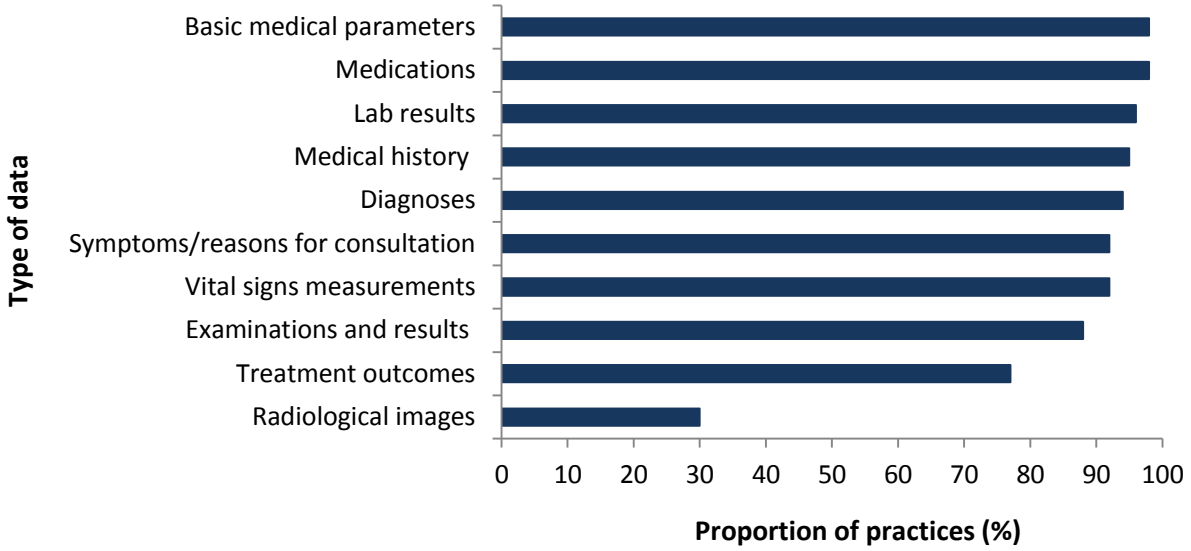
In addition, there are a number of clinical databases derived from these clinical systems. Both the General Practice Research Database (GPRD) and The Health Information Network (THIN) rely on the Vision system.[130,131] Another widely used database of patient data for research is QResearch, derived from the EMIS systems.[132] At the national level, data from individual practice computer systems are also extracted for QOF and currently stored in the Quality Management and Analysis System (QMAS).[133] Prescribing Analysis and Cost (PACT) data are collected in England for monitoring and budget setting.[133] From April 2013, a central extraction system will be introduced for all GP practices in England. One of the initial roles of the General Practice Extraction Service (GPES) will be to extract data from GP practice clinical systems for QOF.[134]

1.6.3 Universal clinical language

The standard clinical terminology used In England is the Read code system.[135] It contains over 80,000 codes that comprehensively cover all elements of clinical practice, including signs and symptoms, diagnoses, treatments and investigations and administrative information (Figure 1.4).[135] Read Codes are mapped to International Classification of Diseases and Related Health Problems 9th and 10th Revisions (ICD-9/10), Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures 4th revision (OPCS-4), British National Formulary (BNF) and the Anatomical Therapeutic Chemical Classification System (ATC).[136] Further changes to the language system are being introduced, with Read Codes to be replaced by the Systematised Nomenclature of Medicine Clinical Terms (SNOMED CT).[135] This system is already being used in countries including

Australia, Canada, Sweden and the US. SNOMED CT is planned for implementation across all NHS care settings.[137] The adoption of standard clinical terms within a structured data system throughout the NHS, and the use of internationally applied clinical codes, provides a wealth of comparable data for research.

Figure 1.4 Storage of electronic patient data in the UK, n=257 practices



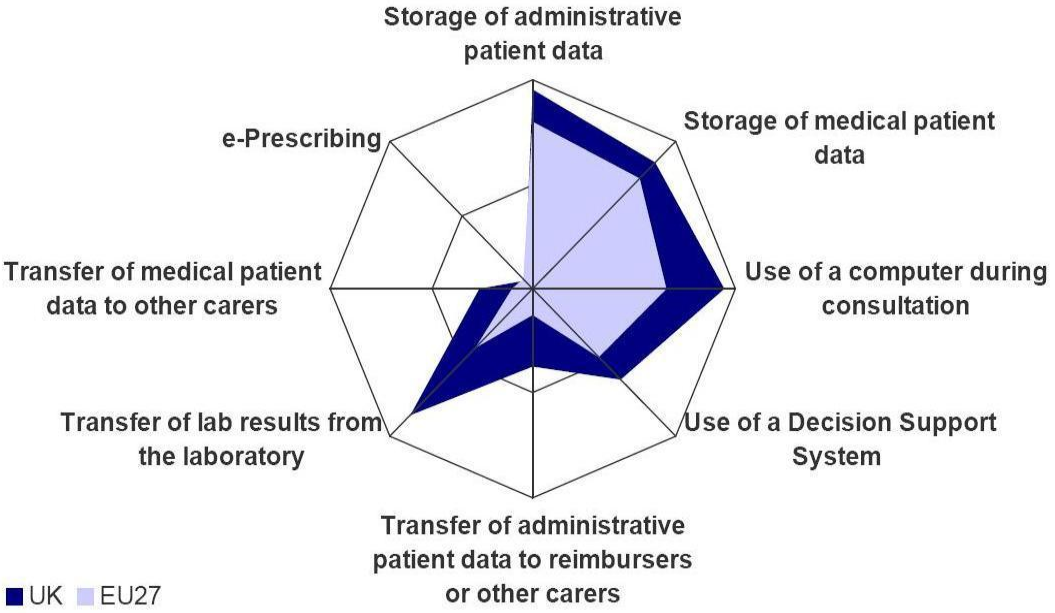
Adapted from Dobrev et al, 2008.[138]

1.6.4 Availability of data

Data used for clinical and non-clinical purposes are already collected and therefore relatively easy to obtain and use (Figure 1.4).[62] While the growth in data collected routinely benefits research, there is also recognition of the need to improve data quality and expand on the types of data being collated.[115,139] Increasingly, more patient and practice-level primary care data are being stored electronically in England (Figure 1.5). This format enables ease of manipulation and quicker transfer of data between users compared with paper versions. Electronic patient databases often contain information on diseases, treatment decisions and patient outcomes (Figure 1.4), therefore making them suitable for use in epidemiological studies of patient safety.[62] Linkage with other data sources, such as mortality data and surveys, can improve the validity of findings.[62,118,140,141] However, as seen in the radar chart (Figure 1.5), application of IT varies among European GPs, including those

in the UK. Predominant uses are during consultations and data storage, with GPs in the UK making more use of IT during consultations and for transferring lab results from the laboratory than colleagues elsewhere in Europe.[138] Beyond this, there is little evidence of electronic transmission of prescriptions from GPs to dispensing pharmacies or digitally-signed prescriptions*, or electronic transfer of patient data to other care providers in the UK or the other 26 Member States of the European Union, and Norway.[138] However, as stated in section 1.6.2, very soon data from clinical systems at all GP practices in England will be extracted by a central service for service improvement.[134]

Figure 1.5 Information technology use by GPs in the UK compared to other European states



Source: Dobrev et al, 2008.[138]

1.6.5 Sentinel monitoring and active surveillance

Patient harm is undesirable but some serious iatrogenic events should never happen, including wrong site surgery and wrong route of chemotherapy administration.[143] These

*The NHS Electronic Prescription Service (EPS) has been rolled out in two stages – release one (R1) in 2004/05 and release two (R2) from 2009 onwards. There have been considerable delays in deploying EPS R2 with only 263 GP practices having EPS R2 capabilities as of August 2012.[142]

events can act as signposts (sentinels) for processes of care that require further investigation. For example, excess mortality is commonly monitored in secondary care but less so in primary care.[144-147] While routine mortality monitoring may be an ineffective signalling method for sentinel events,[145] this technique can be useful for systematic assessment of care processes. In fact, there have been government recommendations for death registers to be set up in general practices and for the monitoring of mortality rates at the practice level.[148]

As well as sentinel event monitoring, routinely collected data can be used to screen for other potentially avoidable failures in medical care. For example, diagnostic errors are one of the most common types of errors reported by healthcare professionals and patients in primary care.[24,73,74,149] Computerised alerts such as drug contraindication warnings, can reduce and prevent errors that may result in harm to patients. Active monitoring systems can be applied at local or national levels to detect unusual patterns in patient outcomes for predicting future behaviour and outcomes. This type of system has been effectively applied in public health for preventing and monitoring disease epidemics.[150]

1.6.6 Evidence of routine data-based monitoring

Patient safety screens that use routinely collected data have been adopted in numerous health systems, firstly in the US and Australia but progressively in other countries.[151] For example, the AHRQ PSIs (section 1.2) have been validated in several hospital populations in the US and adapted for use elsewhere, including England.[152-156] Yet the contribution of these measures to safer care is not confirmed.[62,151,152,157] In general, there are sparse published data on the effectiveness of routinely collected data-based safety measures in improving patient outcomes and reducing patient harm.[123,151] Computerised patient data has been used less extensively to specifically monitor safety in primary care. The predominant area in this setting has been the development of indicators for preventable medication-related AEs using EPRs.[158,159]

1.6.7 Validation of indicators

In the last section, I stated that some safety measures derived from routinely collected data, especially the AHRQ PSIs, have been reasonably validated. Despite this, questions remain

over the validity of measures based on routinely collected data in identifying preventable iatrogenic events.[151,157,160] Doubts have also been raised as to whether non-clinical databases contain the necessary data for adequate case-mix adjustment.[118] These AE screens are also affected by unstable estimates due to the unavailability of suitable denominator data, although this issue could be circumvented by the use of surrogate markers.[139]

1.6.8 Coding issues and data quality

Data collected for purposes other than research may lack the clinical richness, or certain information such as disease severity, that assists patient safety evaluations. Indeed, data completeness and accuracy may vary across provider sites,[115,140,141,161] and diagnosis coding can be (favourably or otherwise) biased by the financial incentives of PfP schemes.[141,162,163] Further discussion of data quality is made in Chapter 3.

1.7 Aims of the research

The topic of patient safety monitoring is well established in primary care yet the use of routinely collected data for this purpose is relatively new in England. The primary care setting encompasses numerous care disciplines and an attempt to address safety issues affecting multiple areas of care would be too ambitious for this doctoral project. Accordingly, in this thesis, I present research on safety measures that are specific to general practice.

The research addressed the following aims:

1. Explore the epidemiology of adverse events in general practice using routinely collected data.
2. Examine how routinely collected data can be used in their current state for patient safety measurement within existing quality improvement systems.
3. Consider what obstacles there might be against using routinely collected data for active patient safety surveillance in general practice, at local and national levels.
4. Apply adverse events indicators for general practice that have been developed from available routinely collected data.

1.7.1 Thesis outline

To achieve the aims set out in the last section, a multi-method approach was adopted. This strategy combines evidence and consensus from the clinical setting and analyses using several datasets, to provide evidence on AEs in English general practice. In Table 1.2, I revisit the research aims in the context of the remaining chapters of this thesis.

Table 1.2 Research aims mapped to thesis chapters

Research aim	Thesis chapter
1. Explore the epidemiology of adverse events in general practice using routinely collected data.	Chapter 2 - Literature review. Chapter 5 - Adverse events recorded in local data. Chapter 6 - Adverse events recorded in national data. Chapter 7 - Unplanned admissions for diabetic emergencies. Chapter 8 - First unplanned admissions for cancer.
2. Examine how routinely collected data can be used in their current state for patient safety measurement within existing quality improvement systems.	Chapter 2 - Literature review. Chapter 9 - Discussion.
3. Consider what obstacles there might be against using routinely collected data for active patient safety surveillance in general practice, at local and national levels.	Chapter 2 - Literature review. Chapter 9 - Discussion.
4. Apply adverse events indicators for general practice that have been developed from available routinely collected data.	Chapter 3 - Data sources. Chapter 4 - Methods. Chapter 5 - Adverse events recorded in local data. Chapter 6 - Adverse events recorded in national data. Chapter 7 - Unplanned admissions for diabetic emergencies. Chapter 8 - First unplanned admissions for cancer.

Chapter 2: Literature review

2.1 Chapter overview

This chapter begins to define the nature and extent of patient safety issues in primary care. Firstly, I determine what types of routinely collected data are used to measure adverse events in this care setting. Secondly, methods of measuring and monitoring patient safety using these data are identified. Finally, I explore the rates and types of adverse events detected from routinely collected data.

2.2 Introduction

A broad spectrum of conditions and diseases, which are often chronic and display relapsing-remitting patterns, is treated and managed in the primary care setting. By comparison, acute episodes of illness are treated in hospital-based specialty care. Consequently, it can be far more difficult to delineate causal relationships between care and AEs in general practice and other areas of primary care. As described in Chapter 1 section 1.3.1, there is increasing and wider use of IT in general practice across England.[138,139] Given this activity, it is surprising that there is little evidence of large scale or national efforts to use routinely collected data for active safety surveillance in this care setting.

There is the potential and need to expand development of patient safety measures beyond secondary care, not least advocated by the Organisation for Economic Co-operation and Development (OECD).[21,154] Newly created measures will complement existing safety monitoring instruments such as reporting and audit,[67,96] allowing for detailed investigations to ascertain the causality of patient harm and identify remediable factors, where appropriate.[164] In the previous chapter, I outlined the main advantages of using existing routinely collected data for quality and safety improvements.[22,165] A main task of patient

safety initiatives is to assess the feasibility of developing AE screening tools using readily available datasets.

2.3 Aims and objectives

To inform the development of safety measures, there must be an understanding of current AEs occurring in primary (non-acute) care. In conjunction, the relationships between information systems and safety monitoring in primary care have to be considered. By synthesising these elements of patient safety, informed advances in the measurement and ultimately improvements to the safety of patient care can be made.

2.3.1 Aims of the literature review

This literature review aimed to describe how routinely collected (administrative) data are used for patient safety measurement and monitoring in primary care. The types of data available in primary care and the nature of medical errors and patient harm measured using these data were established. Particular attention was given to those AEs that may be amenable to organisational change. The findings of the review informed the quantitative analyses presented in later chapters of this thesis.

2.3.2 Objectives of the literature review

By consulting the available literature, this review attempted to:

- Describe the routinely collected data used to measure and monitor adverse events in primary care.
- Identify the types and rates of adverse events attributable to contact with primary care that are detected using routinely collected data.
- Inform analyses of adverse events using routinely collected data from English primary care.

2.4 Methods

I performed a first search of the literature between August 2008 and March 2009. I then made a further search, replicating the original search strategy, in August 2009 to capture relevant literature published in the interim period. The literature review used a range of

sources, including electronic databases such as Excerpta Medica Database (Embase) and Medical Literature Analysis and Retrieval System Online (Medline) to identify peer-reviewed journal articles. Additional searches for relevant publications were made of paper and electronic documents in the public domain, along with websites and contact with experts in the field.

2.4.1 Electronic databases

Peer-reviewed material on patient safety measurement using routinely collected data was collected from several electronic databases (Table 2.1). A combination of Medical Subject Headings (MeSH) and non-MeSH terms were applied.

Table 2.1 Electronic databases used in the literature search

Database	Search period	Search details
Applied Social Sciences Index and Abstracts (ASSIA)	Earliest to 2010	Interface: CSA Illumina. Search screen: command. Search strategy: non-MeSH. Search field: keyword
Cochrane Library	1800 to 2009	Title, Abstract or Keywords in all of the Cochrane Library. Search strategy: non-MeSH.
Excerpta Medica (Embase)	1980 to 2009 week 34	Interface: Ovid. Search method: advanced. Search strategy: MeSH and non-MeSH.
Health Management Information Consortium (HMIC)	1979 to July 2009	Interface: Ovid. Search method: Advanced. Search strategy: non-MeSH.
Institute of Scientific Information (ISI) Web of Science	All years	Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S. Search strategy: non-MeSH. Search field: title, abstract, author keyword, keywords plus.
Medical Literature Analysis and Retrieval System Online (Medline)	1950 to present	Interface: Ovid. Search method: advanced. Search strategy: MeSH and non-MeSH.
PsycInfo	1806 to August week 3 2009	Interface: Ovid. Search method: advanced. Search strategy: MeSH and non-MeSH.

2.4.2 Other data sources

Further searches were made for all other relevant literature, including non-peer-reviewed material. The following sources were used:

- Book chapters;
- Conference proceedings;
- Reference lists of published papers;
- Technical and working papers and reports;

- Unpublished studies;
- Websites (government and safety organisations); and
- Experts in patient safety and/or primary care.

The websites of governments, healthcare and safety and quality organisations, as well as academic institutions were searched to identify relevant reference publications and non-peer reviewed literature (Table A.1).

2.4.3 Search strategy

So that a comprehensive set of relevant publications could be retrieved, a large number of appropriate and clearly defined search terms were used.[166] These statements were selected from commonly applied terms found in the literature on patient safety and primary care. To identify suitable terms for the concepts under review, "free text", index terms and synonyms were compiled.

To ensure that the final list of search terms was adequate and usable in different databases, a comparison of search results from Embase and Medline databases was performed. The full set of terms used is shown in Figure 2.1. Previous literature searches on the same broad research topic have shown that the number and details of the results produced from these two databases are similar. In this review, the number of results was again similar between Embase (n=1326) and Medline (n=1364). The search string was amended according to the search functions and interface of the respective databases (Appendix 2). In each database, individual terms in the three search components (healthcare setting, measure and type of data) were searched first. After this initial process, terms within the individual search components were combined using the "OR" operator. Then the terms for all three search components were joined together using the "AND" operator.

Figure 2.1 Search strategy used to retrieve publications

Search component	Search type		Search syntax
	MeSH	*Free text*	*Boolean operator*
Healthcare setting			
Ambulatory care	x	x	
Ambulatory care facilit*	x	x	
Ambulatory care physician*		x	
Family physician*	x	x	
Family practice	x	x	
General practice	x	x	
General practitioner*	x	x	
Physician*, Family	x		
Primary care	x	x	
Primary health care	x	x	
Measure			
Accident prevention	x	x	**OR**
Adverse event*		x	
Avoidable complication*		x	
Avoidable death*		x	
Diagnostic error*	x	x	
Foreign bodies	x		
Healthcare associated injur*		x	
Iatrogenic disease*	x	x	
Medical error*	x	x	
Medication error*	x	x	
Outcome and Process Assessment (Health Care)	x	x	
Outcome Assessment (Health Care)	x	x	
Patient care	x	x	
Patient outcome		x	
Patient safety		x	**AND**
Patient safety index		x	
Patient safety indicator*		x	
Patient safety indices		x	
Postoperative complication*	x		
Preventable complication*		x	
Quality assessment*	x	x	
Quality improvement*		x	
Quality indicator*	x	x	
Quality Indicators, Health Care	x		
Safety	x	x	
Safety assessment*		x	
Safety improvement*		x	
Safety management	x	x	
Sentinel event*	x	x	
Type of data			
Administrative data		x	**OR**
Billing data		x	
Billing record*		x	
Computer* medical record* system*	x	x	
Consultation record*		x	
Discharge data		x	
Discharge summary*		x	
Electronic data		x	
Hospital Information System*	x	x	
Hospital record*	x	x	
Information system*	x	x	
Inpatient data		x	
Medical record*	x	x	
Routine data		x	
Routinely collected data		x	

2.4.4 Study selection

The purpose of the review was to synthesise the evidence across primary care on how administrative data are applied in patient safety research and practice, and to consider what the potential uses are for these data in detecting and monitoring AEs. Accordingly, data at the individual patient and staff levels were of interest, along with research at practice, local and national levels. International data were also considered, where available and appropriate. Data on the severity of harm, risk factors and preventability also were extracted, where available. This information can be used to identify AEs that should never occur (especially harm resulting in severe and permanent injury or death), events that are amenable to organisational change, as well as inform strategies to reduce patient risk factors.

2.4.4.1 Inclusion criteria

Studies were selected for inclusion using the selection methodology used by the AHRQ during the development of the AHRQ PSIs.[1] Studies on the quality of care were deliberately not excluded as safety is often perceived to be a dimension of quality.[167] However, in order for these studies to be eligible for inclusion in the review, they had to meet the explicit inclusion criteria that follow:

- Report original research (observational or experimental); and
- Apply routinely collected data[*] collected in any healthcare setting; and
- Measure at least one potential or actual adverse patient outcome(s)[†] that is explicitly attributed to contact with primary or ambulatory[‡] care; and
- Provide numerical results for the adverse patient outcome(s) measured (e.g. frequency of injury, hospital admission or death).

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[*] Routinely collected data were defined as patient information, usually in electronic format, collected clinical and non-clinical purposes, including financial reimbursement of service providers.[141]

[†] Adverse patient outcome (measurable patient endpoint) was defined as an unexpected outcome due to healthcare treatment and not due to patient illness or expected outcome of treatment.[168]

[‡] Ambulatory care was included in the literature search given the overlap in services provided in this setting and primary care.

2.4.4.2 Exclusion criteria

The following criteria were used to exclude articles from the review:

- Non-original research; and
- No application of routinely collected data; and/or
- Measurement of medical errors* rather than AEs†; or
- Without explicit measurement of AEs that were attributed to treatment in primary or ambulatory care; or
- Measurement of AEs but without providing numerical data for outcome measures; or
- Predominantly reporting of diagnosis or treatment of specific diseases; or
- Predominantly describing or evaluated teaching or research tools; or
- Publications not in English.

To aid the selection process, a hierarchy of exclusion criteria was applied. This ranking system facilitated the selection process, especially when there were multiple reasons for excluding a citation. The rankings in order of importance for exclusion were:

1. Not healthcare-related.
2. Not safety-related.
3. Safety but not in a primary or ambulatory care setting.
4. Not original research (e.g. review or discussion paper).
5. No application of routinely collected data.
6. No numerical data on any adverse patient outcomes measured.
7. Predominantly reporting of diagnosis, treatment, teaching or research (including non-primary care studies).
8. Non-English language publication.

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*Medical errors are actions or omissions by staff at a general practice that were unanticipated, should not have happened, should not reoccur, and that may have or did result in harm to a patient, and may be preventable.[9]

†Adverse events are injuries caused by medical management and that are not due to the underlying disease, but that may increase length of hospital stay, result in temporary or permanent disability at the time of discharge, or both.[23]

2.4.5 Data extraction

Publications were initially screened for duplication by examining titles and abstracts. Where titles or abstracts were ambiguous or abstracts were not available, full versions of publications were obtained to determine eligibility for review. The reason(s) for exclusion was recorded for any publication deemed ineligible. For all publications, a set of data was extracted (Table 2.2).

Table 2.2 Data extracted from publications

Study section	Data field
Design	Study type
	Setting
Participants	Participants
	Recruitment/sampling method
	Response rate
	Inclusion criteria
	Exclusion criteria
Variables	Adverse event type/exposure
	Predictor variable(s)
	Confounding variable(s)
	Outcome(s)
Data sources/measurement	Method
	Bias(es) accounted for
	Data type(s)
	Measurement instrument(s)
	Measure(s)
Statistical methods	Quantitative variable(s)
	Analysis
	Risk adjustment(s)
Results	Participants
	Outcome(s)
	Study limitation(s)
	Interpretation

2.4.6 Data synthesis

The STROBE structured checklist was used to guide the review process.[169] After remaining ineligible studies were removed, the data fields shown in Table 2.3 were populated for each study by electronic data entry.

Table 2.3 Data fields for data entry

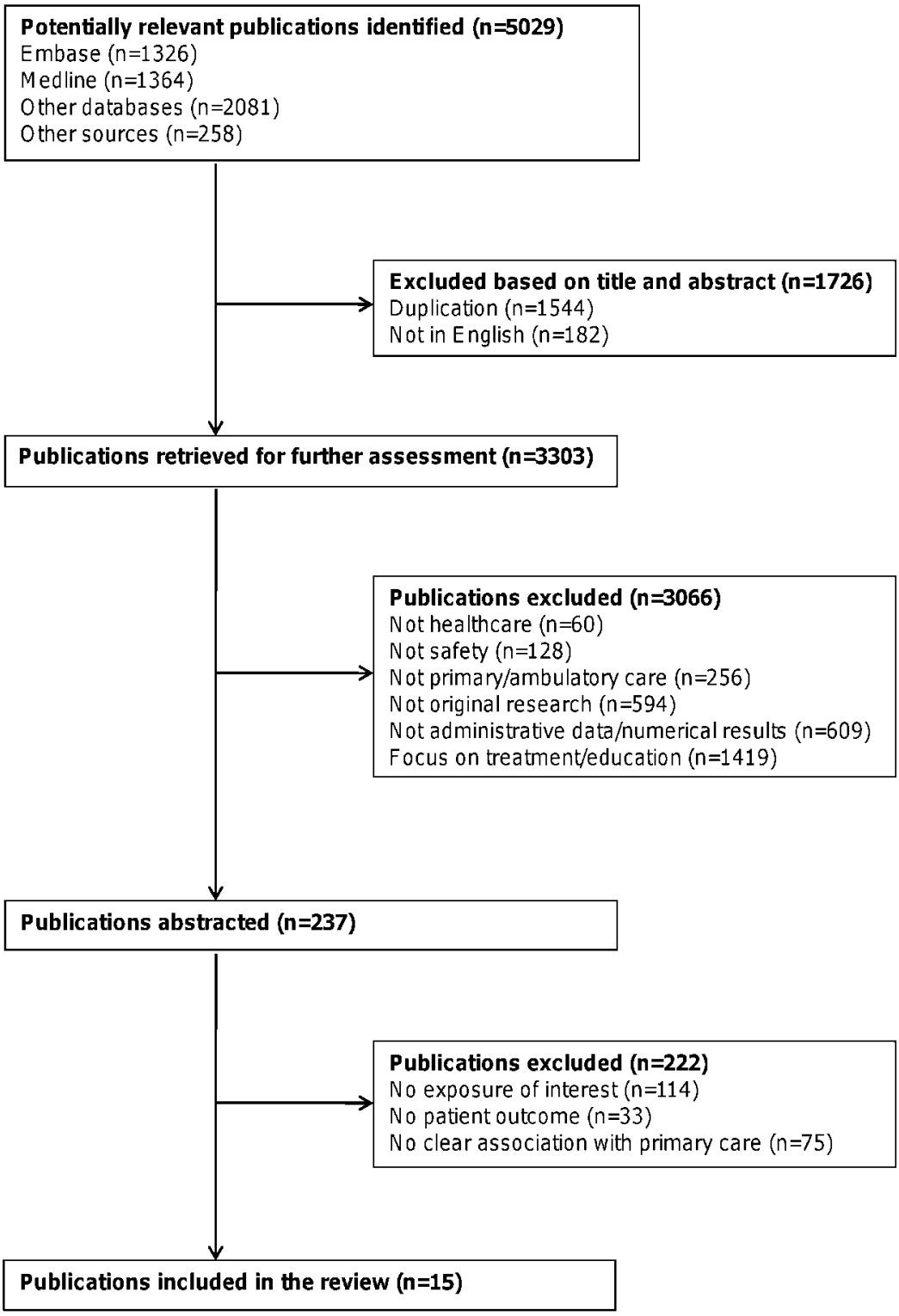
Indicator	Data
Description	Brief free text outline of study
Drug group(s)	Entered where applicable
Drug name(s)	Entered where applicable
Patient outcome(s)	Adverse patient outcome(s) measured
ICD code(s)	Entered where applicable and available
Numerator/denominator values	Entered where applicable and available
Exclusion(s)	Exclusion criteria, where applicable
Data type(s)	Sources of data used
Source(s)	Study reference(s)

Studies reporting on drug-related incidents were only included in the review if patient outcomes were described and measured, and there were also measurements of the severity or preventability of the adverse drug event. Studies that solely reported on adverse reactions caused by medications were excluded as these events can be an expected outcome of treatment.[170] Where there was insufficiently detailed information about the elements of care associated with medical errors and AEs, "treatment" was noted as the default care component related to the AE.

2.5 Results

From searching the electronic databases, 4,771 publications were retrieved (Figure 2.2). A further 258 publications were identified from "grey literature" and hand searching of publication reference lists. Of the abstracted 237 publications, 15 were included in the review. No publications were identified that specifically addressed the use of routinely collected data for patient safety measurement or monitoring in primary care.

Figure 2.2 Study selection process



The majority of studies included in the review were cross sectional (n=9/15), with the remainder using cohort or population-based designs (Table 2.4). One study used a simulated population dataset.[145] Two thirds of studies took place in the US (n=10/15) with study periods spanning from 1990 to 2005, and publication dates from 1990 to 2008. The study time period was not reported for one study.[171] The duration of data collection, or study period, ranged from three months to eight years.[172,173]

The majority of studies used more than one type of data (n=12/15). The largest number of data sources used was in two related studies which drew from health provider reports, hospital discharge summaries, emergency department notes, computer-generated signals, electronic clinic notes and administrative incident reports.[6,174] All but one study focused on adult care. Few studies placed an age restriction on their participants (n=6),[94,164,174-177] although the age range of patients in three studies with adult participants was unknown.[112,172,178]

2.5.1 Assessment of reliability

Approximately half of the studies that assessed medical records or reports used more than one reviewer.[8,24,94,112,172,174,178,179] Where inter-rater agreement was calculated, good or excellent inter-rater agreement was reported,[6,8,94,172,174,178] except in one study where poor agreement was documented.[112] There was no evidence of quality assessment in three studies.[171,176,180] Reporting of methodology varied, with only seven studies providing details of inclusion and/or exclusion criteria applied. There was a wide range of samples in the included studies, ranging from self-selected GP practices,[171] groups of practices ranging from one to 30 sites,[6,24,94,164,172,174,178] single hospitals, state-wide healthcare[8,112,171,176,177,179-181] to national level evaluations.[173] Overall, definitions of AEs and other variables measured were clearly defined in the studies.

Table 2.4 Characteristics of reviewed studies

Study, Country	Study period (months)	Study design	Methods	Sample (N) (n=cases)	Measures	Results for primary/ambulatory care
Budnitz et al, US[179]	2004 - 2005 (24 months)	Cross sectional	Medical records, surveillance data	n=21,298	Emergency department visits	3487 patients admitted. 2.4 ADEs per 1,000 population, 95% CI 1.7-3.0.
Field et al, US[6]	1999 - 2000 (12 months)	Cohort (nested)	Administrative data, reports, medical records	n=1,523 ≥=1 years	ADEs	421 preventable ADEs. 5% ADEs identified through more than one source.
Fischer et al, US[24]	1991 - 1996 (66 months)	Cross sectional	Administrative data	N=948,628 n=35	AEs	29 preventable. 3.7 AEs per 100,000 visits in 5.5 years.
Gandhi et al, US[94]	1999 - 2000 (9 months)	Cohort	Patient survey, medical records	N=1879 n=143 ≥=1439	ADEs, prescribing errors	62 potential ADEs, 3 preventable ADEs.
Gurwitz et al, US[174]	1999 - 2000 (12 months)	Cross sectional	Administrative data, reports, medical records	N=27,617 n=1523 ≥=1 years	ADEs	50.1 ADEs per 1,000 person-years. 421 (27.6%) preventable, 13.8 per 1,000 person-years.
Guthrie et al, Scotland[145]	2001-2004 (3 years)	Cohort (population based)	Administrative data	N=405,000	Excess mortality	10 excess deaths per year. Large number of false alarms generated by all 3 models.
Korst et al, US[181]	1997 (12 months)	Cohort (population based)	Administrative data	N=507,592 n=1,853 Females only	Admission	MediCal patients (odds ratio 1.60, 95% CI 1.46-1.80) and patients of African American ethnicity (odds ratio 1.24, 95% CI 1.10-1.41) at greater risk of admission.
Menec et al, Canada[177]	1990 and 1996 (24 months)	Cross sectional	Administrative data, medical records	N=1,863 ≥=1,863	Admission	High continuity of care associated with reduced odds of ACS admission (adjusted odds ratio 0.67, CI 0.51-0.90).
Morris et al, England[164]	1999 - 2002 (36 months)	Cross sectional	Primary care data, medical records	N=49,658 n=507 ≥18 years	ADEs	1% incidence. Approx. 60% of events due to 4 indicators.
Patel et al, England[173]	1998 - 2005 (84 months)	Cross sectional (population based)	Administrative data	N=13,706,765 n=447,071	Admission	0.50% of hospital episodes due to ADRs (1998-2005). 76,692 hospital episodes due to ADRs (2004-2005).

Pirmohamed et al, England [176]	2001 - 2002 (5 months)	Cross sectional	Administrative data, medical records	N=18,820 n=1225 ≥=1 years	Admission	6.5% prevalence. 307 definitely avoidable ADRs, 773 possible avoidable.
Singh et al, US[112]	2004 - 2005 (12 months)	Case control	Administrative data, medical records	N=25,594 n=652 Adults only	Diagnostic errors, admission, service use	76,692 hospitalisations for ADRs (2004-2005)
South Bedfordshire Practitioners' Group, England[171]	Unknown	Cross sectional	Medical records, reports	N=23 n=7 Children only	Poor treatment for UTI, admission	Most common error was failure to investigate possible UTIs (n=7).
van Walraven et al, Canada[180]	1996 - 1997 (9 months)	Cross sectional	Medical records, administrative data	N=1,402 n=240	Physician communication, readmission	27% patients urgently readmitted within 3 months. Patients seen by physicians who received discharge summary had decreased adjusted risk of readmission (relative risk 0.74, 95% CI 0.50-1.11).
Weingart et al, US[178]	2001 - 2002 (10 months)	Cohort	Computerised physician order entry data, medical records	N=267 n=21 Adults only	ADEs, communication improvement	Prescription filling identified as problematic by 48% of patients. Approx. 81% of ADEs were reported electronically (n=17).
Weingart et al, US[172]	2000 (3 months)	Cohort	Electronic portal data, medical records	N=24,034 n=3 Adults only	ADEs, physician decision to override alert	3481 consecutive alerts assessed, 91 were overrode. ADEs in written prescriptions for alerted medication in 122 patients.
Woods et al, US[8]	1992 (12 months)	Cohort (population based)	Administrative data	N=14,700 n=587	AEs, admission	70 AEs in ambulatory care, of which 31 were preventable.

Key: ADE – adverse drug event; ADR – adverse drug reaction; AE – adverse event; Approx. – approximately; CUSUM – cumulative sum; PDRM – preventable drug-related morbidity; US – United States of America; UTI – urinary tract infection

2.5.2 Excluded studies

During the initial stages of data processing, 1,544 out of 5,029 publications were excluded because of duplication. Further studies were removed due to unavailability in English (n=128/5,029). In the next stages, exclusions were made following assessment of studies' titles and abstracts using the exclusion criteria listed in section 2.4.4.2. Out of the 3,064 publications that were excluded, 39% were not experimental or observational studies, did not apply routinely collected data or did not provide numerical results (n=1,201/3,064). A small group of studies were excluded for not reporting healthcare-related research (n=60/3,064).

After retrieval of full articles for the remaining 239 studies, the majority were excluded (n=222/239). The most common reason for exclusion at this stage of data extraction was no documentation of patients having had primary care contact prior to the occurrence of the AE(s) (n=114/222). Other excluded studies measured medical errors only or reported on hospitalised patients who had AEs in non-acute care but did not provide adequate details about the adverse patient outcomes.

2.5.3 Sources of routinely collected data

Most of the studies did not use data collected in primary care (Table 2.5). Paper or electronic hospital medical records, including prescription charts and computer-generated signals, were the most common data sources used in the included studies (n=17/35). Conversely, patient records from primary care or ambulatory care were only used in eight studies and fewer studies made use of incident reports (n=4/35) or patient/clinician surveys.[94,176,177,180]

Table 2.5 Frequency of data use in the reviewed studies, by type of data, n=35

Type of data	Frequency of use
Hospital medical record/administrative data	15
GP/ambulatory records	8
Incident reports	4
Patient surveys	3
Population based data (including census)	2
Clinician surveys	1
Computer-generated signals	1
Prescription charts	1

2.5.3.1 Data from primary care

Three out of the eight studies that incorporated primary care or ambulatory care data were conducted outside of the US. All of these three studies took place in the UK; one study was performed in Scotland and two in England. The eight studies used different types of GP data ranging from a simulated dataset, electronic patient records, to GP recall of their experiences.

2.5.4 Measurement and monitoring

There appears to be little overlap in the types of AEs detected by different measurement methods.[6] Computer generated signals and electronic notes may be useful for flagging potential AEs. Yet these sources suffer from poor sensitivity.[6] Both routinely collected data from primary and secondary care were used for case identification in the reviewed studies, and were often implemented in tandem with other data sources, such as medical records.[112,164,177,180]

2.5.5 Types and rates of adverse events

Patient outcomes that were explicitly described and measured in the studies included GP contact, hospital admissions and death (Table 2.6). In five studies, patient injuries were measured in the form of physical or mental disability, or injuries requiring further treatment. The categories of AEs applied in the reviewed studies broadly represent dispensing and prescribing of drugs, drug levels and laboratory results and treatment (including diagnostic

errors). Estimates of AEs in primary or ambulatory care derived from a single source of routinely collected data included 3.7 AEs per 100,000 visits over 5.5 years and 4.8 AEs per 1,000 consultations.[8,24] Not all studies included operational definitions for errors and patient harm. In seven studies, there was limited detail about the measures used and no reporting of numerator values for calculations.[8,24,171,172,176,178,179]

2.5.5.1 Adverse drug events

A higher prevalence of adverse drug events (ADEs) was noted in the older population.[173,174,179] Gurwitz et al (2003) found a rate of 50.1 ADEs per 1,000 person-years in patients aged 65 years and older.[174] Budnitz et al (2006) detected 4.9 adverse drug events per 1,000 population per year in patients of the same age range.[179] In the general adult population, the incidence rate of ADEs was 1%, calculated by queries run on electronic data (n=507/49,658).[164] These incidents were often attributed to the same types of drugs, with four indicators accounting for 59.6% of ADEs (n=302/507).[164] These indicators represented cardiovascular medications, diuretics, non-opioid analgesics and anticoagulants (Table 2.6).[164,172,174,176] Drugs in these categories were frequently implicated in adverse incidents among older patients and associated with subsequent hospital admissions.[173,174,179]

Table 2.6 Examples of adverse events identified from the literature

Patient outcome	Adverse event	Drug class (where applicable)	Drug name or type "(where applicable)"
Admission or emergency department contact			
	Acute urinary retention	Analgesics; Anticholinergic agents	Opiates
	Adrenocortical failure	-	-
	Anaphylaxis	-	-
	Bradycardia	Beta-blockers	
	Confusion and altered mental status	Analgesics; Antidepressants	Opiates
	Constipation	Analgesics; Antidepressants	Opiates
	Electrolyte disturbance	Antidepressants; Diuretics; Hypertension and heart failure drugs	ACE inhibitors/All receptor antagonists
	Gastrointestinal complaints*	Analgesics; Anticoagulants; Antidepressants; Antiplatelet drugs; Corticosteroids; Drugs used in rheumatic diseases and gout	Clopidogrel; Naproxen; NSAIDs; Prednisolone; Warfarin
	Gestational pyelonephritis	-	-
	Gout	Diuretics	
	Haemorrhagic CVA	Analgesics	NSAIDs
	Hyperglycaemia	Corticosteroids	Prednisolone
	Hyponatraemia	Antidepressants	
	Hypotension	Hypertension and heart failure drugs; Antidepressants; Beta-blockers; Diuretics	ACE inhibitors/All receptor antagonists
	Loss of seizure control	Antiepileptic drugs	Phenytoin
	Malignant hyperthermia	Anaesthetics and therapeutic gases	
	Mental disorders	Opioids; Psychoactive drugs; Sedatives and hypnotics	
	Neurological condition†	-	
	Osteoporotic fracture	Corticosteroids	Prednisolone

*Including bleeding, gastritis and peptic ulceration.
†Including dystonia.

	Otologic condition*	-	
	Renal/genitourinary condition†	Analgesics; Diuretics; Hypertension and heart failure drugs	ACE inhibitors/All receptor antagonists; NSAIDs
	Systemic lupus erythematosus	-	
	Systemic sclerosis	-	
	Vomiting	Analgesics	Opiates
Admission or emergency department contact; GP practice or hospital contact			
	Hyperthyroidism and hypothyroidism	Thyroid and antithyroid drugs	
	Respiratory condition‡	Beta-blockers; Bronchodilators	
	Worsening of PD symptoms	Drugs used in nausea and vertigo	Metoclopramide
	Anorexia, nausea and vomiting, diarrhoea, visual disturbances, fatigue	Cardiac glycosides	Digoxin; Digoxin immune FAB
	Clinical jaundice	Lipid-regulating drugs	Statins
	Diarrhoea	PPIs	
Emergency department treatment			
	Epistaxis due to drug interaction	Anticoagulants and analgesics	Warfarin and aspirin
	Fall or broken bone	Sedatives and hypnotics	
GP practice or hospital contact			
	CHF and/or fluid overload, heart block or advanced bradycardia	Drugs used in rheumatic diseases and gout; Hypertension and heart failure drugs; Positive inotropic drugs	ACE inhibitors; Digoxin; NSAIDs
	Hyperkalaemia	Hypertension and heart failure drugs	
	Hypokalaemia	Diuretics	
	Second myocardial infarction	Antiplatelet drugs	Aspirin
	Peripheral oedema	CCBs	
Other			
	Drug interaction	Anticoagulants	Warfarin and clarithromycin
	Tremor	Drugs used in diabetes	

*Including ototoxic hearing loss.
†Including impairment and scarring.
‡Including wheezing and exacerbation of asthma or COPD.

Readmission	
	Emergency readmission within 3 months of discharge

Key: AE - Adverse event; ACS - Ambulatory care sensitive (conditions); ACE inhibitors - Angiotensin-converting enzyme inhibitors; Beta-blockers - Beta-adrenoceptor blocking drugs; CCBs - Calcium channel blockers; CVA - Cerebrovascular accident; COPD - Chronic obstructive pulmonary disease; CHF - Congestive heart failure; Digoxin immune FAB - Digoxin immune antigen-binding fragments; NSAIDs - Non steroidal anti-inflammatory drugs; PD - Parkinson's Disease; PPIs - Proton pump inhibitors

2.5.5.2 Severity of adverse events

Six studies assessed the severity of patient injuries. The extent of harm was measured by patient endpoints such as admission, and reviewer assessments based on a rating scale or severity categories.[8,24,94,174,179] For instance, Gurwitz et al (2003) labelled AEs by categories of "significant, serious, life-threatening, or fatal" and Fischer et al (1997) rated event severity from "emotional only", "temporary-insignificant (no delay in recovery)" to "death".[24,174] Across the reviewed studies, there were few cases of the most severe patient harm compared to cases of less severe and more temporary types of injuries. The proportion of patients who had life threatening incidents of harm or died ranged from 0.7% to 10% of patients[*]. The smallest proportions of the most severe harm among patient groups were reported by Fischer et al (1997) and Gandhi et al (2005), with only a single case of fatal or life-threatening injury identified in each study, (n=1/29) and (n=1/62) respectively.[24,94] In spite of their low incidence, the most severe cases of AEs were also those that were potentially preventable.[8]

2.5.6 Other patient outcomes

The reviewed studies measured patient endpoints other than the AEs themselves. I now describe the two main alternative outcomes that were recorded.

2.5.6.1 Hospital admissions

Access to secondary care was reported in 12 studies that investigated hospital admissions (n=9), readmissions (n=1), or emergency department visits (n=2). When looking at data from the US, Budnitz et al (2006) found that 16.7% (95% confidence interval (CI) 13.1-20.3) of patients with adverse drug reactions (ADRs) who were treated in the emergency department were subsequently hospitalised.[179] When looking at admissions by age group, the annual rate of hospitalisation for ADEs was estimated to be highest in patients aged 65 years and older at 1.6 admissions per 1,000 patients (95% CI 0.7-2.5).[179]

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[*]The proportion of patients who experienced the most severe adverse events would range between 0.7% and 16.7% of all patients who had an adverse event if hospital admission is included as a measure of severity, based on Woods et al's study (2007).[8]

In England, ADRs were responsible for 6.5% of admissions at two hospitals (95% CI 6.2-6.9).[176] Patients who were admitted for drug-related adverse reactions tended to be older than patients with other causes of admission (median age 76 versus 66 years, and inter-quartile range (IQR) 65 to 83 versus 46 to 79 years, 95% CI 8-10).[176] This study used a broad definition of ADRs that was originally proposed by Edwards and Aronson (2000), and found more female patients were admitted for ADRs than for other reasons (59% compared to 52%, 95% CI 4-10).[170,176] Applying a questionably more restrictive definition of ADRs based on ICD-10 codes, Patel et al (2007) estimated a lower rate of admissions due to the effects of drugs.[173] They attributed 0.56% of admission episodes in England during 2005 to ADRs, identified through primary or secondary diagnoses.[173]

2.5.6.2 Death

Four studies measured the rate of death in patients who had an AE. In one other study, Guthrie et al (2008) determined the sensitivity of a statistical model to detect excess deaths in a population-based sample.[145] The mortality rate was low in the four studies, ranging from 0.15% (n=28/18,820) to 3.5% (n=1/29) of patients.[8,24,174,176] Bleeding was identified as a common cause of death (n=4/11),[174] especially gastrointestinal bleeding associated with ADRs (n=15/28).[176] Other causes of death associated with drugs included renal failure (n=5/28),[176] drug toxicity (n=2/11)[174] and peptic ulcer (n=1/11).[174]

2.5.7 Risk factors and preventability

Not only did the reviewed studies provide examples of routinely collected data used to estimate the occurrence of AEs in non-acute care, but some of the 15 studies also attempted to identify predictors and assess the preventability of these incidents.

2.5.7.1 Causal factors for adverse events

Two thirds of the studies investigated potential causes of AEs (n=10/15). The most common factors were prescribing errors,[174] poor communication between clinicians[178,180] and diagnostic errors.[112,171] Diagnostic and treatment errors that included missed or delayed diagnoses, poor note taking and failure to investigate were common causes of AEs.[8,24,112,171] Such errors were attributed to between 24.4% (n=34/139) and 36% (n=466/1,296, 95% CI 21.8-50.2) of AEs.[8,112]

2.5.7.2 Risk factors for adverse events

Few studies considered risk factors for AEs, with no patterns identified.[177,179-181] In a Canadian study, van Walraven et al (2002) found that poor continuity of care and the unavailability of hospital discharge summaries were associated with increased risk of AEs.[180] Another Canadian study, by Menec et al (2006), found that higher continuity of care was protective against admissions and readmissions for 28 ambulatory care sensitive (ACS) conditions (the AEs of interest) in patients aged 67 years or older (0.67, 95% CI 0.51-0.90).[177]

2.5.7.3 Preventability of adverse events

Approximately 76,000 hospital admissions per year are estimated to be due to preventable AEs in ambulatory care in the US, of which 10% result in death.[8] Six out of the seven studies investigating the preventability of AEs were drug-related studies.[6,94,164,174,176,178] Avoidable harm associated with drugs can be reliably detected using computer-generated signals.[6] Pirmohamed et al (2004) estimated that 71.8% of admissions in their English sample were due to potentially avoidable adverse drug reactions (n=880/1,225).[176] Among these admissions, 12.2% were deemed definitely preventable.[176] The proportion of ADEs assessed as avoidable in the seven studies ranged from 1% to 42.2%.[164,174]

2.6 Discussion

This review has examined the use of routinely collected data to measure AEs in primary care. I found evidence of data derived from hospital sources being used to detect patient harm in non-acute settings, within the limited range of routinely collected data. Research remains focused on drug-related events and the use of secondary care services. The frequency of ADEs, patient groups at high risk of events and some of the errors associated with these events are well documented. The 15 studies were mostly descriptive in nature, estimating the incidence or prevalence of potential or actual harm and/or explored potential risk factors for AEs.

2.6.1 Sources of routinely collected data

One of the objectives of this literature review was to explore the availability of routinely collected data in primary care. This review identified a small number of relevant studies, a

minority of which were conducted in the UK. As such, the list of data routinely collected and available for purposes other than originally intended in primary care is far from complete. Nevertheless, this review does offer an indication of how these data might be used in conjunction with other sources (Table 2.5). Electronic patient records from hospitals and GP practices were the routinely collected data sources that were most frequently used in the reviewed studies.

2.6.2 Measurement and monitoring

The second of the three study objectives was to identify how routinely collected data are used for measuring and monitoring patient harm in primary care. The findings emphasise the dominance of drug-related studies in the primary care domain and in nationally reported incidents of harm.[7] This review found no patterns in the use of routinely collected clinical and non-clinical data for monitoring safety in primary care, perhaps partly explained by the disparity in research methods and study samples. As shown by the majority of studies that used multiple data sources, measurement of AEs and the effective tailoring of safety improvement strategies require information from more than one source to compensate for the limitations of individual sources.

2.6.3 Types and rates of adverse events

The third and final objective of the review was to identify the types of AEs recorded in routinely collected data and their estimated rates of occurrence. Given the myriad of designs adopted by the reviewed studies, it was difficult to derive a summative estimate of patient harm. This is a long-standing issue in patient safety research.[21] Comparisons between studies were hampered by inconsistent definitions of measurements. Where rates of AEs were provided by authors, these estimates varied considerably because of the divergent patient populations and non-comparable units of measurement. Taking the findings of two reviewed studies, Fischer et al (1007) reported a rate of 3.7 AEs per 100,000 consultations while Woods et al (2007) reported a rate of 4.8 AEs per 1,000 consultations.[8,24] Yet at the crude level, the number of AEs detected in the two studies was not too different at 35 AEs (Fischer et al) and 70 events (Woods et al, 2007).[8,24]

In earlier sections, I stated that ADRs and ADEs have consistently received more research attention and that severe AEs were less frequently identified than temporary or less serious injuries. Several studies concluded that events deemed to cause the most severe harm were potentially avoidable. The types of AEs detected in the reviewed studies were limited, with hospital admissions, death and drug-related events being the principal categories of patient harm measured. I have also noted the impact of study heterogeneity on the review process. Besides the issues I have already raised, there were also discrepancies in the care settings where studies took place, which included ambulatory care and outpatient departments. The poor representation of English primary care in the review and incompatibility with the care settings investigated emphasise the need for more research specific to general practice and other non-acute care settings in England.

2.6.4 Limitations of the review

As with all research using secondary sources of data, the accuracy of findings is dependent on the accuracy of original data entry. This is particularly true for studies reliant on routinely collected data. Due to the heterogeneous methodologies applied in the reviewed studies, it was not possible to perform detailed comparisons of study results, such as meta-analyses. Future reviews may choose to use a more sophisticated literature selection strategy for identifying studies based on specific AEs or patient outcome types.

2.6.4.1 Excluded studies

In earlier sections of this Discussion, I considered the findings in relation to the diverse characteristics of the studies. However, the review applied selection criteria that may have been overly-restrictive. That is, some studies focusing on ADRs but relevant to the review will have been excluded. Adverse reactions to drugs are often not attributable to unsafe care and, in many instances, are unavoidable. Conversely, detrimental effects of medication treatment contribute to morbidity and mortality and should be considered in future research.

This review also excluded studies on medical errors without explicitly defined adverse outcomes. Errors do not always lead to actual AEs, although there is potential for harm, and can rarely be detected using routinely collected data. Despite this rationale and because

medical errors are an integral part of the patient safety paradigm, further research should consider the assessment of errors when measuring patient harm. Not least, in doing so, contributory factors and remedial steps in the health system can be ascertained.

2.6.5 Generalisability

Over half of the studies were carried out in the US and many of the findings may only be applicable to the US and countries with similar health systems. A small number of studies was reviewed, almost all of which contained adult samples, such as only patients aged 65 years and older. Aside from other case-mix characteristics, the diseases encountered by patients of different age groups will vary. AEs will differ by disease and patient profiles (as well as other factors) and therefore the applicability of findings for other patient groups is constrained by the limited selection of reviewed studies.

In section 2.5.5.2, I commented on the severity of AEs measured in the reviewed studies. The generalisability of the severity assessments is doubtful for the following reasons. Few studies assessed severity (n=6), they lacked common measurement techniques and there was insufficient evidence that the inter-rater reliability of case reviewers was determined. Recall my statement in section 2.6.4 on results being dependent on the accuracy of the data source. This line of reasoning is also true for measurement of the severity of patient harm. Events not severe enough to warrant medical treatment, that are undetected or where patients do not present for treatment, will be not be recorded in routinely collected data. Thus, these types of AEs may be under-represented in current estimates of patient harm but are nevertheless incidents that should be taken account of in safety improvements.

2.6.6 Contributions of the review

Tools for quality improvement in the NHS that incorporate routinely collected data have been steadily improving. In addition to software created by commercial companies, in-house bespoke performance monitoring systems have been created for local needs by PCTs, the Public Health Observatories* and other organisations. These activities are not reflected

*Public Health Observatories will become part of Public Health England from April 2013.[182]

in the volume of research based on routinely collected data for detecting and monitoring patient harm in primary care. This review has synthesised the literature on this topic. Studies from different countries have been compared to provide an international perspective, highlighting the need for more research in the English primary care setting.

2.6.7 Recommendations from the review

Remarkably little is known about the errors and AEs occurring in community care, dentistry and other areas of primary care. Based on the evidence from the 15 reviewed studies, future research, policy development and clinical practice should consider the following themes for improving patient safety in primary care:

- Use multiple methods to detect AEs, incorporating quantitative and qualitative measures.
- Further explore the suitability of routinely collected data for safety monitoring.
- Identify risk factors for AEs.
- Investigate common medical errors that result in patient harm, including diagnostic problems, communication breakdowns and management failures.
- Evaluate the impact of AEs on patient outcomes.
- Validate and review existing patient safety measurement tools.

2.6.8 Findings from informal consultations with clinicians

To supplement the evidence gained from the literature review on the nature and extent of patient safety issues in primary care, snapshot views were obtained from four GPs and a medical student in England on uses of routinely collected data for patient safety measurement in this care setting.[183] All five discussions were conducted in person at the participants' usual places of work or study between June 2010 and January 2011. The anecdotal findings provided an outline of patient safety concerns experienced by staff in general practice, as well an indication of staff awareness and uses of routinely collected data to improve patient safety.[183] Opinions of how routinely collected data can be successfully adapted into safety monitoring tools were also obtained.[183]

During the discussions, participants assessed ten candidate patient safety indicators on their suitability for application in English general practice.[183] The indicators assessed were identified from the literature review as being in current use or have the potential to be applied in this care setting, or identified as a national health priority for investigation by the Department of Health. This face validity exercise informed the quantitative analysis components of the project, presented in Chapters 5 to 8. Two of the indicators were selected for further investigation (admissions for short term complications of diabetes - emergency admissions for diabetic ketoacidosis and coma and first time emergency admissions for cancer). A third, general adverse event measure was included in analyses. I state the reasons for choosing each of the three measures in the next chapter and then each indicator is described in detail in later chapters.

2.6.9 The next stages of the project

As competition drives forward the collection of data in all areas of the NHS, there are ample opportunities to use these data for resource efficient safety monitoring. This review of the literature has demonstrated that further research is needed to determine the feasibility of measuring AEs using routinely collected datasets. The next steps will involve measurement of AEs attributed to primary care and detected by readily available data collected in the English health system (NHS). Estimates of patient harm generated by these data should be validated with other sources.[62,184] In light of the limited use of routinely collected data for monitoring safety in the non-acute setting in England, barriers to their use and solutions to these problems will also be explored in this thesis.

Chapter 3: Data sources

3.1 Chapter overview

Recall the research aims set out in Chapter 1. In Chapters 1 and 2, I assessed the scope of routinely collected data to monitor, and provide information about, patient harm in primary care (research aims 1, 2 and 3) and identified measures of potential AEs (research aims 1 and 2). To quantify the epidemiology of AEs in general practice (research aim 1) and to further explore methods in which routinely collected data can be used for safety measurement (research aim 4), analyses were conducted using multiple data sources. In this chapter, I state the rationale for the three indicators selected for analyses in Chapters 5 to 8 and present an overview of the data sources used.

3.2 Selection of the three measures

A list of indicators that are research-operational or in current clinical use was compiled from the literature review reported in Chapter 2 and Department of Health policy publications (Chapter 2 section 2.6.8). From this list, a set of ten potential patient safety indicators were shortlisted for assessment by four GPs and one medical student. The assessments were performed during informal consultations which are not reported in this thesis due to their supplementary nature to this project, but they are described in the referenced publication.[183] Out of the ten indicators assessed by the reviewers, two were selected for analysis. One other general AE measure was included in the analyses. All the indicators were selected because of their inter-setting applicability; the impact of the respective diseases and conditions spans across the entire health system. The three AE measures were:

- Adverse events (AEs) with assigned complication codes,
- Emergency admissions for diabetic emergencies, and

- First emergency admissions for cancer.

3.3 Rationale for the selection

The measures were chosen because of the relatively high prevalence of the associated disease (diabetes), burden to the health system (AEs, diabetes and cancer), presence of disease-specific measures (diabetes and cancer) and relevance to current national health frameworks and initiatives (diabetes and cancer).

3.3.1 Adverse events with designated codes

Both empirical research and the informal consultations (Chapter 2) highlighted the prevalence of drug-related harm in safety awareness and research.[183] Iatrogenic AEs with designated diagnosis codes include ADEs but also refer to non-drug related events, such as intra-procedure misadventures. There are built-in codes specifically for these events in the primary care and secondary care information systems that were available for use in this research. As such, it was possible to calculate a baseline rate of explicitly identified incidents beyond what is already known about ADEs.

3.3.2 Emergency admissions for diabetes and cancer

Aside from investigating AEs directly, the consequences of potentially unsafe care also need to be considered. For any disease or condition, emergency admission is an undesirable outcome, and particularly so for undiagnosed diseases, as well as being costly to service providers. These types of health service uses are well recorded in routinely collected data. Diabetes and cancer are key target areas for improvements to services and patient outcomes that have been identified by the UK government and echoed by health interest groups and third sector parties. Both diseases have national clinical guidelines for treatment and management. Adherence to protocols and guidance are likely to improve the outcomes of patients with these diseases and reduce the likelihood of patients experiencing disease-related AEs.

Unplanned admissions for diabetic emergencies (namely diabetic ketoacidosis and diabetic coma) were assessed as a promising adverse event measure based on routinely collected

data.[183] Despite receiving a lower overall score, "first time emergency admission for cancer in patients without a prior cancer diagnosis", was also selected for further investigation. There were three main reasons for selecting this indicator. Firstly, improving cancer outcomes is a government priority. Secondly, relevant outcome data are available for its measurement. Thirdly, I investigated this measure in a collaborative project with colleagues in the Department of Primary Care and Public Health at Imperial College London, the output of which feeds into this project and is reported in Chapter 8.[185] Each of the measures is contextualised in the relevant chapters but before presenting the analyses, it would be helpful to firstly describe the data used in this project and also the analysis methods applied (Chapter 4).

3.4 Data sources

Given the evidence of the strengths and limitations of respective data sources (Chapter 1 section 0), one can expect that comprehensive examination of AEs requires the use of multiple measurement methods.[96,184] Safety improvement strategies that make use of existing resources are preferable, as is the streamlining of the number of indicators.[14] It is with these caveats in mind that I drew on a selection of data sources to address the aims of this project. Before I present the quantitative methods used in this project, it would be helpful to outline the data sources used (Table 3.1). In the next sections, I will describe each of the sources in turn.

Table 3.1 Data sources, coding and measures

Care setting	Data source	Coding	Measure
Primary care	Primary Care Trust - NHS Brent	READ chapters S, T, U	Adverse events
Secondary care	Hospital Episode Statistics (HES)	ICD-10 blocks S00-T98, V01-Y98	First-time emergency admission for cancer
Combined	General Practice Research Database (GPRD)	READ, ICD-10 and Townsend scoring	Adverse events Emergency admissions for diabetic hyperglycaemic emergencies First-time emergency admission for cancer
Other	Index of Multiple Deprivation (IMD)	Postcodes	Deprivation score for patients' place of residence and GP practices in 2007
	NHS Information Centre	Practice codes -	Full Time Equivalent (FTE) GPs in 2010 National Diabetes Audit results for rates of diabetes and diabetic complications
	National Statistics Postcode Directory (NSPD)	Lower Super Output Areas (LSOAs)	Rural/urban classification for patients' place of residence and GP practices in 2010
	Quality and Outcomes Framework (QOF)	Practice codes	Practice performance

3.5 Data from a Primary Care Trust

The Applied Research Unit at NHS Brent is affiliated with the Department of Primary Care and Public Health at Imperial College London (hereafter referred to as PCPH).[186] Through this association, I obtained access to anonymised electronically recorded patient data from the PCT. At the time of analyses, there were 97 primary care practice sites in NHS Brent, including services such as Accident and Emergency Primary Medical Service and Community Dermatology.[187,188] Of these practice sites, 79 were general practices,[187] and 26 of these general practices were voluntary participants of the Brent Clinical Information Management System (CIMS) project. This scheme collected clinical, administrative and demographic data about patients, including details of treatment and prescribing, coded using the Read classification system. Data from the CIMS project were collected from the PCT by PCPH in 2007 for patients registered at participating practices in NHS Brent during the 2007 calendar year.

3.5.1 Ethical considerations

Approval to use CIMS data from NHS Brent was received by PCPH for research projects conducted within the department from Brent Local Research Ethics Committee. The electronic data were in a pseudo-anonymised format and stored on a computer server that was physically housed at the South Kensington campus of Imperial College London. Remote access to the data was obtained to enable the data to be transferred to a secure, private computer network at the Dr Foster Unit (DFU) at Imperial College London, where I carried out all the analyses for this project.

3.5.2 Description of the dataset

The dataset from NHS Brent consisted of data files for each of the Read Code 5-byte (version 2) chapters A-Z, with additional data files for ethnic coding and GP practice details. The data fields within this dataset were arranged by patient observation. Each consultation record contained data on practice identification number, local patient identification number, Read code, a 30 character description of the consultation, the date of consultation, age of patient and sex of patient.

3.6 Hospital Episode Statistics (HES)

Hospital Episode Statistics (HES) is a "data warehouse" that contains information on all patient contact with the NHS and associated NHS treatment in England.[189] The DFU has permission from the National Information Governance Board for Health and Social Care (NIGB) to hold HES data under Section 251 of the National Health Service Act 2006. Data in HES is stored by episodes of care for each Finished Consultant Episode (FEC) of care under a consultant or allied health professional.[189] The end of an episode of care is indicated by discharge from hospital (including internal and external transfers) or admission to the care of another consultant.[189] Three datasets are available which contain data on admissions, outpatients and accident and emergency contacts, respectively.[190]

3.6.1 Characteristics of HES data

For the purposes of this project, inpatient HES data were used and so only the HES admissions dataset will be described in this section. HES data are available by financial year (1st April to 31st March of the following year) and contain approximately 16 million episodes of care records per year.[190] For each record, there are over 50 fields available to be populated.[190] As well as patient's demographic data (including date of birth and sex), information is also recorded on where they were treated (hospital site and NHS trust), when the admission occurred (admission and discharge dates) and clinical details of diagnosis and treatment, including whether the admission was planned or not.[190] Since 2007-08, the HES admissions dataset contains 20 diagnosis fields, with the first field denoting the primary reason for admission.[190] There are also 24 procedure and operation fields, the first of which denotes the main operation of the episode.[190]

3.6.2 Data cleaning

When HES data are received at DFU, these data are cleaning by DFU data management staff and further processed by colleagues at Dr Foster Intelligence (DFI).[191] For example, unfinished or duplicate episodes, incomplete spells, invalid discharge date, age group, sex, elective admission status or length of stay are removed before the data are used for research.

3.7 General Practice Research Database

As mentioned in Chapter 1 section 1.5.7, the GPRD was superseded by the Clinical Practice Research Datalink (CPRD) in April 2012 but as the former was in operation at the time of the project, references will be made to the GPRD and not CPRD throughout this thesis. The GPRD has been used extensively for epidemiological and healthcare research. It is well validated and renowned for its representational coverage of the UK population.

3.7.1 Data coverage

Data provided by the GPRD for this research were from the October 2010 build of the GPRD database. For this time period, the GPRD contained data for 12.1 million patients.[130] This number included the up-to-research-standard records of 4.87 million currently actively registered patients, and 5.77 million inactive patients who either died or were transferred out of the participating practice.[130]

3.7.2 Strengths and weaknesses of GPRD data

3.7.2.1 Strengths of the database

- Wide international use of database with validation for many diseases, conditions and treatments, [192-195] including comparison with HES.[192]
- Population coverage - approximately 8% of UK population and over 590 GP practices.
- Detailed datasets of clinical and non-clinical data.
- Linkage available with disease registries, secondary care and death data.
- Data have received “preliminary cleaning” by GPRD to ensure they meet “research standard”.

3.7.2.2 Weaknesses of the database

- Only general practices using the Vision computer system can participate in GPRD.[130]
- Voluntary participation by practices with pay incentive (10p per patient per year).[130]
- Limited free linked data available under a MRC license for academic institutions (correct at time of application for GPRD data. The MRC licence has since expired and

a new arrangement for access to data should be made to the CPRD via the Independent Scientific Advisory Committee, ISAC).[130]

3.7.3 GPRD for monitoring adverse events

Patient harm associated with drugs or other forms of treatment in general practice have been well investigated using GPRD data.[192,195-197] Yet fewer studies have taken advantage of the longitudinal nature of the database to explore non-drug-related AEs.[197,198]

3.7.4 Dataset for this project

Data were obtained under the Data Linkage Scheme. Integrated hospital admissions data from Hospital Episode Statistics (HES), central mortality data from the Office of National Statistics (ONS) and social deprivation by Index of Multiple Deprivation (IMD) 2007 scores were included in the dataset. It was therefore possible to conduct a detailed exploration of the relationships between potential risk factors, AEs, and other patient outcomes.

3.7.5 Data cleaning

The raw dataset contained records for 100,000 patients who were registered at 584 participating GP practices during the study period (1st January 1999 to 31st December 2008). Basic cleaning of the dataset removed the records of:

1. Patients with invalid sex field, n=3.
2. Patients missing valid clinical, medical or consultation data, n=404.
3. Patients without valid Read coded fields, n=2,047.
4. Patients missing registration date, year of birth or where the first registration date at the GP practice was after the date of the patient's first ever recording in the computer system, n=3.
5. Patients residing outside of England, n=18,328.
6. Patients who did not have any consultations (in any location, with any type of staff) during the study period, n=4,452.

Once cleaned, data for 74,763 patients registered at 457 practices remained. More cleaning was carried out for the analyses reported in Chapters 6 to 8. The results of this data

preparation are reported in the respective chapters. In the next sub-sections, I describe nuances of the dataset that are worthy of note and that had implications for the analyses.

3.7.6 Registration period

In the GPRD dataset, unique patient identifiers are GP practice-dependent; new patient identifiers are assigned to patients when they join a practice. Thus, it is not possible to track patients who transfer out of one practice and who then register with other practices. Given this artefact of the dataset, only the first registration period of each patient at their current GP practice was included in analyses.

3.7.7 Ethnicity

Data on patients' ethnic classification were only available through the linked HES data, i.e. only patients who had an admission record also had valid ethnicity data. It follows then that ethnicity status was recorded for approximately a quarter of the patients in the original raw dataset (24,307/100,000 patients). Ethnicity data were provided in 13 categories (including a category for "data not entered"). Due to small numbers and to improve consistency when comparing results, I aggregated the ethnicity groups into 6 categories that correspond with the current ethnicity categories used by HES and ONS.[189,199]

3.7.8 Referrals

The recording of referrals in the GPRD dataset was poor.

3.7.9 Social deprivation

Only 35,207/100,000 patients in the raw GPRD dataset had a valid Index of Multiple Deprivation (IMD) score. A code for missing deprivation status was created for analyses. Deprivation was measured by population weighted quintiles provided by GPRD and derived from IMD scores.

3.7.10 Data on admissions

Admissions are reliably recorded in English general practice and have been used in prior primary care studies.[197,200] Nevertheless, completeness of admission information can be improved by linkage with secondary care data. In the GPRD dataset, diagnoses on admission

and date of admission from linked HES data improved the accuracy of estimates on hospitalisations associated with safety incidents occurring in non-acute care.

3.7.11 Recording of death

Similar to the availability of linked admissions data, causes and date of death provided through linked data from the ONS enabled more accurate estimates of patient outcomes that occur after AEs. Within the core GPRD dataset, death data are reportedly well recorded and derived using an in-house algorithm.[201] The linked ONS central mortality data are extracted mainly from death certificates.[202] During cleaning of the dataset, I discovered that the GPRD and ONS death fields in the obtained dataset did not fully match. However, the discrepancies were few in number. For example, 30 records with valid ONS death data were missing date and causes of death in the corresponding GPRD fields.

Nevertheless, these records did contain date of death as indicated from HES or ONS data. There were also 8 records where the date of death in GPRD and ONS fields did not match. The difference in the recorded date of death ranged between 1 and 40 days, with the date in the ONS derived field preceding over the date in the GPRD field. These differences may be attributed to variation in data processing between GP practices participating in the GPRD and the ONS, with the ONS providing absolute recording of deaths.

3.7.12 Data fields not used

A variable for life events was derived for each patient based on whether there had ever been Read codes indicating divorce, bereavement, homelessness or unemployment in their records. Place of residence was also derived from the “Residence Types” code in the GPRD data, which was used to generate a binary flag to indicate whether patients lived alone. Data were too poorly populated for all three variables for them to be included in the analyses.

3.8 Other data sources

Together with the three main datasets, further data were obtained from several publically available data sources. I now describe each of the additional datasets in relation to the analyses conducted.

3.8.1 Index of Multiple Deprivation (IMD), 2007

The Index of Multiple Deprivation (IMD) measures socio-economic deprivation across seven domains; "income deprivation", "employment deprivation", "health deprivation and disability", "education, skills, and training deprivation", "barriers to housing and services", "living environment deprivation" and "crime" are measured.[203] Higher IMD scores indicate greater deprivation.

In the GPRD dataset, deprivation scores for patients derived using the IMD for 2007 were provided and applied in Chapters 6 to 8. For analyses using the HES standalone dataset (Chapter 8), the IMD scores for patients' place of residence and GP practices were mapped by postcodes. IMD scores by postcodes have been previously created by a colleague at DFU, whereby IMD scores by Lower Super Output Area (LSOA) were mapped to postcodes using a postcode to geography level lookup table.

3.8.2 NHS Information Centre

In Chapter 7 – Emergency admissions for diabetic hyperglycaemic emergencies, comparisons were made between the study results and nationally reported data on admission rates. These national data were obtained from the NHS Information Centre (and in conjunction with QRESEARCH) and the National Diabetes Audit (NDA).[204-206] In Chapter 8, I use data on the number of full time equivalent (FTE) GPs, excluding GP retainers and registrars in 2010. These data were previously obtained from the NHS Information Centre by a colleague in PCPH for departmental use.[207] These data were available by age group, sex and country of primary medical qualification.

3.8.3 National Statistics Postcode Directory (NSPD)

For the analyses in Chapter 8, the rural/urban classification for patients' place of residence and GP practices were defined using the 2010 National Statistics Postcode Directory (NSPD), from the ONS.[208] Classifications were available at the LSOA level, which were then mapped to the corresponding postcodes of patients' homes and GP practices using the online GeoConvert tool from the Census Dissemination Unit at the University of Manchester.[209] The three categorises used were:

- Urban >10K;
- Town and fringe and village; and
- Hamlet and isolated dwellings.

3.8.4 Quality and Outcomes Framework data

The Quality and Outcomes Framework (QOF) was first implemented in England in the 2004/05 financial year. This is a voluntary performance-related payment system for NHS GP practices.[210] It enables comparisons to be made on the quality and delivery of health services, using points-based indicators within four domains (clinical, organisational, patient experience and additional services).[210] Higher scores indicate better performance, with a maximum attainable score per practice of 1,000 points. Annual results are publically available at national, local and practice levels. [210] QOF data for the most recent financial year available (2010/11) contains data on 134 indicators, with data collected from 8,245 GP practices for over 55 million patients in England (99.7% of registered patients).[211]

In Chapter 8, five QOF measures were mapped to practices using the unique identifier code assigned to each practice. The overall practice performance, two cancer indicators and two patient experience of access indicators were assessed by averaging each indicator score over the years of the study (the patient experience indicators were only available for the latter two years of the study period). These data were downloaded from the NHS Information Centre for Health and Social Care's website for the three years covering 1st April 2007 to 31st March 2010 (from 1st April 2008 for the two patient experience measures).[212]

The cancer indicators were:

- CANCER 01 – "register of patients with a diagnosis of cancer excluding non-melanotic skin cancers from 1st April 2003", and
- CANCER 03 – "percentage of patients with cancer who have been diagnosed within the last 18 months and have had a patient review recorded as occurring within 6 months of the practice receiving confirmation of the diagnosis".[212]

The patient experience of access indicators were:

- Patient Experience 07 – "percentage of patients who were able to obtain a consultation with a GP within 2 working days", and
- Patient Experience 08 – "percentage of patients who were able to book an appointment with a GP more than 2 days ahead".[212]

3.9 Elements of analyses

3.9.1 Follow-up time

The amount of time individual patients' contribute to the study, time at risk, was calculated separately for the three AE measures.[213] The unit of calculated follow-up time was years. Only approximate estimates were possible using year of birth as patients' dates of birth were unavailable in the GPRD dataset. The calculations took into account of leap years:[213]

$$\text{Follow} - \text{up (years)} = \frac{(\text{end date} - \text{start date})}{365.25}$$

Where:

End date = Date of death, transfer out of practice or study end date (31st December 2008), whichever occurred first **OR** date of AE of interest.

Start date = Study start date (1st January 1999) or first registration date at practice if date of birth was after 1st January 1999, whichever occurred last.

3.9.2 Patient endpoints

After experiencing an AE in general practice, patients may be admitted to hospital and/or die. These endpoints are routinely and reliably recorded. Even though these and other patient outcomes are not always attributable to unsafe care, further investigations are warranted when these outcomes are preceded by iatrogenic harm. Admission rates can be inaccurate markers of healthcare quality.[214,215] Yet unplanned admissions can also be valid indicators of poor quality or unsafe care in the primary care setting. For example, if an admission with a primary diagnosis of a potential AE occurs soon after a GP consultation, the patient's pre-admission contact with health services should be examined to identify the root cause of the cause of admission and remedial factors, if applicable.

3.9.3 Defining emergency admission

As defined in HES, an emergency admission is one that is not from a waiting list, booked or planned.[189] instead, a patient is admitted by accident and emergency (A&E) services, GP, bed bureau, consultant outpatient clinic or other means including the A&E department of another care provider.[189] This definition was used in the analyses reported in Chapters 6 to 8.

3.9.4 Comorbidities

To determine the effects of comorbidities on patient safety outcomes in this project, and to assess the validity of two commonly applied comorbidity measures, the Charlson Comorbidity Index and the John Hopkins Adjusted Case Group (ACG) Case-Mix System were used. A further composite comorbidity measure based on Charlson Index disease groupings was applied. I now describe these three comorbidity measures.

3.9.4.1 Adjusted Case Group (ACG) System

The ACG case mix system was created at Johns Hopkins University in the US specifically for use in ambulatory (or non-acute) care and has been applied internationally, including in English general practice.[216-218] This adjustment method takes into consideration the potential for patients to have multiple diagnoses over a set period of time and the ACG system can be used to predict healthcare use.[219,220] Unlike other risk adjustment methods, the ACG system takes into account clinical need of patients and the burden of diseases when assigning patients to comorbidity groups. It has been used to assess comorbidities in the UK using GPRD data.[218,221]

The structure of the system is as follows:

1. **Adjusted clinical groups (ACGs)** – 106 mutually exclusive health status categories based on morbidity, age and sex. These are used for calculating costs.
2. The ACGs are used to assign patients to **Resource Utilisation Bands (RUBs)**, indicating severity of morbidity. The six RUB groups are:
    - 0 – No or only invalid diagnoses
    - 1 – Healthy user

- 2– Low
- 3 – Moderate
- 4 – High
- 5 – Very high

3. **Aggregated diagnosis groups (ADGs)** – All ICD-10 (and Read codes) are categorised into 32 morbidity markers per patient. These unique morbidity groupings are based on "…specific clinical criteria and demand on healthcare services".[222] Patients are assigned to single or multiple ADGs. The ADGs can be aggregated into 12 Collapsed ADGs (CADGs). Due to copyright restrictions, the mapping of ADGs to CADGs could not be reproduced in this thesis. ADG assignment is based on 5 dimensions:
    - Duration
    - Severity
    - Diagnostic certainty
    - Type of etiology
    - Expected need of specialty care
4. **Expanded diagnosis clusters (EDCs)** – There are 5 MEDC types (Administrative, Medical, Surgical, Obstetric/Gynaecological and Psychosocial). Within these types, there are 27 Major EDC (MEDCs) clinical categories/disease clusters. Each ICD/Read code is mapped to one of 267 EDCs. Within each EDC, the associated ICD and Read codes share similar diagnostic (and therapeutic) characteristics.

3.9.4.2 Use of ACG measures in this project

The ACG software was applied only to the GPRD dataset. Comorbidity measures were created for the entire dataset, with no distinction made between the three AE measures or measure-specific criteria. As such, the end date used to derive ACG weights for each patient was either date of death, date of transfer out of practice or the study end date, whichever occurred first. By ignoring end dates relevant to the individual AE measures, the derived ACG variables were not valid for use in all analyses. To explain, some conditions included in developing the ACG weights will have occurred after the outcome(s) of interest. To include these conditions in analyses where the response variable is the outcome of interest would bias the results. Where variables derived from the ACG software have been used, this is denoted in the relevant sections of the thesis. It should also be noted that original US

spellings are retained for ACG derived variables and intentionally used throughout this thesis.

3.9.4.3 ACG derivations

To derive the ACG weights, only Read codes in the medical history category of the GPRD dataset ("enttype=2") were used as the quality of coding in other categories, such as Disease Registries and Diabetes, was unknown and potentially inconsistent and/or poor. The ACG software distinguishes between data for patients aged <65 years (labelled by ACG as "non-elderly") and patients aged ≥65 years (labelled "elderly"). Therefore the dataset was processed in two batches, using the "lenient diagnostic certainty" option which does not limit the number of diagnoses per patient included in processing, unlike the "stringent diagnostic certainty".[223] Patients were assigned up to 32 ADGs, presented as binary flags. These flags were aggregated into CADGs, with a third binary measure of MEDC flags. Counts of the number of EDCs per patient (maximum 267) were also included in analyses, and a fifth and final ACG measure of categories derived from RUB scores.

3.9.4.4 Charlson Index

The Charlson Index was originally developed for use in the hospital setting to predict mortality within one year of admission. The index has been extensively used in healthcare research, with up-to-date translations for the ICD-10 classification system.[224] In the primary care setting, the index has been adapted for use with Read and OXMIS coding.[225,226]

The original Charlson Index and Khan et al's adaptation for Read/OXMIS codes were derived from 17 disease categories (Table 3.2). Khan et al's version consists of 3,156 codes and was adapted from Deyo et al's modification of the Charlson Index.[226] No changes were made to the original specification. In line with Khan et al's methodology, the overlaps in 13 Read/OMXIS codes corresponding to diabetes and peripheral vascular disease were coded as diabetes.[226] Cancers were coded into separate groups, with exclusions for benign cancer (B7), cancer in situ (B8) and neoplasms of uncertain behaviour (B9).[226]

Table 3.2 Disease categories used to derive Charlson Index scores

Charlson disease category	Score weight
AIDS	6
Cancer	2
Cerebrovascular disease	1
Chronic pulmonary disease	1
Congestive heart disease	1
Dementia	1
Diabetes	1
Diabetes with complications	2
Hemiplegia	2
Metastatic tumour	6
Mild liver disease	1
Moderate liver disease	3
Myocardial infarction	1
Peptic ulcer disease	1
Peripheral vascular disease	1
Renal disease	2
Rheumatological disease	1

There is a relative dearth of studies comparing the performance of different versions of the Charlson Indices on UK primary care data. Studies in secondary care indicate that Elixhauser's comorbidity index performs better than Deyo et al's.[227-229] Ideally, I would have compared two commonly used adaptations of the Charlson Index - Deyo et al's and Elixhauser et al's indices.[230,231] The Elixhauser modified Charlson Index contains 30 disease categories, in contrast to the 17 disease groups in the original Charlson and Deyo et al's adapted indices.[230-232] Given the potentially cumbersome nature of analyses using 30 disease groups and issues surrounding small numbers, and the lack of evidence on using the Charlson Index on non-hospital data, only Deyo et al's version of the Index was used in this project.

3.9.4.5 Disease group flags

In addition to the comorbidity measures created using the ACG software and the Charlson Index, I applied disease flags in the analyses. These binary flags corresponded to the 17

disease categories used to derive Charlson comorbidity scores for each patient. As mentioned in section 3.9.4, an extra 18th (composite) flag was created to indicate whether a patient had any of the 17 diseases.

3.9.5 Continuity of care

Continuity of care, described as "the quality of care over time", can be considered in terms of longitudinal, relational, flexible and team boundaries.[233,234] Continuity of care is particularly important for patients with chronic conditions and who may access health services more frequently than other patients.[234,235]

3.9.5.1 The Continuity of Care (COC) Index

The distribution of consultations by individual patients among staff members was measured by the Continuity of Care (COC) Index.[236] The COC has the advantage of not requiring data on patients' designated doctor (or other relevant staff member), and takes into account the consultation patterns and total numbers of consultations of individual patients.[236] Only patients who had at least two consultations during the study period were allocated a COC score, as recommended by the Index's creators.[236] By excluding patients who had less than two consultations, it was possible to reduce potential bias arising from complete discontinuity caused by infrequent consultations. Only consultations at the GP practice or by telephone and with a doctor or nurse were used to calculate COC scores.[236] The formula for calculating each patient's COC score is:[236]

$$\mathrm{COC} = \frac{\sum_{j=1}^{s} n_j^{\,2} - n}{n\,(n-1)}$$

Where

n = total number of consultations (at GP practice or by telephone)

n_j = number of visits to clinician j

s = number of clinicians (GPs or nurses)

Possible COC values range from 0 to 1. The COC score was converted to a categorical variable (low, moderate and high continuity of care) based on rankings weighted by the sample population.

3.10 Software

The following software items were used in the project:

- Endnote X3 and X4;
- GeoConvert from the Census Dissemination Unit (CDU), University of Manchester;
- GPRD Gold Browsers July 2010;
- Johns Hopkins ACG® System 9.01i;
- Windows Media Player version 11;
- Microsoft Office Word and Excel 2007 and 2010;
- NHS Clinical Terminology Browser Version 1.04; and
- SAS Version 9.2 TS Level 2MO.

Chapter 4: Analysis methods

4.1 Chapter overview

In this chapter, I outline the statistical methods used in Chapters 5 to 8. In the previous chapter, I gave an overview of the measures and data sources included in the analyses. I begin this chapter by revisiting these two components of the analysis. Then, I describe the analysis techniques that feature in the following chapters. Finally, I consider alternative statistical methods to those applied.

4.2 The adverse event measures

Recall the measures described in Chapter 3:

- Adverse events (AEs) with assigned complication of care codes,
- Unplanned admissions for diabetic emergencies, and
- First unplanned admissions for cancer.

These measures were investigated using a number of data sources, of which the main datasets are outlined in the following section. Definitions, including diagnosis codes, are provided in the relevant chapters (Chapters 5 to 8).

4.3 The data sources

Also recall the main datasets described in Chapter 3:

- Data from a PCT, NHS Brent,
- Secondary care data from the Hospital Episodes Statistics (HES), and
- Primary care data from the General Practice Research Database (GPRD).

I will refer to these measures and datasets throughout this chapter.

4.4 Analyses at patient-level

A combination of patient-level and practice-level analyses are presented in the subsequent four chapters. Before describing the analysis techniques used in practice-level analyses (section 4.7), I explain how patient-level analyses in Chapters 5 to 8 were performed. Further methodological detail on chapter-specific analyses can be found in the respective chapters.

4.4.1 Estimates of rates

Chapters 5 to 8 include calculated rates of AEs. The types of data and measures used differ between the chapters (Table 4.1).

Table 4.1 Rate estimates by thesis chapter and data type

Chapter	Type of data	Type of rate	Unit of measurement
Chapter 5 - Adverse events recorded in local data	Local (NHS Brent)	Point prevalence	Consultations (per 1,000 consultations)
Chapter 6 - Adverse events recorded in national data	National (GPRD)	Incidence	Person time (per 1,000 person years)
Chapter 7 - Unplanned admissions for diabetic emergencies	National (GPRD)	Incidence – crude	Person time (per 1,000 person years)
		Incidence - adjusted	Population (per 100,000 population)
Chapter 8 - First unplanned admissions for cancer	National (HES and GPRD)	Incidence – crude and adjusted	Person time (per 10,000 person years)

4.4.2 Crude calculations

Descriptive analyses are presented in Chapter 5 to 8. In each chapter, initial descriptive bivariate analyses explored the associations between the predictor variables and the outcomes of interest. The associations between variables were examined using chi-square tests (categorical data), Mann Whitney U tests (non-normally distributed ordinal data), t-tests (normally distributed continuous data) and Spearman rank correlation (non-normally distributed data). The results of these analyses are not reported in full, but where appropriate.

In Chapters 6 to 8, the main statistical measure of interest was the relative risk (or risk ratio, RR). Odds ratios (ORs) were also estimated in Chapter 8 (section 4.5). Following descriptive analyses, these measures were calculated by crude and then multiple regression, which adjusts for potential confounders. Additional adjustments were made for clustering of patients at GP practices (section 4.8.1).

4.5 Regression modelling

To calculate ORs for binary outcomes, logistic regression is conventionally used. In these models, the outcome (probability of its occurrence) is transformed by the logit link function to derive log odds for the outcome.[237] This method is applied in Chapter 8.

I now turn to the calculation of RRs, which are easier to interpret from raw results than ORs. The first step in deciding which type of regression to use is to determine how the outcome of interest is distributed. A Poisson distribution would be appropriate for ordinal (count) outcomes (such as number of AEs or number of admissions), where the outcome is rare (low probability of occurrence) and there is a large enough number of the outcome for the data to be approximated to the normal distribution.[238] This assumption is valid for the analyses of Chapters 6 and 7. Poisson regression is fitted on a log scale, with the outcome transformed using the log link function.[238]

For dichotomous outcomes (such as death status or whether a first-time admission is an emergency or not), modelling based on the binomial distribution is more appropriate. The conventional approach is to approximate ORs to RRs using logistic regression but this has the disadvantage of potentially over-estimating RRs, especially if the outcome is not rare. An alternative is to use log-binomial regression, which was used in Chapters 6 to 8. Like Poisson regression, this method for calculating RRs requires the data to be transformed using the log link function. While the log of the odds of the outcome is used to generate ORs, the log of the risk of the outcome is used to calculate RRs.[239] Log binomial regression for calculating the relative risk of dichotomous outcomes has been documented in the literature since the mid-1980s but is not commonly applied.[240-242]

4.5.1 Technical issues

The relatively low reported use of log-binomial regression is partly due to its technical caveats. The key issue is model non-convergence.[240,243,244] Failed convergence is often caused by estimates being on the boundary of the parameter space* (often due to the inclusion of continuous covariates and/or poor selection of starting values for the parameters in the model).[241,245] In such a situation, modified Poisson regression using the Generalized Estimating Equations (GEE) method can be applied even for dichotomous and/or common outcomes.[246-248] Furthermore, problems of misclassification (using an incomplete set of predictor variables) and large standard errors (SEs) when there is a binary outcome can be resolved by using this method.[244] I will return to Poisson regression with GEE later (section 4.8.2.2).

Other technical problems experienced in regression analyses arise from correlated observations (such as repeated events in patients) and clustering (such as patients within a GP practice) which violated the assumptions of chosen statistical distributions and result in over-dispersion. Excess of zero counts in datasets also affected model fit. These scenarios occurred in this project and their impact on the statistical choices that I made will be explained in the following sections.

4.5.2 Generalized linear models

Unlike general linear models where the predictor variables and outcome are assumed to have a linear relationship, Poisson and log-binomial regression use (logarithmic) transformation of the outcome to derive a linear relationship.[249] These models are known as generalized linear models. The RRs (and ORs using log-binomial regression) are calculated as Maximum Likelihood Estimates (MLEs)†.

4.5.3 Multiple regression

This type of regression is used when the independent effect of each predictor on the outcome is of interest and simultaneous control of multiple confounders is sought.[250] In the

*Invalid parameter values, outside of the 0-1 interval.

†Regression coefficients that maximise the likelihood function – the most likely values for the observed data.[14, 15]

next sections, I explain how adjusted regression models were built in (used in Chapters 6 and 8) and discuss solutions to the technical issues encountered during this process (section 4.5).

4.6 Model fitting

To account for variation in person-time contributed by individual patients to the study, follow-up time as person years was included as an offset (constant) term (log of follow-up years) in crude and adjusted models, where applicable. Where models contained an offset term, this is indicated in the relevant sections of Chapters 6 and 7. Crude and adjusted models were developed using the PROC GENMOD procedure in SAS. PROC GENMOD has the benefit of allowing both continuous and discrete predictor variables to be fitted and also accommodates solutions to non-convergent models.

4.6.1 Selection of variables

The stepwise method was used to select variables for multiple regression models. This method was chosen over the other two most common selection methods (backwards and forwards elimination) because it allows for greater flexibility in deciding which variables to keep in the model.[251] The stepwise process is not without faults though, including potential over-estimation of model performance.[249,251] All predictors were included in the initial model and then eliminated one at a time on the basis of their p-values.[249,252] A p-value of 0.1 was used in crude analyses as the threshold for variables to be retained and included in the initial adjusted models. Predictors with p-values of 0.05 or less were considered statistically significant and retained for model fitting.

4.6.2 Contribution of predictor variables

Separate models were fitted for each of the comorbidity variables; models for Charlson score, disease categories based on the Charlson Index, ADGs, ACGs, MEDCs, RUBs and count of EDCs were fitted to examine the explanatory power of each measure (Chapter 3 section 3.9.4 for information about comorbidities).

To crudely assess the contribution (statistical significance) of each predictor variable in the model, the Wald statistic was used. Final decisions on the retention of predictors in

regression models were made using likelihood ratio values as Wald statistics are prone to under-estimation caused by inflation of the SE when the regression coefficient is large and also when sample sizes are small (less of an issue in this project).[253,254]

4.6.3 Goodness of fit

In unadjusted analyses, the model's dispersion parameter can be used to assess the model's fit (how much of the variance of the outcome is explained by the predictor variables):

$$\text{Dispersion parameter} = \frac{\text{deviance or chi square}}{\text{degrees of freedom (df)}}$$

Models with a dispersion parameter greater than 1 are assume to have a poor fit. The fit of crude models were assessed using Akaike and Bayesian Information Criteria (AIC and BIC, respectively), with smaller values indicating better model fit.[255] When GEE is used, the AIC and BIC measures are no longer valid (and not given in PROC GENMOD). In this situation, model fit can be assessed by the Quasi-Likelihood under the Independence model Criterion (QIC).[256] As with AIC and BIC values, smaller QIC values indicate better model fit .[256] In adjusted analyses, the model fit was also assessed graphically in plots of the residuals* by the predicted values.[255,258]

4.7 Analyses at practice-level

To assess whether there was variation in recorded AEs by GP practice, the rate of AEs was calculated for each GP practice in Chapter 6. To control for variation in rates due to particular patient profiles, the age and sex of patients were adjusted for (standardised by). Of the two methods to produce rates that are comparable between patient groups with different age and/or sex structures, the indirect method was used. Standard populations (stratified by age and sex) required for direct standardisation were not available for the outcome of interest.[259]

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*In regression, residuals refer to the difference between the outcome and the predicted values.[257]

4.7.1 Standardisation of adverse event measures

Neither practice list sizes nor national data for AEs by age and sex were available to calculate indirectly standardised rates of adverse events (Chapter 6). Therefore, the internal method of indirect standardisation by age and sex was applied, with the expected numbers (denominator values) derived from the sample.[260] The standardisation method can be presented as:[204]

$$\text{Standardised adverse event ratio} = \frac{\text{Observed number of events}}{\text{Expected number of events}} \times \text{Rate in sample}$$

Where the expected number of events is calculated by:[255]

$$\text{Expected number of events} = \text{Total events in sample x Proportion of events in group}$$

To calculate the indirectly standardised rate, the standardised adverse event ratio was multiplied by 100.

It was assumed that there was consistency in the standardised adverse event ratio within age groups and sex of patients. It was also assumed that the sum of observed values was equal to the sum of expected values, or expressed differently, the marginal mean of ratios was fixed at 1.[261] An advantage of using indirect standardisation is that this method produces more robust results than direct standardisation when there are small numbers of the outcome(s) of interest or unstable rates.[262] This argument is valid for the analyses in Chapter 6 as adverse events were rare and there was variation in this outcome between patients by age and sex. When creating funnel plots of the indirectly standardised rates of adverse events (Chapter 6 section 6.4.2), 95% (2SD) and 99.8% (3SD) control limits for the data were calculated using the exact method based on the Poisson distribution.

4.8 Technical issues revisited

I now further consider the difficulties associated with regression modelling that were described in section 4.5.1 and set out solutions to these problems.

4.8.1 Clustering of patients

The analyses in this project feature repeated measures at patient and practice levels. It thus follows that assumptions of events occurring randomly or independently of each other are void. Therefore, clustering (or heteroscedasticity) at the practice-level and/or repeated events in individual patients must be taken into account in adjusted analyses.

4.8.2 Over-dispersion

Where the variance of the outcome is considerably larger than the mean, over-dispersion (or heterogeneity) is suspected. This interpretation has an element of subjectivity. As an arbitrary guide, a variance value ≥1 unit of the mean may be considered "large" for Poisson models.[263] For both Poisson and binomial models, the dispersion parameter can be calculated to test for over-dispersion (section 4.6.3). A ratio value greater than 1 indicates over-dispersion and that the distribution is unsuitable for the data.[263,264] In this situation, there may be under-estimation of the SEs that result in the production of narrower confidence intervals than are appropriate for the data.[263,264]

In the previous section, I stated two causes of over-dispersion (repeated measures and clustering). Other reasons for over-dispersion include misclassification, non-linear terms and interactions between predictors. Where the causes of over-dispersion are not assumed to lie in these reasons, there are several methods to manage variability greater than one would expect to find in a Poisson distribution. These methods will now be discussed.

4.8.2.1 Robust standard errors

Huber's sandwich variance estimator is used to derive robust parameter values (MLEs) without reliance on assumptions about the underlying model, which itself may be incorrect. This method is commonly referred to "sandwich" estimation because the estimated variance matrix lies between the matrices of the original model-based variance.[265] Poisson regression with robust error variance (sandwich estimation) is performed in PROC GENMOD by using the "repeated" statement to invoke the Generalised Estimating Equations (GEE) method (section 4.8.2.2).[244]

4.8.2.2 Generalised Estimating Equations (GEE) method

The Generalised Estimating Equations (GEE) method can compensate for clustering and over-dispersion. This method is particularly useful when data are longitudinal and not normally distributed (determined by running normal quantile-quantile (Q-Q) plots of the outcome and also by examining the residuals of the adjusted models). GEE uses both quasi-likelihood estimation and robust SEs (section 4.8.2.1) to correct for clustering.[266] Missing data are assumed to be missing at random in GEE, thus Wald tests were applied to determine the effects of clustering on the SEs.[266]

In the PROC GENMOD procedure, GEE is invoked by using the "repeated" statement.[244] After the "repeated" statement, the unit of repetition should be declared using the "subject" statement. To account for over-dispersion in PROC GENMOD, the "subject" would be the patient (referring to the unique patient identifier code in analyses).[244] In the case of accounting for clustering of patients within practices, the "subject" would now be GP practice (referring to the unique practice identifier code in analyses) and thus changing from the use of an individual identifier to a cluster identifier.[247]

In all analyses incorporating GEE presented in this thesis, the independent working correlation structure for modelling the associations between repeated measures was applied.[265,267] This is the default working correlation matrix for GEE in PROC GENMOD and was selected based on the assumption that observations within subject (events at a GP practice) were not equally correlated.[244] Analyses using GEE benefit from minimal penalties for model misclassification (using the wrong working correlation structure).[268]

4.8.2.3 Adjustment using goodness of fit ratios

Alternatively, a factor for over-dispersion can be included in the model based on the square root of the deviance or Pearson chi square value over the degrees of freedom (df). The scale parameter is available through the "PSCALE" (for Pearson chi square) and "DSCALE" (for deviance) functions in PROC GENMOD. These functions adjust the SEs of the regression coefficient (multiplies SEs by the scale parameter) to produce more conservative estimates of the SEs, using the quasi-likelihood method.[258]

4.8.3 Excess zeros counts

When an ordinal outcome variable is used (such as count of AEs and count of admissions), there are likely to be excess zero counts (no occurrence of the event of interest). Continuous outcomes were presented graphically to detect this phenomenon in the data. Statistical solutions to address excess zeros are outlined in the next section and also discussed in the respective chapters (Chapters 6 and 7).

4.8.4 Solutions to excess zeros and over-dispersion

4.8.4.1 Negative binomial regression

So far I have discussed two methods to address over-dispersion (application of GEE and scale parameters). Now I will briefly outline some modelling techniques that are suitable when there are excess zero counts and over-dispersion. The first model is negative binomial (NegBin) regression. This type of regression accommodates over-dispersed data but may produce poor fitting models when there are "excess zeros", given inclusion of unobserved heterogeneity in the model.[269]

4.8.4.2 Zero-inflated regression models

A second option would be to build a zero-inflated model, either zero-inflated Poisson (ZIP) or zero-inflated negative binomial (ZINB) versions.[270] The latter, ZINB, is advantageous when the data are over-dispersed.[258] Both NB regression and ZINB regression use the gamma distribution to account for over-dispersion.[258] Either NB regression or ZIP regression would account for both excess zero counts and over-dispersion but unlike NB regression, ZIP regression does not consider between-subject heterogeneity. Zero-inflated and negative-binomial regression models can be built in PROC GENMOD.

4.8.4.3 COPY algorithm

Where regression models fail to converge, alternative methods for calculating RRs include applying robust Poisson regression (section 4.8.2.1), the COPY method using log-binomial regression or non-linear least squares.[271] The COPY method produces approximate MLEs

(section 4.5.2) but this method is affected by outliers and model misspecification*.[241,245] The algorithm is used to create one dataset with a given number (c-1) simulations of the original data and one copy (c) of the dataset with reversed values of the outcome variable.[245] The estimated SE is then multiplied by the square root of the number of simulations (c) to take into account of the inflated sample size. A minimum of 100 simulations, or copies, is recommended, although models that used 1,000 copies or more have resulted in approximated MLEs close to the MLEs of the original dataset.[245,271,272]

4.8.4.4 Non-linear least squares estimation

Poor model fit indicated by the MLE being on the boundary of the parameter space (and ultimately non-convergence) may require the use of estimators not restricted to a specific distribution.[258] By fitting models using the least squares method, parameter values are derived from the minimum residual sum of squares.[258,273] In SAS, non-linear least squares regression is calculated using the PROC NLIN procedure.[258] This approach is more challenging than Poisson regression and the associated variations that have been mentioned already, from both mathematical and programming perspectives. Given the alternative modelling approaches already proposed in this chapter to address the technical issues raised and the requirement of switching to a different SAS procedure, non-linear least squares regression was not attempted in this project.

4.8.4.5 Comparison of methods

I assessed the performance of models by applying the Vuong test. This distribution-free test was used to compare firstly, Poisson models with GEE and ZIP models, and secondly, NegBin models with ZINB models, using a SAS macro downloaded from the SAS website.[274,275] Better performance of original Poisson with GEE models or NegBin models, compared to zero-inflated models, was determined by non-statistically significant Z scores in the Vuong test.[275,276]

*This is caused by erroneous assumptions about the model, such as incorrectly retained or removed variables, use of an incorrect function or inappropriate distribution.

4.9 Alternative analysis approaches

There are two additional statistical approaches that could be considered for tackling excess zeros and over-dispersion. The first is Cox proportional hazards survival analysis (commonly referred to as Cox regression). Although this method can take into account unequal patient-time, it was not applied in this project because the rare nature of the outcomes of interest (and high amount of censoring) would have resulted in inflated SEs and potentially incorrect RR estimates.[245] Indeed, the performance of Cox regression does not seem to be superior to Poisson regression with robust variance estimates or log-binomial regression in models with binary outcomes.[241]

The second approach is hurdle modelling, which is suitable for repeated outcomes (such as multiple AEs and readmissions).[277] However, hurdle analyses cannot be performed by the PROC GENMOD procedure in SAS. Finally, multi-level modelling can take into account clustering and over-dispersion. This approach may be favoured over GEE models when there is more than one cluster level, which GEE is unable to accommodate. Multi-level models can also not be built in PROC GENMOD. To maintain analytical consistency, and because of the availability of alternative modelling techniques within the preferred PROC GENMOD procedure, I did not use Cox regression, hurdle or multi-level models. Relatively new statistical solutions to the issues of over-dispersion, multi-level clustering and excess zero counts are possible when using software other than SAS, but this was beyond the scope of this project.[278]

Chapter 5: Adverse events recorded in local data

5.1 Chapter overview

This chapter presents descriptive analyses of data from NHS Brent on adverse events that were captured in a computerised medical system. The analyses offer insights into data recording at the local level, the types of events that are recorded and highlight some of the limitations of using relatively small datasets to detect potentially harmful incidents.

5.2 Local data

Use of population-level databases for performance monitoring, service planning and resource allocation, payment, and to some extent for research, is well established in primary care.[279] Much of the available data is routinely collected, including General Medical Services (GMS) data, Prescribing Analysis and Cost (PACT) data and the raw data entered onto computer systems at individual GP practices. Novel methods of monitoring AEs can be developed from the data-rich environment of general practice. Before sophisticated data-driven safety tools can be built, the scope of recorded AEs has to be examined. With this rationale in mind, I conducted descriptive analyses to determine the types and frequencies of AEs recorded in routinely collected data from a London PCT.

5.2.1 The Borough of Brent

Brent, in north-west London, is served by NHS Brent (formerly Brent Teaching Primary Care Trust). In the 2008/09 financial year, the PCT received £432 million in funding from the government, of which £61 million was allocated to primary care services including 31 community services.[187] A further £39 million was spent on drugs prescribed in general practice.[187]

Brent is the most ethnically and culturally diverse Borough in London. Over half of the 263,500 residents (55%) are from black and minority ethnic groups.[280] According to the 2001 Census, 36% of Brent residents were born outside of the UK.[280] Approximately 35.5% of all Brent residents are aged between 25 and 44 years and half of its residents from ethnic minority groups are under 30 years of age.[280,281] Compared to national rates, Brent has a greater proportion of unemployed residents (4.98% versus 3.35%) and single parent households (8.19% versus 6.42%).[281] Approximately 32.4% of households in Brent have at least one person with a limiting long term illness.[281] By considering the demography of its population, one can then begin to consider the health challenges facing Brent.

5.2.2 Definition of adverse event

Consistently applied definitions will facilitate the design of, and comparison with, future studies. In the first chapter, I characterised "medical error", "adverse event" and "patient harm" (Chapter 1 section 1.2.3). I now revisit these definitions specifically for this chapter. In the following analyses, AEs are defined as temporary or permanent injuries caused by medical management and are not due to underlying disease nor are expected outcomes of treatment.[24,282,283] AEs can be caused by medical errors arising from actions or omissions that are unanticipated, unintended and should not reoccur.[9] To demonstrate, imagine the scenario where a GP fails to prescribe appropriately by co-prescribing a potassium-sparing diuretic and an angiotensin-converting enzyme (ACE) inhibitor to a patient without valid indication.[51] As a result of adhering to this prescription, the patient develops hyperkalaemia and requires admission to hospital.[51]

5.2.3 Objectives of the analyses

To achieve the study aim stated at the end of Chapter 1, the analyses in this chapter were intended to:

- Determine the types of AEs that are identified by designated Read codes for complications of care and are recorded electronically at GP practices in Brent that participated in the Clinical Information Management System (CIMS) project.

Determine the rates of AEs that are identified by designated Read codes for complications of care and are recorded electronically at GP practices in Brent that participated in the Clinical Information Management System (CIMS) project.

5.3 Methods

The dataset analysed has been described in Chapter 3 section 3.5.

5.3.1 Data extraction

AEs that may be attributable to medical care were identified through the Clinical Terms stored in the electronic CIMS. Valid AEs (as defined in section 5.2.2) were mapped to the following Read Code chapters:

- "Injury and Poisoning" (Chapter S);
- "Causes of injury and poisoning" (Chapter T); and
- "External causes of morbidity and mortality" (Chapter U).[284]

A full list of the Read Codes used in the analysis is shown in Table A.9. The Clinical Terminology Browser Version 1.04 was used to identify the appropriate codes to be applied in the data extraction and analysis.[284] Where ethnicity was analysed, categories from the 2001 Census were applied.[199]

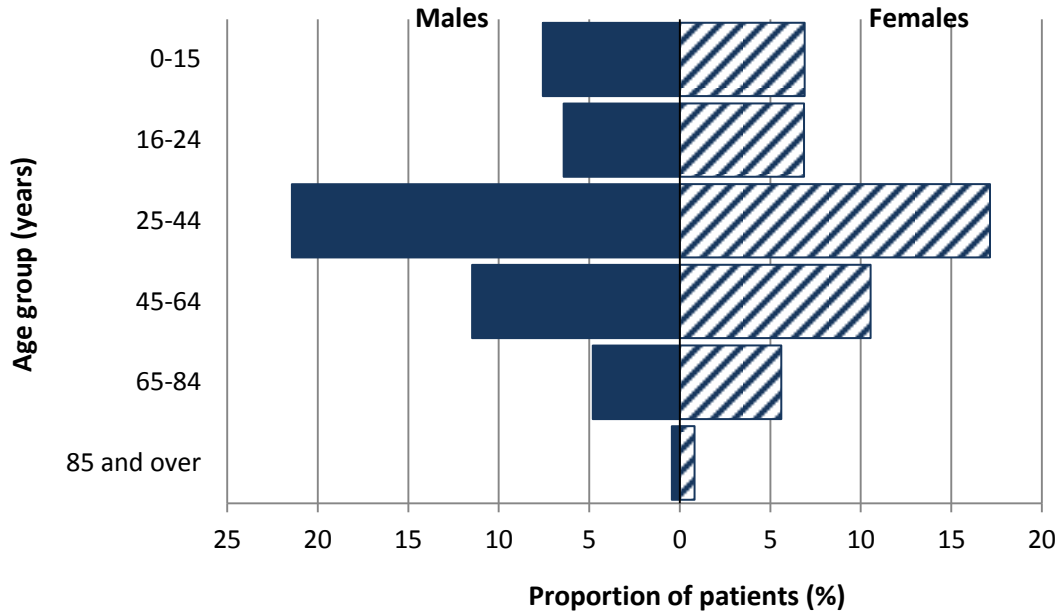
5.4 Results

Before presenting the estimated rate of AEs, I describe the demography of the study sample.

5.4.1 Patient characteristics

Data were available from 25 practices out of the 26 GP practices participating in CIMS. Records were available for 73.7% of registered patients at the 25 practices (n=78,027/105,877). After cleaning of duplicate or missing data, 81.6% of the original consultation records remained valid (n=1,118,072/1,370,659). The average age of patients was 37 years (n=78,027), ranging from under 1 year to 104 years. Across the six age groups, the largest proportion of patients were aged between 25 and 44 years (38.6%; n=78,027) (Figure 5.1).

Figure 5.1 Population distribution of Brent CIMS dataset, n=78,027



The sample contained slightly more male patients (52.1%; n=40,675/78,027) than female patients. Ethnicity was recorded for 43.1% of patients (n=33,649/78,027) and available for 619,992 consultations (Table 5.1). Approximately half of patients with recorded ethnicity were of Asian ethnicity (n=17,111/33,649).

Table 5.1 Age, sex and ethnicity of patients in the Brent CIMS dataset, n=33,649

		Ethnicity*					
		White	Black	Asian	Other	Mixed	NOS†
Sex	Male	3999	1826	8914	754	551	152
	Female	5002	2482	8197	910	690	172
Age group (years)	0-15	731	605	2387	144	143	78
	16-24	1063	453	2043	327	159	48
	25-44	3174	1487	6775	717	470	138
	45-64	1993	983	4078	310	264	32
	65-84	1719	762	1729	145	200	24
	≥85	321	18	99	21	5	

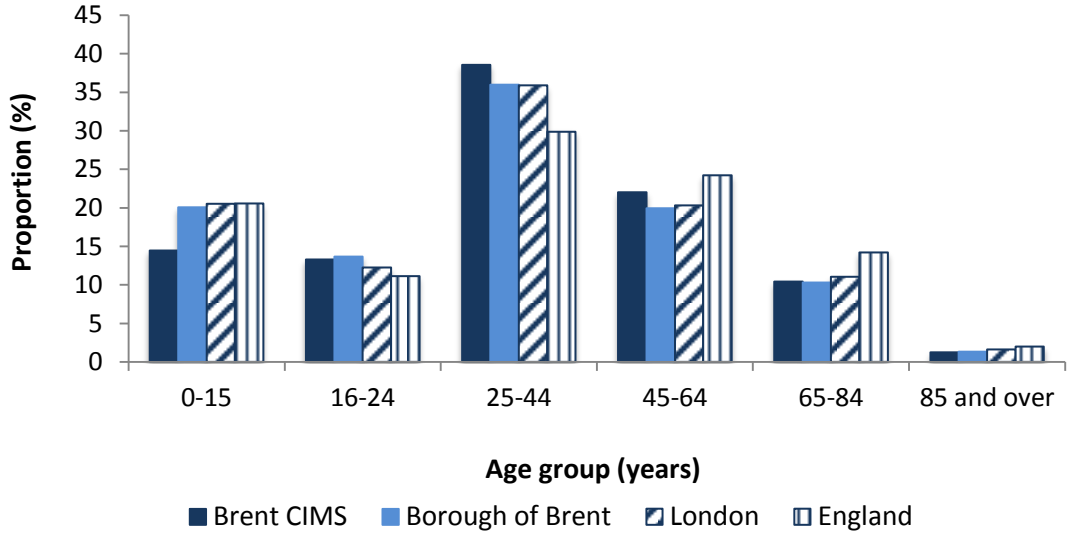
*Missing ethnicity data for 44,378 patients.
†Not otherwise specified.

Patients of white ethnicity tended to be older than patients of other ethnicities, with an average age of 44 years (n=9,001/33,649; range from under 1 year to 104 years). In contrast, patients of Asian ethnicity had an average age of 37 years (n=17,111/33,649; range from under 1 year to 102 years). Patients of "Other" ethnicities tended to be youngest out of all patients with known ethnicity, with an average age of 36 years (n=1,664/33,649; range from under 1 year to 96 years).

5.4.2 Data representativeness

The representativeness of CIMS data to the Brent population was assessed using data from the 2001 Census for the Borough of Brent, London and England on **age**, **sex** and **ethnicity**. For the first comparison variable of age, compared to the rest of England, Brent has a relatively young population with 33.3% of the Borough's residents being aged 24 years or under (n=87,749).[281] In the study sample, 27.8% of patients were in the same age group (n=21,660) (Figure 5.2). There was a greater proportion of people aged between 25 and 64 years in the study sample (60.6%; n=47,266) compared to the official estimates for Brent (55.2%; n=145,478).[281] In terms of the older population, there was little difference in the proportion of people aged 65 years and older recorded in the 2001 Census and the CIMS dataset (11.5%; n=30,237 compared to 11.7%; n=9,101, respectively).[281]

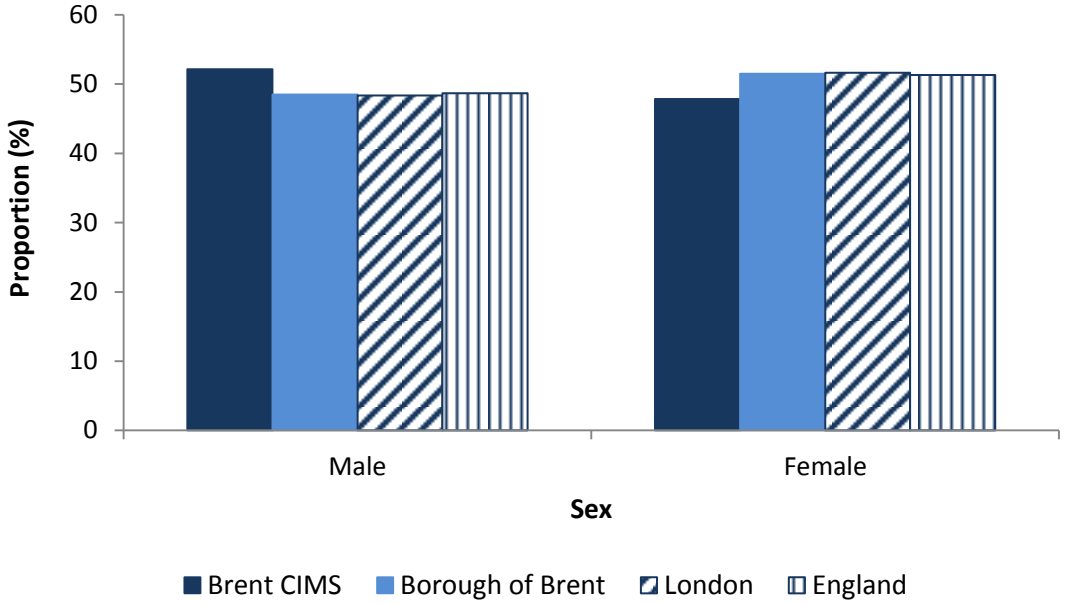
Figure 5.2 Representativeness of sample by age group, compared to the Borough of Brent, London and England



Source: Office of National Statistics.[281]

On the second of the three comparison markers (Figure 5.3), compared to the Borough of Brent (48.5%), London (48.4%) and England (48.7%), there was a greater proportion of male patients in the Brent CIMS dataset (52.1%; n=78,027).[281]

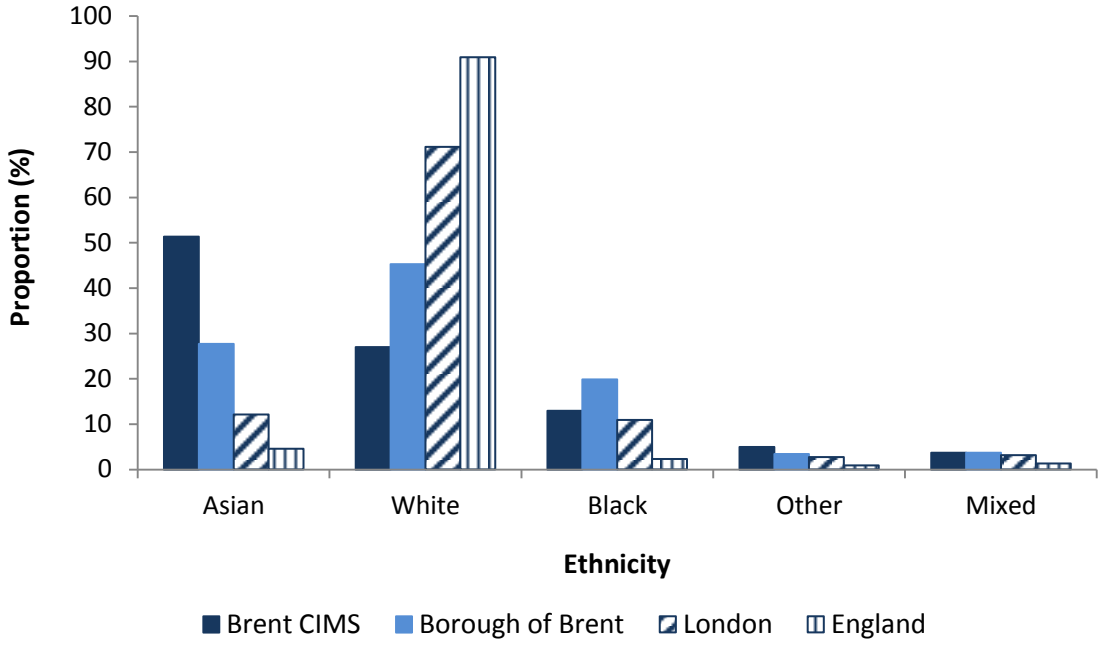
Figure 5.3 Representativeness of sample by sex, compared to the Borough of Brent, London and England



Source: Office of National Statistics.[281]

For the final comparison by ethnicity (Figure 5.4), compared to the Borough of Brent (27.7%), London (12.1%) and England (4.6%), the proportion of Asian patients in the Brent CIMS dataset was greatest (51.3%; n=33,325).[281] Although less of a marked increase, the proportion of patients classed as being of "Other" ethnicity was also greater in the CIMS dataset (5%; n=33,325) compared to the other datasets. Conversely as depicted in Figure 5.4, the proportion of patients of white ethnicity in the CIMS is considerably smaller (27.0%; n=33,325) than in the Borough of Brent (45.3%), London (71.2%) and England (90.9%).[281] The proportion of patients of black ethnicity in the CIMS dataset (12.9%; n=33,325) was smaller than recorded for the Borough of Brent (19.9%), but larger than for London (10.9%) and England (2.3%).[281]

Figure 5.4 Representativeness of sample by ethnicity, compared to the Borough of Brent, London and England*



Source: Office of National Statistics.[281]

5.4.3 Complications of care

Overall, a rate of 1.67 AEs per 1,000 consultations was recorded among patients in Brent (n=1,118,072; 95% CI 1.59-1.74). There was wide variation in the number of cases of AEs at the 23 GP practices with recorded AEs, ranging from 0.28 AEs per 1,000 consultations to 2.74 AEs per 1,000 consultations.

The rate of recorded complications related to surgery in the CIMS dataset was 0.44 cases of complications per 1,000 consultations (n=1,118,072; 95% CI 0.41-0.47). Female patients experienced more complications (59.9%), with 38.3% of complications recorded in women aged between 25 years and 64 years (n=188/491). Patients aged 15 years or less (3.26%) and those aged 85 years or older (4.28%) were least likely to have a surgical complication.

*Data for the "Not otherwise specified" (NOS) ethnicity category were not available in the comparison datasets and is therefore not reported in Figure 5.4.

In 77.0% of surgical complications, the cause was "Other procedure complications not elsewhere classified" (n=378/491). Nearly two thirds of complications in this category occurred in female patients (n=235/378; 62.2%). Four out of five of the most common surgical complications fell into the "Other procedure complications not elsewhere classified" category (Table 5.2). The exception was mechanical complications, which falls into the category of "Complications of certain procedures". Where ethnicity was indicated, complications were most frequently recorded in patients of Asian (n=107/262) and white (n=101/262) ethnicities.

Table 5.2 The five most frequently recorded surgical complications (rate per 1,000 consultations), n=409/491

Type of surgical complication	Cases, n	Rate
Postoperative infection (includes wound infections)	285	0.25
Other procedure complication NEC*	48	0.04
Mechanical complications	43	0.04
Operation wound disruption	19	0.02
Peri-operative haemorrhage or haematoma	14	0.01

5.4.4 Medical accidents

Few accidents occurring during medical or surgical care were recorded in the CIMS dataset. There was a rate of 0.05 medical accidents per 1,000 consultations (n=1,118,072; 95% CI 0.04-0.06). A greater proportion of medical accidents were recorded in male patients (61.8%; n=34/55). By age group, more medical accidents occurred in patients aged between 45 years and 64 years (30.9%; n=17/55). The most common type of recorded medical accident was accidental cut, puncture, perforation or haemorrhage during medical care (n=49/55). In 60.7% of cases, the patient was of Asian ethnicity (n=17/28).

5.4.5 Adverse drug events

The rate of adverse drug events (ADEs) was 1.18 per 1,000 consultations (n=1,118,072; 95% CI 1.11-1.24). Among the 23 practices where patients had recorded ADEs, there were 2 or

*Not elsewhere classified. Includes surgical emphysema, failed intubation and postoperative pain.

fewer cases of ADEs per 1,000 consultations. The rate ranged between 0.10 ADEs per 1,000 consultations to 2.32 ADEs per 1,000 consultations in the 23 practices.

Looking at events corresponding to Read Chapter T ("Causes of injury and poisoning") codes, the rate of adverse drug reactions (ADRs) was 0.76 per 1,000 consultations (n=1,118,072; 95% CI 0.74-0.79). The results in Table 5.3 show that over half of the drug-related events recorded with Read Chapter T codes occurred in female patients (57.2%; n=487/851). In contrast, the number of drug-related events recorded with Read Chapter U ("External causes of morbidity and mortality") codes was similar among male and female patients (52.1%; n=243/467). For events recorded with codes from either Read Chapter, the most events were recorded in patients aged between 65 and 84 years (Table 5.3). I will return to the results by Read Chapter U in a later sub-section of this chapter, section 5.4.6.

Table 5.3 Cases of adverse drug events by age and sex, n=1,317

Characteristic		Read Chapter T		Read Chapter U		Brent pop. size[280,281]
		n	(%)	n	(%)	
Sex	Female	487	57.2	223	47.9	135,658
	Male	364	42.8	243	52.1	127,806
Age group (years)	0-15	55	6.5	12	2.6	52,169
	16-24	42	4.9	<5	-	35,580
	25-44	167	19.6	48	10.3	93,601
	45-64	236	27.7	168	36.1	51,877
	65-84	315	37.0	220	47.2	26,828
	≥85	36	4.2	15	3.2	3,409

5.4.5.1 Events by drug categories

Data on ADRs corresponding to Read Chapter T codes were mapped to categories from the British National Formulary (BNF). These categories are based on the systems of the body and elements of medical care (Table 5.4).[285] No drug name was available in 106 cases of adverse reactions. Drugs used to treat infections were most frequently associated with ADRs and include those from the penicillin family, which accounted for 22.4% of recorded ADRs (n=191/851). Systemic antibiotics, drugs primarily affecting the autonomic nervous

system and those that affect the cardiovascular system were among the medications most commonly recorded as causing adverse reactions (Table 5.4).

Table 5.4 Adverse drug reactions by British National Formulary body system category (rate per 1,000 consultations), n=851

Body system category	Cases, n	Rate
Infections	311	0.28
Cardiovascular system	226	0.20
Central nervous system	124	0.11
General (including ADRs NOS and diagnostic agents/kits)*	108	0.10
Immunological products and vaccines	40	0.04
Other†	30	0.01
Endocrine system	12	0.03

5.4.5.2 Adverse drug events by age

In patients aged under 16 years, antibiotics were the predominant cause of ADRs (n=38/55). Amoxicillin (n=17) and penicillin (n=13) were the two most frequently identified types of antibiotics. Vaccines were also frequently associated with ADRs (n=12/55). Likewise, antibiotics were associated with 66.7% of drug-related events in young adults aged between 16 and 24 years (n=28/42). Antibiotics were also a common cause of recorded ADRs in patients aged between 25 and 44 years, accounting for 47.9% of adverse reactions (n=80/167). In 11.4% of ADRs occurring in patients in this age group, no named drug was associated with the event (n=19/167).

Among adults aged between 45 and 64 years, 30.9% of ADRs were caused by antibiotics (n=73/236), while statins (n=27) and beta-blockers (n=25) also frequently caused adverse effects. Of all drug types, patients aged 65 to 84 years were most likely to experience adverse effects from antibiotics (n=91/315). In another 14.9% of cases, reactions not otherwise specified were responsible (n=47/315), with statins contributing to a further 12.4% of ADRs in this age group. In older patients aged 85 years and older, 22.2% of adverse

*NOS –Not otherwise specified.
†Includes anaesthesia; eye, ear, nose, and oropharynx, and skin; gastro-intestinal system; malignant disease and immunosuppression; musculoskeletal and joint diseases; nutrition and blood; obstetrics, gynaecology, and urinary-tract disorders; respiratory system.

reactions were attributed to antibiotics (n=8/36) and the same number of events was caused by drugs without a specified name.

5.4.6 External causes of morbidity and mortality

Chapter U was introduced to the 5-byte (version 2) Read codes following the addition of "Chapter XX External causes of morbidity" to the ICD-10.[286,287] The new Chapter U is an updated version of Read Chapter T – "Causes of injury and poisoning".[287] There were 467 drug or associated substance-related complications of care recorded with Chapter U codes (Table 5.5). The fewer events identified by codes from this newer Read chapter compared to Chapter T codes may be due to its relatively recent addition to the Read coding system.

Table 5.5 The five most frequently recorded types of drug associated with complications of care mapped to Read Chapter U codes (rate per 1,000 consultations), n=400/467

Type of drug	Cases, n	Rate
Angiotensin-converting-enzyme (ACE) inhibitors	238	0.21
Angiotensin II receptor antagonists (ARBs)	110	0.10
Antibiotics	25	0.02
Statins	19	0.02
Calcium-channel blockers	16	0.01

Nearly half of ADR cases identified by Read Chapter U codes occurred in patients aged between 65 and 84 years (47.2%; n=467). Few cases were recorded in patients aged under 25 years (n=15). Out of all the events identified with Chapter U codes, one case was not a drug-related event but involved ophthalmic diagnostic and monitoring devices. Overall, the most common type of drug associated with recorded adverse effects was ACE inhibitors, accounting for 51.0% of all drug-related events with Read Chapter U codes (n=467) (Table 5.5). Where ethnicity was recorded, 45.7% of complications related to drugs or biological substances occurred in patients of Asian ethnicity (n=370).

5.4.7 Other incidents of patient harm

There was a rate of 0.35 "other" (not otherwise stated) AEs per 1,000 consultations (n=1,118,072; 95% CI 0.32-0.38). These events were more common among female patients (61.7%; n=243/394) and nearly half of all recorded cases were in patients aged between 25

and 44 years (47.7%; n=394). There were 221 cases of suicide and intentional self-harm in the CIMS dataset and 162 cases of self-poisoning. Less than 3% of "other AEs" were coded as other types of external causes of morbidity and mortality, including 9 cases relating to injury by MRI contrast media.

5.5 Discussion

This study examined AEs recorded using Read codes in English general practice, from a small dataset from a PCT. There were low rates of undesirable events, with adverse effects of drugs being the most common type of recorded incident. Other types of AEs that were detected included medical and surgical complications and acts of self-harm and suicidal intent. Some of these events are likely to indicate episodes of patient harm that occurred in secondary care but were either not detected in that care setting or did not manifest before discharge from hospital.[155]

5.5.1 Evidence on drug-related events

A relatively high number of drug-related events were recorded in patients aged 65 years and older. Other studies conducted in the UK and the US have found similar results.[173,179] My analyses indicate that drugs with long established clinical usage often cause adverse effects, echoing the findings Pirmohamed et al and Budnitz et al.[176,179] Furthermore, I found that 8.96% of patient records where an ADR was noted did not contain information about the drug category or drug name.

5.5.2 Study strengths and limitations

Studies on AEs in English general practice have typically focused on measuring drug-related morbidity and mortality. In this study, I attempted to capture a broader sense of potential patient harm, regardless of whether the incident was drug-related or not. This inclusive approach was reflected in the selection of AEs based on the presence of a corresponding Read code for an iatrogenic event.

These analyses were of a preliminary and descriptive nature, using diagnoses mapped to only three chapters of the Read system. Although there is an extensive range of clinical practice terms in the system, the Read codes are arranged within a rigid coding hierarchy.

Consequently, it is possible that events without a designated AE code but nonetheless eligible for inclusion in this study may have been missed. As outlined in Chapter 3, there was limited clinical detail contained in the dataset from NHS Brent. One example of its restrictive nature was the lack of information about patients' treatments and their diseases and conditions. Due to this, it was not possible to adjust for potential confounders such as comorbidities, disease severity and polypharmacy, nor evaluate the preventability of recorded events.

5.5.3 Implications for further analyses

The analyses of data from one computer system at one PCT have highlighted elements of data management that are crucial for successful monitoring of patient harm. No single method of safety measurement is adequate.[7,173,288,289] The results of this study suggest that routinely collected data from general practice may be suitable to flag up unusual patterns in patient outcomes. Given the low number of events detected at the local level, attention should also be turned into using data collected nationally on a routine basis to develop safety surveillance tools for general practice.

5.6 Conclusions

In this chapter, I have described the types of AEs recorded in routinely collected, electronic general practice data. These events include incidents following procedures or surgeries and adverse drug reactions. The quality of data within general practice information systems is relatively good compared to other care settings. This is largely due to collection of these data for quality monitoring and performance-based financial incentives. Even so, early detection and screening systems for patient harm that rely solely on these data can only identify potential medical errors and AEs. In order to improve the clinical value of AE measurement in general practice and elsewhere in primary care, multiple data sources should be used.

Chapter 6: Adverse events recorded in national data

6.1 Chapter overview

In Chapter 5, I explored the epidemiology of adverse events recorded at the local level. This chapter quantifies and describes the nature and extent of adverse events in general practice at the national level, using GPRD data. Analyses extend to a comparison of local and national estimated rates of adverse events. The chapter ends with a discussion on the suitability of GPRD data for this type of research and the comorbidity measures applied.

6.2 Rationale

When considering the epidemiology of recorded adverse events (AEs) and the potential for routinely collected data to be used in patient safety surveillance, it is logical to firstly consider the role of existing data. The use of available data sources for quality measurement may be preferable to develop new datasets in times of financial restraints.[165] As there are designated diagnosis codes for AEs in secondary care (ICD 10 codes) and primary care (Read codes), it would be prudent to explore how well these codes are populated and to describe the AEs that they correspond to.

Studies often use data from one care setting and from few sources, which may under-estimate the true rate of patient harm.[173,290,291] A review of the literature (Chapter 2) found that research on AEs was focused on drug-related events, relied on data routinely collected in hospitals and was under-representative of primary care in England. The range of patient outcome measured in these studies is limited, typically focusing on admissions (including length of hospital stay and high dependency care), readmissions and mortality. It is therefore important to incorporate data from multiple sources and care settings to form a more complete understanding of AEs occurring in non-acute care.

6.2.1 Definition of outcomes

An operational definition of "adverse event" was provided in the previous chapter (Chapter 5 section 5.2.2). Emergency admission was defined in Chapter 3 section 3.9.3 and deaths were described in Chapter 3 section 3.7.11.

6.2.2 Aims and objectives

From the published literature and analyses presented in Chapter 5, one might expect that certain patient groups experience more AEs, including older patients, ethnic minority groups and patients with more complex care needs.[91,292,293] However, the relationships between other characteristics, such as the level of continuity of care received by a patient, and patient harm are less established.[235,294]

6.2.2.1 Aims of analysis

With gaps in knowledge about risk factors for AEs in general practice, this study was intended to quantify the rate of AEs recorded in the English general practice care setting. The second aim was to identify predictors for patient harm recorded in routinely collected electronic data. The third aim was to explore the outcomes of patients who experience recorded safety incidents.

6.2.2.2 Objectives of analysis

The following objectives were set to meet the three aims of this study:

1. Measure the incidence of adverse events (AEs) in the English general practice population, identified by diagnosis codes designated for complications of care in the Read classification system (Read chapters S, T and U).
2. Identify patient risk factors associated with recorded AEs in the English general practice population, identified by Read codes for complications of care.
3. Explore the health service use of patients with recorded adverse events in the English general practice population, identified by Read codes for complications of care.

4. Explore the outcomes (emergency admissions and death) of patients with recorded AEs in the English general practice population, identified by Read codes for complications of care.

6.3 Methods

6.3.1 Study design

This study was cross-sectional in design. The analyses were hypothesis generating, intended to assess the suitability of routinely collected data for measuring AEs in general practice.

6.3.2 Data extraction

The method of extracting records of interest from the GPRD dataset has been stated in Chapter 4 and the same process as set out in Chapter 5 was used to identify AEs. In short, diagnosis codes were extracted from three Read Code chapters that describe external causes of injury and poisoning and include diagnosis codes for complications of medical and surgical care. The Read chapters were:

- "Injury and Poisoning" (Chapter S);
- "Causes of injury and poisoning" (Chapter T); and
- "External causes of morbidity and mortality" (Chapter U).[284]

6.3.3 Cleaning of adverse event records

Exclusion criteria were implemented to improve the accuracy of estimating the incidence of AEs. These criteria are explained in the following three sub-sections.

6.3.3.1 Ordering by first consultation

Recorded AEs were only study-valid if they occurred after the first consultation of the patient's first registration period with the current GP practice. This criterion was also applied to patient outcomes of emergency admission and death (outcomes were valid only if they occurred after the first consultation). This rule reduced the likelihood of capturing events and outcomes attributable to care other than at the current GP practice.

6.3.3.2 Multiple code entries

Only the first occurrence of a Read code for an AE per consultation record was included in the study. Subsequent recordings of identical read codes during the same consultation were excluded as these codes may be due to data entry errors, and would not contribute new information to the study. Where there were multiple different Read codes for complications of care for a single consultation, further investigation was carried out to determine the validity of these codes. Read terms and classifications were used to guide this process. In all detected cases, multiple Read codes were associated with the same AE and so these records were processed as one AE per consultation.

The date associated with the AE (event date) was the same as the consultation date in the majority of cases. A minority of events occurred before the date of the consultation associated with the AE. For these cases, data cleaning excluded the following events:

- Records of allergy/intolerance but without an associated consultation date.
- Records of allergy/intolerance and linked to a previous consultation that occurred more than one year ago but without supporting AE codes.
- Linkage to a previous consultation that occurred up to one year ago, not recorded in the "medical history" section and not a surgical AE.

6.3.3.3 Lag time

When looking at repeated events, a patient's risk period can be defined as either discrete (new event cannot occur until previous event has ended) or continuous. The latter type of risk period may be more realistic, in that patients can experience multiple AEs during the same time period. No guidance was available in the literature on defining a suitable "washout" period for measuring AEs in the non-acute setting. Therefore, to distinguish between new events and existing recorded events for an individual patient, an arbitrary time interval was applied whereby events occurring less than 30 days apart were considered to be related. In this scenario, only the index event was eligible for inclusion in analyses.

6.3.4 Statistical method

Related to lag time, valid repeated (multiple) events at patient and practice levels will influence the statistical approach used. To take into account the potential clustering of AEs (outcome of interest) by patient, a continuous version of the outcome variable was used in the form of the rate of events (per person). Clustering of patients at practices was managed by applying the Generalized Estimating Equation (GEE) method. As explained in Chapter 4 section 4.5, the log transformation of patients' follow-up time was included as an offset term in the regression models for predicting the risks of having an AE and emergency admission. Further details of GEE and the statistics for this chapter are provided in Chapter 4.

6.4 Results

In this section, I present the estimated rates of AEs and then crude and adjusted results by type of outcome (AEs, admissions and then death). The patterns of service use in patients who had at least one AE are also described.

6.4.1 Incidence of adverse events

There were 2,048 AEs (1,817 AE codes) recorded in 1,774 patients at 387 GP practices between 1999 and 2008. Thus, 2.37% of the study population experienced at least one AE during the study period (n=74,763). Table 6.1 shows that the most AEs experienced by a patient during the study period was 9 events (n=1 patient). Less than an eighth of patients who had an AE experienced more than one AE (12.3%; n=218/1,774). In all except 30 cases of AEs, the event was recorded on the same day as the consultation.

Table 6.1 Number of adverse events per patient, n=74,763

Adverse events, n	Patients, n	(%)
0	72989	(97.6)
1	1556	(2.08)
2	184	(0.25)
3	26	(0.03)
4	1	(<0.01)
5	2	(<0.01)
6	4	(0.01)
9	1	(<0.01)

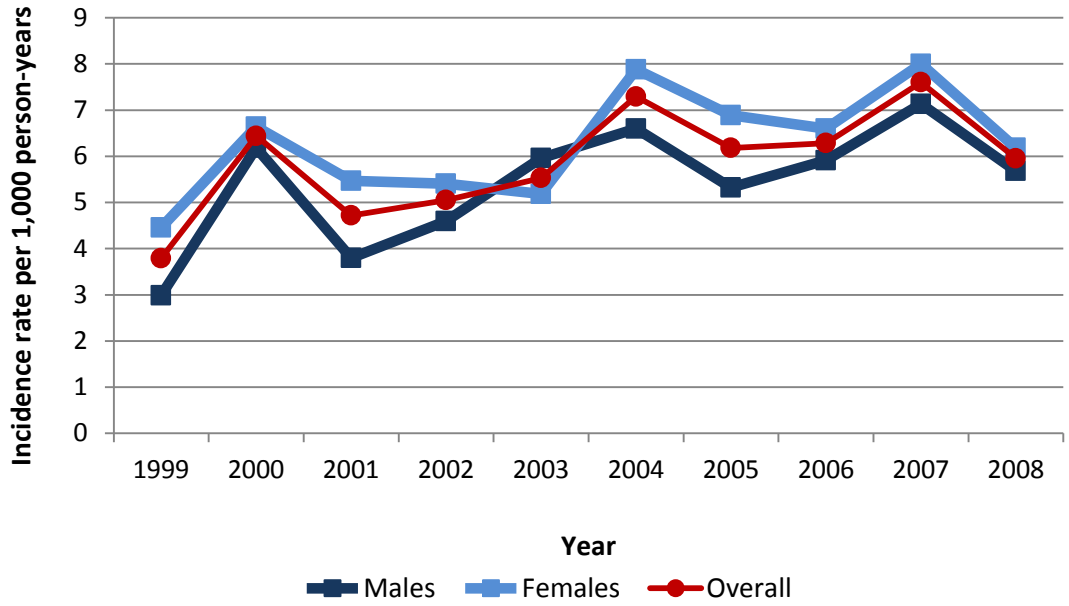
Patients were followed up for 341,261 person-years. The average follow-up time for all patients in the study sample was 7 (SD 3.51) years, compared to 5 (SD 2.87) years for patients who had at least one AE, p<0.001 (Table 6.2).

Table 6.2 Follow-up time of patients, n=74,763

Follow-up time (years)	Patients, n			RRs (95% CI)	P-value
	All	≥1 adverse event	(%)		
<1	5628	196	(3.48)	3.94 (3.24-4.78)	<.001
1-3	16227	542	(3.34)	3.27 (2.81-3.81)	<.001
4-6	12186	550	(4.51)	4.21 (3.66-4.85)	<.001
7-10	40722	486	(1.19)	1	

The overall incidence was 6.0 AEs per 1,000 person-years (95% CI 5.74-6.27). The rate of AEs increased over the study period (Figure 6.1). The lowest incidence of AEs was in the first year of the study, 1999, when there were 3.79 events per 1,000 person-years (95% CI 3.05-4.66). The highest rate was in 2007, when there were 7.60 events per 1,000 person-years (95% CI 6.77-8.51).

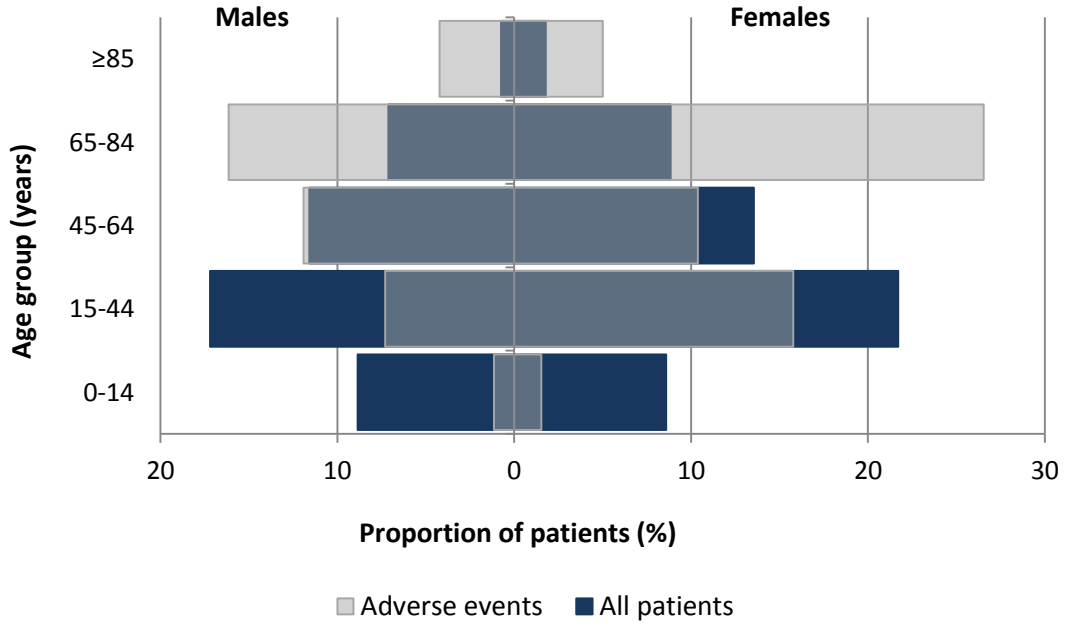
Figure 6.1 Incidence rate of adverse events by sex and year (per 1,000 person-years)



Over the ten years of the study, the rate of AEs was lower in male patients who had an overall rate of 5.54 events per 1,000 person-years (n=854/2,048; 95% CI 5.18-5.93) compared to 6.38 events per 1,000 person-years in female patients (n=1194/2,048; 95% CI 6.02-6.75). In male patients, the incidence ranged from 2.98 events per 1,000 person-years (95% CI 2.04-4.21) in 1999 to 7.13 events per 1,000 person-years (95% CI 5.96-8.47) in 2007. In female patients, the lowest rate was 4.46 events per 1,000 person-years (95% CI 3.39-5.76) in 1999 while the highest rate was 8.0 events per 1,000 person-years (95% CI 6.85-9.28) in 2007.

The demography of patients who had at least one AE was compared with the overall population by age and sex, using data for 2004 as a proxy for the middle year of the study. There were proportionally fewer younger patients who had AEs compared to their representation in the overall population, especially for patients aged less than 15 years at entry to the study (Figure 6.2). The opposite was true for the oldest patients, who were over-represented in the proportion of patients who experienced at least one AE. Over a quarter of AEs (26.5%) occurred in female adults aged between 65 and 84 years (n=3,341/37,816). The fewest events were recorded in female children aged from under one year to 14 years (1.15%; n=3,250/37,816).

Figure 6.2 Age and sex of all patients compared to patients with at least one adverse event, 2004



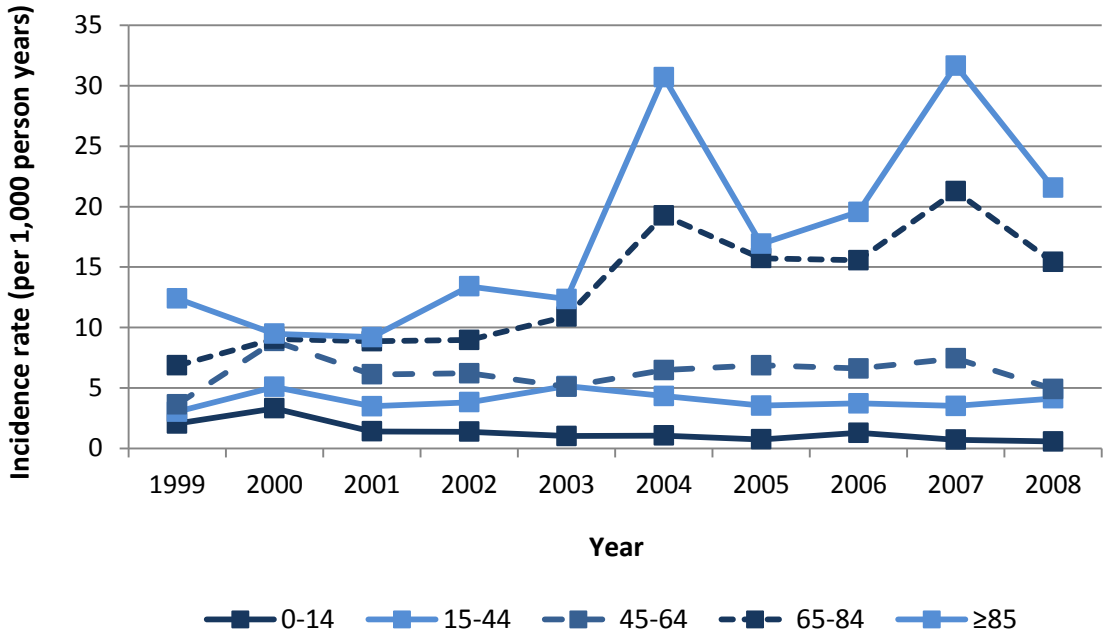
Overall, the highest rate of events occurred in the oldest patients (aged 85 years and over), who experienced 18.8 events per 1,000 person-years (95% CI 16.0-21.9) (Table 6.3).

Table 6.3 Incidence rate of adverse events by age group (rate per 1,000 person-years), n=2,048 events

Age group (years)	Adverse events, n	Person time (years)	Rate (95% CI)
0-14	76	60277	1.26 (0.99-1.58)
15-44	526	132270	3.98 (3.64-4.33)
45-64	543	86666	6.27 (5.75-6.82)
65-84	742	53474	13.9 (12.9-14.9)
≥85	161	8575	18.8 (16.0-21.9)

There were notable fluctuations in the rate of AEs by age groups over the study period. Marked variation in the incidence rate was seen in older patients, especially in adults aged 85 years or older in whom the rate of events ranged from 9.21 events per 1,000 person-years (95% CI 3.70-19.0) in 2001 to 31.7 events per 1,000 person-years (95% CI 21.9-44.3) in 2007. A rise in new cases of recorded AEs was also seen in patients aged between 65 and 84 years over the ten years studied. In patients of this age group, the lowest rate was 6.86 events per 1,000 person-years (95% CI 4.40-10.2) in 1999 and increased to 21.3 events per 1,000 person-years (95% CI 17.8-25.2) in 2007 (Figure 6.3).

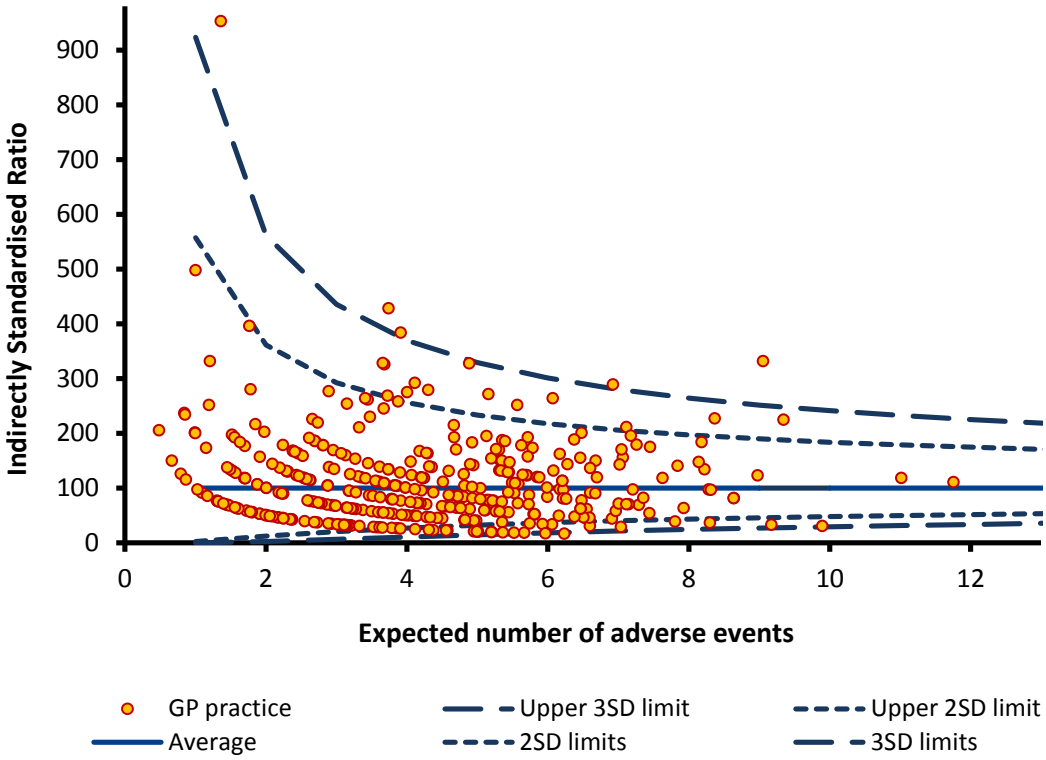
Figure 6.3 Incidence rate of adverse events by age group and year (per 1,000 person-years)



6.4.2 Incidence rate by practice

On average, there were 164 (SD 84.3) patients per practice included in the study, ranging from 19 to 595 patients per practice (n=457 practices). The majority of practices (84.9%) had registered patients with at least one recorded AE during the study period. On average, these practices had 4 (SD 3.94) patients who had one or more events, ranging from 1 to 30 patients per practice (n=388 practices). Exploring the rate of AEs by practice, five practices were above the 99.8% control limit indicating that these practices had more cases of AEs than would be expected given the total number of registered patients at those practices, after adjustment for age and sex of the practice population. There were 61 practices that fell below the 99.8% limit, indicating that these practices had fewer cases of AEs than would be expected based on the total number of patients at those practices (Figure 6.4).

Figure 6.4 Incidence rate of adverse events, indirectly standardised by age group and sex, 1999-2008, n=387/457 practices



6.4.3 Risk factors for adverse events

6.4.3.1 Crude associations with adverse events

In crude calculations, all variables were significant at the 95% level except for deprivation, mild liver disease and consultation within 30 days after hospital discharge (Table 6.4). There were no patients in the sample with recorded Auto-Immune Deficiency Disease (AIDs) so this variable was excluded from further analyses and will not be reported hereafter. P-values for the calculations in this section are $p<0.0001$ unless reported otherwise.

Patients who were most at risk of having an AE were those aged 65 to 84 years old when they entered the study (RR 11.9, 95% CI 9.90-14.3), female (RR 1.31, 95% CI 1.20-1.43), married (RR 3.06, 95% CI 2.34-3.99), registered at practices in the North West (RR 1.46, 95% CI 1.05-2.04; p=0.026) or the South East Coast regions (RR 1.45, 95% CI 1.04-2.04; p=0.030). Patients who were registered at their practice for the longest periods of time (RR 1.36, 95% CI 1.18-1.57), with the highest continuity of care scores (RR 7.27, 95% CI 4.66-11.3) or a high number of consultations at the GP practice, by telephone or home visit (RR 7.79, 95% CI 6.39-9.49) were also at greater risk of having an AE. Patients of unknown ethnicity were statistically least at risk of having an AE compared to patients of known ethnicity (RR 0.56, 95% CI 0.34-0.90; p=0.016).

An elevated comorbidity status (measured by the Charlson Index score) also raised the risk of having an AE, albeit a small increase (RR 1.05, 95% CI 1.05-1.06). High resource users, defined by the Resource Utilization Band (RUB) score, were most at risk of an AE (RR 54.1, 95% CI 17.4-168). Further results by comorbidities can be found in the Appendices (Table A.10).

Patients who had a consultation within 30 days after a referral request (RR 1.98, 95% CI 1.60-2.45) or a consultation within 30 days of hospital discharge (RR 4.23, 95% CI 1.06-16.9; p=0.041) were at greater risk of an AE. There was a positive linear relationship between the number of admissions that patients had during the study period and their risk of having an AE; patients who had 5 or more admissions were most at risk of an AE (RR 5.17, 95% CI 4.61-5.79).

Table 6.4 Risk factors for reported adverse events, crude results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic	Patients, n			RR (95% CI)	P-value
	All	≥1 adverse event	(%)		
Age group at study start (years)					<0.0001
0-14	20952	131	(0.63)	1	
15-44	32176	542	(1.68)	2.58 (2.14-3.11)	<0.0001
45-64	13582	547	(4.03)	5.36 (4.45-6.45)	<0.0001
65-84	7149	525	(7.34)	11.9 (9.90-14.3)	<0.0001
≥85	904	29	(3.21)	7.95 (5.50-11.5)	<0.0001
Sex					<0.0001
Male	36089	743	(2.06)	1	
Female	38674	1031	(2.67)	1.31 (1.20-1.43)	<0.0001
Ethnicity					<0.0001
Asian	585	15	(2.56)	1	
Black	441	15	(3.40)	1.26 (0.63-2.49)	0.514
Mixed	148	4	(2.70)	1.34 (0.49-3.63)	0.567
White	15909	688	(4.32)	1.26 (0.78-2.03)	0.350
Other	355	8	(2.25)	0.69 (0.30-1.59)	0.380
Unknown	57325	1044	(1.82)	0.56 (0.34-0.90)	0.016
Marital status					<0.0001
Single	5019	61	(1.22)	1	
Married	7082	282	(3.98)	3.06 (2.34-3.99)	<0.0001
Other status	1359	50	(3.68)	3.7 (2.62-5.23)	<0.0001
Unknown	61303	1381	(2.25)	1.94 (1.51-2.48)	<0.0001
Deprivation					0.174
Least deprived	41787	933	(2.23)	1	
Quintiles 2,3,4	19482	502	(2.58)	1.09 (0.99-1.21)	0.083
Most deprived	6954	178	(2.56)	1.09 (0.94-1.26)	0.278
Unknown	6540	161	(2.46)	1.14 (0.98-1.33)	0.099
Practice region					<0.0001
East Midlands	1491	30	(2.01)	1	
East of England	10765	288	(2.68)	1.28 (0.92-1.79)	0.139
London	4215	114	(2.70)	1.35 (0.95-1.92)	0.098
North East	3526	98	(2.78)	1.27 (0.89-1.83)	0.192
North West	8079	248	(3.07)	1.46 (1.05-2.04)	0.026
South Central	9122	212	(2.32)	1.08 (0.77-1.52)	0.655
South East Coast	7493	219	(2.92)	1.45 (1.04-2.04)	0.030
South West	9830	200	(2.03)	1.04 (0.74-1.46)	0.817
West Midlands	11988	177	(1.48)	0.82 (0.58-1.15)	0.243
Yorkshire & The Humber	8254	188	(2.28)	1.16 (0.82-1.62)	0.405
Length at practice (years)					<0.0001
Low	24925	209	(0.84)	1	
Moderate	24918	565	(2.27)	0.83 (0.72-0.97)	0.017
High	24920	1000	(4.01)	1.36 (1.18-1.57)	<0.0001
Continuity of care					<0.0001
Low	9572	19	(0.20)	1	
Moderate	21711	522	(2.40)	5.67 (3.63-8.86)	<0.0001
High	21678	687	(3.17)	7.27 (4.66-11.3)	<0.0001

Not valid	21802	546	(2.50)	6.6 (4.23-10.3)	<0.0001
Number of all consultations					<0.0001
Low	25051	51	(0.20)	1	
Moderate	24944	318	(1.27)	4.01 (2.99-5.38)	<0.0001
High	24768	1405	(5.67)	15.8 (12.0-20.0)	<0.0001
Consultation*					<0.0001
No	4465	12	(0.27)	1	
Yes	70298	1762	(2.51)	4.53 (2.63-7.81)	<0.0001
Number of consultations†					<0.0001
Low	25709	98	(0.38)	1	
Moderate	24064	316	(1.31)	2.1 (1.69-2.62)	<0.0001
High	24990	1360	(5.44)	7.79 (6.39-9.49)	<0.0001
Referral					0.011
No	69907	1595	(2.28)	1	
Yes	4856	179	(3.69)	1.21 (1.05-1.40)	0.009
Number of referrals					0.013
0	69907	1595	(2.28)	1	
1	2942	103	(3.50)	1.11 (0.91-1.34)	0.305
≥2	1914	76	(3.97)	1.37 (1.11-1.68)	0.003
Referral ≤30 days before next consultation					<0.0001
No	73391	1697	(2.31)	1	
Yes	1372	77	(5.61)	1.98 (1.60-2.45)	<0.0001
Admission					<0.0001
No	58153	935	(1.61)	1	
Yes	16610	839	(5.05)	2.49 (2.28-2.71)	<0.0001
Number of admissions					<0.0001
0	58153	935	(1.61)	1	
1	6566	160	(2.44)	1.22 (1.04-1.43)	0.014
2	3462	139	(4.02)	1.93 (1.63-2.28)	<0.0001
3-4	3380	196	(5.80)	2.67 (2.31-3.08)	<0.0001
≥5	3202	344	(10.7)	5.17 (4.61-5.79)	<0.0001
Admission ≤30 days before next consultation					0.099
No	74750	1772	(2.37)	1	
Yes	13	2	(15.4)	4.23 (1.06-16.9)	0.041
Charlson Index score, mean (SD)	0.59 (2.45)	2.04 (4.73)	-	1.05 (1.05-1.06)	<0.0001
Resource utilization band (RUB)					<0.0001
Healthy	6762	2	(0.03)	1	
Low to moderate	42428	329	(0.78)	8.39 (2.69-26.1)	<0.0001
High to very high	25373	1443	(5.69)	54.1 (17.4-168)	<0.0001

*At GP practice, telephone or home visit.
†At GP practice, telephone or home visit.

6.4.3.2 Model selection for adjusted analyses

Before presenting the results of adjusted regression analyses, it would be helpful to explain the process of selecting regression models. The choice between different modelling methods is further explained in section 6.3.4 and Chapter 4.

The mean of the response variable (number of AEs) was approximately equal to the variance (0.027 compared to 0.037, respectively). Assuming that the data fit a Poisson distribution, the variance to mean ratio did not indicate the presence of over-dispersion (Chapter 4 section 4.8.2 for definition). However, there were excess zero counts of the response variable (Chapter 4 section 4.8.3), as 97.6% of patients in the sample did not have an AE during the study period. To begin exploring the modelling options, adjusted regression models were fitted using NB regression but this approach produced models of poor fit (Chapter 4 section 4.6.3 for details of goodness-of-fit assessments). Therefore, further models were produced using Poisson with GEE and ZIP regression. As the data were not over-dispersed (which can occur when there are excess zero counts) and in favour of adjusting for clustering of patients at practices which is not possible by ZIP regression in PROC GENMOD, Poisson regression with GEE was used in final adjusted modelling. The limitations of this choice are addressed in the Discussion (section 6.5.2) and Chapter 4.

Eight models were developed to assess the contribution of the different comorbidity measures and to prevent collinearity (linear associations between these variables). The model containing disease flags based on disease categories used to derive Charlson Index scores performed best, producing a QIC score of 11625.7 (Table 6.5). Although this QIC score is high, indicating that the model is a sub-optimal fit for the data, the score is much lower than for the null model (QIC score of 91087.4).

Table 6.5 Fit of adjusted Poisson regression models for predicting risk factors for having an adverse event, using the generalized estimating equations (GEE) method

Model	Comorbidity variables	Quasi-Likelihood under the Independence model Criterion (QIC)
1	Charlson score	95118.6
2	Composite Charlson Index measure	95163.1
3	Disease flags derived from Charlson Index scoring	11625.7
4	Aggregated Disease Groups (ADGs)	93607.0
5	Collapsed Aggregated Disease Groups (CADGs)	91836.2
6	Major Expanded Diagnosis Clusters (MEDCs)	97751.3
7	Number of Expanded Diagnosis Cluster (EDC) groups	95418.5
8	Resource Utilization Band (RUB)	95218.2
9	Null model	91087.4

6.4.3.3 Adjusted associations with adverse events

After adjusting for other variables and clustering of patients at practices, there was no longer a statistically significant difference between male and female patients in their risks of having an AE (p=0.871) (Table 6.6). Ethnicity (p=0.480), marital status (p=0.228), practice region (p=0.208) and continuity of care (p=0.279) were also no longer significant predictors of having an AE.

Compared to patients of other ages, patients aged between 65 and 84 years were still most at risk of having an AE (adjusted RR of 4.55, 95% CI 3.66-5.64 compared to unadjusted RR of 11.9, 95% CI 9.90-14.3). Patients registered at practices in the North West of England were still at greater risk of having an AE compared to patients of practices in other regions (RR 1.51, 95% CI 1.00-2.27; p=0.048). Other predictors of an AE were a high number of consultations at the practice, by telephone or home visit (RR 1.49, 95% CI 1.10-2.02; p=0.010) and having five or more admissions (RR 1.99, 95% CI 1.58-2.50).

In contrast to crude results, longer length of time registered at the practice had a protective effect against having an AE (RR 0.45, 95% CI 0.38-0.52 and RR 0.44, 95% CI 0.38-0.52 for moderate and long lengths of registration time, respectively). Similarly, having at least one referral request was protective against having an AE (RR 0.56, 95% CI 0.43-0.74 for one referral and RR 0.61, 95% CI 0.44-0.84; p=0.003 for two or more referral requests). Yet

patients who had a referral request within 30 days of their next consultation remained more at risk of an AE (RR 1.87, 95% CI 1.24-2.80; p=0.003).

Comorbidities* associated with greater risk of an AE were diagnoses of diabetes without complications (RR 1.30, 95% CI 1.10-1.54; p=0.002), hemiplegia (RR 2.03, 95% CI 1.08-3.80; p=0.028), myocardial infarction (RR 1.61, 95% CI 1.20-2.15), peptic ulcer disease (RR 1.66, 95% CI 1.29-2.14), peripheral vascular disease (RR 1.63, 95% CI 1.33-2.01) and renal disease (RR 1.39, 95% CI 1.17-1.64).

*Recorded in patient's records and may have occurred at any time.

Table 6.6 Risk factors for reported adverse events, adjusted results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic		Crude		Adjusted	
		RR (95% CI)	P-value	RR (95% CI)	P-value
Age group at study start (years)			<0.0001		<0.0001
	0-14	1		1	
	15-44	2.58 (2.14-3.11)	<0.0001	2.06 (1.68-2.52)	<0.0001
	45-64	5.36 (4.45-6.45)	<0.0001	2.91 (2.37-3.57)	<0.0001
	65-84	11.9 (9.90-14.3)	<0.0001	4.55 (3.66-5.64)	<0.0001
	≥85	7.95 (5.50-11.5)	<0.0001	3.96 (2.53-6.19)	<0.0001
Sex			<0.0001		0.871
	Male	1		1	
	Female	1.31 (1.20-1.43)	<0.0001	1.01 (0.91-1.11)	0.871
Ethnicity			<0.0001		0.480
	Asian	1		1	
	Black	1.26 (0.63-2.49)	0.514	1.50 (0.74-3.04)	0.261
	Mixed	1.34 (0.49-3.63)	0.567	1.80 (0.59-5.49)	0.299
	White	1.26 (0.78-2.03)	0.350	0.90 (0.54-1.48)	0.669
	Other	0.69 (0.30-1.59)	0.380	0.83 (0.36-1.89)	0.652
	Unknown	0.56 (0.34-0.90)	0.016	0.85 (0.51-1.41)	0.524
Marital status			<0.0001		0.228
	Single	1		1	
	Married	3.06 (2.34-3.99)	<0.0001	1.22 (0.94-1.58)	0.134
	Other status	3.70 (2.62-5.23)	<0.0001	1.16 (0.79-1.69)	0.457
	Unknown	1.94 (1.51-2.48)	<0.0001	1.07 (0.84-1.35)	0.603
Practice region			<0.0001		0.208
	East Midlands	1		1	
	East of England	1.28 (0.92-1.79)	0.139	1.32 (0.85-2.04)	0.211
	London	1.35 (0.95-1.92)	0.098	1.40 (0.73-2.66)	0.310
	North East	1.27 (0.89-1.83)	0.192	1.48 (0.95-2.30)	0.081
	North West	1.46 (1.05-2.04)	0.026	1.51 (1.00-2.27)	0.048
	South Central	1.08 (0.77-1.52)	0.655	1.18 (0.79-1.76)	0.427
	South East Coast	1.45 (1.04-2.04)	0.030	1.36 (0.90-2.03)	0.141
	South West	1.04 (0.74-1.46)	0.817	1.17 (0.77-1.78)	0.470
	West Midlands	0.82 (0.58-1.15)	0.243	1.01 (0.66-1.53)	0.983
	Yorkshire & The Humber	1.16 (0.82-1.62)	0.405	1.30 (0.84-2.02)	0.244
Length at practice (years)			<0.0001		<0.0001
	Low	1		1	
	Moderate	0.83 (0.72-0.97)	0.017	0.45 (0.38-0.52)	<0.0001
	High	1.36 (1.18-1.57)	<0.0001	0.44 (0.38-0.52)	<0.0001
Continuity of care			<0.0001		0.279
	Low	1		1	
	Moderate	5.67 (3.63-8.86)	<0.0001	0.92 (0.81-1.05)	0.206
	High	7.27 (4.66-11.3)	<0.0001	0.92 (0.78-1.09)	0.342
	Not valid	6.60 (4.23-10.3)	<0.0001	0.67 (0.40-1.12)	0.123
Number of all consultations			<0.0001		<0.0001
	Low	1		1	
	Moderate	4.01 (2.99-5.38)	<0.0001	3.93 (2.61-5.91)	<0.0001
	High	15.8 (12.0-20.9)	<0.0001	7.37 (4.78-11.4)	<0.0001

Number of consultations*			<0.0001		<0.0001
	Low	1		1	
	Moderate	2.10 (1.69-2.62)	<0.0001	0.93 (0.69-1.25)	0.618
	High	7.79 (6.39-9.49)	<0.0001	1.49 (1.10-2.02)	0.010
Number of referrals			0.013		<0.0001
	0	1		1	
	1	1.11 (0.91-1.34)	0.305	0.56 (0.43-0.74)	<0.0001
	≥2	1.37 (1.11-1.68)	0.003	0.61 (0.44-0.84)	0.003
Referral ≤30 days before next consultation			<0.0001		0.008
	No	1		1	
	Yes	1.98 (1.60-2.45)	<0.0001	1.87 (1.24-2.80)	0.003
Number of admissions			<0.0001		<0.0001
	0	1		1	
	1	1.22 (1.04-1.43)	0.014	0.97 (0.78-1.20)	0.750
	2	1.93 (1.63-2.28)	<0.0001	1.21 (0.96-1.53)	0.106
	3-4	2.67 (2.31-3.08)	<0.0001	1.28 (1.01-1.61)	0.038
	≥5	5.17 (4.61-5.79)	<0.0001	1.99 (1.58-2.50)	<0.0001
Disease flags					
Cancer			<0.0001		0.320
	No	1		1	
	Yes	3.16 (2.58-3.86)	<0.0001	1.13 (0.90-1.43)	0.293
Cerebrovascular disease			<0.0001		0.107
	No	1		1	
	Yes	3.81 (3.18-4.57)	<0.0001	1.23 (0.97-1.56)	0.083
Congestive heart disease			<0.0001		0.256
	No	1		1	
	Yes	4.52 (3.66-5.59)	<0.0001	1.18 (0.90-1.53)	0.232
Chronic pulmonary disease			<0.0001		0.171
	No	1		1	
	Yes	1.46 (1.31-1.63)	<0.0001	1.10 (0.97-1.24)	0.157
Dementia			0.001		0.406
	No	1		1	
	Yes	2.45 (1.54-3.90)	<0.0001	0.82 (0.49-1.37)	0.446
Diabetes without complications			<0.0001		0.005
	No	1		1	
	Yes	3.46 (3.06-3.92)	<0.0001	1.30 (1.10-1.54)	0.002
Diabetes with complications			<0.0001		0.377
	No	1		1	
	Yes	4.95 (3.59-6.82)	<0.0001	1.21 (0.82-1.78)	0.343
Hemiplegia			<0.0001		0.115
	No	1		1	
	Yes	4.40 (2.36-8.19)	<0.0001	2.03 (1.08-3.80)	0.028
Metastatic tumour			<0.0001		0.950
	No	1		1	
	Yes	3.36 (1.90-5.92)	<0.0001	1.02 (0.55-1.89)	0.949
Moderate liver disease			0.008		0.336
	No	1		1	
	Yes	7.62 (2.46-23.7)	<0.0001	2.97 (0.85-10.4)	0.088
Myocardial infarction			<0.0001		0.009
	No	1		1	
	Yes	4.76 (3.82-5.93)	<0.0001	1.61 (1.20-2.15)	0.001

*At GP practice, telephone or home visit.

Peptic ulcer disease		<0.0001		0.004
No	1		1	
Yes	4.08 (3.27-5.09)	<0.0001	1.66 (1.29-2.14)	<0.0001
Peripheral vascular disease		<0.0001		<0.0001
No	1		1	
Yes	5.29 (4.35-6.43)	<0.0001	1.63 (1.33-2.01)	<0.0001
Renal disease		<0.0001		0.001
No	1		1	
Yes	4.50 (3.95-5.13)	<0.0001	1.39 (1.17-1.64)	<0.0001
Rheumatological disease		<0.0001		0.146
No	1		1	
Yes	3.26 (2.67-3.98)	<0.0001	1.18 (0.96-1.46)	0.113

6.4.4 Service use

Certain consultation and referral characteristics were associated with greater risk of having an AE. I now examine patients' patterns of service use.

6.4.4.1 Consultations prior to index adverse event

On average, patients who had at least one AE had 69 (SD 61.1) consultations at any time before their index AE (p<0.001) and an average of 39 (SD 46.5) consultations with a doctor or nurse at the practice, by telephone or on home visit (p<0.001). Less than 1% of patients who had at least one AE did not have any consultations with a doctor or nurse at the practice, by telephone or home visit before their index AE (n=16/1,774; p<0.001).

During the year before their first AE, 96.3% of patients had at least one consultation at the GP practice, by telephone or home visit (n=1,708/1,774; 19,466 consultations). On average, patients had 11 (SD 16.9) consultations each at any of the three locations, ranging from 1 to 200 consultations. For the 13,601 consultations with valid recording of consultation length, the average length of consultations was 10.5 (SD 16.3) minutes.

6.4.4.2 Referrals requests before index adverse event

Of the patients who had at least one AE, 8.17% (n=145/1,774) had at least one referral before their index AE (RR 1.33, 95% CI 1.06-1.68; p=0.016). Over half of these patients only had one referral (53.1%; n=77/145). In the year before their index AE, 1.35% of patients had at least one referral (mean 1, SD 0.28 referrals), ranging from 1 to 2 referrals per patient (n=24/1,774 patients, 26 referrals). Where the referral speciality was known, 38.9% of

referrals were to urology (n=7/18 referrals). The other known specialties were general surgery (n=6 referrals), ophthalmology (n=3 referrals) and trauma and orthopaedics (n=2 referrals). Approximately half of referrals in the year preceding the first AE were recorded as routine (n=13/26), with the remaining referrals recorded as two week wait (n=1) or of unknown urgency status (n=12).

6.4.4.3 Consultations after index adverse event

Most patients who had at least one AE had one or more consultations following their index event (97.6%; n=1,731/1,774). Out of the 66,965 consultations that patients had after their first AE, 81.4% were at the GP practice, by telephone or home visit (n=54,524/66,965). On average, patients who had at least one AE had 32 (SD 35.3) consultations in any of the three locations after their index AE and during the study period, ranging from 1 to 392 consultations per patient.

6.4.4.4 Referrals requests after index adverse event

In 2.25% of patients who had at least one AE, a referral request was made after their index AE (n=40/1,774 patients, 74 referrals). On average, patients had 2 (SD 3.96) referral requests each, ranging from 1 to 26 referrals post-index AE per patient during the study period. Where referral speciality was known, two thirds of referrals were for urology (n=36/55 referrals). Referrals were also made to general surgery (n=12 referrals), ophthalmology (n=3), oral surgery (n=1) and trauma and orthopaedics (n=2). No speciality coding was provided for a quarter of referral requests post-index AE (n=19). The majority of referrals were recorded as routine (n=59/74), with 6 urgent referrals, 1 two week wait and 8 referrals where the urgency status was unknown.

6.4.5 Risk factors for emergency admissions

In the next section of the Results, I describe the predictors of unplanned admissions identified from crude and adjusted analyses.

6.4.5.1 Crude associations with emergency admissions

There were 55,320 admissions among 16,610 patients during the study period (Table 6.7). P-values for in this section are p<0.0001 unless reported otherwise. Analyses were performed to determine whether having an AE was an independent predictor of emergency admission, as a proxy measure of an adverse outcome. In Table 6.7 and Table 6.9, AE variables are the last to be presented and are in bold typeface. In crude analyses, having an AE was associated with increased risk of emergency admission (RR 2.82, 95% CI 2.73-2.90), patients who had more than one AE were at greatest risk (RR 3.69, 95% CI 3.44-3.96). Other risk factors for having an (all-cause) unplanned admission were older age (85 years or older) at study entry (RR 5.29, 95% CI 4.98-5.63), being female (RR 1.31, 95% CI 1.29-1.33), white ethnicity (RR 1.07, 95% CI 1.01-1.14; p=0.028), marital status other than single or married (RR 2.35, 95% CI 2.20-2.52) and living in areas of unknown deprivation status (RR 4.87, 95% CI 4.74-50).

Patients registered at practices in the South East Coast region (RR 2.03, 95% CI 1.89-2.18), who had a high continuity of care score (RR 3.50, 95% CI 3.29-3.71), high number of consultations at the GP practice, by telephone or home visit (RR 3.47, 95% CI 3.37-3.57), with two or more referral requests during the study period (RR 1.59, 95% CI 1.53-1.65) or a referral within 30 days of their next consultation (RR 1.74, 95% CI 1.67-1.82) were also at greater risk of an emergency admission. There was a small but statistically significant difference in the risk of admission between patients by Charlson Index score (RR 1.05, 95% CI 1.00-1.05). Conversely, patients who were the highest resource users, as measured by the Resource utilization band (RUB) score, had an increased risk of admission (RR 9.00, 95% CI 8.18-9.90). Further results by comorbidity markers can be found in the appendices (Table A.11).

Table 6.7 Risk factors for emergency admission during study period, crude results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic	Patients with ≥1 emergency admission, n			RR (95% CI)	P-value
	All	≥1 adverse event	(%)		
Age group at study start (years)					<0.0001
0-14	3134	48	(1.53)	1	
15-44	6373	251	(3.94)	1.69 (1.65-1.74)	<0.0001
45-64	3813	276	(7.24)	2.45 (2.38-2.52)	<0.0001
65-84	2909	254	(8.73)	4.76 (4.62-4.90)	<0.0001
≥85	381	10	(2.62)	5.29 (4.98-5.63)	<0.0001
Sex					<0.0001
Male	7157	347	(4.85)	1	
Female	9453	492	(5.20)	1.31 (1.29-1.33)	<0.0001
Ethnicity					<0.0001
Asian	367	15	(4.09)	1	
Black	263	14	(5.32)	1.06 (0.97-1.16)	0.201
Mixed	84	3	(3.57)	0.77 (0.66-0.90)	0.001
White	11705	650	(5.55)	1.07 (1.01-1.14)	0.028
Other	230	6	(2.61)	0.71 (0.64-0.79)	<0.0001
Unknown	3961	151	(3.81)	0.08 (0.07-0.08)	<0.0001
Marital status					<0.0001
Single	777	22	(2.83)	1	
Married	1873	136	(7.26)	1.99 (1.89-2.08)	<0.0001
Other status	380	20	(5.26)	2.35 (2.20-2.52)	<0.0001
Unknown	13580	661	(4.87)	1.63 (1.56-1.70)	<0.0001
Deprivation					<0.0001
Least deprived	3836	181	(4.72)	1	
Quintiles 2,3,4	7582	398	(5.25)	4.20 (4.11-4.29)	<0.0001
Most deprived	2530	129	(5.10)	3.66 (3.56-3.76)	<0.0001
Unknown	2662	131	(4.92)	4.87 (4.74-5.00)	<0.0001
Practice region					<0.0001
East Midlands	170	9	(5.29)	1	
East of England	2888	141	(4.88)	1.71 (1.60-1.84)	<0.0001
London	918	34	(3.70)	1.52 (1.40-1.63)	<0.0001
North East	606	29	(4.79)	1.01 (0.93-1.10)	0.758
North West	2032	143	(7.04)	1.65 (1.53-1.77)	<0.0001
South Central	2171	107	(4.93)	1.53 (1.42-1.64)	<0.0001
South East Coast	2173	123	(5.66)	2.03 (1.89-2.18)	<0.0001
South West	1933	84	(4.35)	1.12 (1.04-1.21)	0.002
West Midlands	1923	85	(4.42)	1.25 (1.16-1.34)	<0.0001
Yorkshire & The Humber	1796	84	(4.68)	1.37 (1.27-1.47)	<0.0001
Length at practice (years)					<0.0001
Low	3210	78	(2.43)	1	
Moderate	6188	282	(4.56)	0.78 (0.76-0.80)	<0.0001
High	7212	479	(6.64)	0.92 (0.89-0.94)	<0.0001
Continuity of care					<0.0001
Low	673	4	(0.59)	1	
Moderate	5085	262	(5.15)	2.72 (2.56-2.89)	<0.0001
High	6006	338	(5.63)	3.50 (3.29-3.71)	<0.0001
Not valid	4846	235	(4.85)	3.15 (2.97-3.35)	<0.0001
Number of all consultations					<0.0001

Low	2174	15	(0.69)	1	
Moderate	5064	110	(2.17)	1.78 (1.72-1.85)	<0.0001
High	9372	714	(7.62)	4.76 (4.61-4.92)	<0.0001
Consultation*					<0.0001
No	317	3	(0.95)	1	
Yes	16293	836	(5.13)	3.04 (2.79-3.31)	<0.0001
Number of consultations†					<0.0001
Low	2639	28	(1.06)	1	
Moderate	4884	122	(2.50)	1.52 (1.47-1.57)	<0.0001
High	9087	689	(7.58)	3.47 (3.37-3.57)	<0.0001
Referrals					<0.0001
No	15202	751	(4.94)	1	
Yes	1408	88	(6.25)	1.46 (1.42-1.50)	<0.0001
Number of referrals					<0.0001
0	15202	751	(4.94)	1	
1	930	48	(5.16)	1.37 (1.33-1.42)	<0.0001
≥2	478	40	(8.37)	1.59 (1.53-1.65)	<0.0001
Referral ≤30 days before consultation					<0.0001
No	16134	806	(5.00)	1	
Yes	476	33	(6.93)	1.74 (1.67-1.82)	<0.0001
Charlson Index score	1.14 (3.59)	2.40 (5.46)		1.05 (1.05-1.05)	<0.0001
Resource utilization band (RUB)					<0.0001
Healthy	383	0	-	1	
Low to moderate	6647	96	(1.44)	2.34 (2.13-2.58)	<0.0001
High to very high	9566	743	(7.77)	9.00 (8.18-9.90)	<0.0001
Adverse event					**<0.0001**
No	**15771**	**0**	**-**	**1**	
Yes	**839**	**839**	**(100)**	**2.82 (2.73-2.90)**	**<0.0001**
Number of adverse events, mean (SD)	**0.06 (0.27)**	**1.15 (0.44)**		**1.67 (1.65-1.70)**	**<0.0001**
Multiple adverse events					**<0.0001**
No	**16506**	**735**	**(4.45)**	**1**	
Yes	**104**	**104**	**(100)**	**3.69 (3.44-3.96)**	**<0.0001**

6.4.5.2 Model selection for adjusted analyses

There was an excess of zero counts in the sample, with 77.8% of patients not having any admissions during the study period. The data was also over-dispersed, with the variance of the continuous response variable (number of admissions) being much larger than the mean (9.39 compared to 0.74, respectively). Along with Poisson with GEE, adjusted regression models were also built with NB and ZIP regression to determine the most appropriate method for the data. Similar to the reasoning in section 6.4.3.2, Poisson with GEE was

*At GP practice, telephone or home visit.
†At GP practice, telephone or home visit.

selected for final adjusted regression analyses because of the ability to adjust for clustering of patients at practices.

Eight regression models were fitted, one for each of the comorbidity measures (Table 6.8). The best fitting model for predicting emergency admissions was model 3 which included comorbidity disease flags derived from Charlson Index categories (Table 6.8). The QIC score for this model was 5736.1, indicating that the model performed much better than the null model which had a QIC score of 47049.3.

Table 6.8 Fit of adjusted Poisson regression models for predicting risk factors for admission, using the generalized estimating equations (GEE) method

Model	Comorbidity variables	Quasi-Likelihood under the Independence model Criterion (QIC)
1	Charlson score	3087.1
2	Composite Charlson Index measure	23355.6
3	Disease flags derived from Charlson Index scoring	5736.1
4	Aggregated Disease Groups (ADGs)	18180.4
5	Collapsed Aggregated Disease Groups (CADGs)	20375.7
6	Major Expanded Diagnosis Clusters (MEDCs)	18793.0
7	Number of Expanded Diagnosis Cluster (EDC) groups	23555.5
8	Resource Utilization Band (RUB)	22542.4
9	Null model	47049.3

6.4.5.3 Adjusted associations with emergency admissions

After adjusting for all other variables and taking into account of clustering of patients at practices, having an AE was still associated with increased (though weaker) risk of admission (RR 1.27, 95% CI 1.14-1.42) (Table 6.9). The risk of admission between male and female patients was no longer statistically significant (p=0.216). Likewise, marital status (p=0.181), number of referral requests (p=0.062) and referrals within 30 days of the next consultation (p=0.173) were also no longer associated with the risk of unplanned admission. Adjusted risk factors for emergency admission were age 85 years or older on entry to the study (RR 2.25, 95% CI 1.95-2.59), living in the most deprived areas (RR 1.17, 95% CI 1.06-1.29; p=0.001) and having a high number of consultations in any primary care location (RR 2.17, 95% CI 1.89-2.49).

Although the number of referral requests was no longer statistically significant at the 95% level, patients who had two or more referrals remained at greater risk of an admission (RR 1.19, 95% CI 1.02-1.40; p=0.028). Patients of unknown ethnicity were less at risk of emergency admission compared to patients with known ethnicity (RR 0.11, 95% CI 0.09-0.14). By comorbidities, the diseases associated with greatest risk of (all-cause) emergency admission were cancer (RR 2.08, 95% CI 1.82-2.37) and metastatic tumour (RR 2.12, 95% CI 1.51-2.98), moderate liver disease (RR 2.29, 95% CI 1.11-4.74; p=0.026) and hemiplegia (RR 4.18, 95% CI 2.26-7.73).

Table 6.9 Risk factors for emergency admission during study period, adjusted results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic		Crude		Adjusted	
		RR (95% CI)	P-value	RR (95% CI)	P-value
Age group at study start (years)			<0.0001		<0.0001
	0-14	1		1	
	15-44	1.69 (1.65-1.74)	<0.0001	1.41 (1.31-1.53)	<0.0001
	45-64	2.45 (2.38-2.52)	<0.0001	1.52 (1.37-1.69)	<0.0001
	65-84	4.76 (4.62-4.90)	<0.0001	1.86 (1.67-2.07)	<0.0001
	≥85	5.29 (4.98-5.63)	<0.0001	2.25 (1.95-2.59)	<0.0001
Sex			<0.0001		0.216
	Male	1		1	
	Female	1.31 (1.29-1.33)	<0.0001	1.03 (0.98-1.09)	0.215
Ethnicity			<0.0001		<0.0001
	Asian	1		1	
	Black	1.06 (0.97-1.16)	0.201	1.16 (0.88-1.53)	0.300
	Mixed	0.77 (0.66-0.90)	0.001	0.88 (0.69-1.11)	0.267
	White	1.07 (1.01-1.14)	0.028	1.00 (0.88-1.14)	0.995
	Other	0.71 (0.64-0.79)	<0.0001	0.77 (0.59-1.01)	0.056
	Unknown	0.08 (0.07-0.08)	<0.0001	0.11 (0.09-0.14)	<0.0001
Marital status			<0.0001		0.181
	Single	1		1	
	Married	1.99 (1.89-2.08)	<0.0001	1.04 (0.92-1.19)	0.510
	Other status	2.35 (2.20-2.52)	<0.0001	0.95 (0.79-1.14)	0.592
	Unknown	1.63 (1.56-1.70)	<0.0001	1.09 (0.96-1.24)	0.202
Deprivation			<0.0001		<0.0001
	Least deprived	1		1	
	Quintiles 2,3,4	4.2 (4.11-4.29)	<0.0001	1.05 (0.97-1.14)	0.224
	Most deprived	3.66 (3.56-3.76)	<0.0001	1.17 (1.06-1.29)	0.001
	Unknown	4.87 (4.74-5.00)	<0.0001	0.62 (0.52-0.74)	<0.0001
Practice region			<0.0001		0.051
	East Midlands	1		1	
	East of England	1.71 (1.60-1.84)	<0.0001	0.92 (0.59-1.42)	0.703
	London	1.52 (1.40-1.63)	<0.0001	1.12 (0.71-1.75)	0.628
	North East	1.01 (0.93-1.10)	0.758	0.88 (0.53-1.45)	0.611
	North West	1.65 (1.53-1.77)	<0.0001	0.93 (0.60-1.44)	0.748
	South Central	1.53 (1.42-1.64)	<0.0001	1.04 (0.67-1.60)	0.869
	South East Coast	2.03 (1.89-2.18)	<0.0001	1.00 (0.65-1.56)	0.986
	South West	1.12 (1.04-1.21)	0.002	0.81 (0.52-1.24)	0.328
	West Midlands	1.25 (1.16-1.34)	<0.0001	0.94 (0.61-1.45)	0.767
	Yorkshire & The Humber	1.37 (1.27-1.47)	<0.0001	1.06 (0.68-1.65)	0.793
Length at practice (years)			<0.0001		<0.0001
	Low	1		1	
	Moderate	0.78 (0.76-0.80)	<0.0001	0.58 (0.54-0.62)	<0.0001
	High	0.92 (0.89-0.94)	<0.0001	0.51 (0.47-0.55)	<0.0001
Continuity of care			<0.0001		<0.0001
	Low	1		1	
	Moderate	2.72 (2.56-2.89)	<0.0001	1.06 (1.00-1.12)	0.068
	High	3.50 (3.29-3.71)	<0.0001	1.08 (1.00-1.18)	0.054
	Not valid	3.15 (2.97-3.35)	<0.0001	0.78 (0.68-0.89)	<0.0001
Number of all consultations			<0.0001		<0.0001
	Low	1		1	
	Moderate	1.78 (1.72-1.85)	<0.0001	1.49 (1.35-1.64)	<0.0001

High	4.76 (4.61-4.92)	<0.0001	2.17 (1.89-2.49)	<0.0001
Number of consultations*		<0.0001		<0.0001
Low	1		1	
Moderate	1.52 (1.47-1.57)	<0.0001	0.90 (0.82-0.99)	0.032
High	3.47 (3.37-3.57)	<0.0001	1.02 (0.90-1.15)	0.758
Number of referrals		<0.0001		0.062
0	1		1	
1	1.37 (1.33-1.42)	<0.0001	0.95 (0.85-1.07)	0.419
≥2	1.59 (1.53-1.65)	<0.0001	1.19 (1.02-1.40)	0.028
Referral ≤30 days before next consultation		<0.0001		0.173
No	1		1	
Yes	1.74 (1.67-1.82)	<0.0001	1.13 (0.95-1.34)	0.172
Disease flags				
Cancer		<0.0001		<0.0001
No	1		1	
Yes	5.40 (5.23-5.56)	<0.0001	2.08 (1.82-2.37)	<0.0001
Cerebrovascular disease		<0.0001		0.563
No	1		1	
Yes	2.59 (2.49-2.70)	<0.0001	1.03 (0.93-1.14)	0.561
Congestive heart disease		<0.0001		<0.0001
No	1		1	
Yes	4.86 (4.67-5.05)	<0.0001	1.65 (1.44-1.89)	<0.0001
Chronic pulmonary disease		<0.0001		0.010
No	1		1	
Yes	1.40 (1.37-1.43)	<0.0001	1.09 (1.02-1.17)	0.008
Dementia		<0.0001		0.083
No	1		1	
Yes	2.33 (2.12-2.55)	<0.0001	0.84 (0.69-1.02)	0.075
Diabetes without complications		<0.0001		0.020
No	1		1	
Yes	2.36 (2.30-2.43)	<0.0001	1.16 (1.03-1.30)	0.014
Diabetes with complications		<0.0001		0.035
No	1		1	
Yes	3.21 (2.97-3.46)	<0.0001	1.30 (1.05-1.62)	0.017
Hemiplegia		<0.0001		0.101
No	1		1	
Yes	10.1 (9.35-12.0)	<0.0001	4.18 (2.26-7.73)	<0.0001
Metastatic tumour		<0.0001		0.009
No	1		1	
Yes	9.64 (9.03-10.3)	<0.0001	2.12 (1.51-2.98)	<0.0001
Mild liver disease		<0.0001		0.059
No	1		1	
Yes	3.18 (2.82-3.59)	<0.0001	1.51 (1.05-2.18)	0.027
Moderate liver disease		<0.0001		0.073
No	1		1	
Yes	11.3 (9.41-13.5)	<0.0001	2.29 (1.11-4.74)	0.026
Myocardial infarction		<0.0001		0.003
No	1		1	
Yes	3.39 (3.23-3.57)	<0.0001	1.31 (1.13-1.52)	<0.0001
Peptic ulcer disease		<0.0001		0.019
No	1		1	

*At GP practice, telephone or home visit.

	Yes	2.57 (2.43-2.71)	<0.0001	1.26 (1.06-1.49)	0.009
Peripheral vascular disease			<0.0001		0.078
	No	1		1	
	Yes	3.67 (3.51-3.84)	<0.0001	1.18 (1.00-1.39)	0.055
Renal disease			<0.0001		0.051
	No	1		1	
	Yes	3.05 (2.96-3.14)	<0.0001	1.15 (1.01-1.30)	0.040
Rheumatological disease			<0.0001		0.302
	No	1		1	
	Yes	2.45 (2.34-2.56)	<0.0001	1.07 (0.94-1.22)	0.294
Adverse event			**<0.0001**		**<0.0001**
	No	**1**		**1**	
	Yes	**2.82 (2.73-2.99)**	**<0.0001**	**1.27 (1.14-1.42)**	**<0.0001**

6.4.5.4 Admissions for adverse events

In 3.59% of all admissions, an AE was recorded as a cause of admission (n=1, 987/55,320 admissions). Few patients who had one or more admissions for an AE also had at least one AE before their first AE admission (1.29%; n=16/1,238). All except 5 of these patients had one AE before their admission; the five patients experienced two AEs each.

6.4.6 Admissions prior to index adverse event

Out of the patients who had an AE, 28.2% also had at least one admission in the year before their index AE (n=500/1,774 patients, 978 admissions). On average, these patients had 2 (SD 2.21) admissions each in the year prior to their first AE, ranging from 1 to 31 admissions per patient. In 46 of these admissions, AE was a recorded cause of admission.

6.4.6.1 Admissions after index adverse event

Out of the patients who had an AE, 31.2% had at least one admission after their initial AE (n=553/1,774 patients). In these patients, there were 2,087 admissions during the study period with an average of 4 (SD 5.59) admissions per patient, ranging from 1 to 92 admissions. An adverse event was recorded as a cause of admission in 5.94% of these admissions (n=124/2,087).

6.4.7 Risk factors for deaths

In the next section of the Results, I describe the predictors of death identified from crude and adjusted analyses.

6.4.7.1 Crude associations with death

There were 3,963 deaths during the study period, including 108 deaths following AEs. For the same reason as investigating emergency admissions, the independent risk of having an AE on death as a potential iatrogenic outcome was assessed. AE variables are the last to be presented in Table 6.10 and Table 6.12 and are in bold typeface. Among patients who had at least one AE, 10.0% died during the study period (n=178/1,774). The average age of the 178 patients who had at least one AE and also died was 77 (SD 13.8) years, ranging from 22 to 101 years. Another 59 patients who had at least one AE died after the end of the study (during 2009 or 2010). P-values in this section are p<0.0001 unless reported otherwise.

No patients who died had a consultation within 30 days of a hospital discharge and therefore this variable has been excluded from analyses. A crude model with Charlson Index score as the predictor for death failed to converge. Therefore, this variable is not reported in the crude results. The average Charlson score of patients who died was 2.62 (SD 5.93), compared to an average score of 4.37 (SD 7.78) in patients who had at least one AE and died.

In crude analyses, having an AE (RR 1.90, 95% CI 1.64-2.19), and in particular more than one AE (RR 2.47 95% CI 1.76-3.47), increased the risk of death (Table 6.10). Other risk factors for death were older age at entry into the study (RR 467, 95% CI 326-670 for patients aged 85 years or older), being female (RR 1.09, 95% CI 1.02-1.16, p=0.008), white ethnicity (RR 5.03, 95% CI 2.79-9.04), marital status other than single or married (RR 11.6, 95% CI 8.67-15.4) and living in areas of unknown deprivation status (RR 1.48, 95% CI 1.33-1.63). Registration at practices in the West Midlands compared to other regions of England had a protective effect against death in crude analyses (RR 0.56, 95% CI 0.45-0.69).

Patients also had increased risk of death if they were registered with the practice for the longest lengths of time (RR 1.61, 95% CI 1.49-1.74), followed-up for between 4 and 6 years (RR 1.14, 95% CI 1.03-1.27; p=0.010) or with a high continuity of care score (RR 1.18, 95% CI 1.05-1.32; p=0.005). A high number of consultations at the GP practice, by telephone or

home visit (RR 1.45, 95% CI 1.35-1.56), two or more referral requests (RR 1.52, 95% CI 1.30-1.77), five or more admissions during the study period (RR 6.48, 95% CI 6.00-7.00) and high resource use as measured by the Resource Utilization Band score (RR 8.23, 95% CI 6.27-10.8) were also crude predictors of death. Further results by comorbidities are in the Appendices (Table A.12).

Table 6.10 Risk factors for death during study period, crude results from log-binomial regression using the generalized estimating equations (GEE) method

Characteristic	Deaths, n			RR (95% CI)	P-value
	All	≥1 adverse event	(%)		
Age group at study start (years)					<0.001
0-14	33	1	(3.03)	1	
15-44	222	8	(3.60)	4.74 (3.24-6.94)	<0.0001
45-64	749	36	(4.81)	36.8 (25.6-53.0)	<0.0001
65-84	2328	113	(4.85)	217 (151-310)	<0.0001
≥85	631	20	(3.17)	467 (326-670)	<0.0001
Sex					0.008
Male	1816	81	(4.46)	1	
Female	2147	97	(4.52)	1.09 (1.02-1.16)	0.008
Ethnicity					<0.001
Asian	12	0	-	1	
Black	9	0	-	1.09 (0.46-2.61)	0.843
Mixed	2	1	(50.0)	0.73 (0.16-3.26)	0.680
White	1557	77	(4.95)	5.03 (2.79-9.04)	<0.0001
Other	12	0	-	1.82 (0.81-4.08)	0.145
Unknown	2371	100	(4.22)	2.18 (1.21-3.92)	0.009
Marital status					<0.001
Single	58	4	(6.90)	1	
Married	406	16	(3.94)	4.79 (3.65-6.30)	<0.0001
Other status	189	12	(6.35)	11.6 (8.67-15.4)	<0.0001
Unknown	3310	146	(4.41)	4.55 (3.51-5.88)	<0.0001
Deprivation					<0.001
Least deprived	1915	86	(4.49)	1	
Quintiles 2,3,4	1227	52	(4.24)	1.38 (1.29-1.48)	<0.0001
Most deprived	382	18	(4.71)	1.19 (1.07-1.33)	0.001
Unknown	439	22	(5.01)	1.48 (1.33-1.63)	<0.0001
Practice region					<0.001
East Midlands	93	1	(1.08)	1	
East of England	604	29	(4.80)	0.90 (0.73-1.11)	0.314
London	279	11	(3.94)	1.07 (0.85-1.34)	0.589
North East	186	12	(6.45)	0.84 (0.66-1.07)	0.152
North West	473	15	(3.17)	0.94 (0.75-1.16)	0.548
South Central	500	24	(4.80)	0.88 (0.71-1.09)	0.253
South East Coast	487	26	(5.34)	1.05 (0.85-1.30)	0.663
South West	506	15	(2.96)	0.82 (0.66-1.01)	0.063
West Midlands	402	18	(4.48)	0.56 (0.45-0.69)	<0.0001
Yorkshire & The Humber	433	27	(6.24)	0.84 (0.67-1.04)	0.113
Length at practice (years)					<0.001
Low	1040	24	(2.31)	1	
Moderate	1214	56	(4.61)	1.16 (1.06-1.25)	0.001
High	1709	98	(5.73)	1.61 (1.49-1.74)	<0.0001
Follow-up time (years)					<0.001
<1	486	6	(1.23)	1	
1-3	1255	32	(2.55)	0.88 (0.79-0.97)	0.014
4-6	1238	65	(5.25)	1.14 (1.03-1.27)	0.010
7-10	984	75	(7.62)	0.26 (0.23-0.28)	<0.0001
Continuity of care					<0.001
Low	411	6	(1.46)	1	
Moderate	603	32	(5.31)	0.57 (0.50-0.65)	<0.0001
High	1240	70	(5.65)	1.18 (1.05-1.32)	0.005

Not valid	1709	70	(4.10)	1.63 (1.45-1.82)	<0.0001
Number of all consultations					<0.001
Low	860	3	(0.35)	1	
Moderate	1100	29	(2.64)	1.23 (1.13-1.35)	<0.0001
High	2003	146	(7.29)	2.27 (2.10-2.46)	<0.0001
Consultation*					0.001
No	249	4	(1.61)	1	
Yes	3714	174	(4.68)	0.79 (0.69-0.90)	<0.0001
Number of consultations†					<0.001
Low	1163	22	(1.89)	1	
Moderate	1064	28	(2.63)	0.92 (0.85-1.00)	0.051
High	1736	128	(7.37)	1.45 (1.35-1.56)	<0.0001
Referral					<0.001
No	3609	165	(4.57)	1	
Yes	354	13	(3.67)	1.39 (1.25-1.54)	<0.0001
Number of referrals					<0.001
0	3609	165	(4.57)	1	
1	201	9	(4.48)	1.31 (1.14-1.50)	<0.0001
≥2	153	4	(2.61)	1.52 (1.30-1.77)	<0.0001
Referral ≤30 days before next consultation					0.078
No	3874	174	(4.49)	1	
Yes	89	4	(4.49)	1.21 (0.99-1.48)	0.068
Admission					<0.001
No	2023	81	(4.00)	1	
Yes	1940	97	(5.00)	3.28 (3.09-3.49)	<0.0001
Number of admissions					<0.001
0	2023	81	(4.00)	1	
1	426	8	(1.88)	1.80 (1.62-1.99)	<0.0001
2	335	6	(1.79)	2.72 (2.43-3.03)	<0.0001
3-4	442	17	(3.85)	3.68 (3.33-4.05)	<0.0001
≥5	737	66	(8.96)	6.48 (6.00-7.00)	<0.0001
Resource utilization band (RUB)					<0.001
Healthy	134	0	-	1	
Low to moderate	1008	3	(0.30)	1.76 (1.33-2.32)	<0.0001
High to very high	2819	175	(6.21)	8.23 (6.27-10.8)	<0.0001
Adverse event					**<0.001**
No	**3785**	**0**	**-**	**1**	
Yes	**178**	**178**	**(100)**	**1.90 (1.64-2.19)**	**<0.0001**
Multiple adverse events					**<0.001**
No	**3934**	**149**	**(3.79)**	**1**	
Yes	**29**	**29**	**(100)**	**2.47 (1.76-3.47)**	**<0.0001**
Admission for adverse event					**<0.001**
No	**3682**	**152**	**(4.13)**	**1**	
Yes	**281**	**26**	**(9.25)**	**4.45 (4.00-4.96)**	**<0.0001**

*At GP practice, telephone or home visit.
†At GP practice, telephone or home visit.

6.4.7.2 Model selection for adjusted analyses

As used for crude estimates of risk factors for death, adjusted models were built using log-binomial regression with GEE to account for patient clustering by practice. These models failed to converge (Chapter 4 section 4.5.1). To overcome this problem, modified Poisson regression models using GEE were applied instead.

In section 6.4.7.1, I reported that the crude log-binomial model of Charlson Index score as the predictor of death failed to converge. In spite of the original exclusion, Charlson score was included in the Poisson with GEE models (Table 6.11). The model with Charlson score achieved relatively reasonable fit (QIC score of 21800.1) but the best performing model featured a count of Expanded Diagnosis Cluster (EDC) groups. This model achieved a much lower QIC score than the null model (QIC score of 21475.3 compared to 32959.3, respectively).

Table 6.11 Fit of adjusted Poisson regression models for predicting risk factors for death, using the generalized estimating equations (GEE) method

Model	Comorbidity variables	Quasi-Likelihood under the Independence model Criterion (QIC)
1	Charlson score	21800.1
2	Composite Charlson Index measure	21872.6
3	Disease flags derived from Charlson Index scoring	21993.2
4	Aggregated Disease Groups (ADGs)	22678.3
5	Collapsed Aggregated Disease Groups (CADGs)	23398.2
6	Major Expanded Diagnosis Clusters (MEDCs)	22604.4
7	Number of Expanded Diagnosis Cluster (EDC) groups	21475.3
8	Resource Utilization Band (RUB)	21967.8
9	Null model	32959.3

6.4.7.3 Adjusted associations with death

After adjustment and taking clustering into account, there was no longer any statistical difference in the risk of death among patients who had an AE and patients who had not (p=0.396) (Table 6.12). Having an admission for an AE (RR 1.22, 95% CI 1.09-1.37) or five or more admissions (RR 1.89, 95% CI 1.71-2.10) remained predictors of death. Patients' age at study entry remained a strong predictor of death with patients aged 85 years or older at

greatest risk of death (RR 212, 95% CI 145-310). Female patients were less at risk of death compared to male patients (RR 0.85, 95% CI 0.81-0.89). Compared to patients of known ethnicity, patients of unknown ethnicity were at greater risk of death (RR 1.70, 95% CI 1.06-2.72; p=0.027). Patients living in areas of unknown deprivation status (RR 1.30, 95% CI 1.19-1.43) or who had been registered with the practice for the longest lengths of time (RR 1.94, 95 % CI 1.79-2.11) remained most at risk of death. Patients with a high number of consultations at any location (RR 1.32, 95% CI 1.18-1.48) or a high continuity of care score (RR 1.23, 95% CI 1.15-1.33) were at greater risk of death, but having a high number of consultations at the practice, by telephone or home visit with a GP or nurse was not significantly associated with risk of death (RR 0.95, 95% CI 0.85-1.04; p=0.266).

Patients registered at practices in the West Midlands compared to other regions (RR 0.65, 95% CI 0.49-0.86, p=0.003) and patients who were followed up for between 7 and 10 years (RR 0.09, 95% CI 0.08-0.10) were less at risk of death. Patients with any comorbidity, as measured by the Charlson Index, had almost five times greater risk of death than patients without any of the comorbid diseases (RR 4.87, 95% CI 4.58-5.17). Specifically, patients with recorded chronic pulmonary disease (RR 11.6, 95% CI 10.8-12.5), dementia (RR 10.4, 95% CI 9.36-11.6), metastatic tumour (RR 13.2, 95% CI 11.7-14.8) or moderate liver disease (RR 12.3, 95% CI 8.62-17.7) were at greatest risk of death.

Table 6.12 Risk factors for death during study period, adjusted results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic	Crude		Adjusted	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Age group at study start (years)		<0.0001		<0.0001
0-14	1		1	
15-44	4.74 (3.24-6.94)	<0.0001	4.55 (3.12-6.64)	<0.0001
45-64	36.8 (25.6-53.0)	<0.0001	38.9 (26.8-56.6)	<0.0001
65-84	217 (151.3-310)	<0.0001	147 (101-213)	<0.0001
≥85	467 (326-670)	<0.0001	212 (145-310)	<0.0001
Sex		0.008		<0.0001
Male	1		1	
Female	1.09 (1.02-1.16)	0.008	0.85 (0.81-0.89)	<0.0001
Ethnicity		<0.0001		<0.0001
Asian	1		1	
Black	1.09 (0.46-2.61)	0.843	1.01 (0.56-1.83)	0.971
Mixed	0.73 (0.16-3.26)	0.680	2.18 (0.61-7.82)	0.233
White	5.03 (2.79-9.04)	<0.0001	1.44 (0.90-2.31)	0.126
Other	1.82 (0.81-4.08)	0.145	1.21 (0.62-2.35)	0.578
Unknown	2.18 (1.21-3.92)	0.009	1.70 (1.06-2.72)	0.027
Marital status		<0.0001		0.129
Single	1		1	
Married	4.79 (3.65-6.30)	<0.0001	1.09 (0.87-1.36)	0.454
Other status	11.6 (8.67-15.4)	<0.0001	1.17 (0.93-1.48)	0.180
Unknown	4.55 (3.51-5.88)	<0.0001	1.19 (0.96-1.46)	0.114
Deprivation		<0.0001		<0.0001
Least deprived	1		1	
Quintiles 2,3,4	1.38 (1.29-1.48)	<0.0001	1.14 (1.04-1.25)	0.007
Most deprived	1.19 (1.07-1.33)	0.001	1.26 (1.13-1.41)	<0.0001
Unknown	1.48 (1.33-1.63)	<0.0001	1.30 (1.19-1.43)	<0.0001
Practice region		<0.0001		0.002
East Midlands	1		1	
East of England	0.90 (0.73-1.11)	0.314	0.85 (0.65-1.11)	0.233
London	1.07 (0.85-1.34)	0.589	0.81 (0.62-1.07)	0.139
North East	0.84 (0.66-1.07)	0.152	0.86 (0.65-1.14)	0.302
North West	0.94 (0.75-1.16)	0.548	0.83 (0.63-1.09)	0.189
South Central	0.88 (0.71-1.09)	0.253	0.76 (0.58-1.00)	0.047
South East Coast	1.05 (0.85-1.30)	0.663	0.74 (0.56-0.96)	0.025
South West	0.82 (0.66-1.01)	0.063	0.84 (0.64-1.10)	0.200
West Midlands	0.56 (0.45-0.69)	<0.0001	0.65 (0.49-0.86)	0.003
Yorkshire & The Humber	0.84 (0.67-1.04)	0.113	0.79 (0.60-1.03)	0.086
Length at practice (years)		<0.0001		<0.0001
Low	1		1	
Moderate	1.16 (1.06-1.25)	0.001	1.82 (1.69-1.97)	<0.0001
High	1.61 (1.49-1.74)	<0.0001	1.94 (1.79-2.11)	<0.0001
Follow-up time (years)		<0.0001		<0.0001
<1	1		1	
1-3	0.88 (0.79-0.97)	0.014	0.63 (0.58-0.69)	<0.0001
4-6	1.14 (1.03-1.27)	0.010	0.51 (0.46-0.56)	<0.0001
7-10	0.26 (0.23-0.28)	<0.0001	0.09 (0.08-0.10)	<0.0001
Continuity of care		<0.0001		<0.0001
Low	1		1	
Moderate	0.57 (0.50-0.65)	<0.0001	1.12 (1.03-1.22)	0.006

High	1.18 (1.05-1.32)	0.005	1.23 (1.15-1.33)	<0.0001
Not valid	1.63 (1.45-1.82)	<0.0001	1.11 (0.98-1.26)	0.101
Number of consultations		<0.0001		<0.0001
Low	1		1	
Moderate	1.23 (1.13-1.35)	<0.0001	1.15 (1.05-1.26)	0.004
High	2.27 (2.10-2.46)	<0.0001	1.32 (1.18-1.48)	<0.0001
Consultation*		0.001		0.531
No	1		1	
Yes	0.79 (0.69-0.90)	<0.0001	0.96 (0.84-1.09)	0.530
Number of consultations†		<0.0001		0.542
Low	1		1	
Moderate	0.92 (0.85-1.00)	0.051	0.97 (0.90-1.05)	0.480
High	1.45 (1.35-1.56)	<0.0001	0.95 (0.85-1.04)	0.266
Referral		<0.0001		
No	1		1	
Yes	1.39 (1.25-1.54)	<0.0001	1.09 (0.95-1.23)	0.210
Number of referrals		<0.0001		0.712
0	1		1	
1	1.31 (1.14-1.50)	<0.0001	1	
≥2	1.52 (1.30-1.77)	<0.0001	0.97 (0.81-1.16)	0.712
Referral ≤30 days before consultation		0.078		0.739
No	1		1	
Yes	1.21 (0.99-1.48)	0.068	0.97 (0.80-1.17)	0.739
Admission		<0.0001		
No	1		1	
Yes	3.28 (3.09-3.49)	<0.0001	1.48 (1.35-1.63)	<0.0001
Number of admissions		<0.0001		<0.0001
0	1		1	
1	1.80 (1.62-1.99)	<0.0001	1	
2	2.72 (2.43-3.03)	<0.0001	1.12 (1.02-1.23)	0.013
3-4	3.68 (3.33-4.05)	<0.0001	1.24 (1.13-1.36)	<0.0001
≥5	6.48 (6.00-7.00)	<0.0001	1.89 (1.71-2.10)	<0.0001
Expanded Diagnosis Clusters (EDCs) groups		<0.0001		0.498
Low	1		1	
Moderate	1.58 (1.43-1.74)	<0.0001	1.03 (0.95-1.12)	0.439
High	3.01 (2.75-3.30)	<0.0001	1.00 (0.90-1.10)	0.963
Adverse event		**<0.0001**		**0.396**
No	**1**		**1**	
Yes	**1.90 (1.64-2.19)**	**<0.0001**	**0.95 (0.83-1.08)**	**0.403**
Multiple adverse events		**<0.0001**		**0.970**
No	**1**		**1**	
Yes	**2.47 (1.76-3.47)**	**<0.0001**	**0.99 (0.72-1.37)**	**0.970**
Admission for adverse event		**<0.0001**		**0.001**
No	**1**		**1**	
Yes	**4.45 (4.00-4.96)**	**<0.0001**	**1.22 (1.09-1.37)**	**0.001**

*At GP practice, by telephone or home visit.
†At GP practice, by telephone or home visit.

6.4.8 Performance of comorbidity measures

The output of analyses in this chapter presented an opportunity to compare the performance of Khan et al's version of the Charlson Index and the ACG software. When selecting which comorbidity measure to include in adjusted regression models for predicting the risk of having an adverse event, none of the ACG variables performed better than the disease flags derived from the Charlson Index (section 6.4.3.2). The two models with CADGs and ADGs performed better than the model with Charlson Index scores. In fact, performance of the CADG model was similar to that of the null model.

For predicting the risk of an emergency admission, Charlson Index based-disease flags performed best again (section 6.4.5.2). All comorbidity measures performed better than the null model. The models with ADGs, MEDCs, CADGs and RUBs fitted the data better than the model containing Charlson Index scores. Like with modelling the risk of emergency admission, all models with comorbidity measures performed better than the null model in predicting the risk of death (section 6.4.5.2). The model containing EDC counts performed best, followed by the model with Charlson Index scores.

6.5 Discussion

I begin the final section of this chapter with a précis of the study results, comparing these findings from national data with those from local data in Chapter 5. The section concludes with reflections on the study's methodological limitations.

6.5.1 Summary of main findings

The first objective of this chapter was to measure the incidence of AEs in the English general practice population. Between 1999 and 2008, an incidence rate of 6.0 AEs per 1,000 person-years was detected in national GPRD data (n=341,261 person-years; 95% CI 5.74-6.27). Analyses of local data from NHS Brent collected in 2007 produced an estimated rate of 1.67 AEs per 1,000 consultations (n=1,118,072 consultations; 95% CI 1.59-1.74). Those analyses in Chapter 5 also identified 491 surgical complications, 1,317 ADEs and a further 467 AEs recorded as external causes of morbidity and mortality at 23 GP practices. In this chapter, 2,048 recorded AEs were identified in 1,774 patients at 387 GP practices between 1999 and 2008. It is difficult to compare these two sets of results with published estimates given the

heterogeneity of study methods and limited research within the NHS (Chapter 2 section 2.5.3.1). The estimated rate using NHS Brent data is far lower than de Wet and Bowie's (2009) estimate of 28.4 incidents of harm per 1,000 consultations which was derived from trigger tool assessment of electronic records at five Scottish practices.[295] On the other hand, that rate of 1.67 AEs per 1,000 consultations is comparable to estimates of 0.037 AEs per 1,000 consultations and 4.8 AEs per 1,000 consultations from two US studies that used larger samples than de Wet and Bowie.[8,24]

The second objective was to identify patient risk factors for recorded AEs. In analyses from Chapter 5 and this chapter, adverse events were more commonly recorded in older patients, especially those aged 65 and 84 years. This predictor is well documented in the literature.[177,179,295] Other risk factors identified in this chapter were registration at practices in the North West of England, having a high number of consultations at the practice, by telephone or home visit, 30 days or less between referral and the next consultation and having five or more admissions. Patients with recorded hemiplegia, myocardial infarction, peptic ulcer disease or peripheral vascular disease had at least one and a half times greater risk of having an AE compared to patients without the respective diseases.

The third objective was to explore the health service use of patients with recorded AEs. The majority of patients who had an AE also had at least one consultation at the GP practice, by telephone or home visit in the 12 months before their index AE and also following this AE. Few patients had a referral request before their first AE, with up to two referrals per patient being made. Even fewer patients had a referral request after their index AE, 8.17% of patients before compared to 2.25% of patients after. Other referral details were sparsely populated in the dataset. The paucity of similar research conducted in England mean that interpretation of the findings relating to the second and third study objectives is difficult. Yet it also demonstrates the importance of developing the research area and the value of this study to the field.

The fourth and final objective was to explore the outcomes (emergency admissions and death) of patients with recorded AEs. Older patients (especially aged 85 years or older), patients who lived in the most deprived areas and patients with a high number of consultations (in any primary care location) were most at risk of an emergency (all-cause)

admission. The associations between increasing patient age, and deprivation status, with emergency admissions in England have been described by Bankart et al (2011), among others.[214,296-298] Patients who had at least one AE were also at greater risk of admission but not of death. However, patients who had at least one admission for an AE, or five or more (all-cause) admissions, were at greater risk of death. While longer registration time at the practice was protective against an emergency admission, this factor was a predictor for death, as was having a high continuity of care score. Patients with metastatic tumour or moderate liver disease had higher risk of an emergency admission and death. The monotonic association between secondary care service use denoted by the number of admissions, but not of GP consultations*, and mortality risk is logical given that patients with more severe or complex diseases may have greater intensity of hospital contact but not necessarily of more general practice care.

6.5.2 Methodological issues

The cohort approach to the analyses in this chapter used the AE variable as both predictor and outcome measures. By doing so, I was able to explore the temporal sequencing between AEs and multiple outcomes (admissions and death). I now reflect on the study's technical deficits, expanding on the discussion of section 6.5.1, and in terms of future research. The first caveat of the analyses is the measurement of many predictors and outcomes. By multiple statistical testing, it is possible that spurious statistically significant associations between variables were identified. To somewhat counter this issue, a higher threshold for statistical significance is recommended for more conservative estimates (Chapter 4 section 4.6.1).

6.5.2.1 Accurate identification of cases

Despite the cleaning process undertaken (section 6.3.3) to improve the accuracy of case ascertainment, false positive cases of AEs might have been included in the study. While data are collected for research by the GPRD, they are not intended specifically for investigating patient safety. Incidents occurring as part of the disease process, expected treatment effects or events related to previous AEs may have been unintentionally coded as AEs. The

*At GP practices, by telephone or home visit with a GP or nurse.

reviewed studies in Chapter 2 highlighted the research practice of using multiple data sources to enhance data quality. Individual datasets may be affected by a number of biases related to reimbursement, management, patient groups and the nuances of the software itself.[299,300] In this study, additional information from case notes and interviews with patients and practice staff would have facilitated the distinction between discrete episodes of AEs.

6.5.2.2 Case-mix adjustments

In order to identify remediable factors in the organisation and delivery of care in general practice, key drivers of quality and safety must be identified. Very few practice variables were available in the GPRD dataset, with no data on list size or staff demography. The data were unsuitable for linkage to other sources due to their anonymised nature. These properties of the dataset narrowed the list of potential confounders that could be adjusted for and also restricted the examination of processes of care that may be associated with patient harm. Characteristics including patient age, continuity of care, deprivation, length of registration time at practice and geographical region of the practice were identified as risk factors for having an AE and/or emergency admission and/or death. To better understanding the roles of patient and practice characteristics, one also needs to consider how they may modify the effects of other characteristics on the outcomes of interest.

6.5.2.3 Temporal incongruence

In section 6.5.2, I commented on the exploration of causality in this study. Both a high number of consultations* and admissions were associated with greater risk of having an AE. Having a high number of consultations (in any primary care location) was also associated with increased risk of an emergency admission. For these two predictors, no distinction was made on whether the proposed risk factors occurred before or after the outcome. As such, the roles may be reversed. For example, having a higher number of admissions may predict patients' high number of consultations. To establish causality, it will be necessary to delineate the chronology of events in future research.

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*In any primary care location, or specifically at GP practice, telephone or home visit.

Similarly, although marital status was not significantly associated with any of the three outcomes, this variable represented patients' "current status" at the time of data submission by the GP practice to GPRD, and not patients' status at the time of the event(s) of interest. Hence, associations between this variable, other predictors and outcomes may be inaccurate. Another time-related issue is the possible lag between adverse event, or symptom onset, and related consultation. Delayed presentation may affect event recording, even though the "event date" field in patient records is intended for recording the date associated with the event. Patient delays to consultation may also affect the distinction between separate AE episodes, particularly if events occur close together in time.

Furthermore, the recording of event dates is dependent on the recall of patients, which can be erroneous. Not least, the arbitrary lag time I set to distinguish between AE episodes may be an inappropriate length, although there is no indication of this from the literature (section 6.3.3.3). A final note on event ordering; this study analysed data only from patients' first registration period at a GP practice. Some patients may have had multiple valid transfers out of a practice over the study period. Bias from excluding such patients, and others by transfer status, was briefly explored during data cleaning. No significant differences were identified in the age or sex of patients who transferred out of their current practice and those who did not. Likewise, there was no statistically significant difference in the two characteristics between patients who had multiple transfers out and patients with either just one or no transfer out of their current GP practice.

6.5.2.4 Comorbidity measures

Earlier in this Discussion (section 6.5.2.2), I addressed the subject of inadequate comorbidity adjustment. In this section, I return to that topic in more detail. No comorbidity measure accounts for all co-existing conditions in a studied population. The Charlson Index (and its modified versions) is perhaps the most widely used comorbidity measure in health research and, consequently, also well validated in different populations.[224-226] Still, there is little documentation of its use in English general practice and so the use of Khan et al's version of the Index (and two additional Index-derived measures) in this project contributes evidence for its validation for this setting (Chapter 3 section 3.9.4.4). Some technical qualities of Khan et al's adaptation require attention, namely the use of fewer diagnosis codes compared to

other versions, such as Elixhauser's modified Index.[301] This second measure has demonstrated better performance in non-acute populations (Chapter 3 section 3.9.4.4 for further discussion).[302] Khan et al's modified measure was based on an ICD-9-CM code version of the Charlson Index.[226] Due to this, the resulting translation for Read codes may be affected by incomplete mapping between taxonomies but, nevertheless, may still be most appropriate for the English general practice population.

Like the Charlson Index, ACG measures have been used in ambulatory care populations, including GPRD samples.[221,303] The value of time-naïve ACG fields for case-mix adjustment in this project has been contemplated in Chapter 3 section 3.9.4.2. Paediatric and obstetric data are often excluded from Charlson Index derivations. Data separation also features in the use of the ACG software, with separate calculation of ACG weights for adult and children recommended.[304] Neither the suggested modifications to Charlson or ACG measures were applied in this project. As the ACG software was designed for the US population, the default case-mix weights are set for that population and may not be accurate for the English general practice population.[305]

Overall, neither set of comorbidity measures displayed absolute best performance. The Charlson Index score performed less well than Charlson-based disease flags in modelling the risk of adverse events and emergency admissions. The latter measure performed best out of all comorbidity measures for these two outcomes. In models to predict death, the two measures had similar performances to each other but counts of EDCs from the ACG software was the best performing comorbidity measure. Besides the restrictions described already in this section and in Chapter 3, a further technical issue to note is the inclusion of conditions and diseases that may have resolved, which is related to the time-naivety of the ACG variables.[221] The potential problem of misclassification can only be rectified through the use of additional data as suggested in section 6.5.2.1.

6.5.3 Patient outcomes

First-time and subsequent AEs were included in calculations. To inform service delivery and patient safety monitoring, more sophisticated analyses should determine whether having a first AE predicts the occurrence of future adverse events. As stated in section 6.5.1, the estimated rate of AEs was lower than some reported rates for the non-acute setting.

Plausible independent and combined reasons for the low incidence rate in this study are: lack of presentation in general practice (AEs causing low levels of patient harm); presentation in secondary care instead of general practice (AEs causing high levels of patient harm); failure to record AEs using the designated complication of care codes; failure to diagnose AEs; and failure to capture AEs that do not correspond to the basic set of diagnosis codes used in the analyses.

Some of the measured AEs have corresponding external causes of morbidity and mortality (ICD-10 Y codes). These codes are typically used for secondary diagnoses. As primary and all secondary HES and ONS diagnosis fields were included in the analyses, it is unlikely that valid diagnoses in the ICD-10 "Y" code block will have been excluded. No attempt was made to link AEs with subsequent outcomes (emergency admissions and death). Although a temporal relationship was identified in the measurement of admissions and death subsequent to AEs and/or admissions for AEs, direct causality was not established but should be explored in future research.

6.5.4 Implications for clinical care and health policy

This study has applied national data from ten years, using validated coding systems and outcome measures, to identify temporal trends in the epidemiology of recorded AEs in general practice in England. The rates of AEs were low, but concur with findings from other studies, although further external validation is recommended. Within the framework for measuring and monitoring patient harm, there must be room to assess the amenability of detected events. As suggested in section 6.5.2.1, some AEs may not be due to medical errors or indeed be preventable. There is a growing evidence base around preventable ADEs in the non-acute setting but information on non-drug related incidents in general practice and elsewhere in primary care is still fragmented, locally-orientated and without definitive priorities for service improvement or research (Chapters 2 and 5). The identified high-risk patient groups for adverse events and other adverse outcomes (emergency admission and death) will inform safety improvement initiatives and steer research on patient harm.

Chapter 7: Unplanned admissions for diabetic emergencies

7.1 Chapter overview

This chapter examines the recording of unplanned (emergency) admissions for diabetic ketoacidosis and coma using GPRD data. I identify risk factors for this outcome and describe the health service use of patients who had one or more of these admissions. In the final section of the chapter, the limitations of the data and the value of data linkage for this study are discussed.

7.2 Introduction

I gave justifications for examining emergency admissions for diabetic emergencies in Chapter 3 section 3.3. In the next section of this chapter (section 7.2.8), I develop the rationale for this study. Before this, I describe diabetes, its complications and their treatments within the context of the NHS.

7.2.1 Definition of diabetes

Diabetes mellitus (DM) is a group of disorders that share common features, notably impaired glucose metabolism.[306] Diabetes is a chronic and progressive disease. The most common are Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) and, to a lesser extent, gestational diabetes. Symptoms of diabetic disorders include weight loss, blurred vision, polydipsia, polyuria, polyphagia, repeated skin infections and tiredness.[307-309] T1DM often has a rapid onset and commonly occurs at a younger age compared to T2DM.[308]

Signs of T1DM also include hyperglycaemia (random testing of blood glucose concentration higher than 11 mmol/litre and ketonuria), acidosis and ketonaemia.[308,310] In contrast, patients with T2DM may present with non-specific symptoms or be asymptomatic.[309,311] Patients are considered to have T2DM if they do not have T1DM, monogenic or secondary diabetes.[311] Diabetes is diagnosed by the presence of the acute hyperglycaemic symptoms listed at the start of this paragraph and/or the following test results with at least two tests performed on different days:

- Fasting plasma glucose ≥ 7.0mmol/litre (l) or 126mg/decilitre (dl), or
- Random venous plasma glucose concentration ≥ 11.1mmol/l or 200mg/dl, or
- 2 hour plasma glucose concentration ≥ 11.1mmol/l or 200mg/dl 2 hours after 75g oral glucose tolerance test (OGTT).[306,309]

7.2.2 Prevalence of diabetes

Diabetes is a major global health problem, with a worldwide projected prevalence of 4.4% by 2030.[312] Approximately 90% of people with diabetes have T2DM. Historically, T1DM has been the most prevalent form of diabetes in younger people. It is most commonly diagnosed in children aged between 10 and 14 years.[313] In recent years, not only has there been a continuing rise in the incidence of T1DM in children,[314,315] but there are also more diagnoses of T2DM in young people across the world.[316-318] Approximately 23,000 people aged under 25 years have been diagnosed with diabetes in the UK, of which 20,500 people were diagnosed with T1DM.[319]

In England, 2.9 million adults have been diagnosed with diabetes and the prevalence is expected to reach 4 million people by 2025.[210,320] The accuracy of diabetes diagnosis in the UK has been under scrutiny, with undiagnosed diabetes estimated to affect one percent of the UK population.[321-323] As a consequence of the rising new cases of diabetes, there are considerable demands on health resources. A key method of ameliorating the burdens of diabetes care on the health and social system is the reduction of preventable diabetic complications.

7.2.3 Diagnosis, treatment and management

To address the challenge of meeting the needs of patients with diabetes, one needs to consider the schema of public health - prevention, diagnosis, treatment and management. In England there are national policies that cover these four tenets for a number of diseases and conditions, with the aims of improve the quality of care and reducing variation in patient outcomes across the country. For diabetes, there is the National Service Framework (NSF) for diabetes.[324,325] Despite almost a decade of implementing the NSF, there remains unacceptable national discrepancies in the quality of care for patients with diabetes.[326]

I now briefly map diabetes to the mentioned schema, at the point of diagnosis. Diabetes can be diagnosed by symptoms, during a routine health check or when a patient presents with a diabetic, typically hyperglycaemic, emergency. Confirmation of diagnosis is through measurement of glycaemic status. Treatment for diabetes may involve insulin and/or medication. Education and lifestyle changes, such as controlled diet and exercise, are important in managing diabetes. There is a strong emphasis on diabetes care being delivered by integrated multidisciplinary teams (MDTs), including a structured educational programme on treatment regime, diet and self-management.[308,311] For patients aged under 18 years who have suspected T1DM, same day referral to specialist paediatric diabetes care is recommended by the National Institute for Clinical Excellence (NICE).[308]

7.2.4 Diabetic complications

Compared to the general population of the same age, patients with T1DM have approximately 2.6 times greater risk of death and patients with T2DM have approximately 1.5 times greater risk of death.[327] Along the continuum of undesirable outcomes in patients with diabetes, a wide range of complications are associated with the disease. While the aetiologies of insulin-dependent and non-insulin dependent diabetes are markedly different, the sequelae of the two disorders are similar.[310] These can be classed as macrovascular (such as cardiovascular disease - angina, myocardial infarction, cardiac failure and stroke), microvascular (such as diabetic retinopathy, neuropathy and nephropathy) and other complications (such as sexual dysfunction, complications during pregnancy, depression and psychological ill-health).[306,308,311]

7.2.5 Diabetic emergencies

Acute diabetic complications resulting in medical emergencies can arise from extremely high blood glucose levels (hyperglycaemia). In patients with T1DM, diabetic ketoacidosis (DKA) is the more common form of hyperglycaemic emergency. In patients with T2DM, Hyperosmolar Hyperglycaemic State (HHS) also known as hyperosmolar non-ketotic (HONK) coma is more common.[307] Patients may also fall into a diabetic coma when they have low blood glucose levels (hypoglycaemia). These hyperglycaemic and hypoglycaemic complications are hereafter collectively referred to as diabetic emergencies. Such states, especially diabetic ketoacidosis, can be secondary to severe acute diseases, such as myocardial infarction and pneumonia.[328] Other precipitating factors include poor insulin management (including non-compliance) and excess alcohol intake.[328-330]

7.2.5.1 Treating diabetic emergencies

Hospital treatment of diabetic emergencies is needed, unless there is an absence of dehydration or acidosis, in accordance with established clinical guidelines.[307-309,331] These emergencies affect a large proportion of patients with diabetes; approximately 11% of patients in England with T1DM experienced an episode of DKA between 2004 and 2009.[332] Even though the mortality rate for patients with DKA is declining in England (estimated at less than five percent of patients), emergency admissions for this preventable complication are increasing.[333] In England, the (indirectly standardised by age and sex) rate of admissions for DKA was 2.17 admissions per 10,000 resident population in 2002 compared to 2.68 admissions per 10,000 resident population in 2008.[205] Between April 2009 and March 2010, there were 14,183 emergency admissions for DKA in England, of which 20 percent were patients aged under 15 years.[334] Over half of patients aged under 20 years who are admitted for diabetes do not have a prior diagnosis of diabetes.[335]

There are a number of conditions that can arise during treatment of diabetic emergencies, and which may be useful external markers of the severity of the admission.[310] Four of the most common and serious adverse effects of treatment are (with corresponding ICD-10 diagnosis code in brackets):

- Hyperkalaemia (E87.5) and hypokalaemia (E87.6);

- Hypoglycaemia (E16.0, E16.1 and E16.2);
- Cerebral oedema (G93.6); and
- Pulmonary oedema (J81).

7.2.6 Burden of care

Diabetes-related care is extremely costly, requiring approximately ten percent of the NHS budget, equating to approximately £9 billion per year.[320] The estimated cost of managing the most common type of diabetes, T2DM, is between £1,080 and £1,738 per patient, per year.[336-338] One in ten patients admitted to hospital has diabetes. These patients account for an approximate excess of 81,000 bed days per year (based on the mean length of stay) and experience longer hospital stays and more readmissions than patients without diabetes.[337,339,340] As well as hospital costs and social services (such as residential or nursing care homes), additional management of microvascular and macrovascular complications contributes to an estimated spend of £5,132 per patient with diabetic complications.[337,341] Patients with diabetic complications, especially microvascular complications, are also more likely to have loss of earnings compared to patients with no complications.[342]

7.2.7 Recording of diabetes and diabetic complications

Data on diabetes care are collected for reimbursement, quality monitoring and research. Consequently, data for the whole country are available albeit with inconsistent quality.[133] Discharge coding of diabetes is poor for inpatient care, with approximately 24% of patients missing appropriate codes.[343] Within primary care, where the majority of diabetes care occurs, there are known coding and classification errors, including incorrect and under-diagnosis of diabetes.[323,344,345] Across classification systems, there are also irregularities in coding (Chapter 1 section 1.6.8). I will return to diagnosis coding later (section 7.3.1).

7.2.8 Rationale for analysis

I now summarise the issues raised so far in this chapter and in doing so, clarify the reasons for conducting this research. Firstly, acute diabetic emergencies can have potentially long term effects, such as permanent neurological impairment, and place great burdens on the health service. As diabetic emergencies are preventable, these conditions warrant investigation for the purpose of health service improvement. This belief is supported by

evidence of considerable variation across England in the rates of admissions for DKA and the treatment of this and other diabetic emergencies.[332,346] Partly as a consequence of regulatory performance reporting, national data collected on the management of diabetic emergencies are available for secondary analysis. These data have already shown promise for measuring the quality of primary care services.[297,347-349]

Theoretically, with the availability of effective treatments and explicit protocols for managing diabetes and associated complications, there should be low rates of serious morbidity and mortality in patients with diabetes (patient compliance permitting).[350] Of course, in reality, the situation is far more complex because patients with diabetes often have multiple chronic comorbidities as well as episodes of acute complications. As well as the behaviour of patients themselves affecting their outcomes, provider behaviour is also important. Studies have found complex associations between practice characteristics, such as nurse staffing levels, and diabetes care in primary care.[351-354]

In short, DKA and other acute emergencies are serious but avoidable complications of diabetes. Data on their treatments are captured in primary and secondary care computer systems. By examining emergency admissions for DKA and diabetic coma and patients' access of services, we can better understand the patient and organisational factors associated with the occurrence of these diabetic complications.

7.2.8.1 Aims of analysis

This study explores the characteristics of patients who had one or more emergency admissions for a diabetic emergency, namely diabetic ketoacidosis or coma due to hyperglycaemia or hypoglycaemia, in England between 1999 and 2008. Routinely collected data were used to address the objectives set out in the next section (section 7.2.8.2).

7.2.8.2 Objectives of analysis

The three objectives of the analyses were:

1. Determine the incidence of emergency admissions for diabetic ketoacidosis and diabetic (hyperglycaemic or hypoglycaemic) coma using linked GPRD and HES data in:
    a. all patients; and

   b. patients diagnosed with diabetes.
2. Identify predictors of emergency admissions for diabetic ketoacidosis or diabetic (hyperglycaemic or hypoglycaemic) coma in patients diagnosed with diabetes.
3. Describe the patterns of service use (consultations and emergency admissions) of patients who have at least one emergency admission for diabetic ketoacidosis or diabetic (hyperglycaemic or hypoglycaemic) coma.

7.3 Methods

A cross-sectional approach was used to measure the rate of unplanned admissions for diabetic emergencies. Crude and adjusted (indirectly standardised by age and sex) rates were calculated for the two denominator populations – all patients and patients with known diabetes. Analyses were focused on patients with diabetes as the conditions of interest are predominantly complications of the disease and preventable in diagnosed patients. For more details about the standardisation method, Chapter 4 section 4.7.1.

7.3.1 Defining diabetes

Read codes for diabetes were extracted from the NHS Clinical Terminology Browser (Appendices Table A.13).[284] Further aggregation of diabetes types was made to avoid problems with small numbers in analyses (Table 6.1).

Table 7.1 Original and aggregated groupings of diabetes by type

Type of diabetes	Aggregated group
Type 1 (Insulin-dependent) diabetes mellitus	Type 1
Type 2 (non-insulin-dependent) diabetes mellitus	Type 2
Gestational diabetes mellitus	Other
Malnutrition diabetes mellitus	Other
Neonatal diabetes mellitus	Other
Other diabetes mellitus	Other
Unspecified diabetes mellitus	Other

To ensure complete identification of patients with diabetes, as well as using Read codes for the corresponding types of diabetes shown in Table 7.1, the description of the medical code (unique GPRD code for the term selected by the person who entered the data at GP practice)

was also used to select patients who did not have a diabetes diagnosis recorded elsewhere (Appendices Table A.14). These diabetes-related terms were grouped as shown in Table 7.2.

Table 7.2 Clinical entries related to diabetes

GPRD Entity Code	Category
18	Diabetic register
22	Diabetes annual check
26	Current Diabetes status
59	Ankle neuropathy
65	Diabetic consultation
91	Diabetes concerns
97	Insulin dosage
117	Foot pulse right leg
118	Foot pulse left leg
134	Visual acuity right eye
135	Visual acuity left eye

7.3.2 Diseases associated with diabetes

To meet the overarching study aim and study objective number 3, diagnoses related to diabetes were identified to better ascertain the service use and outcome (death) of patients diagnosed with diabetes and who had at least one diabetic emergency admission. Diabetes-related diagnoses used in the 2010/11 National Diabetes Audit were applied, along with adapted version of diagnoses grouped by McEwen et al[*].[355,356] Other diagnoses related to diabetes were added, including drug-related outcomes in young people with T1DM.[329]

7.3.3 Defining diabetic emergency

In section 7.2.7 and Chapter 1 section 1.6.8, I raised the issue of variation in coding between classification systems. One example is the lack of distinction between hyperglycaemic and hypoglycaemic comas in the ICD-10 system where diabetes mellitus with any coma is denoted by the fourth character subdivision of ".0" and ketoacidosis with the subdivision of

[*] McEwen et al are reported to have included ICD-10 codes V00-V89. I have used an expanded set of codes, ICD-10 V01-99, as there is no ICD-10 V00 code block and there also seems to be no good reason to exclude the V90-99 codes.[355]

".1". In contrast, there is separation of diabetic comas in the Read classification system (Appendices Table A.15).

In these analyses, HES data were used to identify emergency admissions for hyperglycaemic emergencies and therefore the ICD-10 coding distinctions applied. The definition of emergency admission has been stated in Chapter 3 section 3.9.3. Guided by these classifications, diabetic emergencies were categorised as being either diabetic ketoacidosis or diabetic coma. All causes of admission recorded in the HES linked dataset with ICD-10 E10-E14 codes and the fourth character of ".0" or ".1" were mapped to the appropriate complication. For convenience, emergency admissions for diabetic emergencies will hereafter be referred to by the abbreviation DEA (diabetic emergency admission).

7.3.4 Selection of predictor variables

Variables included in the analyses were chosen because of their known or suspected associations with diabetes and diabetic complications.[219,348,351,354,357]

7.3.5 Type of analysis

Only crude analyses were performed in this study. The decision not to conduct adjusted analyses was made in light of the exploratory nature of the study and the low numbers of patients with diabetes and DEAs identified over the ten years studied. As explained in Chapter 4 section 4.6, the log transformation of patients' follow-up time was included as an offset term in the regression models for predicting the risk of DEAs.

7.4 Results

Before presenting the estimated incidence of DEAs and analyses of risk factors and service usage, I describe the demography of the study sample.

7.4.1 Patient characteristics

The cleaned GPRD dataset (Chapter 3 section 3.7.5) contained the records of 74,763 patients at 457 GP practices. Among these patients, 1,359 were identified with a primary care diagnosis of diabetes (identified by Read codes) at 217 GP practices. There were 1,616 diagnoses of diabetes among the 1,359 patients (Table 7.3). Out of these diagnoses, 5.57%

of diagnoses were for type 1 diabetes, T1DM, (n=90/1,616) and 39.1% of diagnoses were for type 2 diabetes, T2DM (n=632/1,616). The majority of "Other diabetes" diagnoses were for unknown subtype (95.8%; n=460/480) (section 7.3.1). Comparing the types of diagnoses by sex, there was little difference in the number of T1DM diagnoses among male and female patients (n=49 and n=48, respectively). For recorded T2DM diagnoses, there were more diagnoses in male patients (52.5%; n=350/667) than female patients (47.5%; n=317/667). There was little difference the number of "Other diabetes" diagnoses between the sexes, with 49.3% of recorded and inferred (from medical code descriptions, section 7.3.1) diagnoses in male patients (n=660/1,338) compared to 50.7% of diagnoses in female patients (n=678/1,338). For T1DM, diagnoses were more common in younger patients, with 45.3% of diagnoses recorded in patients aged up to 44 years (n=44/97). For T2DM, 54.9% of diagnoses were in patients aged 65 years or older and there were no diagnoses in patients aged less than 15 years (n=366/667). For "Other diabetes", there were few recorded diagnoses at either extreme of age groups, with the most diagnoses in patients aged between 45 and 64 years out of all age groups (n=484/1,338).

Table 7.3 Types of diabetes diagnoses by age group and sex, n=1,359 patients

Age group (years)	T1DM				T2DM				Other diabetes			
	Males		Females		Males		Females		Males		Females	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
0-14	3	6.12	7	14.6	0	-	0	-	29	4.39	30	4.42
15-44	18	36.7	16	33.3	20	5.71	28	8.83	135	20.5	153	22.6
45-64	16	32.7	14	29.2	146	41.7	107	33.8	265	40.2	219	32.3
65-84	11	22.6	11	22.9	167	47.7	163	51.4	208	31.5	233	34.4
≥85	1	2.04	0	-	17	4.86	19	5.99	23	3.48	43	6.34

There were 32 patients who had one or more DEAs during the study period. Three of these patients did not have a primary care diagnosis of diabetes during the study period. Of the remaining 29 patients who were diagnosed with diabetes, 27 patients were diagnosed before their index DEA. The type of diabetes was unknown in approximately half of patients with a recorded diagnosis (48.1%; n=13/27), while 37% of patients received a diagnosis of T1DM before their first DEA (n=10/27). Only one patient who had a DEA also had a recorded complication of treatment, hypokalaemia, for the same admission (section 7.2.5).

7.4.2 Multiple admissions

The majority of patients had one DEA during the study period, ranging up to 6 DEAs per patient. The most DEAs occurred in 2008 (n=10) and the fewest DEAs occurred in 1999 and 2002, when there was only one DEA during each year (Table 7.4).

Table 7.4 Number of diabetic emergency admissions (DEAs) by discharge year, n=32 patients

Discharge year	DEAs, n	(%)	Patients, n
1999	1	(2.38)	1
2000	3	(7.14)	3
2001	3	(7.14)	3
2002	1	(2.38)	1
2003	2	(4.76)	2
2004	6	(14.3)	5
2005	8	(19.2)	7
2006	6	(14.3)	6
2007	2	(4.76)	2
2008	10	(23.8)	7

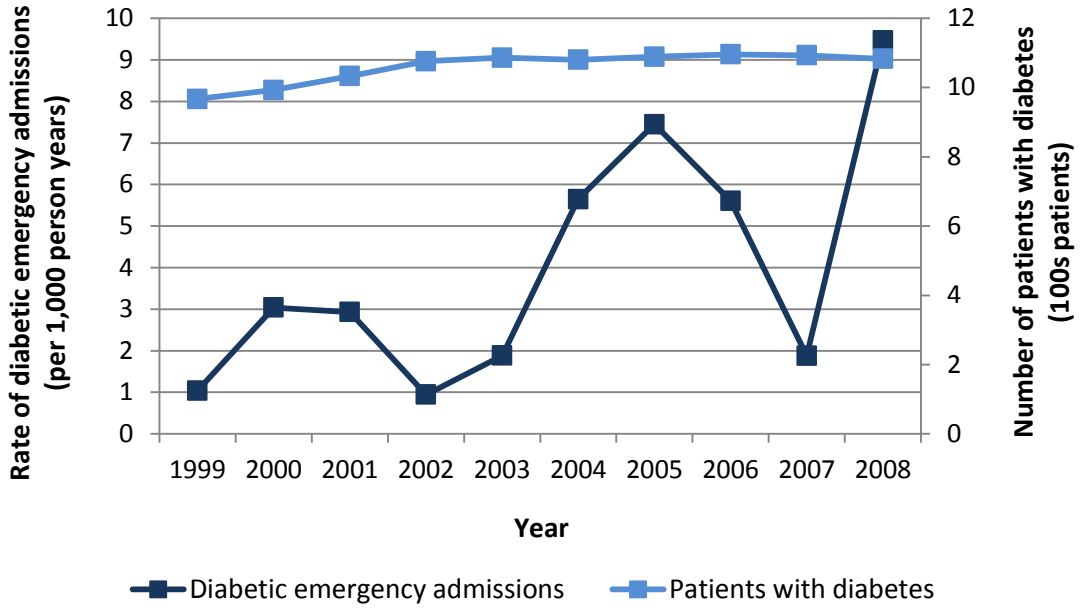
7.4.3 Incidence

There were 42 DEAs in 32 patients at 28 GP practices between 1999 and 2008. The overall follow-up time was 341,261 person years. From the sample of 74,763 patients, there was a rate of 0.12 DEAs per 1,000 person years during the study period.

7.4.3.1 Incidence in patients with diabetes

Over the ten years studied, there were 3.97 DEAs per 1,000 person years in patients with diabetes, with 10,571 person years of follow-up time. There were marked fluctuations in the overall rate of DEAs, ranging from 0.94 DEAs per 1,000 person years in 2002 to 9.47 DEAs per 1,000 person years in 2008 (Figure 7.1).

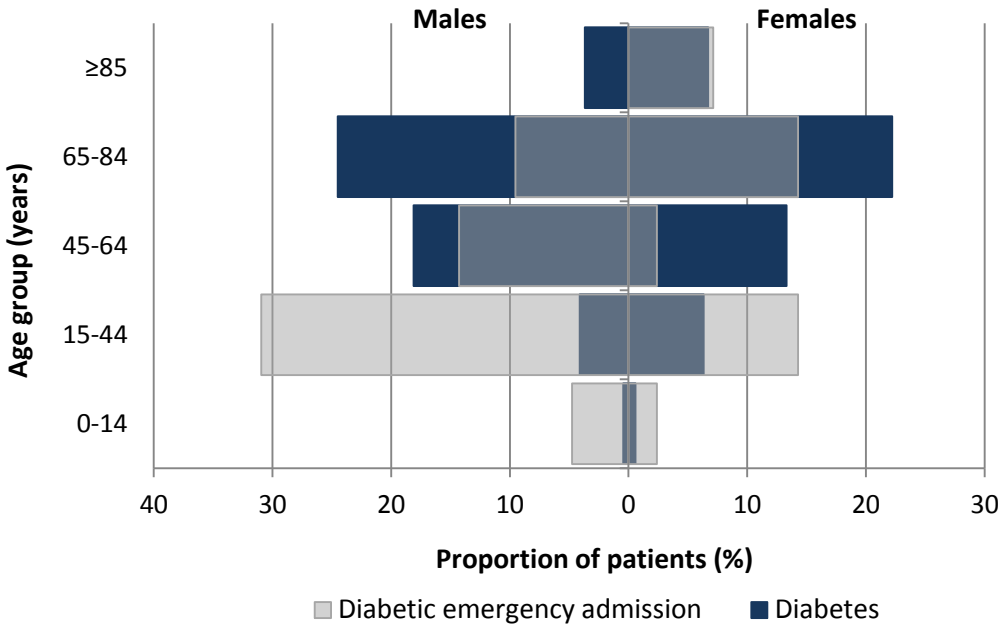
Figure 7.1 Rates of diabetic emergency admissions and diabetes by year, 1999-2008



There was wide variation between patients of different age groups in the rate of DEAs. Limited interpretations of the rates can be made given the low number of admissions during the study period. There were no admissions in at least three years for patients in each of the five age groups. The number of male (n=15) and female (n=14) patients who had at least one DEA was similar but the number of DEAs per patient was greater in male patients, and so there was a greater rate of DEAs in male patients compared to female patients, 4.67 DEAs per 1,000 person years compared to 3.26 DEAs per 1,000 person years.

Figure 7.2 shows that compared to the age and sex distribution of the study sample, the greatest proportion of DEAs was in male patients aged between 15 and 44 years (n=13/42 admissions). Compared to the proportion of patients in the diabetic sample, the proportion of patients who had DEAs in this sub-group was eight times greater (Figure 7.2).

Figure 7.2 Age and sex distribution of patients diagnosed with diabetes compared to those who had one or more diabetic emergency admissions, 1999-2008



The rate of diabetic emergency admissions ranged from 1.97 DEAs per 1,000 person years in patients aged between 65 and 84 years to 34.1 DEAs per 1,000 person years in patients aged 0 to 14 years during the study period (Table 7.5).

Table 7.5 Incidence rate by age group and follow-up time, per 1,000 person years

Age group (years)	DEAs, n	Person time (years)	Incidence rate (95% CI)
0-14	3	88.0	34.1 (7.03-99.7)
15-44	19	971.9	19.6 (11.8-30.5)
45-64	7	3435.7	2.04 (0.82-4.20)
65-84	10	5077.3	1.97 (0.94-3.62)
≥85	3	997.8	3.01 (0.62-8.79)

The prevalence of diabetes in the study population (in bold blue type) was lower than published national rates, based on data available during study period (Table 7.6). In fact, unlike the national trend of increasing prevalence, there was a decrease from 4.05 cases per 100 patients in 1999 to 2.69 cases per 100 patients in 2008. However, when comparing the estimated prevalence (cumulative frequency rather than point prevalence) from these

analyses with published estimates only for the three years where data from all sources were available, the estimated rates from this study lie between those from the National Diabetes Audit, QRESEARCH and QOF.[206,210,326]

Table 7.6 Comparison of national and study prevalence rates of diabetes mellitus (per 100 patients), 1999-2008

Dataset	Year									
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
NDA*					3.25	3.51	3.74	3.79	3.91	4.13
QOF†						3.34	3.55	3.65	3.87	4.07
QRESEARCH‡			1.18	1.36	1.58	1.96	2.27	2.57		
Study§	**4.05**	**3.86**	**3.28**	**3.23**	**3.20**	**2.86**	**2.82**	**2.72**	**2.70**	**2.69**

Sources: NHS Information Centre for Health and Social Care[210,326] and QRESEARCH.[206]

The estimated crude and standardised rates of DEAs fluctuated over the study period (in bold blue type), which was not reflected in the published estimates (Table 7.7). The crude rate of DEAs per 100,000 population was lower than published rates. Conversely, age and sex standardised rates of DEAs in the study sample were higher for 4 out of the 7 years where published data were available.

Table 7.7 National and study incidence rates of emergency admissions for diabetic ketoacidosis and diabetic coma (per 100,000 population), 1999-2008

Type of rate	Year									
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Crude**				21.5	21.5	22.5	24.4	25.8	26.6	26.8
Crude	**4.18**	**11.7**	**9.5**	**3.0**	**5.9**	**15.9**	**20.7**	**14.9**	**4.9**	**24.8**
Age and sex standardised††				21.7	21.5	22.6	24.4	25.8	26.7	26.8
Age and sex standardised	**11.4**	**31.8**	**26.0**	**8.2**	**16.1**	**36.2**	**49.7**	**40.8**	**13.6**	**47.8**

Sources: NHS Information Centre for Health and Social Care.[204,210]

*NDA data are for 1st January to 31st March of the following year. Patients with a first diabetes diagnosis during the audit year are excluded.
†QOF data are for the financial year - 1st April to 31st March of the following year.
‡QRESEARCH data are point prevalence estimates on 1st April of a given year.
§Study data are cumulative frequency counts for a calendar year.
**Denominator: ONS mid-year resident population estimate.
††Denominator: ONS mid-year resident population estimate.

7.4.4 Methodological issues

Given the excess of zero counts of the response variable (number of DEAs) in the study sample, modelling using zero-inflated Poisson (ZIP) regression was considered (Chapter 4 section 4.8.4.2). Despite the skewness, there was little variation in the number of recorded DEAs in the sample. All except five out of 1,359 patients had either no admissions or one admission for a diabetic emergency during the study period. With this distribution, one might consider fitting a binomial regression model using a binary outcome flag for "one or more DEAs" and "no DEAs". However, to incorporate the differences in the length of time that patients were included in the study (Chapter 4 section 4.5), Poisson regression with a continuous outcome variable was more appropriate for calculating relative risks. The second stage of crude analyses featured the generalized estimating equations (GEE) method to account for clustering at the practice-level (Chapter 4 section 4.8.2.2).

7.4.4.1 Exclusions from analyses

Several disease groups that feature in Charlson Index score categories were not included in crude or adjusted analyses due to low numbers or no occurrences of these diseases in the study sample during the study period. These diseases were cancer, cerebrovascular disease, hemiplegia, moderate liver disease, renal disease and rheumatological disease.

Crude Poisson regression models for several comorbidity markers failed to converge due to all patients having the condition. No outputs are provided for these conditions:

- Chronic Medical: Unstable - ADG 10;
- Chronic Specialty: Stable-Ear, Nose, Throat - ADG 13;
- Chronic Specialty: Unstable-Orthopedic - ADG 16;
- Chronic Specialty: Unstable-Ear, Nose, Throat - ADG 17;
- Chronic Medical: Stable - CADG6; and
- Endocrine - MEDC 6.

7.4.4.2 Final dataset for analyses

As stated in section 7.4.1, there were three patients who had DEAs but did not have a diagnosis of diabetes during the study period. These patients were excluded from further

analyses as the denominator group of interest was patients with diabetes. Thus, the following analyses used data on 1,359 patients who had a recorded diagnosis of diabetes at any time up to the end of the study period, including 29 patients who had at least one DEA, from 217 GP practices. Due to small numbers in some categories, the 10 original practice regions were combined into the four NHS SHA clusters (Appendices Table A.16).[358] P-values reported in this section are p<0.0001 unless stated otherwise.

7.4.5 Risk factors for diabetic emergency admissions

On average, patients were 57 years old (SD 17.3 years) when they entered the study (n=1,359). Patients who had at least one DEA were younger (mean 46 years, SD 22.1 years, n=29) than those who did not have any DEAs during the study period (mean 57 years, SD 17.1 years, n=1,330), p=0.011. In the overall sample, the average length of time that patients were registered at their GP practice before exiting the study was 18.9 (SD 14.9) years. Patients who had at least one DEA tended to have been registered for longer (mean 19.7 years, SD 14.8 years) than the other patients, although this difference was not statistically significant (p=0.781).

There was also no statistically significant difference in follow-up time between patients with diabetes who had at least one DEA (mean 8.43 years, SD 2.29 years) and those who did not (mean 7.76 years, SD 3.13 years), p=0.135. The Charlson Index score was low in both groups, but significantly different between patients who had at least one DEA (mean score 0.17, SD 0.38) and patients who did not have a DEA (mean score 3.26, SD 6.83, n=1,330), p=0.005.

Patients who had at least one DEA had fewer consultations at the GP practice, by telephone or home visit during the study period (mean 37.2 consultations, SD 35.2 consultations) than patients who did not have any DEAs (mean 78.6 consultations, SD 65.5 consultations, n=1,330), p<0.0001. Similarly, patients who had at least one DEA also had fewer admissions overall during the study period (mean 2.93 admissions, SD 2.42 admissions) compared to patients who did not have a DEA (mean 4.95 admissions, SD 7.90 admissions, n=1,155), p<0.0001. There was no difference in the number of referrals between those patients who had a DEA (mean 1.50 referrals, SD 0.58 referrals) and patients who did not (mean 1.92 referrals, SD 2.13 referrals, n=156), p=0.693.

7.4.6 Crude associations with diabetic emergency admissions

In crude analyses, the 95% significance level was assigned as the cut-off for determining the statistical significance of variables. At this level, ethnicity (p=0.068), number of consultations at the GP practice, by telephone or home visit (p=0.003) and the Charlson score (0.006) were associated with having a DEA.

Table 7.8 presents the crude Poisson regression results. Compared to patients with diabetes aged under 15 years (reference group), older patients were less at risk of having a DEA. In patients aged between 15 and 64 years when they entered the study, the relative risk (RR) was 0.27, 95% CI 0.08-0.90; p=0.032. In patients aged 64 years and older the RR was lowest at 0.22 (95% CI 0.06-0.80, p=0.021). Patients who had the most consultations at the GP practice, by telephone or home visit were least at risk of having a DEA (RR 0.29, 95% CI 0.11-0.77; p=0.013). Patients with higher Charlson Index scores were also less at risk of a DEA (RR 0.76, 95% CI 0.62-0.92; p=0.006). Further results by comorbidities are reported in the Appendices (Table A.17). These results include lower risk of DEA in patients with diabetes and chronic pulmonary disease (COPD) compared to patients without COPD (RR 0.24, 95% CI 0.06-0.99; p=0.048). Patients with diabetes and mild liver disease were at greater risk of a DEA than patients without mild liver disease (RR 6.75, 95% 0.93-49.19; p=0.059).

Table 7.8 Risk factors for diabetic emergency admission (DEA) in patients with diabetes, crude results from Poisson regression

Characteristic	Patients with diabetes, n			RR (95% CI)	P-value
	All	≥1 DEA*	(%)		
Age group at start of study (years)					0.141
<15	31	3	(9.68)	1	
15-64	841	18	(2.14)	0.27 (0.08-0.90)	0.032
≥65	487	8	(1.64)	0.22 (0.06-0.80)	0.021
Sex					0.297
Male	691	15	(2.17)	1	
Female	668	14	(2.10)	0.71 (0.38-1.35)	0.300
Ethnicity					0.068
White	304	4	(1.32)	1	
Non-white	965	24	(2.49)	2.61 (0.93-7.36)	0.069
Unknown	90	1	(1.11)	0.89 (0.10-7.92)	0.913
Marital status					0.118
Married	196	2	(1.02)	1	
Status other than married	76	2	(2.63)	2.78 (0.39-19.74)	0.306
Unknown	1087	25	(2.30)	3.45 (0.83-14.36)	0.088
Deprivation (quintiles)					0.279
Least deprived	309	6	(1.94)	1	
Quintiles 2,3,4	184	3	(1.63)	0.67 (0.17-2.59)	0.561
Most deprived	627	14	(2.23)	1.23 (0.51-2.94)	0.643
Unknown	239	6	(2.51)	1.98 (0.77-5.11)	0.157
Practice region					0.598
London	333	6	(1.80)	1	
Midlands and East	409	11	(2.69)	1.3 (0.50-3.34)	0.593
North	466	9	(1.93)	1.78 (0.74-4.30)	0.198
South	151	3	(1.99)	1.34 (0.39-4.56)	0.645
Time at practice (years)					0.975
Low	445	8	(1.80)	1	
Moderate	458	12	(2.62)	0.94 (0.40-2.22)	0.890
High	456	9	(1.97)	1.02 (0.44-2.38)	0.968
Continuity of care					0.432
Low or moderate	882	21	(2.38)	1	
High	446	8	(1.79)	0.73 (0.35-1.49)	0.386
Not valid	31	0	-	-	-
Consultations†					0.003
Low	438	12	(2.74)	1	
Moderate	456	11	(2.41)	1.14 (0.56-2.32)	0.711
High	465	6	(1.29)	0.29 (0.11-0.77)	0.013
Referrals					0.973
No	1199	25	(2.09)	1	
Yes	160	4	(2.50)	1.02 (0.40-2.60)	0.973
Charlson Index score, mean (SD)	3.20 (6.77)	0.83 (2.04)		0.76 (0.62-0.92)	0.006
Resource Utilization Band (RUB)					0.727
Healthy, low or moderate	232	5	(2.16)	1	
High to very high	1127	24	(2.13)	1.18 (0.46-3.01)	0.733

*DEA – Diabetic emergency admission.
†At GP practice, by telephone or home visit.

7.4.6.1 Crude associations with diabetic emergency admissions, adjusted for GP practice

The crude Poisson regression model for grouped continuity of care scores, with adjustment for clustering of patients in practices did not converge and so no results for this model are reported in Table 7.9. Once clustering was accounted for, only the number of consultations at GP practice, by telephone or home visit (p=0.031) and Charlson score (p=0.022) were statistically significantly associated with having a DEA in patients with diabetes. The relative risks did not differ between unadjusted (crude) and adjusted (for clustering) results, but confidence intervals were generally wider in the adjusted results and p-values also changed accordingly.

Compared to patients aged under than 15 years, adults remained less at risk of an unplanned admission for a diabetic emergency. The RR was 0.27 (95% CI 0.08-0.87; p=0.028) for patients aged between 15 and 64 years and RR 0.22 (95% CI 0.06-0.87; p=0.031) for patients aged 65 years and older. Compared to patients who had fewer consultations at the practice, by telephone or home visit, patients who had the greatest number of consultations were least at risk of a DEA (RR 0.29, 95% CI 0.11-0.78; p=0.015). A higher Charlson score had a protective effect against DEAs (RR 0.76, 95% CI 0.59-0.96; p=0.022). Patients with diabetes and COPD remained less at risk of a DEA than patients without COPD (RR 0.24, 95% CI 0.06-0.97; p=0.045) while patients with mild liver disease were more at risk of a DEA (RR 6.75, 95% CI 1.19-38.4; p=0.031). Further results by comorbidities are in the Appendices (Table A.18).

Table 7.9 Risk factors for diabetic emergency admission (DEA) in patients with diabetes, crude results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic	Crude		Adjusted	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Age group at start of study (years)		0.141		0.392
<15	1		1	
15-64	0.27 (0.08-0.90)	0.032	0.27 (0.08-0.87)	0.028
≥65	0.22 (0.06-0.80)	0.021	0.22 (0.06-0.87)	0.031
Sex		0.297		0.487
Male	1		1	
Female	0.71 (0.38-1.35)	0.300	0.71 (0.28-1.82)	0.479
Ethnicity		0.068		0.138
White	1		1	
Non-white	2.61 (0.93-7.36)	0.069	2.61 (0.88-7.72)	0.082
Unknown	0.89 (0.10-7.92)	0.913	0.89 (0.10-7.58)	0.912
Marital status		0.118		0.102
Married	1		1	
Status other than married	2.78 (0.39-19.7)	0.306	2.78 (0.39-19.7)	0.306
Unknown	3.45 (0.83-14.4)	0.088	3.45 (0.80-14.8)	0.095
Deprivation (quintiles)		0.279		0.583
Least deprived	1		1	
Quintiles 2,3,4	0.67 (0.17-2.59)	0.561	0.67 (0.18-2.46)	0.545
Most deprived	1.23 (0.51-2.94)	0.643	1.23 (0.46-3.30)	0.682
Unknown	1.98 (0.77-5.11)	0.157	1.98 (0.50-7.86)	0.330
Practice region		0.598		0.827
London	1		1	
Midlands and East	1.30 (0.50-3.34)	0.593	1.30 (0.46-3.66)	0.626
North	1.78 (0.74-4.30)	0.198	1.78 (0.57-5.56)	0.320
South	1.34 (0.39-4.56)	0.645	1.34 (0.34-5.22)	0.678
Time at practice (years)		0.975		0.986
Low	1		1	
Moderate	0.94 (0.40-2.22)	0.890	0.94 (0.38-2.33)	0.896
High	1.02 (0.44-2.38)	0.968	1.02 (0.32-3.28)	0.977
Consultations*		0.003		0.031
Low	1		1	
Moderate	1.14 (0.56-2.32)	0.711	1.14 (0.45-2.88)	0.776
High	0.29 (0.11-0.77)	0.013	0.29 (0.11-0.78)	0.015
Referral		0.973		0.977
No	1		1	
Yes	1.02 (0.40-2.60)	0.973	1.02 (0.34-3.07)	0.977
Charlson Index score	0.76 (0.62-0.92)	0.006	0.76 (0.59-0.96)	0.022
Resource Utilization Band (RUB)		0.727		0.714
Healthy, low or moderate	1		1	
High to very high	1.18 (0.46-3.01)	0.733	1.18 (0.47-2.93)	0.725

*At GP practice, by telephone or home visit.

7.4.7 Health service use

I now describe patients' health service access (consultations and emergency admissions) before and after their first unplanned admission for a diabetic emergency.

7.4.7.1 Consultations prior to index diabetic emergency admission

The majority of patients who had at least one DEA also had one or more consultations (in any location and with any type of staff) in the 12 months preceding their index DEA (n=27/32 patients, 377 consultations). In the 6 months before the index DEA, 78.1% of patients had at least one consultation (n=25/32 patients, 106 consultations). On average, these patients had 4 (SD 3.78) consultations each, ranging from 1 to 14 consultations per patient, in any location and with any staff type. Patients who had consultations at the practice, by telephone or home visit during the 6 month period had a total of 80 consultations (n=21 patients). On average, these patients had 4 (SD 2.75) consultations each, ranging from 1 to 10 consultations per patient. The majority of the 80 consultations were recorded as taking place with a GP (n=58; 72.5%).

7.4.7.2 Consultations after index diabetic emergency admission

Out of the 32 patients who had at least one DEA, 84.4% had one or more consultations at the GP practice, by telephone or home visit after their index DEA but also during the study period (n=27/32 patients, 656 consultations). Among these 27 patients, there was an average of 24 (SD 24.7) consultations per patient after the first DEA, ranging from 1 to 81 consultations per patient. From the 517 consultation records with valid time data, the average length of consultations post index DEA was 11 (SD 13.9) minutes, ranging from 1 to 249 minutes.

7.4.7.3 Admissions

On average, patients with diabetes had 4.31 (SD 7.50) admissions (all-cause), ranging from 0 to 189 admissions during the study period. There was little difference in the number of admissions (all-cause) between patients who had at least one DEA (median 3, IQR 2-5 admissions) and patients who did not have any DEAs (median 3, IQR 1-5 admissions).

7.4.7.4 Admissions before index diabetic emergency admission

In the 12 months before the index DEA, 28.1% of patients had an admission (n=9/32 patients, 10 admissions), 8 of these admissions (n=7 patients) occurred in the 6 months preceding the first DEA. Patient had an average of 1 (SD 0.33) admission each in the 6 months prior to the first DEA, ranging from 1 to 2 admissions per patient. The causes of these admissions included T1DM (n=1 admission), T2DM (n=6), stroke (n=2) and respiratory disease (n=2). Admissions may have had multiple recorded causes.

7.4.7.5 Admissions after index diabetic emergency admission

After their index DEA, 56.3% of patients had at least one further admission during the study period (n=18/32 patients, 53 admissions). These patients had an average of 3 (SD 2.53) admissions each, ranging from 1 to 11 admissions per patient. In the majority of admissions, diabetes was recorded as a cause of admission (n=42/53). Cardiovascular disease was also a common diagnosis (n=11/53). Less than one fifth of subsequent admissions were for diabetic emergencies, which included one admission for diabetic coma (n=5/18 patients, n=10/53 admissions).

7.4.8 Deaths

Of all the patients with diabetes, 256 died during the study period and one more patient died who had at least one DEA but was not diagnosed with diabetes before death (Table 7.10). Two deaths were of patients with recorded T1DM and 29 deaths were of patients with recorded T2DM. The remaining patients who died had recorded “Other diabetes” diagnoses. Over two thirds of patients with diabetes who died did not have diabetes listed as a cause of death (68.8%; n=176/256). Diabetes was recorded as the underlying cause of death of 12 patients with diabetes (4.69%) and as an additional cause of death of 68 patients (26.6%). Other causes of death included cardiovascular disease (26.2%; n=67/256), neoplasms (18.4%; 47/256), infection (6.25%; n=16/256) and renal failure (1.17%; n=3/256).

There were only three alcohol-related deaths, where one case was the underlying cause of death related to alcohol (alcoholic cirrhosis of liver). Alcoholic cirrhosis of liver, acute intoxication and alcoholic liver disease (unspecified) were recorded as secondary causes of

death of the three patients. None of these patients had T1DM or an unplanned admission for a diabetic emergency.

As for the four conditions that are potential complications of treating diabetic emergencies (section 7.2.5), three patients had pulmonary oedema recorded as a secondary cause of death and heart failure as the underlying cause. The eight patients who had one or more DEAs and died during the study period were aged between 38 years and 88 years at death, with an average age of 71.3 (SD 18.6) years. Six of these deaths were caused by diabetes, including one death attributed to diabetic ketoacidosis. In four out of the six deaths, the underlying cause of death was diabetes.

7.4.8.1 Crude associations with death

In addition to the comorbidity markers not presented in earlier results due to non-convergence of models (section 7.4.4.1), three other ACG flags (pregnancy - CADG 12, genetic - MEDC 12 and neonatal - MEDC 18) and the mild liver disease comorbidity flag were omitted from the results that follow as there were no deaths in patients who met the criteria for any these categories. In crude analyses using log-binomial regression, the models for grouped continuity of care scores and follow-up time (with death as the binary response) did not converge and so no results are reported for these two explanatory variables. P-values reported in this section are $p<0.0001$ unless stated otherwise.

Among the 1,359 patients with diabetes, 73.0% of patients were of non-white ethnicities, n=187/256 (Table 7.10). Patients in this sub-group had less risk of death (RR 0.87, 95% CI 0.79-0.96; p=0.007) compared to patients of white ethnicity, being registered at practices in northern areas of England increased the risk of death in patients with diabetes (RR 1.17, 95% CI 1.01-1.35; p=0.031). The Charlson Index and the majority of other comorbidity measures did not display statistically significant associations with risk of death in the study sample (Table 7.10 and Appendices Table A.19). Further results by comorbidities are in the Appendices (Table A.19). Unsurprisingly, patients with diabetic complications were at increased risk of death (RR 1.17, 95% CI 1.07-1.29; p=0.003) compared to patients without complications (Table A.19). However, having a DEA was not a significant predictor of death in patients with diabetes, p=0.725.

Table 7.10 Risk factors for death in patients with diabetes, crude results from log-binomial regression

Characteristic	Deaths, n			RR (95% CI)	P-value
	All	≥l DEA*	(%)		
Age group at start of study (years)					0.648
0-14	0	0	-	-	-
15-44	6	0	-	1	
45-64	55	1	(1.82)	1.23 (0.77-1.98)	0.391
65-84	175	6	(3.43)	1.24 (0.78-1.97)	0.369
≥85	20	0	-	1.30 (0.80-2.13)	0.286
Age group at study exit (years)					0.465
0-14	0	0	-	-	-
15-44	1	0	-	1	-
45-64	28	1	(3.57)	1.70 (0.42-6.84)	0.457
65-84	154	4	(2.60)	1.68 (0.42-6.74)	0.462
≥85	73	2	(2.74)	1.57 (0.39-6.30)	0.525
Sex					0.172
Male	123	3	(2.44)	1	
Female	133	4	(3.01)	1.07 (0.97-1.19)	0.174
Ethnicity					0.059
White	62	1	(1.61)	1	
Non-white	187	6	(3.21)	0.87 (0.79-0.96)	0.007
Unknown	7	0	-	0.96 (0.73-1.26)	0.767
Marital status					0.186
Married	29	0	-	1	
Status other than married	9	0	-	0.73 (0.49-1.10)	0.136
Unknown	218	7	(3.21)	0.94 (0.82-1.08)	0.378
Deprivation (quintiles)					0.775
Least deprived	53	3	(5.66)	1	
Quintiles 2,3,4	36	0	-	1.08 (0.92-1.27)	0.372
Most deprived	126	3	(2.38)	1.00 (0.87-1.15)	0.961
Unknown	41	1	(2.44)	0.99 (0.83-1.18)	0.876
Practice region					0.105
London	61	1	(1.64)	1	
Midlands and East	81	2	(2.47)	1.11 (0.95-1.29)	0.185
North	96	3	(3.13)	1.17 (1.01-1.35)	0.031
South	18	1	(5.56)	1.00 (0.77-1.29)	0.976
Time at practice					0.397
Low	89	2	(2.25)	1	
Moderate	83	2	(2.41)	0.97 (0.86-1.09)	0.614
High	84	3	(3.57)	0.92 (0.81-1.04)	0.182
Number of consultations†					0.128
Low	106	5	(4.72)	1	
Moderate	81	2	(2.47)	0.89 (0.79-1.00)	0.060
High	69	0	-	0.92 (0.81-1.04)	0.166
Referral					0.730
No	214	5	(2.34)	1	
Yes	42	2	(4.76)	1.02 (0.90-1.17)	0.723

*DEA – Diabetic emergency admission.
†At GP practice or by telephone and with GP or nurse.

Number of admissions					0.685
Low	39	1	(2.56)	1	
Moderate	96	3	(3.13)	0.95 (0.82-1.09)	0.452
High	121	3	(2.48)	0.94 (0.82-1.08)	0.356
Charlson Index score	4.95(8.28)	0.57(1.51)		1.00 (0.99-1.01)	0.511
Resource Utilization Band (RUB)					0.355
Low to moderate	29	2	(6.90)	1	
High to very high	227	5	(2.20)	0.93 (0.81-1.07)	0.298
Diabetic emergency admission (DEA)					**0.725**
No	**249**	**0**	**-**	**1**	
Yes	**7**	**7**	**(100)**	**0.94 (0.66-1.34)**	**0.746**

7.4.8.2 Crude associations with death, adjusted for GP practice

The following results are from crude log-binomial analyses that took into account clustering of patients at practices (Table 7.11). After adjusting for clustering by GP practice, non-white patients with diabetes remained less at risk of death compared to white patients (RR 0.87, 95% CI 0.79-0.97; p=0.010). Patients with diabetes registered at practices in northern England were still at greater risk of death compared to patients of practices in other regions of England (RR 1.17, 95% CI 1.03-1.33; p=0.020). Further results by comorbidities are in the appendices (Table A.20), these include greater risk of death in patients with unspecified diabetic complications (RR 1.17, 95% CI 1.06-1.29; p=0.001) compared to patients without any diabetic complications. Also, patients with diabetes and recorded myocardial infarction were at greater risk of death (RR 1.17, 95% CI 1.05-1.31; p=0.004).

Table 7.11 Risk factors for death in patients with diabetes, crude results from log-binomial regression using the generalized estimating equations (GEE) method

Characteristic	Crude		Adjusted	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Age group at start of study (years)		0.648		0.720
<15	-	-	-	-
15-44	1		1	
45-64	1.23 (0.77-1.98)	0.391	1.23 (0.76-1.99)	0.394
65-84	1.24 (0.78-1.97)	0.369	1.24 (0.77-1.99)	0.377
≥85	1.30 (0.80-2.13)	0.286	1.30 (0.80-2.12)	0.283
Age group at death (years)		0.465		0.595
<15	-	-	-	-
15-44	1		1	
45-64	1.70 (0.42-6.84)	0.457	1.70 (0.42-6.83)	0.457
65-84	1.68 (0.42-6.74)	0.462	1.68 (0.41-6.83)	0.466
≥85	1.57 (0.39-6.30)	0.525	1.57 (0.39-6.30)	0.525
Sex		0.172		0.180
Male	1		1	
Female	1.07 (0.97-1.19)	0.174	1.07 (0.97-1.19)	0.176
Ethnicity		0.059		0.058
White	1		1	
Non-white	0.87 (0.79-0.96)	0.007	0.87 (0.79-0.97)	0.010
Unknown	0.96 (0.73-1.26)	0.767	0.96 (0.73-1.26)	0.767
Marital status		0.186		0.197
Married	1		1	
Status other than married	0.73 (0.49-1.10)	0.136	0.73 (0.50-1.07)	0.105
Unknown	0.94 (0.82-1.08)	0.378	0.94 (0.84-1.05)	0.263
Deprivation (quintiles)		0.775		0.732
Least deprived	1		1	
Quintiles 2,3,4	1.08 (0.92-1.27)	0.372	1.08 (0.91-1.27)	0.377
Most deprived	1.00 (0.87-1.15)	0.961	1.00 (0.87-1.16)	0.964
Unknown	0.99 (0.83-1.18)	0.876	0.99 (0.81-1.19)	0.885
Practice region		0.105		0.126
London	1		1	
Midlands and East	1.11 (0.95-1.29)	0.185	1.11 (0.96-1.28)	0.160
North	1.17 (1.01-1.35)	0.031	1.17 (1.03-1.33)	0.020
South	1.00 (0.77-1.29)	0.976	1.00 (0.72-1.37)	0.980
Time at practice		0.397		0.341
Low	1		1	
Moderate	0.97 (0.86-1.09)	0.614	0.97 (0.87-1.08)	0.592
High	0.92 (0.81-1.04)	0.182	0.92 (0.82-1.03)	0.141
Number of consultations*		0.128		0.095
Low	1		1	
Moderate	0.89 (0.79-1.00)	0.060	0.89 (0.79-1.00)	0.058
High	0.92 (0.81-1.04)	0.166	0.92 (0.81-1.03)	0.154
Referral		0.730		0.726
No	1		1	
Yes	1.02 (0.90-1.17)	0.723	1.02 (0.90-1.17)	0.724
Number of admissions		0.685		0.640

*At GP practice or by telephone and with GP or nurse.

Low	1		1	
Moderate	0.95 (0.82-1.09)	0.452	0.95 (0.82-1.09)	0.460
High	0.94 (0.82-1.08)	0.356	0.94 (0.82-1.07)	0.332
Resource Utilization Band (RUB)		0.355		0.343
Low to moderate	1		1	
High to very high	0.93 (0.81-1.07)	0.298	0.93 (0.80-1.07)	0.320

7.5 Discussion

In the final section of this chapter, I present the key findings from the analyses and interpret the results in the context of existing evidence, before suggesting directions for further investigation.

7.5.1 Summary of main findings

The first objective of this chapter was to determine the incidence of emergency admissions for diabetic ketoacidosis and diabetic hyperglycaemic or hypoglycaemic coma (collectively referred to as DEAs). There was a low rate of DEAs in the study sample, estimated at 0.12 admissions per 1,000 person years between 1999 and 2008. In patients with diagnosed diabetes, the rate was higher at 3.97 admissions per 1,000 person years during the same ten year period.

The second objective was to identify predictors of DEAs in patients diagnosed with diabetes. Older age was associated with a lower risk of DEAs, patients with diabetes aged 65 years or older being least at risk of a DEA (RR 0.22, 95% CI 0.06-0.87; p=0.031). A high number of consultations at the GP practice, by telephone or home visit also had a protective effect against DEAs in patients with diabetes (RR 0.29, 95% CI 0.11-0.78; p=0.015). Patients with diabetes and more and/or complex comorbidities, measured by the modified Charlson Index, were least at risk of a DEA (RR 0.76, 95% CI 0.59-0.96; p=0.022).

The third objective was to describe the patterns of service use (consultations and emergency admissions) of patients who have at least one DEA. In the 6 months prior to the index DEA, 65.6% of patients with diabetes had at least one consultation at the GP practice, by telephone or home visit (n=21/32; 80 consultations) and 21.9% of patients with diabetes had an emergency admission (n=7/32; 8 admissions). There were eight deaths of patients who had one or more DEAs during the study period. Diabetes was recorded as the

underlying cause of death for six of the deaths. After adjusting for clustering of patients at practices, non-white ethnicity remained a protective factor against death in patients with diabetes (RR 0.87, 95% CI 0.79-0.97; p=0.010). Patients with diabetes registered at practices in northern areas of England (RR 1.17, 95% CI 1.03-1.33; p=0.020) and those who had diabetes and myocardial infarction (RR 1.17, 95% CI 1.05-1.31; p=0.004) were at greater risk of death. Patients who had diabetic complications, though not specifically diabetic ketoacidosis or diabetic coma, also had greater risk of death (RR 1.17, 95% CI 1.06-1.29; p=0.001).

7.5.2 Estimating rates

As with all analyses using data collected for other purposes, the quality of data may be sub-optimum for the needs of the research. In this study, calculations were affected by low numbers of both the numerator and denominator populations of interest. To meet the project aims of exploring several safety measures in general practice, the dataset obtained from the GPRD contained records for a cross sectional selection of patients at participating practices. For this reason, the dataset contained far fewer records for patients with the conditions of interest than if the cohort consisted only of the patient sub-groups of interest (patients with diabetes and patients who had one or more DEAs).

Nevertheless, the GPRD contains a representative sample of the general population and so, if there was a reasonable number of patients with the outcome in the dataset, one might expect calculated rates to be similar to published national estimates. The definition of "reasonable number" is subjective, yet in this study with 42 DEAs in 32 patients at 28 GP practices over a ten year period, one might consider the number to be low. Hence, caution must be made in interpreting the results. Findings of low rates and wide variation may also be artefacts of coding practices, whereby the recording of the variables of interest (such as diabetes) remains poor as the population increases. I will return to coding concerns later (section 7.4.7.5).

7.5.2.1 Rates of diabetes and diabetic emergency admissions

Even though there were few records of DEAs during the study period, this finding is of value given limited research about predictors for DEAs, especially using national datasets. The

availability of data over 10 years in this study also contributes to our understanding of national trends in DEAs over time. It is difficult to compare the results to published data given the unstable rates due to low numbers in this study. For example, contrary to results from the National Diabetes Audit (NDA), I found that the overall rate of diabetic emergency admissions was higher in male patients than female patients despite there being only one more male patient than female patients (Table 7.7).[359] The NDA data are less complete than QOF data and dependent on voluntary participation but, like in this study, it includes all patients with diabetes in analyses, regardless of age. Both the NDA and these analyses identified more male than female patients registered with diabetes, although population prevalence models used by the NDA predict a greater prevalence of diabetes in females.[326,360]

7.5.3 Risk factors

The finding that a high number of consultations at the GP practice, by telephone or home visit and the presence of complex and/or multiple comorbidities have protective effects against DEAs in patients with diabetes may seem counter-intuitive at first. Yet one might reason that increased contact with health services improves disease management and patient adherence to treatment, as well as prevention of disease complications. The relationships between patient factors were not investigated in this study but there are likely to be interactions between the volume of consultations, comorbidities and care needs. To screen for potential patient harm and be of relevance to clinical practice, further exploration of the associations between such characteristics must be made.

7.5.4 Deaths in patients with diabetes

As well as exploring risk factors for DEAs in patients with diabetes, this study also investigated predictors for death in these patients. In crude analyses, having one or more unplanned admissions for diabetic emergencies was not found to be a statistically significant predictor of death (p=0.725).

Excess deaths attributable to diabetes or of patients with diabetes are a public health concern, given that patients with diabetes have a markedly increased risk of death and the potential avoidability of many of these deaths.[361] Gulliford and Charlton (2009) and Walker

et al (2011) showed that for patients with T2DM aged 30 years or older, relative mortality was higher in female patients, those who were younger at diagnosis and also within the first two years after diagnosis.[357,362] Studies have shown wide variation across England in admission rates for diabetes (and acute diabetic complications) even where there is high attainment in incentivised quality measures for the disease.[219,348] Studies commonly identify an association between deprivation and adverse patient outcomes but socioeconomic deprivation demonstrates a complex relationship with other factors, including age and sex of patients.[348,357]

The results in this chapter indicated no distinction between types of diabetes in the relative risk of death. In crude regression analyses, with adjustment for clustering of patients at practices, no statistically significant difference was found between male and female patients in their risk of death (p=0.180). I included patients of all ages in the analyses and did not calculate age at diagnosis (unlike Gulliford and Charlton, 2009). Instead, I used ages at study entry and exit.[362] Neither of the age variables were significant risk factors for death (p=0.720 for age at study entry and p=0.595 for age at study exit). Deprivation, as measured by population-weighted quintiles converted from IMD scores, was not found to be a significant predictor of unplanned admissions for diabetic emergencies or death in patients with diabetes. However, the results may have been affected by how the IMD quintile variable was derived. The quintiles were accurate for the original GPRD dataset but I did not re-calibrate the quintiles in the final dataset after data cleaning; the quintiles were not weighted to the sample population but were weighted to the GPRD population.

Cardiovascular disease was the main cause of death in patients with diabetes in this study and patients who had a recording of myocardial infarction were at greater risk of death, reflecting evidence from the literature. There were few cases where diabetic emergencies and other diabetic complications were identified as a cause of death. It has been suggested that drug and alcohol-related deaths are common in young patients with T1DM.[330] With low numbers of patients with a recorded T1DM diagnosis over the ten year study period (1.07% of those diagnosed), it is difficult to generate meaningful interpretations of the results. Of the three patients with diabetes whose deaths were attributed to alcohol, none of them had a recorded diagnosis of T1DM. Under-reporting of diabetes in death certificates may also detrimentally affect the accuracy of estimates in this study.[355,363,364]

7.5.5 Undiagnosed diabetes

It is recognised that diagnosis of diabetes suffers from miscoding, misclassification and misdiagnosis.[321,323] There is controversy over the number of patients who present with DKA but who do not have a prior diagnosis of diabetes, with estimates from European countries ranging from 12.8% to over 50%.[335,365] Delayed diagnosis of T1DM, and hence lack of diabetes management, may be a reason for the increasing frequency of DEAs.[366,367] I did not explore this proposition because of the low numbers of patients who had a DEA in the sample. The picture is further clouded by indications that non-recording of diabetes in patients who are admitted to hospital and known to have diabetes does not have a detrimental effect on length of stay, day case admissions or readmissions.[368] This finding by Whitson et al suggests that diabetes may often be appropriately recorded in secondary care. Yet there remain the issues of non-diagnosis and delayed treatment of diabetes in general practice.[365,366]

7.5.6 Impact of general practice organisation

The anonymised nature of the GPRD dataset and limited detail about practices hampered the investigation of practice risk factors for DEAs. For example, one might expect the rates of DEAs to be lower at practices that offer diabetes clinics or specialist diabetes care.[369] Other practice characteristics such as baseline prevalence of diabetes, staffing levels and staffing types can also affect the number of diabetes-related admissions.[347] In this study, continuity of care was not found to be associated with risk of having a DEA but with more practice data, the nuances of continuity of care can be further explored. These aspects include practice size (ratio of staff to list size) and patient preferences for treatment and outcomes.[347,370,371]

7.5.7 Methodological issues

The analyses in this chapter benefitted from the availability of a large dataset with data spanning 10 years. It was possible to explore temporal trends in unplanned emergency admissions for diabetic emergencies and to perform preliminary investigations of service use prior to and after the DEAs. However, there were low numbers of the outcomes of

interest and therefore, interpretation of the results must be cautious. In the following sections, I outline the main methodological limitations of this study.

7.5.7.1 Selected variables

In observational research, there will be residual confounders. In these analyses, a small selection of variables was included and some potentially important factors were not accounted for. Certain patient characteristics are associated with increased risk of diabetic ketoacidosis and other diabetic emergencies, including younger age, lower body mass, lower parental educational attainment, preceding infection and psychological illness.[335,365,372] These known risk factors were not included in the analyses, except for age as a generic confounder, but they should be considered in future research, where possible and appropriate.

7.5.7.2 Accurate identification of patients

As diabetes is under-diagnosed and inconsistently coded, I attempted to improve the accuracy of identifying recorded diabetes diagnoses by including patients who did not have a recorded diagnosis but where coding indicated that diabetes was likely to be present (section 7.2).[373] It is known that data for younger patients are more prone to inconsistent coding.[345]

7.5.7.3 Data quality

The dataset was obtained under the now defunct MRC licence for academic research and so the granted linked HES and ONS data (GPRD Integrated dataset) were of a restricted nature (unlike the non-academic GPRD GOLD dataset, which allows for more extensive data extraction). Despite being nationally representative, data submitted to the GPRD by individual practices still varies in quality. For example, there were a large number of zero values for the length of consultation. Data in this field not only documents the duration of consultations, but also logs the length of time that the record was accessed (hence the consultation entries for less than one minute in length).[374] It is difficult to determine which records were for genuine consultations and which were not.

7.5.7.4 Limitations of data linkage

One major restriction of the GPRD integrated dataset was the availability of hospital data, and associated ethnicity status, for only 24,307 out of the 100,000 patients in the original dataset. There were even fewer records with linked death data from the ONS, with valid data for only 3,094 patients. Unlike the presence of a designated main (underlying) cause of death field, the dataset did not contain a field for the primary cause of admission. Therefore, it was not possible to distinguish between the main and secondary causes of admission or to accurately attribute admissions to diabetes (and diabetic complications). When determining the temporal placements of admissions, the date of discharge was used as date of admission was not available. As admission date missing, length of hospital stay was not measurable. The length of time between general practice contact and admission was also only crudely estimated using discharge date.

7.5.7.5 Coding inconsistencies

With the narrower definition of diabetes since the coding rules for QOF changed in 2006, one would expect more similarity between the prevalence estimates from the analyses and the QOF estimates from 2006 onwards (Table 7.6). Rather than the expected pattern, this study showed a slight decline in the prevalence of diabetes. This finding may be due to changes in coding practices over time beyond the QOF rules. The dataset is also affected by another caveat of GPRD data – incorrect recording of diagnosis date.[375] Instead of recording the first date that a patient presents with a disease or condition, used as a proxy measure of the index diagnosis, the date might instead be indicative of other events, including the first time that the information is entered onto the computer system or the first recording of an event that was discussed in a previous consultation.[375] There are secondary fields that may assist in determining the appropriateness of dates, such as episode type, but the completeness and accuracy of these fields are also uncertain.

7.5.8 Further research

To develop the analysis beyond that presented in this chapter, greater use of the GPRD dataset could be made. For example, indicators for family groups and also whether patients were receiving state welfare benefits could be used as proxy measures for risk factors

identified in other studies.[335,365,372] Other methods to improve the accuracy of identifying patients with diabetes include using prescribing data and clinical intermediate outcome markers such the levels of blood glucose (glycosylated haemoglobin, HbA_{1C}), blood pressure or cholesterol.[321,345,376] These measures can be used to assess the adequacy of diabetes control and overall quality of care. Additional data on the involvement of diabetes specialist teams in hospital admissions would improve assessments of adherence to policies on the management of diabetic emergencies.[310] Information on the number of bed days is also needed to determine whether younger patients are spending less time in hospital with DEAs than in previous years.[335,377]

7.5.9 Conclusion

These analyses were intended to provide a better understanding of the characteristics of patients with diabetes who have unplanned admissions for diabetic emergencies. As expected given the relatively young age of patients with T1DM which is most commonly associated with diabetic ketoacidosis, I found that adults were at less risk of having a DEA. Patients who had more consultations at the GP practice, by telephone or home visit and those who had more complex care needs were less likely to have a DEA. Admissions and consultations in the 6 months prior to the first DEA were common.

Although there were few deaths attributable to diabetic emergencies in patients with diabetes, there was a statistically significant difference in the risk of death between patients of white and non-white ethnicities. Patients with diabetes registered at practices in northern England, and those with recorded diabetes and myocardial infarction, were at greater risk of death. Based on these preliminary findings, further research may assist the identification of patients who are at the greatest risk of harm. Through engaging these patients in self-management, their quality of life can be improved and the burdens on the health system can also be reduced.

Chapter 8: First unplanned admissions for cancer

8.1 Chapter overview

This chapter contains the final analyses of the project. I examine the recording of first time unplanned (emergency) admissions for cancer in national data, as a proxy measure of cancer diagnosis by the emergency route. I present two separate pieces of analyses identifying risk factors for such admissions, firstly using secondary data from HES and then using general practice data from the GPRD. Results from both sets of analyses are then compared and discussed.

8.1.1 Acknowledgements

I conducted the analyses presented in section 8.2 (Study 1 – analyses using HES data) as part of a study in collaboration with Alex Bottle (lead researcher), Camille Parsons, Azeem Majeed, Michael Soljak and Paul Aylin at the Department of Primary Care and Public Health, Imperial College London. Preliminary analysis was performed by Camille Parsons. I conducted the final analyses for this study, with statistical input from Alex Bottle. All analyses of Study 2 (section 8.4) were performed by me.

8.2 Rationale

Cancer is the leading cause of mortality in adults aged under 75 years in England, with new cancer diagnoses estimated to reach 299,000 cases by 2020.[378,379] Over 30% of cancers are preventable and the majority of cancers are responsive to treatments.[380] As the delivery of chemotherapy and adjuvant regimes becomes more sophisticated and advances continue in our genetic understanding of the disease, we must ensure that patients receive safe and high quality care that enables them to achieve the best health outcomes possible. While

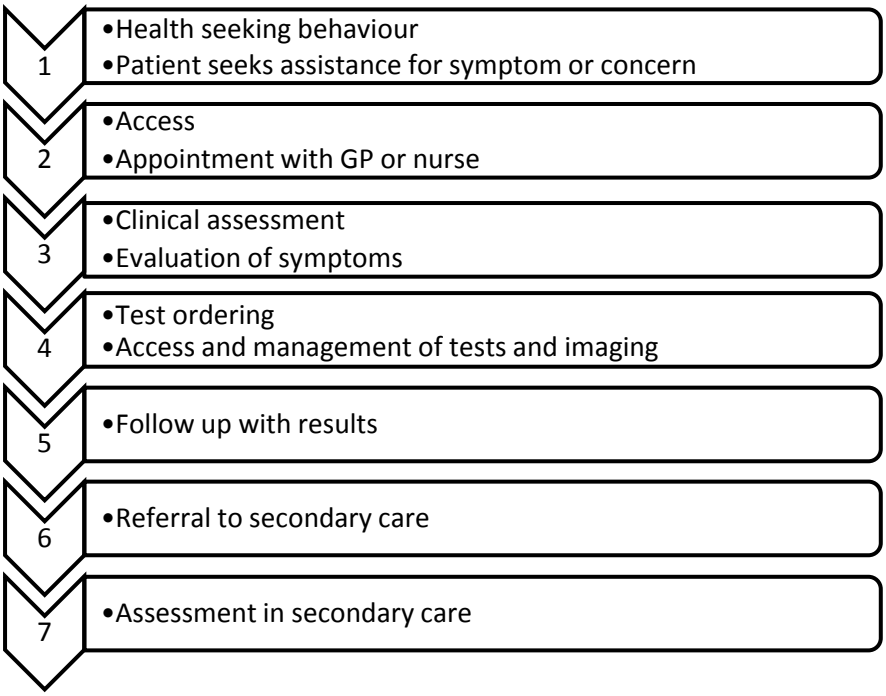
cancer survival rates are improving for the most common cancers (breast, lung, prostate and colon) in England, there is controversy over the quality, and in particular the efficiency, of cancer services compared to other countries.[381-383] Numerous studies have found the outcomes of patients with cancer to be relatively worse in England than in other countries in Europe, Canada and the United States of America.[384-386] It is believed that diagnostic errors and delays combined with late diagnosis of cancers are largely attributable to the relatively poor survival and high mortality rates.[386,387]

To reduce late diagnosis, as part of the government's Cancer Reform Strategy, the National Awareness and Early Diagnosis Initiative (NAEDI) was set up to promote the risks and symptoms of cancer among the general population, and to encourage early presentation and improve uptake of screening programmes.[378] Economic modelling for the five most common cancers in either sex, taking into account cancer stage at diagnosis, has demonstrated that earlier diagnosis improved patient outcomes (life expectancy) and increases cost-effectiveness in the NHS.[388] Analyses by the National Audit Office indicate that 532,000 bed days and £106 million per year can be saved through reductions in the number of emergency admissions and length of hospital stays.[389] At the local level, variation in the quality of cancer care across England has been noted. Differences extend from spending on cancer care, urgent referral rates, emergency admissions, to consultation patterns prior to referral.[83,389-391]

8.2.1 Role of primary care in cancer care

To improve the consistency of cancer care in England and to reduce diagnostic delays, primary care engagement is crucial.[392,393] The majority of patients begin their cancer care journey with one or more consultations with their GP, who act as the gatekeeper to further investigations and specialised treatment. Due to this, it is vital that GPs appropriately refer patients with suspected cancer for timely diagnosis and treatment. At any point along the primary care pathway (Figure 8.1), errors or inappropriate care may cause delays in referral and/or diagnosis.[387,394]

Figure 8.1 Primary care patient pathway



Source: National Patient Safety Agency, 2010.[394]

8.2.2 Definition of delayed and late diagnosis

Before exploring the emergency route to cancer diagnosis, it would be helpful to consider the terminology commonly associated with the early stages of a patient's cancer journey. The main two elements are presentation and diagnosis. The negative descriptions attached to these elements are typically "delayed", "late" and "missed". Presentation concerns the behaviour of patients in seeking health services. Diagnosis typically refers to health professional or health provider behaviour, but can be mediated by patient behaviour. Distinct patient groups have been identified as having greater risk of late presentation for suspected cancers.[387,395] It is not within the scope of my study to examine patient presentation and so I will proceed with a focus on the element of diagnosis.

Taking perhaps the most obvious description, "missed", we can define this as the failure to correctly diagnosis a cancer, whether cancer has been suspected or not. The definition of diagnosis as "late" is inconsistently applied but usually refers to cancer diagnosed at a late stage with considerable tumour growth and potential metastases.[396,397] The final description, "delayed" can refer to multiple points before diagnosis whereby timely diagnosis is

prevented. This includes the mediating effect of patient delay on prompt diagnosis, from initial signs and symptoms to contact with a health professional (usually a GP).[395]

As stated previously (section 8.2), delayed diagnosis is a key reason for poor patient outcomes, and can be attributed to patient, clinician or health provider behaviours. Common causes of delay by clinicians include misdiagnosis, inadequate examination, use of inappropriate tests and failing to act upon negative or inconclusive test results.[387,394,398] There are many causes of health system delays, including inadequate communication between primary and secondary care and errors in the processing of referral requests and results of investigations.[387,399] To improve patient outcomes, both "delayed" and "late" diagnoses of cancer need to be reduced. For this to be possible, the choices that patient make in accessing cancer care within the context of their overall health service usage must be understood.

8.2.3 Cancer diagnosis through the emergency route

Patients who are diagnosed with cancer via the emergency route (by unplanned admission) typically have later stage diseases and poor prognoses.[391,400] Emergency admission was defined in Chapter 3 section 3.9.3. Almost a quarter of patients diagnosed with cancer in England during 2007 presented as emergencies (23%, n=225,965), with wide variation in the number of admissions by cancer type and patient characteristics as well as between PCTs.[389,401] The presence of an active malignancy is a predictor of 7-day mortality in patients admitted as an emergency.[402] Any of these findings alone make reasonable grounds for further investigation but their collective presence indicates that closer examination is warranted for patients diagnosed with cancer by emergency presentation.

Research evidence shows that certain patient groups, such as those living in more deprived areas, with rarer cancers or who are relatively younger or older, represent a greater proportion of first emergency admissions for cancer.[391,403-405] With this knowledge, one might hypothesise that patients who are diagnosed with cancer during an emergency admission may have fewer comorbidities, and therefore have had fewer consultations and referrals prior to diagnosis, compared to patients diagnosed through the standard route of GP referral for specialist assessment.[391] The relationships between living in rural areas, distance to facilities for investigations and treatment, population demography, as well as

primary care attributes such as size of GP practices and GP training also warrant further attention.[406,407]

8.2.4 Aims and objectives

As part of the government priority to improve cancer outcomes, the number of patients diagnosed with cancer from emergency presentations must be reduced. In the next sub-section, I set out the overall aims and objectives of the two studies presented in this chapter. Study-specific aims are provided later.

8.2.4.1 Overall aims

To achieve improvements in cancer care, the characteristics of patients who are diagnosed by the emergency route and their access of health services prior to diagnosis must be better understood.

8.2.4.2 Overall objectives

To meet the aim stated in the previous section, the following objectives were identified:

1. Measure the rate of first emergency (unplanned) admissions for cancer.
2. Identify patient risk factors for first emergency admissions for cancer.
3. Identify GP practice risk factors for first emergency admissions for cancer.

8.2.5 Structure of this chapter

Unlike the presentation of analyses on adverse events in separate chapters (Chapters 5 and 6), analyses on first emergency admissions for cancer using GPRD and HES data are presented here in a single chapter. As a precursor to analyses with integrated HES, ONS and GPRD linked data, the ability to detect new cases of cancer using only data from secondary care (HES) was assessed. The methods and results of the two studies are presented separately. Descriptions of variables used in these analyses, cross-mapping of codes and descriptions of HES and GPRD data are documented in Chapter 3.

8.3 Study 1 – analyses using HES data

These analyses investigated the associations between patient and practice factors and first emergency admissions for cancer. Unlike anonymised GPRD data, HES data contains patient and practice identifiers that enable linkage with other data sources.

8.3.1 Aims of study 1

The first set of analyses in this chapter identified patient and GP practice risk factors for first unplanned (emergency) admissions for cancer in England, as a proxy measure of cancer diagnosis via the emergency route.

8.3.2 Methods

HES data for three financial years of 2007/8, 2008/9 and 2009/10 were analysed. The study sample consisted of all patients who had a first admission for cancer by any admission method, of which patients who had an emergency admission were of interest. Inpatients, day cases and regular day or night attenders with a primary cancer diagnosis were included. Patients' records were tracked back over 3 years to improve the accuracy of identifying true first cancer admissions.

8.3.2.1 Case ascertainment

Patients may have an unplanned admission for expected side effects of treatment, cancer symptoms or for comorbid conditions. The possibility of including these ineligible cases is reduced by investigating only those patients with a first emergency admission during the study period and with a first (primary) diagnosis of cancer (ICD-10 codes C00–C96, excluding ICD-10 codes C44 and C97.

8.3.2.2 Selection of variables

The variables included in analyses are shown in Table 8.1.

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Table 8.1 Patient and practice characteristics measured in the study

Patient factors	Practice factors
Age	GP age (whether 50 or older)
Sex	GP sex (proportion of female patients)
Ethnicity	Country of medical qualification
Cancer type	Practice list size
Deprivation	Number of full time equivalent (FTE) GPs in the practice
Rurality of residence	Deprivation of GP practice location
	Rurality of practice location
	QOF performance

8.3.2.3 Statistical method

First unplanned cancer admissions were analysed as a binary outcome measure (whether first cancer admissions were unplanned or not unplanned). Bivariate associations between patient and practice factors and the outcome were explored using chi-square test, Pearson's/Spearman's correlation coefficient and t-test/analysis of variance. Crude regression analyses to calculate odds ratios for the first cancer admission being unplanned were conducted. Adjusted regression was then performed, taking into account of clustering of patients in practices by using Generalised Estimating Equation (GEE). Further details about the statistical methods are provided in Chapter 4.

8.3.3 Results

Before presenting the analyses of risk factors, I describe the demography of the sample.

8.3.3.1 Study sample

During the three years studied, there were 4,272,780 patients who had an admission with a primary diagnosis of cancer. Following exclusion of patients who did not have a first time admission during the study period, who had an admission in the three years prior to their index admission, patients with a primary diagnosis code of malignant neoplasms of skin (ICD-10 code C44) or malignant neoplasms of multiple sites (ICD-10 C97) or patients of ineligible practices (missing QOF data, invalid practice codes, list size less than 500 patients), there remained 639,064 patients who had a first time admission for cancer. Of these patients, 21.8% had an unplanned admission (n=139,351/639,064).

8.3.3.2 Crude results

Table 8.2 shows that out of all patients who had a first admission for cancer, the greatest proportions of emergency admissions were in younger and older patients, especially patients aged 85 years or older (44.9%; n=22,367/49,786) and patients aged under 5 years (38.3%; n=783/2,044). Slightly more male patients had an emergency admission for cancer (22.8% compared to 20.9% of female patients who had an admission for cancer). Where ethnicity was known, patients of "other" ethnicities had the greatest proportion of emergency admissions (24.3%; n=1,455/5,978). Unplanned admissions were also greater in patients who were diagnosed with pancreatic cancer, acute leukaemia or bladder cancer (49%, 49.2% and 56.2%, respectively). Patients with Non-Hodgkin's lymphoma and lung cancer had the lowest proportion of emergency admissions (2.2% and 4.1%, respectively). Deprivation showed a linear relationship with emergency admissions for cancer, with the greatest proportion of unplanned admissions (26.4%) recorded in patients living in the most deprived areas (quintile 5).

Table 8.2 Characteristics of patients with a first cancer admission, 2007/08-2009/10

Characteristic	Patients with first cancer admission, n			
	All	Emergency	(%)	P-value
Age group (years)				<0.0001
0-4	2044	783	(38.3)	
5-14	2503	814	(32.5)	
15-44	50666	7041	(13.9)	
45-64	211785	32054	(15.1)	
65-74	175011	34225	(19.6)	
75-84	147269	42067	(28.6)	
≥85	49786	22367	(44.9)	
Sex				<0.0001
Male	312951	71349	(22.8)	
Female	326113	68002	(20.9)	
Ethnic group				<0.0001
White	531657	117837	(22.2)	
Mixed	2063	401	(19.4)	
Asian	11389	2486	(21.8)	
Black	9385	2092	(22.3)	
Other	5978	1455	(24.3)	
Not known	78592	15080	(19.2)	
Cancer type				<0.0001
Acute leukaemia	8336	4087	(49.2)	
Bladder	48333	3696	(56.2)	
Brain & central nervous system	13170	6484	(7.60)	
Breast	101506	4170	(9.40)	
Cervix	5964	779	(7.30)	
Chronic leukaemia	7192	1716	(13.9)	
Colorectal	80508	17285	(27.7)	
Kidney	13653	3157	(39.7)	
Larynx	4764	661	(18.0)	
Lung	62442	24803	(4.10)	
Melanoma	18933	414	(6.50)	
Multiple myeloma	9654	2674	(21.5)	
Non-Hodgkin's lymphoma	23541	5318	(2.20)	
Oesophagus	18946	3407	(22.6)	
Oral	9863	721	(11.7)	
Ovary	12079	3493	(23.9)	
Pancreas	13225	7436	(49.0)	
Prostate	55275	6487	(38.6)	
Stomach	13970	3684	(23.1)	
Testis	4732	445	(28.9)	

Uterus	16017	1036 (26.4)	
Other	96961	37398 (13.1)	
Deprivation (quintiles)			<0.0001
1 (least deprived)	131224	25373 (18.3)	
2	136924	27519 (19.8)	
3	133580	28537 (21.6)	
4	122964	28304 (24.0)	
5 (Most deprived)	113717	29436 (26.4)	
6 (Unknown)	655	182 (29.5)	
Rurality of residence			<0.0001
Urban >10K	496040	111039 (22.4)	
Town and fringe	72445	14897 (20.6)	
Village, hamlet and isolated dwellings	70170	13297 (18.9)	
Not resident in England	409	118 (28.9)	
Year of diagnosis			<0.0001
2007	206656	46421 (22.5)	
2008	214097	46713 (21.8)	
2009	218311	46217 (21.2)	

Note: Table has been published in Bottle et al, 2012.[185]

8.3.3.3 Adjusted results

Once adjusted for all other variables and clustering of patients at GP practices, compared to the oldest patients (aged 85 years or older), patients aged between 15 and 44 years were least likely to have an emergency admission for cancer with odds ratio (OR) 0.15, 95% Confidence Interval (CI) 0.14-0.15; p<0.0001. The adjusted results in Table 8.3 also show that patients who were female (OR 1.07, 95% CI 1.05-1.08; p<0.0001), Asian (OR 1.16, 95% CI 1.08-1.24; p<0.0001), with brain and central nervous system cancers (OR 1.99, 95% CI 1.92-2.07; p<0.0001), with pancreatic cancer (OR 1.91, 95% CI 1.84-1.99; p<0.0001), living in the most deprived (quintile 5) areas (OR 1.46, 95% CI 1.12-1.89; p<0.0001) or living in urban areas (OR 1.04, 95% CI 1.01-1.06; p=0.002) were most likely to have a first admission for cancer that was unplanned.

Table 8.3 Associations between patient characteristics and first unplanned admissions for cancer, crude and adjusted results

Patient characteristic	Crude		Adjusted	
	ORs (95% CI)	P-value	ORs (95% CI)	P-value
Age group (years)		<0.0001		<0.0001
0-4	0.76 (0.70-0.83)	<0.0001	0.20 (0.18-0.22)	<0.0001
5-14	0.59 (0.54-0.64)	<0.0001	0.17 (0.15-0.19)	<0.0001
15-44	0.20 (0.19-0.20)	<0.0001	0.15 (0.14-0.15)	<0.0001
45-64	0.22 (0.21-0.22)	<0.0001	0.20 (0.19-0.20)	<0.0001
65-74	0.30 (0.29-0.30)	<0.0001	0.26 (0.25-0.26)	<0.0001
75-84	0.49 (0.48-0.50)	<0.0001	0.43 (0.42-0.44)	<0.0001
≥85	1	-	1	-
Sex		<0.0001		<0.0001
Male	1	-	1	-
Female	0.89 (0.88-0.90)	<0.0001	1.07 (1.05-1.08)	<0.0001
Ethnicity		<0.0001		<0.0001
White	1	-	1	-
Mixed	0.83 (0.81-0.85)	<0.0001	0.87 (0.85-0.89)	<0.0001
Asian	1.13 (1.06-1.20)	<0.0001	1.16 (1.08-1.24)	<0.0001
Black	1.01 (0.96-1.06)	0.828	1.12 (1.05-1.18)	0.241
Other	0.98 (0.94-1.03)	0.404	1.03 (0.98-1.08)	0.212
Not known	0.85 (0.76-0.94)	0.003	0.93 (0.83-1.04)	<0.0001
Cancer type		<0.0001		<0.0001
Acute leukaemia	1.53 (1.46-1.60)	<0.0001	1.78 (1.69-1.87)	<0.0001
Bladder	0.13 (0.13-0.14)	<0.0001	0.10 (0.10-0.10)	<0.0001
Brain & central nervous system	1.55 (1.49-1.60)	<0.0001	1.99 (1.92-2.07)	<0.0001
Breast	0.07 (0.07-0.07)	<0.0001	0.07 (0.07-0.08)	<0.0001
Cervix	0.24 (0.22-0.26)	<0.0001	0.30 (0.28-0.32)	<0.0001
Chronic leukaemia	0.50 (0.47-0.53)	<0.0001	0.48 (0.45-0.51)	<0.0001
Colorectal	0.44 (0.43-0.45)	<0.0001	0.37 (0.36-0.38)	<0.0001
Kidney	0.48 (0.46-0.50)	<0.0001	0.50 (0.48-0.52)	<0.0001
Larynx	0.26 (0.24-0.28)	<0.0001	0.26 (0.23-0.28)	<0.0001
Lung	1.05 (1.03-1.07)	<0.0001	0.95 (0.93-0.98)	<0.0001
Melanoma	0.04 (0.03-0.04)	<0.0001	0.04 (0.03-0.04)	<0.0001
Multiple myeloma	0.61 (0.58-0.64)	<0.0001	0.55 (0.52-0.58)	<0.0001
Non-Hodgkin's lymphoma	0.47 (0.45-0.48)	<0.0001	0.47 (0.45-0.49)	<0.0001
Oesophagus	0.35 (0.34-0.36)	<0.0001	0.30 (0.28-0.31)	<0.0001
Oral	0.13 (0.12-0.14)	<0.0001	0.13 (0.12-0.14)	<0.0001
Ovary	0.65 (0.62-0.68)	<0.0001	0.68 (0.65-0.71)	<0.0001
Pancreas	2.05 (1.97-2.12)	<0.0001	1.91 (1.84-1.99)	<0.0001
Prostate	0.21 (0.21-0.22)	<0.0001	0.20 (0.19-0.20)	<0.0001
Stomach	0.57 (0.55-0.59)	<0.0001	0.45 (0.43-0.47)	<0.0001
Testis	0.17 (0.15-0.18)	<0.0001	0.30 (0.27-0.33)	<0.0001
Uterus	0.11 (0.10-0.12)	<0.0001	0.11 (0.10-0.11)	<0.0001
Other	1	-	1	-
Deprivation (quintiles)		<0.0001		<0.0001
1 (least deprived)	1	-	1	-
2	1.05 (1.03-1.07)	<0.0001	1.04 (1.02-1.07)	<0.0001
3	1.13 (1.11-1.16)	<0.0001	1.12 (1.09-1.15)	<0.0001
4	1.25 (1.22-1.27)	<0.0001	1.20 (1.17-1.23)	<0.0001
5 (most deprived)	1.61 (1.35-1.91)	<0.0001	1.46 (1.12-1.89)	<0.0001
6 (unknown)	1.46 (1.43-1.49)	<0.0001	1.36 (1.32-1.40)	<0.0001
Rurality of residence		<0.0001		<0.0001
Urban >10K	1.12 (1.09-1.14)	<0.0001	1.04 (1.01-1.06)	0.002
Town and fringe	1	-	1	

Village, hamlet and isolated dwellings	0.90 (0.88-0.93)	<0.0001	0.96 (0.93-0.99)	0.003
Not resident in England	1.57 (1.26-1.96)	<0.0001	1.03 (0.72-1.48)	0.876
Year of diagnosis		<0.0001		<0.0001
2007	1	-	1	-
2008	0.96 (0.95-0.98)	<0.0001	0.96 (0.94-0.97)	<0.0001
2009	0.93 (0.91-0.94)	<0.0001	0.91 (0.90-0.93)	<0.0001

Note: Table has been published in Bottle et al, 2012.[185]

Table 8.4 shows that patients of GP practices where none of the GPs received their medical qualification in the UK had a slightly higher odds of a first emergency admission (OR 1.08, 95% CI 1.04-1.11; p<0.0001). Patients registered at practices that received higher overall QOF performance scores were less likely to have an emergency admission for cancer (OR 0.94, 95% CI 0.91-0.97; p<0.0001). Patients at practices that had a greater mean score for provision of appointments within two working days were also less likely to have an unplanned admission (OR 0.85, 95% CI 0.79-0.92; p<0.0001).

Table 8.4 Association between GP practice characteristics and first unplanned admissions for cancer, crude and adjusted results

Practice characteristic	Crude		Adjusted	
	ORs (95% CI)	P-value	ORs (95% CI)	P-value
List size per 10,000 patients	0.94 (0.92-0.95)	<0.0001	0.97 (0.95-0.99)	0.014
FTE per 10,000 patients	0.98 (0.97-0.99)	<0.0001	0.99 (0.98-1.00)	0.001
Single handed practices				
Single GP	1.16 (1.12-1.19)	<0.0001	1.01 (0.96-1.06)	0.628
>1 GP	1	-	1	-
GPs aged 50 years and over		<0.0001		0.486
None	1	<0.0001	1	
Some	0.97 (0.95-0.99)	0.015	1.00 (0.97-1.02)	0.797
All	1.10 (1.06-1.14)	<0.0001	1.02 (0.98-1.06)	0.343
GPs qualified in the UK		<0.0001		<0.0001
None	1.23 (1.19-1.26)	<0.0001	1.08 (1.04-1.11)	<0.0001
Some	1.06 (1.04-1.08)	<0.0001	1.04 (1.02-1.06)	0.001
All	1	-	1	-
Female GPs		<0.0001		0.31
None	1	-	1	
Some	0.88 (0.86-0.90)	<0.0001	0.98 (0.95-1.01)	0.205
All	0.98 (0.93-1.04)	0.553	1.02 (0.96-1.08)	0.594
Practice deprivation average score[*]	1.01 (1.01-1.01)	<0.0001	1.00 (1.00-1.00)	0.002
Practice deprivation quintile[†]				
<5	1	-	1	-
5 (most deprived)	1.23 (1.21-1.26)	<0.0001	1.01 (0.98-1.03)	0.576
Practice deprivation quintile[‡]		<0.0001		<0.0001
1 (least deprived)	1	-	1	-
2	1.03 (1.01-1.05)	0.011	0.95 (0.93-0.98)	<0.0001
3	1.08 (1.06-1.11)	<0.0001	0.92 (0.90-0.95)	<0.0001
4	1.16 (1.14-1.19)	<0.0001	0.91 (0.88-0.93)	<0.0001
5 (most deprived)	1.31 (1.27-1.34)	<0.0001	0.93 (0.90-0.96)	<0.0001
Rurality of practice[§]		<0.0001		0.33
Urban >10K	0.95 (0.90-0.99)	0.01	1.02 (0.99-1.06)	0.192
Town and fringe	1		1	
Village, hamlet and isolated dwellings	1.13 (1.11-1.16)	<0.0001	0.99 (0.95-1.04)	0.809
QOF total practice performance score[**]	0.85 (0.83-0.88)	<0.0001	0.94 (0.91-0.97)	<0.0001
QOF CANCER01 indicator				
Diagnosis always recorded	1	-	1	-
Diagnosis sometimes or never recorded	0.90 (0.61-1.32)	0.576	0.75 (0.55-1.01)	0.052
QOF CANCER03 indicator				
Patient always reviewed	1	-	1	
Patient sometimes or never reviewed	1.02 (1.00-1.03)	0.06	1.01 (0.99-1.02)	0.567
QOF PE07 indicator[††]	0.72 (0.68-0.77)	<0.0001	0.85 (0.79-0.92)	<0.0001
QOF PE08 indicator[‡‡]	0.83 (0.79-0.87)	<0.0001	0.98 (0.92-1.04)	0.52

Note: Table has been published in Bottle et al, 2012.[185]

[*] Deprivation variables were included in the models one at a time.
[†] Deprivation variables were included in the models one at a time.
[‡] Deprivation variables were included in the models one at a time.
[§] Data missing for 1,013 patients at 10 practices.
[**] Per 100 points.
[††] Appointments within 2 working days (48 hours).
[‡‡] Appointments more than 2 days in advance.

I discuss these results and those of study 2 in section 8.4.4.

8.4 Study 2 – analyses using GPRD data

To improve the accuracy of case ascertainment (correct identification of patients with a first emergency admission for cancer), additional information is required beyond hospital data. When only secondary care data are used, false positive classification of patients as new cases may occur in patients with no previous admission for cancer. On the contrary, these patients may have existing cancer diagnoses not recorded in secondary care data.

8.4.1 Aims of study 2

The second set of analyses in this chapter continued to explore risk factors for first unplanned admissions for cancer in England. As with study 1, this outcome was considered to be a proxy measure of cancer diagnosis via the emergency route. In addition, I estimated the incidence of cancer diagnosis by emergency admission and explored patients' use of health services before admission.

8.4.2 Methods

Data were obtained for patients registered at GP practices that contributed to the GPRD during the study period, 1st January 1999 to 31st December 2008.

8.4.2.1 Case ascertainment

Patients were identified as having a first diagnosis of cancer if they had a valid recorded cancer diagnosis in their general practice records or their emergency admission records, defined by Read codes and ICD-10 codes, respectively. Of these patients, those who were diagnosed by an emergency admission were identified. The diagnosis codes used in sample selection are documented in Appendices Table A.21 and excluded codes in Appendices Table A.22.

Eligible patients were those who had a first recorded cancer diagnosis at any time between 1st January 1999 (or date of study entry, whichever occurred last) and 31st December 2008 (or date of study exit, whichever occurred first). To ensure that the diagnosis corresponded to the patient's first-ever diagnosis, diagnoses beginning from the first record were checked

for valid cancer codes. Where patients had a valid diagnosis of cancer prior to their first diagnosis during the study period, these patients were excluded as false positive cases.

8.4.2.2 Selection of variables

Given limited information about GP practices in the GPRD dataset, only patient characteristics were measured, except for the geographical region of the GP practice location. The selected variables were, in alphabetical order:

- Admissions before diagnosis;
- Age at diagnosis;
- Comorbidity (derived from Charlson Index score and Johns Hopkins ACG case-mix system);
- Consultations before diagnosis;
- Continuity of care;
- Ethnicity;
- Follow-up time;
- Length of time at practice;
- Marital status;
- Deprivation status;
- Practice region;
- Referrals before diagnosis; and
- Sex.

Further information about the selection of variables can be found in Chapter 3.

8.4.2.3 Statistical method

Details of the analysis techniques used in this study have been described in Chapter 4. Crude and adjusted analyses to identify predictors for diagnosis of cancer by emergency admission were conducted using the PROC GENMOD procedure in SAS. As the outcome of interest was discrete in nature, taking one of two values, the data were assumed to fit a binomial distribution. Accordingly, the “log” link function was used in PROC GENMOD to generate crude relative risks, RRs (Chapter 4 section 4.5.1). Adjusted RRs were calculated using

Poisson regression with GEE because models using log-binomial regression with GEE failed to converge (Chapter 4 section 4.5.1).

8.4.3 Results

Before presenting the estimated incidence of first unplanned admissions for cancer and analyses of risk factors and service use, I describe the demography of the sample.

8.4.3.1 Patient characteristics

Out of the 74,763 patients in the cleaned dataset, 5,870 patients had a first diagnosis of cancer at 445 GP practices during the ten years studied. Of these patients, 13.9% were diagnosed during an unplanned admission (n=817/5,870). The majority of patients who received a new cancer diagnosis during an emergency admission had one recorded cancer diagnosis, based on ICD-10 codes (81.0%; n=731/903) with a maximum of two cancer diagnoses during one episode of care. The number of new cancer diagnoses recorded by ICD-10 codes mapped to Read codes ranged between one diagnosis per patient (60.5%; n=715/1,181) and four diagnoses per patient (0.34%; n=4/1,181). Almost all patients who were diagnosed with cancer for the first time by a non-emergency route had only one recorded cancer diagnosis (99.3%; n=5,035/5,071).

Table 8.5 shows the cancer type that was most commonly recorded as the cause of emergency admission was “Other” types of cancer (21.4%; n=193/902), followed by breast cancer (13.6%; n=123/902), then colorectal cancer (11.5%; n=104/902).

Table 8.5 Number of first unplanned admissions by cancer type (ICD-10 codes), n=902 diagnoses

Cancer type	Frequency, n	(%)
Acute leukaemia	8	(0.89)
Bladder	54	(5.99)
Brain & CNS	16	(1.77)
Breast	123	(13.6)
Cervix	7	(0.78)
Chronic leukaemia	9	(1.00)
Colorectal	104	(11.5)
Kidney	21	(2.33)
Larynx	2	(0.22)
Lung	95	(10.5)
Melanoma	10	(1.11)
Multiple myeloma	16	(1.77)
Non-Hodgkin's lymphoma	37	(4.10)
Oesophagus	31	(3.44)
Oral	11	(1.22)
Ovary	18	(2.00)
Pancreas	16	(1.77)
Prostate	84	(9.31)
Stomach	17	(1.88)
Testis	8	(0.89)
Uterus	22	(2.44)
Other cancer	193	(21.4)

Comparison of cancer types by diagnosis route (emergency admission versus non-emergency routes) was difficult because two different classification systems are used in primary and secondary care (Read codes and ICD-10 codes, respectively). A crude match of ICD-10 codes to Read codes was performed so that it was possible to compare the frequency of different cancer types by diagnosis routes (Appendices Table A.21).

The following table provides the frequencies of diagnoses by cancer type for both settings, using Read codes (Table 8.6). The largest proportion of diagnoses through emergency presentations were for cancers of the genitourinary system (43.5%; n=448/1,030) and cancers of the digestive system (19.3%; n=199/1,030). By filtering diagnoses to include only those recorded in diagnoses by both emergency and non-emergency routes, cancers of the

bone, connective tissue, skin and breast were most frequently diagnosed (57.2%; n=309/540).

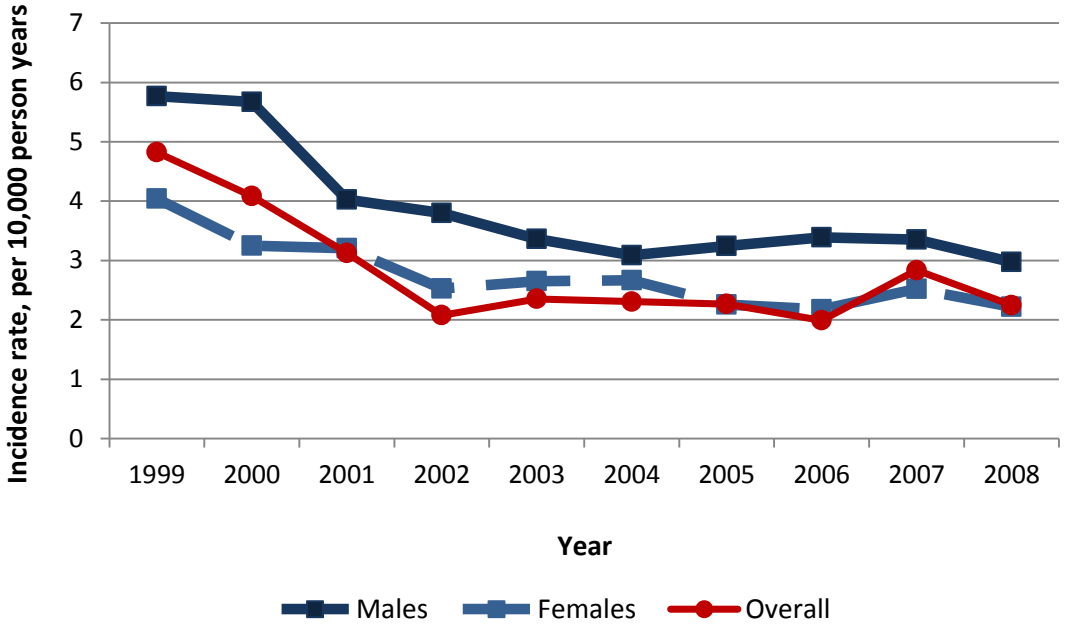
Table 8.6 Number of cancer diagnoses by route to diagnosis, using Read codes

Read classification system		Diagnosis route, n			
Code	Type of malignant neoplasm	Emergency	(%)	Non-emergency	(%)
B0	Lip, oral cavity and pharynx	18	(1.75)	7	(0.14)
B1	Digestive organs and peritoneum	199	(19.3)	59	(1.16)
B2	Respiratory tract and intrathoracic organs	110	(10.7)	36	(0.71)
B3	Bone, connective tissue, skin and breast	149	(14.5)	309	(6.09)
B4	Genitourinary organ	448	(43.5)	68	(1.34)
B5	Other and unspecified sites	18	(1.75)	31	(0.61)
B6	Lymphatic and haemopoietic tissue	88	(8.54)	30	(0.59)
B7	Benign neoplasms	0	-	3850	(75.9)
B8	Carcinoma in situ	0	-	33	(0.65)
B9	Neoplasms of uncertain behaviour	0	-	45	(0.89)
BA	Unspecified nature neoplasm	0	-	2	(0.04)
BB	Morphology of neoplasms	0	-	590	(11.6)
Bz	Neoplasms Not Otherwise Specified	0	-	11	(0.22)

8.4.3.2 Incidence of cancer diagnosis by emergency admission

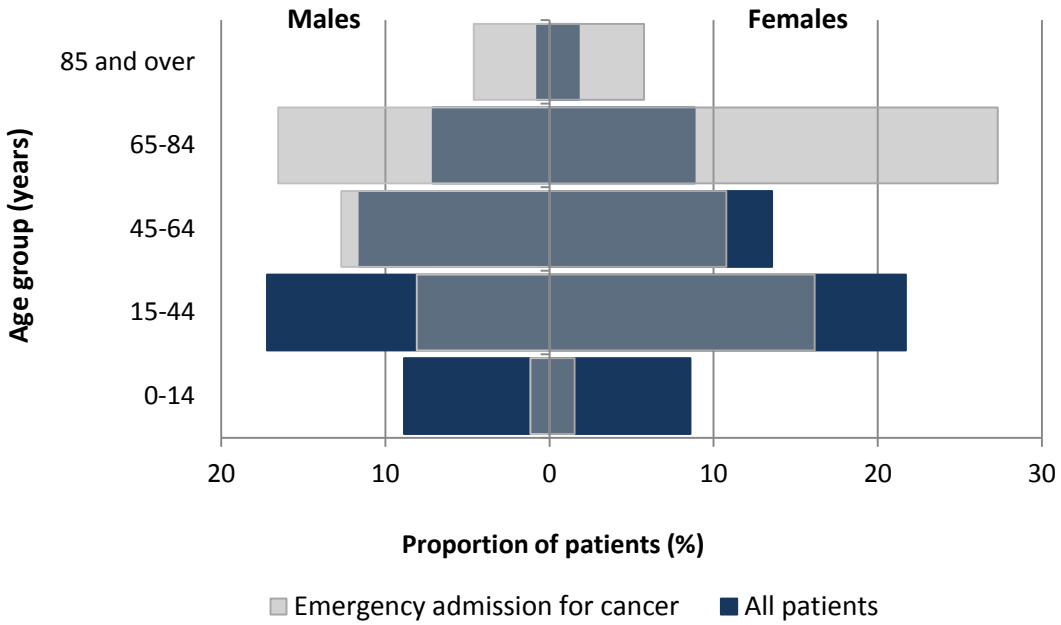
Out of 5,870 patients with a first-time diagnosis of cancer between 1999 and 2008, 13.9% of patients were diagnosed during an emergency admission (n=817/5,870). The overall incidence of first recording (as a proxy for diagnosis) of cancer by emergency admission during the study period was 2.51 patients per 10,000 person years. Over the ten years included in the study, the rate of cancers diagnosed by the emergency route declined, with a slight fluctuation in the penultimate year, 2007 (Figure 8.2). There was a greater overall decrease in the incidence rate in male patients compared to female patients but the rate remained higher in male patients in the final year of the study (2.98 patients per 10,000 person years compared to 2.22 patients per 10,000 person years).

Figure 8.2 Incidence rate of first unplanned admissions for cancer by sex and year (per 10,000 person years), 1999-2008



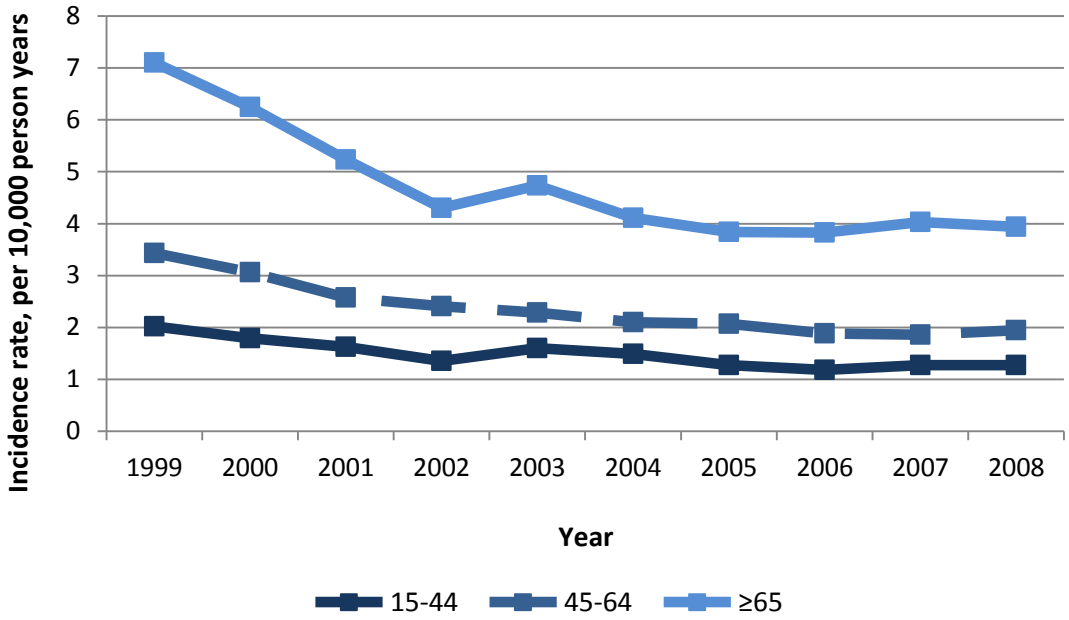
To explore the age and sex distribution of patients who were diagnosed via unplanned admissions, I took a snapshot view of a single year of the study. Data for the calendar year 2004 (crude surrogate for the middle year of the study period) showed that when compared to the overall sample of patients who received a first cancer diagnosis in that year, there was a disproportionally greater number of older patients who were diagnosed via an unplanned admission, especially for female patients aged between 65 and 84 years at diagnosis (Figure 8.3). Less than 5% of male and female patients diagnosed by emergency admissions were in the youngest age group (less than one year to 15 years old).

Figure 8.3 Age and sex distribution of all patients with a first diagnosis of cancer compared to patients diagnosed through the emergency route, 2004



The next figure, Figure 8.4, depicts the temporal trend in first diagnoses by age group. Patients aged less than 15 years were excluded from calculations due to small numbers. Similarly, because few patients aged 85 years or older had a first diagnosis of cancer by emergency admission, the 65 or older and 85 or older age groups were combined. Figure 8.4 shows that the incidence rate of first recorded diagnoses of cancer by unplanned admission decreased over time in all three age groups. The most marked decline was in patients aged 65 years or older, especially between 1999 and 2002.

Figure 8.4 Incidence rate of first unplanned admissions for cancer by age group and year, 1999-2008



8.4.3.3 Risk factors for cancer diagnosis by emergency admission

In the next section of the Results, I describe the predictors of first cancer diagnosis by unplanned admission identified from crude and adjusted analyses.

8.4.3.4 Crude associations with cancer diagnosis by emergency admission

No patients in the sample had records for AIDs, congestive heart disease, diabetes with complications or hemiplegia. Therefore no results are reported for the corresponding comorbidity flags. Crude models of the risk of cancer diagnosis by emergency admission for certain comorbidities did not converge. The respective diseases were cerebro-vascular disease, dementia, mild liver disease, moderate liver disease, peptic ulcer or peripheral vascular disease. Therefore no results are reported for these variables. A model with Charlson Index score as the continuous explanatory variable also did not converge. All p-values reported in this section are $p<0.0001$ unless stated otherwise.

Crude regression models for all variables except those mentioned in the previous sub-section were statistically significant at the 95% level (Table 8.7). Age at diagnosis, length of

time registered at the GP practice, follow-up time and continuity of care showed a positive linear relationship with risk of diagnosis by the emergency route. Female patients were less at risk of diagnosis by this route than male patients (RR 0.73, 95% CI 0.64-0.83). Although ethnicity was a crude predictor of diagnosis by emergency admission, the risk was not statistically different between patients of different ethnicities. Where deprivation status was recorded, patients living in areas classed as not the most or least deprived areas had greatest risk of cancer diagnosis via emergency admission (RR 3.51, 95% CI 2.98-4.14).

Patients who were married (RR 3.19, 95% CI 1.78-5.72) compared to patients who were single, and those who were registered at practices on the South East coast (RR 4.63, 95% CI 1.93-11.09) or the North West (RR 4.17, 95% CI 1.74-10.0) compared to other regions of England were most at risk of a first cancer diagnosis by the emergency route. Patients with at least one condition measured by the Charlson Index were also more at risk (RR 6.55, 95% CI 5.88-7.30). In particular, patients with chronic pulmonary disease were 6 times more likely to be diagnosed by an emergency admission than patients without this condition (RR 6.08, 95% CI 5.28-6.99).

Table 8.7 Risk factors for first diagnosis of cancer, crude results from log-binomial regression using the generalized estimating equations (GEE) method

Characteristic	Patients, n			RR (95% CI)	P-value
	All routes	Emergency admission	(%)		
Age group at diagnosis (years)					<0.0001
0-14	439	6	(1.37)	1	
15-44	2347	3	(0.13)	1.43 (0.69-2.96)	0.340
45-64	1680	12	(0.71)	8.46 (4.22-17.0)	<0.0001
65-84	1197	12	(1.00)	18.1 (9.05-36.1)	<0.0001
≥85	207	16	(7.73)	25.2 (12.5-50.8)	<0.0001
Sex					<0.0001
Male	2418	400	(16.5)	1	
Female	3452	417	(12.1)	0.73 (0.64-0.83)	<0.0001
Ethnicity					<0.0001
Asian	29	6	(20.7)	1	
Black	30	8	(26.7)	1.29 (0.51-3.26)	0.592
Mixed	8	2	(25.0)	1.21 (0.30-4.88)	0.790
White	1924	617	(32.1)	1.55 (0.76-3.17)	0.230
Other	28	6	(21.4)	1.04 (0.38-2.83)	0.945
Unknown	3851	178	(4.62)	0.22 (0.11-0.46)	<0.0001
Marital status					<0.0001
Single	313	12	(3.83)	1	
Married	802	98	(12.2)	3.19 (1.78-5.72)	<0.0001
Other status	128	23	(18.0)	4.69 (2.41-9.13)	<0.0001
Unknown	4627	684	(14.8)	3.86 (2.20-6.74)	<0.0001
Deprivation (quintiles)					<0.0001
Least deprived	2990	187	(6.25)	1	
Quintiles 2,3,4	1738	382	(22.0)	3.51 (2.98-4.14)	<0.0001
Most deprived	716	132	(18.4)	2.95 (2.40-3.63)	<0.0001
Unknown	426	116	(27.2)	4.35 (3.54-5.36)	<0.0001
Practice region					<0.0001
East Midlands	122	5	(4.10)	1	
East of England	835	140	(16.8)	4.09 (1.71-9.78)	0.002
London	345	51	(14.8)	3.61 (1.47-8.83)	0.005
North East	252	38	(15.1)	3.68 (1.49-9.11)	0.005
North West	615	105	(17.1)	4.17 (1.74-10.0)	0.001
South Central	763	92	(12.1)	2.94 (1.22-7.09)	0.016
South East Coast	622	118	(19.0)	4.63 (1.93-11.1)	0.001
South West	834	84	(10.1)	2.46 (1.02-5.94)	0.046
West Midlands	746	90	(12.1)	2.94 (1.22-7.10)	0.016
Yorkshire & The Humber	736	94	(12.8)	3.12 (1.29-7.50)	0.011
Time at practice (years)					<0.0001
Low	1957	176	(9.00)	1	
Moderate	1957	279	(14.3)	1.59 (1.33-1.89)	<0.0001
High	1956	362	(18.5)	2.06 (1.74-2.44)	<0.0001

Follow-up time (years)					<0.0001
<1	988	82	(8.30)	1	
1-3	2032	271	(13.3)	1.61 (1.27-2.03)	<0.0001
4-6	1571	226	(14.4)	1.73 (1.36-2.20)	<0.0001
7-10	1279	238	(18.6)	2.24 (1.77-2.84)	<0.0001
Continuity of care					<0.0001
Low	5378	409	(7.61)	1	
Moderate	164	134	(81.7)	10.7 (9.55-12.1)	<0.0001
High	162	131	(80.9)	10.6 (9.43-12.0)	<0.0001
Not valid	166	143	(86.1)	11.3 (10.1-12.7)	<0.0001
Any consultation before diagnosis					<0.0001
No	752	218	(29.0)	1	
Yes	5118	599	(11.7)	0.40 (0.35-0.46)	<0.0001
Consultation before diagnosis*					0.031
No	2242	340	(15.2)	1	
Yes	3628	477	(13.2)	0.87 (0.76-0.99)	0.030
Consultation ≤30 days before diagnosis					<0.0001
No	5734	704	(12.3)	1	
Yes	136	113	(83.1)	6.77 (6.11-7.50)	<0.0001
Consultation ≤7 days before diagnosis					<0.0001
No	5830	782	(13.4)	1	
Yes	40	35	(87.5)	6.52 (5.70-7.46)	<0.0001
Referral					<0.0001
No	5839	800	(13.7)	1	
Yes	31	17	(54.8)	4.00 (2.89-5.54)	<0.0001
Referral ≤30 days before diagnosis					0.006
No	5866	814	(13.9)	1	
Yes	4	3	(75.0)	5.41 (3.06-9.55)	<0.0001
Admission before diagnosis, mean (SD)	0.11 (0.32)	0.04 (0.20)	-	-	<0.0001
Charlson Index score					<0.0001
0	5785	745	(12.9)	1	
1	43	39	(90.7)	7.04 (6.27-7.92)	<0.0001
≥2	42	33	(78.6)	6.10 (5.14-7.24)	<0.0001
Composite Charlson Index measure					<0.0001
No	5749	718	(12.5)	1	
Yes	121	99	(81.8)	6.55 (5.88-7.30)	<0.0001
Chronic pulmonary disease					<0.0001
No	5809	768	(13.2)	1	
Yes	61	49	(80.3)	6.08 (5.28-6.99)	<0.0001
Diabetes					<0.0001
No	5843	796	(13.6)	1	

* At GP practice, telephone or home visit and with GP or nurse.

Yes	27	21	(77.8)	5.71 (4.62-7.06)	<0.0001
Myocardial infarction					0.017
No	5865	814	(13.9)	1	
Yes	5	3	(60.0)	4.32 (2.11-8.87)	<0.0001
Renal disease					<0.0001
No	5854	803	(13.7)	1	
Yes	16	14	(87.5)	6.38 (5.24-7.76)	<0.0001
Rheumatologic disease					0.017
No	5865	814	(13.9)	1	
Yes	5	3	(60.0)	4.32 (2.11-8.87)	<0.0001

8.4.3.5 Model selection for adjusted analyses

As explained in section 8.4.2.3, log-binomial models using GEE for adjusted regression did not converge. Of the three Poisson with GEE models for the different comorbidity measures that were statistically significant at the 95% level in crude analyses (Table 8.7), the model with grouped Charlson score performed best (lowest QIC score) and so this variable was carried forward for adjusted analyses. As multiple consultation and referral variables were included in adjusted calculations, eight separate models were run for the variable combinations to reduce collinearity caused by correlated variables. The performances of these models are shown in Table 8.8. The model with consultation ≤7 days before diagnosis and referral ≤30 days before diagnosis performed best, producing a QIC score of 6317.1, and was used in final adjusted analyses (Table 8.8). However, this model's QIC score was 670.5 points greater than the null model's score, indicating sub-optimum fit.

Table 8.8 Fit of adjusted Poisson regression models for predicting risk factors for first emergency admissions for cancer, by consultation and referral variable, using the generalized estimating equations (GEE) method

Consultation variable	Quasi-Likelihood under the Independence model Criterion (QIC)	
	Referral before diagnosis	Referral ≤30 days before diagnosis
Consultation ≤30 days before diagnosis	6353.2	6320.3
Consultation ≤7 days before diagnosis	6349.7	6317.1
Consultations, grouped	6814.6	6777.2
Consultations at GP practice, telephone or home visit with GP or nurse, grouped	6573.3	6522.3
Null model		5646.6

8.4.3.6 Adjusted associations with cancer diagnosis by emergency admission

Once adjusted for other characteristics and taken into account clustering of patients at GP practices, patient's age at diagnosis, deprivation status and Charlson Index score remained significant predictors of first diagnosis of cancer by emergency admission at the 95% level (Table 8.9). Ethnicity and continuity of care score were also associated with risk of diagnosis by unplanned admission, although the differences in risk between patient groups for both characteristics were not statistically significant. Patients in the oldest age group at diagnosis (RR 9.23, 95% CI 4.81-17.7; p<0.0001), living in the most deprived areas (RR 1.23, 95% CI 1.02-1.49; p=0.032) and patients with a moderate number/severity of comorbidities* (RR 1.35, 95% CI 1.05-1.75; p=0.020) were most at risk of cancer diagnosis by emergency admission.

*Defined by cumulative Charlson Index score of one.

Table 8.9 Risk factors for first diagnosis of cancer, crude (log-binomial) and adjusted (Poisson with GEE) results using the generalized estimating equations (GEE) method

Characteristic	Crude		Adjusted	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Age group at diagnosis (years)		<0.0001		<0.0001
0-14	1		1	
15-44	1.43 (0.69-2.96)	0.340	1.22 (0.62-2.43)	0.566
45-64	8.46 (4.22-17.0)	<0.0001	4.77 (2.50-9.10)	<0.0001
65-84	18.1 (9.05-36.1)	<0.0001	6.57 (3.42-12.6)	<0.0001
≥85	25.2 (12.5-50.8)	<0.0001	9.23 (4.81-17.7)	<0.0001
Sex		<0.0001		0.275
Male	1		1	
Female	0.73 (0.64-0.83)	<0.0001	0.94 (0.84-1.05)	0.269
Ethnicity		<0.0001		<0.0001
Asian	1		1	
Black	1.29 (0.51-3.26)	0.592	0.75 (0.42-1.33)	0.325
Mixed	1.21 (0.30-4.88)	0.790	0.80 (0.36-1.76)	0.571
White	1.55 (0.76-3.17)	0.230	1.06 (0.59-1.89)	0.845
Other	1.04 (0.38-2.83)	0.945	1.27 (0.62-2.60)	0.512
Unknown	0.22 (0.11-0.46)	<0.0001	0.34 (0.18-0.62)	0.001
Marital status		<0.0001		0.224
Single	1		1	
Married	3.19 (1.78-5.72)	<0.0001	1.27 (0.82-1.96)	0.283
Other status	4.69 (2.41-9.13)	<0.0001	1.09 (0.64-1.87)	0.742
Unknown	3.86 (2.20-6.74)	<0.0001	1.35 (0.88-2.05)	0.166
Deprivation (quintiles)		<0.0001		<0.0001
Least deprived	1		1	
Quintiles 2,3,4	2.95 (2.40-3.63)	<0.0001	1.14 (0.98-1.32)	0.085
Most deprived	3.51 (2.98-4.14)	<0.0001	1.23 (1.02-1.49)	0.032
Unknown	4.35 (3.54-5.36)	<0.0001	0.63 (0.50-0.79)	<0.0001
Practice region		<0.0001		0.352
East Midlands	1		1	
East of England	4.09 (1.71-9.78)	0.002	1.77 (0.78-4.03)	0.170
London	3.61 (1.47-8.83)	0.005	1.84 (0.78-4.30)	0.161
North East	3.68 (1.49-9.11)	0.005	2.00 (0.83-4.79)	0.121
North West	4.17 (1.74-10.0)	0.001	1.75 (0.77-3.98)	0.185
South Central	2.94 (1.22-7.09)	0.016	1.84 (0.81-4.20)	0.146
South East Coast	4.63 (1.93-11.1)	0.001	1.82 (0.80-4.13)	0.152
South West	2.46 (1.02-5.94)	0.046	1.54 (0.68-3.48)	0.301
West Midlands	2.94 (1.22-7.10)	0.016	1.64 (0.71-3.78)	0.244
Yorkshire & The Humber	3.12 (1.29-7.50)	0.011	2.15 (0.94-4.91)	0.069
Time at practice (years)		<0.0001		0.846
Low	1		1	
Moderate	1.59 (1.33-1.89)	<0.0001	1.02 (0.87-1.20)	0.783
High	2.06 (1.74-2.44)	<0.0001	0.99 (0.84-1.15)	0.866
Follow-up time (years)		<0.0001		0.581
<1	1		1	
1-3	1.61 (1.27-2.03)	<0.0001	1.12 (0.90-1.40)	0.308
4-6	1.73 (1.36-2.20)	<0.0001	1.15 (0.92-1.43)	0.209
7-10	2.24 (1.77-2.84)	<0.0001	1.18 (0.92-1.50)	0.186
Continuity of care		<0.0001		<0.0001
Low	1		1	
Moderate	10.7 (9.55-12.1)	<0.0001	1.01 (0.87-1.18)	0.895

High	10.6 (9.43-12.0)	<0.0001	0.99 (0.86-1.14)	0.896
Not valid	11.3 (10.1-12.7)	<0.0001	0.29 (0.25-0.34)	<0.0001
Any consultation before diagnosis		<0.0001		<0.0001
No	1		1	
Yes	0.40 (0.35-0.46)	<0.0001	0.44 (0.37-0.51)	<0.0001
Consultation before diagnosis*		0.031		<0.0001
No	1		1	
Yes	0.87 (0.76-0.99)	0.030	0.54 (0.47-0.63)	<0.0001
Consultation ≤30 days before diagnosis		<0.0001		0.119
No	1		1	
Yes	6.77 (6.11-7.50)	<0.0001	1.14 (0.97 1.34)	0.116
Consultation ≤7 days before diagnosis		<0.0001		0.022
No	1		1	
Yes	6.52 (5.70-7.46)	<0.0001	1.34 (1.05-1.71)	0.019
Referral†		<0.0001		0.036
No	1		1	
Yes	4.00 (2.89-5.54)	<0.0001	1.45 (1.04-2.02)	0.027
Referral ≤30 days before diagnosis		0.006		0.285
No	1		1	
Yes	5.41 (3.06-9.55)	<0.0001	1.76 (0.76-4.09)	0.187
Admission before diagnosis, mean (SD)	0.30 (0.21-0.43)	<0.0001	0.30 (0.20-0.46)	<0.0001
Charlson Index score		<0.0001		0.016
0	1		1	
1	7.04 (6.27 - 7.92)	<0.0001	1.35 (1.05-1.75)	0.020
≥2	6.10 (5.14 - 7.24)	<0.0001	0.83 (0.66-1.04)	0.111

8.4.3.7 Service use

To better understand the characteristics of patients who were diagnosed with cancer through emergency admissions, I compared the access to health services by these patients and patients diagnosed through non-emergency routes. I now describe the consultation, referral and emergency admission patterns of patients in these two groups.

8.4.3.8 Consultations

Patients who had at least one consultation with a GP or nurse at the practice, by telephone or home visit in the 7 days immediately before their first cancer diagnosis were at great risk of diagnosis via an unplanned admission (adjusted RR 1.34, 95% CI 1.05-1.71; p=0.019). During the study period, patients who were diagnosed via non-emergency routes had fewer consultations with a GP or nurse at their GP practice, by telephone or home visit before

*At GP practice, telephone or home visit and with GP or nurse.
†Adjusted results for referral are from regression model that included consultations within 7 days of diagnosis.

diagnosis (mean 0.25, SD 3.16, consultations) compared to patients diagnosed by unplanned admission (mean 7.91, SD 16.3, consultations), t(826)=13.4, p<.001.

8.4.3.9 Referrals

No patients had a recorded referral request in the 7 days immediately before their first diagnosis of cancer, but patients who had at least one recorded referral request were at greater risk of being diagnosed via the emergency route (adjusted RR 1.45, 95% CI 1.04-2.02; p=0.027). Few patients with a first cancer diagnosis during the study period had a recorded referral request before diagnosis, regardless of diagnosis route (0.53%; n=31/5,870). Among the patients diagnosed via the emergency route, the number of referrals before diagnosis ranged between 0 and 17 referrals (2.08%; n=17/817). In comparison, the number of referrals before diagnosis for patients diagnosed by non-emergency routes fell into a much narrower range, between 9 and 5 referrals (n=5,053), t(820)=5.0; p<0.001.

8.4.3.10 Admissions

Patients with a greater average number of prior emergency admissions were less likely to be diagnosed with cancer via the emergency route (adjusted RR 0.30, 95% CI 0.20-0.46; p<0.0001). Regardless of the route to diagnosis, the number of all-cause emergency admissions before the first cancer diagnosis was low, ranging between 0 and 2 admissions in patients diagnosed via the emergency route (n=817/5,870) and between 0 and 3 admissions in patients diagnosed via non-emergency routes (n=5,053/5,870), t(1670)=10.5; p<0.001.

8.4.4 Discussion

The two studies presented in this chapter are not directly comparable. Firstly, different denominator data were used. Study 1 included all patients with a first time admission for cancer while study 2 included all patients with a first time diagnosis for cancer. Yet the numerator was the same; both studies identified patient characteristics associated with cancer diagnosis by emergency admission. Secondly, different units of measurement were used. Study 1 measured ORs while study 2 measured RRs. As the outcome of interest (emergency admission for cancer) in study 1 was common (occurrence in more than 10% of the sample), the ORs from the first study do not approximate to RRs. Nevertheless, the two sets of analyses provide complimentary information to inform policy and practice. Next, I

consider the results in respect to the objectives of this chapter (section 8.2.4) and also the wider context of cancer care in England.

8.4.4.1 Summary of main findings

The first overall objective of this chapter was to measure the rate of first emergency (unplanned) admissions for cancer. Between 1999 and 2008, the incidence of first-time diagnoses (new cases) of cancer by emergency admission was 2.51 patients per 10,000 person years. During these ten years, 13.9% of patients who were diagnosed with cancer for the first time received their diagnosis during an emergency admission (n=817/5,870). Among patients who receive a first-time diagnosis of cancer by admission between 2007/08 and 2009/10, 21.8% were diagnosed by the emergency route (n=139,351/639,064).

These estimates also capture temporal trends in cancer diagnoses via the emergency route in England. Published national figures have tended to use data from one year; NCIN estimated that 23% of cancers were diagnosed by emergency presentations in 2007 and the National Audit of Cancer Diagnosis in Primary Care estimated that 12.9% of diagnosed cancers in 2009/10 were made along the emergency pathway[*].[391,401] The validity of the results shown in this chapter is supported by their similarity to the external figures, using data from the same care settings albeit with far smaller samples.

As for the second and third objectives to identify patient and practice risk factors for first emergency admissions for cancer, the results of the two studies were in concordance. Distinct patient groups at greater risk of diagnosis by emergency admission were identified, namely older patients (especially aged 85 years or older) and those living in the most deprived areas. No breakdown of admissions by cancer type was made in study 2. However, grouping by biological system showed cancers of the digestive system to be commonly diagnosed by the emergency route. While in study 1, pancreatic cancer had one of the highest odds out of all the cancer types for diagnosis by emergency admission.

[*] In the Audit, relevant diagnoses were defined as emergency referrals for suspected cancers that were later confirmed, including emergency hospital presentations without primary care contact. Estimate excludes cancers detected by screening, in-situ carcinomas and non-melanotic carcinomas of the skin.[391]

Practice-level predictors for emergency admissions were investigated in study 1, presenting a mixed picture about the suitability of the outcome measure as a primary care safety indicator. I will discuss the role of measurement in Chapter 9. Expected correlations between this measure and established QOF cancer indicators were not found in adjusted results. More promising inverse associations were detected between diagnosis by emergency admission and practices' overall QOF performance, and patient experiences of access. Despite this finding, additional quality markers should be used to validate outcomes in future research given the well documented equivocal impact of financial incentive schemes, and specifically the QOF, on quality improvement.[353,408-410] Also, interactions between factors need to be explored to better understand findings such as the increased odds of diagnosis by the emergency route for patients at practices where none of the GPs received their medical qualification in the UK.

8.4.4.2 Methodological issues

Studies 1 and 2 were affected by weaknesses inherent to their study designs and the sources of data used. For instance, data in HES are entered by professional, typically non-medically qualified, coders while GPRD data are extracted directly from GP practices and may be entered by different types of staff including GPs, nurses, receptionists and trained medical coders. One finding of the informal consultations was the advocacy by GPs of employing medically qualified staff to enter clinical data into computer systems (Chapter 2 section 2.6.8).[183] The use of these designated coders might improve data accuracy but does not negate the issue of inconsistent coding within GP practices if data are processed by multiple staff, as well as inter-practice variation due to different coding standards and computer systems. Even though there are national NHS clinical coding standards for diagnoses and procedures (ICD-10 and OPCS-4 classifications, as well as SNOMED CT), there is likely to be variation in coding practices between hospitals and Trusts.

I now further discuss limitations relating to the main data sources, HES and the GPRD. I will then consider potential confounders that did not feature in the analyses yet are of interest for future research.

8.4.4.3 Limitations of the data and analyses

As mentioned in section 8.3.2.1 and section 8.4, first recordings of cancer by emergency admission may be attributed to pre-existing diagnoses. Accurate case ascertainment was difficult in study 1, where only HES data were used. For example, there was no information about outpatient appointments to eliminate patients known to be receiving cancer treatment. Patients of practices with less than 500 patients were excluded without exploration of potential differences between these practices, its patients and the practices that were included in analyses. The analyses offer a simple view of the current health care situation, with no exploration of interactions between characteristics such as cancer type and rurality, or the relationships between practice (and patient) variables, as already mentioned in section 8.4.4.1.

Coding for cancer diagnoses is known to be poor in general practice records.[116] By using the integrated HES data in the GPRD dataset, I was better able to detect true positive cases of first cancer diagnosed by emergency admissions. In section 8.4.4.1, I compared the finding that 13.9% of first cancer diagnoses were made by emergency admissions with published national estimates and the higher rate calculated in study 1. One plausible reason for the low estimate (in contrast to study 1's rate) lies with the rigorous sampling criteria applied in study 2 (section 8.4.2.1 for case ascertainment method). By tracking back to patients' first records in the GPRD dataset and cross-referencing between primary and secondary care records, I was able to ascertain first diagnoses over patients' lifetimes. Other studies on this subject tracked back over considerably shorter periods of time (3 years in study 1) and therefore the sampling sensitivity in those studies is likely to be poorer than in study 2.

As set out in Chapter 3 section 3.7, the dataset requested from the GPRD was a random sample of 100,000 patients with no specifications about disease status or other patient traits. Therefore, the sample for study 2 of this chapter and the sample for analyses in Chapter 7 were smaller than if samples for specific disease groups or outcomes of interest had been requested instead. As such, the generalisability of results might be affected. This weakness is somewhat counter-balanced by the use of nationally representative data and robust statistical methods appropriate for the sample size. Additional data triangulation,

such as using case notes and patient interviews, would further improve the accuracy of identifying first time cancer diagnoses by the unplanned route.

Not all fields in the GPRD dataset were of a good level of completeness or accuracy. Referral rates for suspected cancer are known to differ across the country.[83,389-391] This information was not available for study 1 but in study 2, the number of recorded referral requests in general practice was considerably lower than published numbers. To illustrate, 0.53% of patients in study 2 were recorded as having at least one referral request before their first cancer diagnosis compared to 86.5% of patients who had a known type of referral in the National Audit.[391] The stark difference may be partly explained by the narrow definition of referral used in study 2, based solely on data from the referrals section of the GPRD dataset without cross-referencing with investigations and tests recorded in other data sections. Although results by referral for study 2 are included in this chapter for completeness, the low numbers mean that these results should not be extrapolated beyond the study.

8.4.4.4 Case-mix adjustments

Generic and cancer-specific confounders have been adjusted for in studies 1 and 2. Still, there will undoubtedly be factors unaccounted for. Cancer type was only adjusted for in study 1. Further analyses should consider cancer types separately as the epidemiology, treatment and patient outcomes for different cancer types will not be homogeneous. Arguably the most important variable missing from both studies is cancer stage. Linkage of HES and/or GPRD to cancer registries and audits will provide staging and treatment information required to determine the relationship between diagnosis by the emergency route and late diagnosis (as defined in section 8.2.2).[389] Extra data on cancer screening and waiting times between intervals of care will help to establish which patient groups are most affected by poor care and expose the processes that require improvement. However, for many sources of cancer data, delays between data collection and publication or availability of these data for secondary uses can be obstructive for research purposes.[389]

8.4.4.5 Implications for clinical care and health policy

In conclusion, in this chapter I have presented population-level analyses using recent data to determine a range of patient and practice characteristics associated with first diagnoses of

cancer by the emergency route, as a proxy measure of delayed diagnosis. The results feed into national efforts to improve cancer care in England and echo findings from the literature.[391,401,411] Cancer research often focuses on short-term survival, typically up to one year post-diagnosis or completion of treatment. However, patients, carers and community care providers are also interested in longer term prognoses, especially as cancer is often now a chronic disease.[412] Analyses within a short timeframe may be appropriate if assuming that poor patient outcomes are due to delayed diagnosis. Based on this understanding, earlier diagnosis by reducing the number of patients diagnosed by the emergency route would improve both short and long term patient outcomes.

Chapter 9: Discussion

9.1 Chapter overview

In this final chapter of the thesis, I summarise the results of the analyses from Chapters 5 to 8 within the context of the project aims. I then evaluate the methodologies applied and consider current understanding of patient safety indicators. I discuss the strengths and limitations of the project and conclude with suggestions for future applications of patient safety indicators in terms of research, clinical practice and health policy.

9.2 Addressing the aims of the project

I begin by revisiting the aims of this project (Chapter 1 section 1.7) to summarise the key findings. This section brings together the findings from Chapters 2, 5, 6, 7 and 8.

9.2.1 Addressing Aim 1

- **Explore the epidemiology of adverse events in general practice using routinely collected data.**

There have been limited and inconsistent reports on the extent of AEs in general practice in England, not helped by heterogeneous methods applied in previous studies (Chapter 2 section **Error! Reference source not found.**). One of the aims of this project was to provide a robust national estimate of AEs, based on data recorded routinely as part of care in hospital or general practice. I found low rates of AEs defined by designated diagnosis codes for complications of care, DEAs and for first unplanned admissions for cancer (as a proxy measure for diagnosis by the emergency route). Analyses of data from NHS Brent (Chapter 5) produced an estimated rate of 1.67 AEs per 1,000 consultations (95% CI 1.59-1.74). Data from the GPRD (Chapter 6) produced an estimated rate of 6.0 AEs per 1,000 person-years

(95% CI 5.74-6.27). These findings are not too dissimilar to those from some previous studies, but the inconsistent use of denominator populations and units of measurement makes comparisons very difficult.[8,24,295] Among patients with diagnosed diabetes, there were 3.97 DEAs per 1,000 person years (Chapter 7). The proportion of patients with a first emergency admission for cancer ranged between 13.9% and 21.8% of patients diagnosed with cancer, with an incidence of 2.51 patients diagnosed by the emergency route per 10,000 person years (Chapter 8).

Patient and practice characteristics associated with AEs were examined. Older age, certain comorbid conditions and greater service use (GP consultations and emergency admissions) were associated with increased risk of an AE identified by a complication of care code, while there was variation in risk by GP practice region (Chapters 5 and 6). Older age, more GP consultations and having more and/or complex comorbidities were associated with lower risk of a DEA in patients with diabetes (Chapter 7). Older age was again associated with elevated risk of experiencing the final AE measured in this project, first emergency admission for cancer (Chapter 8). Patients living in the most deprived areas were also at greater risk of this outcome, along with patients who had certain diagnoses such as pancreatic cancer (Chapter 8). Associations between first emergency admission for cancer and practice measures of quality varied and did not provide conclusive evidence about the suitability of the outcome for use as safety indicator (Chapter 8).

9.2.2 Addressing Aim 2

- **Examine how routinely collected data can be used in their current state for patient safety measurement within existing quality improvement systems.**

The use of data collected locally and nationally for patient safety measurement and monitoring was reviewed in Chapter 2. The types of routinely collected data currently used for these purposes are limited and mainly originate from secondary care, although there is documented use of electronic patient records from GP practices. The focus of these often small scale (practice or local level) measurements remains drug-related events, using multi-sourced data. In fact, the analyses reported in Chapters 5 to 8 illustrated the importance of using more than one data source to improve the validity of AE measures. More often than not in quality improvement initiatives, patient safety is integrated into other domains of

quality and rarely considered on a standalone basis. Within the framework of performance monitoring at the PCT- (and future CCG-) level, data on patient safety have been collected for benchmarking, to create practice profiles, for service commissioning and in local extensions of the QOF programme (Chapter 2).[183]

9.2.3 Addressing Aim 3

- **Consider what obstacles there might be against using routinely collected data for active patient safety surveillance in general practice, at local and national levels.**

Findings from the literature review and informal consultations reported in Chapter 2 highlighted difficulties in the use of data to improve patient safety in general practice and elsewhere in primary care.[183] The key obstacles were poor communication, cultural barriers, technical data challenges, inadequate skills and knowledge and management issues. A further limitation for monitoring AEs is insufficient clinical detail in most existing routinely collected data to determine the preventability and severity of events. Current use of these data for patient safety is also hindered by scant awareness of their potential applications in general practice or other care settings (Chapter 2 section 2.6.8).[183] Reporting of all safety incidents involving patients only became mandatory in English primary care in 2012. Before this, reporting was sporadic and inconsistent in this setting. Nevertheless, local and national incident reporting schemes are main sources of information about AEs, even though there are known issues of incomplete event capture and scepticism among clinicians on the effectiveness of reporting schemes.[183]

9.2.4 Addressing Aim 4

- **Apply adverse events indicators for general practice that have been developed from available routinely collected data.**

Results of analyses on the three AE indicators measured in this project have been described earlier in this chapter (section 9.2.1) and presented in Chapters 5 to 8. The data sources and analysis methods were described in Chapters 3 and 4, respectively. In essence, the first indicator was a generic measure of AEs recorded in data routinely collected in general practice, to provide a national baseline rate of harm. The second and third measures were indicators of outcomes associated with AEs. The former indicator measured emergency admissions for diabetic emergencies (DEAs), which is a collective term for diabetic

ketoacidosis and diabetic (hyperglycaemic or hypoglycaemic) coma. The latter measured first emergency admissions for cancer. While detailed findings are reported in the respective Chapters 5, 6, 7 and 8, further discussion of the methods adopted to meet the research aims are presented in the following section.

9.3 Meeting the research aims

Now I will discuss how the aims were met by evaluating the research methods used in this project, the sources of data and the analysis methods applied.

9.3.1 Research methods

To address the four aims of this project, multiple methods were applied. While quantitative analyses formed the largest component, they were supported by a literature review and supplementary informal consultations. As well as providing face validity for the indicators explored in this project, the discussions with four GPs and a medical student provided snapshot anecdotal evidence of clinical views and experiences of AE measurement using routinely collected data. The limitations of these consultations, including the small sample and non-random selection, have been described at length elsewhere (Chapter 2 section 2.6.8).[183]

Stringent selection criteria were applied in the literature review which may have been overly-restrictive, for example potentially relevant studies on ADRs were excluded (Chapter 2 section 2.4.4). Relatively few studies were conducted in the UK, with strong dominance from US-based studies. Thus there needs to be caution in generalising findings from the review to the English health system. The patient groups in reviewed studies were also limited, comprising mainly of adult hospital patients. The quality of the studies varied and they lacked common measures for elements such as AE severity, where this was considered. These limitations may not reflect inadequacies of the review process given the comprehensive methodology adhered to, but they may instead accurately portray the incomplete and inadequate evidence base on measurement of patient safety in non-acute care using routinely collected data.

In addressing research aims 1 and 4, I examined three distinct AE indicators. The first generic measure was to provide a baseline estimate of events that are recorded in local and

national datasets. The second and third measures of outcomes associated with AEs were selected due to the high prevalence and hence burden to the health system of the conditions, the availability of disease-specific indicators and the topical nature of the diseases in terms of care improvement. This approach of considering three diverse indicators enabled confirmation that AEs potentially attributable to care received in general practice can be detected using routinely collected data, either directly from patient records or by using more sophisticated tools to deduce harm by proxy.

Additionally, the implementation of three indicators provided evidence on the suitability of routinely collected data for monitoring AEs across a range of diseases and conditions, including the simple use of existing complications of care codes for active surveillance. An alternative research strategy to the one I adopted would be to focus on a single disease or patient group, whereby a more detailed understanding of risk factors and patient outcomes might be achieved. However, as this project was exploratory in nature and with the unknown compatibility of the available datasets with AE detection, the chosen research methods were appropriate. Whether investigating one or multiple diseases or AEs, successful research depends on the quality and nature of available data, which I consider in the next sub-section.

9.3.2 Sources of information

Variable data availability and quality between and within care settings and specialities, and the historical lack of a central repository for healthcare data, in England compounds the difficulties of conducting research in this field. Further obstacles include costs associated with obtaining some datasets and a notorious ethical approval process for certain types of studies. An example of the variation in management of services which affects the delivery of care in primary care is the non-uniformity in GP practice computer systems, arising from the GPSoC scheme. Currently, approximately half of NHS GP practices use computer systems from EMIS which offers several different core system products, but there also exists a myriad of other systems (Chapter 1 section 1.6.2).[128]

One detrimental effect of individual GP practices being able to choose their preferred computer system is the potential increase in coding irregularities between systems, although these can also occur within systems.[183,413] This chaotic data landscape hinders

accurate monitoring of AEs, not least because of potential incomparability of findings from studies which use data from different computer systems. The divergence in data management is emphasised by the fact that until recently, the two largest English primary care datasets available for research purposes, QResearch and the GPRD (superseded by CPRD), were extracted from practices using different computer systems provided by EMIS and INPS, respectively. It should be noted that the new CPRD should have better coverage as it houses data from all four of the main computer systems used in English primary care, as well as having capacity to link with data from across health and social care.[130] Furthermore, the most comprehensive data yet from GP practices should become available through the GPES (Chapter 1 section 1.6.2).[134]

9.3.3 Quality of the data

The value and importance of data triangulation in patient safety indicator research, especially for pilot or exploratory studies, has been raised earlier in this chapter (section 9.2.2).[299,300] As discussed previously (Chapter 6 section 6.5.2.1, Chapter 7 section 7.5.7.5 and Chapter 8 sections 8.4.4.2 and 8.4.4.3), secondary uses of data collected for purposes other than research are reliant on the accuracy and completeness of initial data recording. In the case of GPRD data which have been used extensively to study different diseases and conditions, there may be under-recording of prevalent conditions.[192,193] Analyses of these data are also restricted by the inherent coding structures of the datasets, including nuances of coding practices in primary and secondary care settings (Chapter 5 section 5.5.2). As SNOMED CT becomes more widely adopted as the standard clinical terminology in the NHS, there should be positive effects in terms of the consistency, reliability and comprehensiveness of recorded data (Chapter 1 section 1.6.3).[135]

Potential quality discrepancies beyond the control of original data entry and project analyses may also been present. For instance, delays by patients in presenting with symptoms or AEs, as well as erroneous recall, may contribute to inaccurate records (Chapter 6 section 6.5.2.3). To improve the accuracy of sample selection and detection of true cases of AEs, verification could use further data sourced from case notes, interviews or other material (Chapter 1 section 1.4.2), but this was not feasible in this project (Chapter 8 section 8.4.4.3).

Case mix adjustment was also affected by the limited availability of variables in the main study datasets from NHS Brent, the GPRD and HES (Chapter 5 section 5.5.2, Chapter 7 section 7.5.7.1 and Chapter 8 section 8.4.4.4). There were particularly few GP practice variables available in the first two aforementioned datasets, preventing exploration of their associations with the measured AEs and patient factors. Given the anonymised nature of data from NHS Brent and the GPRD, linkage of these datasets to other sources was not possible (Chapter 6 section 6.5.2.2 and Chapter 7 section 7.5.7.4). Practice list size, number of GPs and other GP practice data were used in study 1 of Chapter 8 but otherwise unavailable. Potential residual practice confounders such as these may be relevant to study 2 of Chapter 8 and other studies in this project.

9.3.3.1 Validation of the data

Another aspect of quality assessment is data validation. There are several methods to determine the discriminative and predictive accuracy of measurements. For example, the sensitivity and specificity of estimates can be assessed by splitting data into development (prediction) and validation datasets. An alternative to this internal form of validation (assessments using the same data) is to conduct external assessments using other data sources. Both methods are dependent on the accuracy of original data recording.[192,414] No internal validation using split datasets was performed in this project. The validity of results was improved by data triangulation from local and national datasets for the generic measure of AEs, although different units of measurement were used in the studies reported in Chapters 5 and 6.

To validate the analyses of DEAs (Chapter 7), results were compared to the literature and other published material. The findings were summarised earlier in this chapter (section 9.2.1) but of further note is that the comparisons to published national data were hampered by small numbers in the study. In spite of this, reasonable data validity was assumed given that the calculated rates of diabetes fell within the estimates from three national sources, the National Diabetes Audit, QRESEARCH and QOF[*]. The studies in Chapter 8 on emergency

[*]Estimates for the years 2004-2006, where data from the study, National Diabetes Audit, QRESEARCH and QOF were all available.

admissions for cancer show how multiple data sources can be used to improve case ascertainment. Building on the use of only HES data in study 1, patient records from HES and the GPRD were cross-matched in study 2 to ensure true identification of first diagnoses of cancer. The rates of diagnoses by emergency admission estimated in the two studies were compared with each other and other studies from the literature (Chapter 8 section 8.4.4.1).

9.3.4 Analysis methods

Validation of data extended beyond assessments of outcomes in this project. The validity of some measures commonly applied in health service research is not well known for non-acute settings. The studies reported in Chapters 6, 7 and 8 applied two sets of comorbidity measures, the Charlson Index and the Johns Hopkins ACG case-mix system. For both of these measures, there is relatively little published evidence on their uses in primary care compared to acute settings, especially in England.[216-218,225,226] Neither set of measures demonstrated conclusive superiority in its ability to explain variation in the data. For example, statistical models containing measures from the Charlson Index performed best in predicting the risk of AEs identified from complications of care codes and first emergency admissions for cancer (Chapters 6 and 8). However, Expanded Diagnosis Cluster (EDC) groups from the ACG system performed best out of all comorbidity measures in predicting the risk of death (Chapter 6).

Technical concerns associated with the comorbidity measures were outlined in Chapter 3 (section 3.9.4). One conspicuous problem was temporal incongruence, whereby conditions and diseases that were resolved before the occurrence of the AEs of interest were not recorded as such and hence may have been incorrectly included as valid comorbidities (Chapter 3 section 3.9.4.2). Issues with event sequencing also affected the studies presented in Chapters 6 and 7, as reverse causality between the outcomes of interest (rates of AEs and DEAs, respectively) and service use (GP consultations, referrals and emergency admissions) could not be determined. However, in acknowledgement of this methodological weakness, additional analyses were conducted where the first AE was the reference point by which service use was measured, i.e. calculation of the frequency and nature of service use before or after the first AE (Chapter 6 section 6.4.4 and Chapter 7 section 7.4.7). In the studies of

Chapter 8, the outcome of interest was the first AE (emergency admission for cancer), thus the chronology of service use in relation to the event was easily determined.

The explanatory factors included in this project were by no means exhaustive but exploration of these variables and their relationships with the AEs through multiple statistical testing may have generated spurious statistically significant results (Chapter 6 section 6.5.2). By increasing the threshold for statistical significance in the analyses, undesired effects from multiple testing were reduced (Chapter 4 section 4.6.1). Small numbers hindered exploration of interactions between variables, although such relationships may be present. The issue of small sample size was particularly relevant to the study on DEAs in Chapter 7 and the study 2 of Chapter 8 on emergency admissions for cancer, which may have resulted in insufficient statistical power to detect even large effects. A separate analytical matter relates to regression model selection for the studies in Chapters 6 to 8, which was governed by the ability to adjust for clustering of patients at individual practices (Chapter 6 sections 6.4.3.2, 6.4.5.2 and 6.4.7.2; Chapter 7 section 7.4.4; and Chapter 8 section 8.4.3.5). This factor took priority over the presence of "excess zeros" and/or over-dispersion, which may have been better accounted for by models other than Poisson with GEE.

The technical issues of patient clustering, excess zero counts and over-dispersion were all considered and solutions offered in Chapter 4 sections 4.8 and 4.9. Where relevant, alternative regression models were described in the Results sections of the respective chapters, listed previously. Multi-level modelling was described as being particularly suited for data containing clustering and over-dispersion (Chapter 4 section 4.9). This statistical approach can also accommodate multiple cluster levels (such as the combined clustering of patients at practices, clustering of practices within PCTs and clustering of PCTs in geographical regions). However, this method cannot be programmed using the SAS PROC GENMOD statement and thus, to ensure statistical consistency throughout the project, multi-level modelling was not used. Regardless, this method may be used in future research as an alternative and more statistically powerful method of analysing clustered and over-dispersed data.

9.4 Current knowledge about patient safety indicators

With confirmation that the project aims were met (section 9.2) and understanding of how they were met (section 9.3), I now consider the knowledge about patient safety indicators derived from routinely collected data collated in this project. Attention is given to the types of measures, how they are applied and assessment of their strengths and weaknesses.

9.4.1 Range of patient safety indicators

Through the literature review and informal consultations reported in Chapter 2, measures of AEs due to care received in the primary care setting were identified. For three of the measures, their feasibility for use as safety indicators was examined using routinely collected data from local and national sources. Almost all AE measures were intended for adult populations and as stated in section 9.2.2, drug-related events were the most prominent type of harm investigated. Health service use as an outcome measure for AEs was also commonly reported, typically comprising of unplanned admissions, readmissions and death. These endpoints are universally perceived to be undesirable patient outcomes and have the advantages of being easy to identify and convenient for benchmarking, but they are also crude and sometimes incorrect markers of overall quality as well as safety.

9.4.2 Uses of patient safety indicators

To reiterate the statement made at the end of the previous sub-section, measurement must be fit for purpose. Evidence is weak but exists for changes in clinical and patient attitudes and behaviours in non-acute care settings through the measurement and publication of provider performance data.[371,415-418] In contrast, there is also the perception among staff in primary care that data-driven safety improvement initiatives are resource wasteful and have a low impact on safer delivery of care.[183] The ability of indicators to improve safety depends not only on technical factors (including data quality, validity of the measures and how they are applied), but also relies on the willingness of clinicians, managers and policy makers to participate in patient safety improvement and to implement and adapt metrics according to their respective needs. Therefore, to ensure wider use of routinely collected data for monitoring patient safety, cultural change is needed.[89,419,420] This is all the more important as care continues to be tailored to the individual and patient choice, delineated by the NHS

Constitution, is encouraged.[421] As unpopular a policy as it is, GP-led commissioning may offer the opportunity to develop and implement safety indicators that are locally and clinically relevant, as seen in the QOF+ initiative at NHS Hammersmith and Fulham.[422]

9.4.3 Strengths and limitations of patient safety indicators

Routinely collected data can be applied to screen for different types of patient harm in general practice. With the presence of only a few data fields, basic surveillance algorithms can be implemented which allow for the detection of AEs at local or national levels. The accuracy and detail of safety efforts will depend on the available data. For instance, the validity of case ascertainment can be improved by data from multiple care settings which will invariably require data linkage. However, this method has the advantages of being relatively cheap and easy to manipulate, although data linkage may prove to be more resource costly depending on required linkage complexity, along with the potential for real-time monitoring (Chapter 1 section 1.4.2). There are promising signs for improved access and quality of data, such as the GPES (Chapter 1 section 1.6.2).[134] There is also government commitment to electronic care records across health and social care.[423] Such potential advances in the healthcare data environment support the further research and applications of patient safety indicators based on clinical and non-clinical data.

Safety and quality improvement in healthcare continues to evolve but there is a persisting challenge of how to ensure that implemented measures are meaningful and useful for different parties of interest, including patients and health professionals. This issue extends to the appropriateness of data presentation, while elements such as severity and preventability are only crudely captured through current indicators (Chapter 2 sections 2.5.5 and 2.5.7). There is growing recognition that inclusivity must be integral to plans for improving the quality and safety in the NHS, as evident from recent public consultations on outcome measures.[14] It remains to be seen how well placed current indicators are to provide feedback as part of a national safety monitoring system, and in local schemes. Not only are there limitations in the range of indicators available and the technical requirements for their use (section 9.4.1), but there is also institutionalised weariness and apprehension about quality and safety monitoring which must be overcome if patient safety indicators are to become firmly established within the safety improvement toolkits.[183]

At present, as remarked in Chapter 2 (section 2.6.6), there is a dearth of knowledge about, and consequently also few indicators for, AEs in primary care occurring outside of general practice, including community nursing, dentistry and pharmacy. Through a wider range of data being collected, improved quality of the data and with greater integration of datasets, a more holistic understanding of care spanning all sections of healthcare may be gained (section 9.3.3). Earlier in this chapter, I raised the difficulty of measuring the preventability of harm (section 9.2.3). Prudently, the focus of AE monitoring has been on incidents that are detectable, measureable and amenable to organisational change. Although resources are limited, it may also be worthwhile to consider those AEs that are not yet easily detectable from routinely collected data as well as 'near misses'. Even though these incidents may be less clinically relevant, especially if they result in no or temporary and less severe harm, learning can still be gained from their occurrences and the consequences of these events for patients and staff should be explored (section 2.6.5).

9.5 Strengths and limitations of the project

In recognition of the broad discipline of primary care and the breadth of the patient safety field, I focused on patient harm attributable to care from general practice. I have commented on the strengths and weaknesses associated with the overarching methods used in the project and those pertaining to individual studies. This section is a summary of the project, with attention to research, clinical practice and health policy.

There are a number of strengths to the research presented in this thesis. Firstly, three different AEs were investigated, including a generic measure of harm based on existing complications of care codes. Secondly, local and national data were analysed to demonstrate the suitability and versatility of routinely collected data for safety measurement. Datasets included HES and the GPRD, which are nationally representative and widely validated. These data were obtained for the purposes of this project at no financial cost[*]. Thirdly, the GPRD dataset contained patient-level data spanning ten years which allowed the exploration of temporal trends in recorded AEs. Fourthly, external validation of findings was possible using different datasets for two of the indicators (AEs

[*]Data from the GPRD were obtained for free under the now expired MRC licence for academic research.

derived from complication of care codes and cancers diagnosed by emergency admissions). Additional validation was achieved by comparing results with published literature. Finally, patient groups at high risk of AEs as well as adverse and other outcomes were identified.

Study-specific methodological weaknesses have been discussed in earlier chapters and further summarised in section 9.3. The implications of the project's strengths and limitations on patient safety are outlined in the following two sub-sections.

9.5.1.1 Implications for research

Research on patient safety indicators derived from routinely collected data in general practice remains underdeveloped. Consequently, the field suffers from concentrated efforts using limited data sources in the areas of primary care where common types of AEs have been identified (Chapter 2). Despite this limitation, it is reasonable to first develop measurement expertise in those areas that have been well documented, before applying these skills and knowledge to less well understood areas of care and AEs that are harder to detect. The baseline estimates from AE measures using complication of care codes in Chapters 5 and 6 offer a robust foundation on which to build more sophisticated generic and disease or patient group-specific indicators in general practice and elsewhere in primary care.

Future expectations for such measures will no doubt include real-time alerts for unusual patterns in processes of care or patient outcomes, indicators for entire care pathways and measures that are valid across different health systems. Furthermore, aside from the conventional outcomes of hospital admission, readmissions and mortality, new indicators must address other neglected outcomes that are of interest to patients and other parties, such as quality of life and long term outcomes (Chapter 8 section 8.4.4.5 and section 9.4.3). This project has demonstrated the potential to measure AEs using diagnosis codes from existing medical classification systems. In general practice and elsewhere in English primary care, greater uptake of SNOMED CT will facilitate the international comparability of research due to worldwide application of the terminology system (Chapter 1 section 1.6.3).

9.5.1.2 Implications for clinical practice and policy

This project was exploratory in nature and selection of indicators relied on published material of existing measures. This somewhat pragmatic approach is suitable for research in a relatively novel field where methodological handicaps, as undesirable as they may be, can inform future studies by highlighting deficits in technical abilities and remaining gaps in knowledge. However, to inform practice and health policy, research also needs to be guided by clinical need and organisational status, such as the availability of necessary infrastructure and resources to implement indicator-based safety surveillance. From the perspective of clinical application, each of the three measures from this project can be readily replicated for AE monitoring, although their success will be affected by caveats of the measures, the data and populations of interest (sections 9.3.1 and 9.4.3). The generic AE measures based on complication of care codes may be best suited for active surveillance at either the local or national level as minimal modifications are required.

The results are promising for the continued development of measures using routinely collected data to improve patient safety. Service commissioners and policy makers should consider refinement of current measures but also encourage new metrics to be developed. Attempts to advance indicator development and to better understand patient harm so that AEs can be ameliorated, data must be improved. The proposed “paperless” system for patient records which will unify information across health and social care will hopefully not only add richness and variety to data sources, but will also improve the quality and safety of services through availability of patient data at the point of care (section 9.4.3).[423] Of paramount importance is cooperation between those who manage and use health data across all care settings so that the quality, access and uses of these resources can be optimised for safety improvement, the delivery of care and management of services.

9.6 Conclusion

Few AE measures have been developed specifically for general practice using routinely collected data. The studies presented in this thesis demonstrate some of the AEs that can be detected using available data, but a much wider range of incidents occurring in general practice can also be measured. Examples of how research methods, data sources as well as analysis methods influence the choice of indicators for research have been provided. Our

current knowledge about the types of patient safety indicators, their uses and their strengths and limitations has also been considered. There is scope to expand the application of routinely collected data for safety monitoring in the primary care setting, such as real time surveillance using complication of care coded measures that are readily available.

This relatively new field may deliver great benefits to patient safety improvement but for there to be progress, there must be local and national commitment to these efforts. As stated earlier in this chapter (section 9.4.3), there is currently a government drive for the ambitious overhaul of how patient records are managed.

Appendices

Appendix 1. Outputs from the project

Publications related to the project

1. Bottle A, Tsang C, Parsons C, Majeed A, Soljak M, Aylin P. Association between patient and general practice characteristics and unplanned first-time admissions for cancer: observational study. Br J Cancer. 2012;107(8):1213-1219.
2. Tsang C, Majeed A, Aylin P. Consultations with general practitioners on patient safety measures based on routinely collected data in primary care. JRSM Short Rep. 2012;3:5.
3. Tsang C, Palmer W, Bottle A, Majeed A, Aylin P. A Review of Patient Safety Measures Based on Routinely Collected Hospital Data. Am J Med Qual. 2012;27(2):154-69.
4. Tsang C, Majeed A, Aylin P. Routinely recorded patient safety events in primary care: a literature review. Fam Pract. 2011;29(1):8-15.
5. Tsang C, Majeed A, Banarsee R, Gnani S, Aylin P. Adverse events in English general practice: analysis of data from electronic patient records. Inform Prim Care. 2010;18(2):117-24.

Conference abstracts related to the project

1. Bottle A, Tsang C, Parsons C, Majeed A, Soljak M, Aylin P. (2012) Association between patient and family practitioner characteristics and first-time emergency admissions for cancer. WONCA Europe, Vienna, 4th-7th July 2012 (Oral presentation).
2. Tsang C, Majeed A, Aylin P. (2010) Adverse events in English general practice: analysis using administrative data. International Society for Quality in Health Care Conference, Paris, 11th-13th October 2010 (Accepted for oral poster presentation).
3. Tsang C, Majeed A, Banarsee R, Gnani S, Aylin P. (2010) Adverse events in English general practice. Presented at Society of Academic Primary Care Annual Conference, Norwich, 7th-10th July (Oral presentation, shortlisted for Early Career Researcher's prize).
4. Tsang C, Majeed A, Aylin P. (2010) Recording of adverse events in English general practice: analysis of data from electronic patient records. Patient Safety Congress, Birmingham, 25th-26th May (Poster).
5. Tsang C, Majeed A, Aylin P. (2010) Recording of adverse events in English general practice: analysis of data from electronic patient records. Working Conference Health Services Research in Europe, The Hague, 8th-9th April (Abstract published in conference book).
6. Tsang C, Majeed A, Aylin P. (2010) The use of administrative data to measure adverse events in primary care: evidence from the literature. UK Annual Public Health Forum, Bournemouth, 24th-25th March (Poster).
7. Tsang C, Aylin P, Majeed A. (2009) Patient safety indicators for primary care. National Patient Safety Agency 3rd Annual UK Patient Safety Conference, London, 16th December (Poster).
8. Tsang C, Aylin P, Majeed A. (2009) Patient safety indicators for primary care. International Society for Quality in Health Care Conference, Dublin, 12th-14th October (Poster).
9. Tsang C, Aylin P, Majeed A. (2009) Patient safety indicators for primary care. Abstract presented at the Patient Safety Congress, Birmingham, 31st April-1st May (Poster).

Appendix 2. Literature review material

Table A.1 List of organisations included the website search (Chapter 2)

Accreditation Canada
Action Against Medical Accidents
Agency for Healthcare Research and Quality
American Hospital Association
Australian Council for Safety and Quality in Health Care
Australian Council of Healthcare Standards
Australian Government
Australian Institute of Health and Welfare
Australian Patient Safety Foundation
Canadian Institute for Health Information
Canadian Patient Safety Institute
Danish Society for Patient Safety
Danish Society for Quality in Health Care
Department of Health
Department of Health and Ageing
European Commission
European Society for Quality in Healthcare
Health Foundation
Healthcare Commission
Institute for Healthcare Improvement
Institute for Safe Medication Practices
Institute for Safe Medication Practices, Canada
Institute of Medicine
International Society of Quality in Healthcare
Joint Commission International
King's Fund
Medical Defence Union
Medical Research Council
National Audit Office
National Institute for Clinical Excellence
National Institute for Health Research
National Patient Safety Agency
National Patient Safety Foundation
NHS Institute for Innovation and Improvement
NHS Litigation Authority
Organisation for Economic Co-operation and Development
Patient Safety Observatory
Royal Australian College of General Practice
Royal Australian College of Physicians
Royal College of General Practitioners
Royal College of Physicians and Surgeons of Canada
The Commonwealth Fund
The Joint Commission
United States Department of Veteran Affairs - National Center for Patient Safety
University of Birmingham
University of California San Francisco-Stanford Evidence-Based Practice Center
World Health Organization

Table A.2 Literature search results from ASSIA: Applied Social Sciences Index and Abstracts

#	Search term	Results
1	Ambulatory care	184
2	Ambulatory care facilit	3
3	Ambulatory care physician	0
4	Family physician*	259
5	Family Practice	1525
6	General practice	2685
7	General practitioner*	3682
8	Primary care	5868
9	Primary Health Care	4381
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	12450
11	Accident Prevention	51
12	Outcome assessment*	152
13	Outcome and Process assessment*	7
14	Patient outcome*	517
15	Patient care	2394
16	Patient safety	460
17	Quality assessment*	281
18	Quality improvement*	723
19	Quality indicator*	146
20	Healthcare quality indicators	0
21	Safety assessment*	44
22	Safety improvement*	19
23	Safety Management	18
24	Safety	5725
25	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24	9455
26	Adverse event*	512
27	Avoidable complication*	5
28	Avoidable death*	28
29	Diagnostic error*	14
30	Healthcare associated injuries	0
31	Healthcare associated injury	0
32	Iatrogenic disease*	9
33	Medical error*	106
34	Medication error*	86
35	Patient safety index	0
36	Patient safety indicator*	7
37	Patient safety indices	0
38	Preventable complication*	6
39	Sentinel event*.	15
40	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39	757
41	Administrative data	215
42	Billing data	7
43	Billing record*	9
44	Consultation record*	4
45	Discharge data	91
46	Discharge summar*	38
47	Hospital Information System*	24
48	Information system*	1090
49	Hospital record*	104
50	inpatient data	6
51	Medical Record*	1012
52	Electronic data	52

53	Electronic record*	34
54	Computer* medical record* system*	2
55	Routine data	78
56	Routinely collected data	45
57	41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56	2669
58	25 or 40	10212
59	10 and 57 and 58	45
60	59 limit to English language	42

Search time period: Earliest to 2010. Interface: CSA Illumina. Search method: command. Search strategy: non MeSH terms. Search field: keyword.

Table A.3 Literature search results from Cochrane Library

#	Search term	Results
1	(Ambulatory care facilit):ti,ab,kw	0
2	(Ambulatory care physician):ti,ab,kw	317
3	Ambulatory care	5629
4	Family Practice	6395
5	General practice	11957
6	Family physician*	2864
7	Primary Health Care	17399
8	Primary care	22894
9	General practitioner*	4151
10	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9)	36506
11	Accident Prevention	1089
12	Outcome assessment*	35473
13	Outcome and Process assessment*	9149
14	Patient outcome*	93544
15	Patient care	57676
16	Patient safety	31891
17	Quality assessment*	22061
18	Quality improvement*	11881
19	Quality indicator*	1984
20	Healthcare quality indicator*	290
21	Safety assessment*	9309
22	Safety improvement*	7733
23	Safety Management	3979
24	Safety	42642
25	(#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24)	160676
26	Adverse event*	28143
27	Avoidable complication*	40
28	Avoidable death*	46
29	Diagnostic error*	1673
30	Healthcare associated injur*	257
31	Iatrogenic disease*	243
32	Medical error*	8915
33	Medication error*	1713
34	Patient safety index	6590
35	Patient safety indicator*	410
36	Patient safety indices	6590
37	Preventable complication*	128
38	Sentinel event*	51
39	(#26 OR #27 OR #28 OR #29 OR #30 OR 31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38)	74031
40	Administrative data	814
41	Billing data	495
42	Billing record*	466
43	Consultation record*	2592
44	Discharge data	4390
45	Discharge summar*	1773
46	Hospital Information System*	7997
47	Information system*	22908
48	Hospital record*	25020
49	inpatient data	3288
50	Medical Record*	78141
51	Electronic data	6543

52	Electronic record*	7118
53	Computer* medical record* system*	3636
54	Routine data	5141
55	Routinely collected data	419
56	(#40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55)	86991
57	(#10 AND #25 AND #39 AND #56)	9172
58	(#10 AND (#25 OR #39) AND #56)	17032

**No limit available for language restrictions in advanced search.

Search time period: 1800 to 2009. Search method: advanced. Search strategy: non-MeSH. Search field: title, abstract or keywords.

Where terms were mapped, the fields used in the search were: [mp=abstract:ab, keyword :kw, title:ti].

Table A.4 Literature search results from Embase

#	Search term	Results
1	Ambulatory care.mp. or Ambulatory Care/	8454
2	"Ambulatory care facilit*".sh,ab,tw,ti,ot,kf,hw,kw.	81
3	"Ambulatory care physician*".sh,ab,tw,ti,ot,kf,hw,kw.	26
4	Physicians, Family/ or Family physician*.mp.	35230
5	Family practice.mp. or Family Practice/	25199
6	General practice.mp.	29160
7	Physician*, Family.mp.	175
8	Primary Health Care/ or Primary care*.mp.	45436
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	101083
10	Patient care.mp. or Patient Care/	95526
11	Patient safety.mp.	16485
12	Quality assessment*.mp.	3944
13	Quality improvement*.mp.	5607
14	Quality indicator*.mp.	1619
15	Quality Indicators, Health Care.mp.	1
16	Safety.mp. or Safety/	279637
17	Safety assessment*.mp.	2056
18	Safety Management/ or Safety Management.mp.	48302
19	Safety improvement*.mp.	126
20	Accident Prevention.mp. or Accident Prevention/	5940
21	"Outcome Assessment (Health Care)"/ or "Outcome and Process Assessment (Health Care)"/ or patient outcome.mp.	414568
22	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	746834
23	Patient safety indicator*.mp.	43
24	Patient safety index.mp.	1
25	Patient safety indices.mp.	0
26	Adverse event*.mp.	40647
27	Medical error*.mp.	3800
28	Medication error*.mp.	3840
29	Sentinel event*.mp.	232
30	Healthcare associated injury.mp.	1
31	Healthcare associated injuries.mp.	0
32	Iatrogenic disease*.mp.	10857
33	Postoperative Complications/ or Preventable complication*.mp. or Foreign Bodies/	112023
34	Avoidable death*.mp.	169
35	Avoidable complication*.mp.	122
36	Diagnostic Errors/ or Diagnostic error*.mp.	20084
37	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	187823
38	Administrative data.mp.	1436
39	Medical Records/ or Electronic data.mp. or Medical Records Systems, Computerized/	42857
40	Inpatient data.mp.	97
41	Routine data.mp.	445
42	Routinely collected data.mp.	297
43	Hospital Records/ or Hospital record*.mp.	44147
44	Hospital Information Systems/ or Information Systems/ or Information system*.mp.	24729
45	Discharge data.mp.	1083
46	Billing data.mp.	212
47	Billing record*.mp.	199
48	Consultation record*.mp.	42
49	Discharge summary*.mp.	188
50	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49	70721
51	22 or 37	870381
52	9 and 50 and 51	1326
53	limit 52 to English language	1257

Search time period: 1980 to 2009 week 34. Interface: Ovid. Search method: advanced. Search strategy: MeSH and non-MeSH.

Where terms were mapped, the fields used in the search were: [mp=abstract:ab, keyword heading:kw, keyword heading word:kf, original title:ti, subject heading word:sh, text word:tw].

Table A.5 Literature search results from HMIC Health Management Information Consortium

#	Search term	Results
1	Ambulatory care.mp. or Ambulatory Care/	415
2	"Ambulatory care facilit*".sh,ab,tw,ti,ot,kf,hw,kw.	8
3	"Ambulatory care physician*".sh,ab,tw,ti,ot,kf,hw,kw.	6
4	Physicians, Family/ or Family physician*.mp.	212
5	Family practice.mp. or Family Practice/	196
6	General practice.mp.	14486
7	Physician*, Family.mp.	8
8	Primary Health Care/ or Primary care*.mp.	21114
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	31584
10	Patient care.mp. or Patient Care/	16756
11	Patient safety.mp.	1936
12	Quality assessment*.mp.	497
13	Quality improvement*.mp.	3067
14	Quality indicator*.mp.	321
15	Quality Indicators, Health Care.mp.	0
16	Safety.mp. or Safety/	19272
17	Safety assessment*.mp.	54
18	Safety Management/ or Safety Management.mp.	82
19	Safety improvement*.mp.	81
20	Accident Prevention.mp. or Accident Prevention/	297
21	"Outcome Assessment (Health Care)"/ or "Outcome and Process Assessment (Health Care)"/ or patient outcome.mp.	3395
22	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	40585
23	Patient safety indicator*.mp.	19
24	Patient safety index.mp.	0
25	Patient safety indices.mp.	0
26	Adverse event*.mp.	661
27	Medical error*.mp.	247
28	Medication error*.mp.	397
29	Sentinel event*.mp.	24
30	Healthcare associated injury.mp.	2
31	Healthcare associated injuries.mp.	0
32	Iatrogenic disease*.mp.	69
33	Postoperative Complications/ or Preventable complication*.mp. or Foreign Bodies/	3
34	Avoidable death*.mp.	121
35	Avoidable complication*.mp.	9
36	Diagnostic Errors/ or Diagnostic error*.mp.	21
37	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	1463
38	Administrative data.mp.	187
39	Medical Records/ or Electronic data.mp. or Medical Records Systems, Computerized/	2601
40	Inpatient data.mp.	4
41	Routine data.mp.	190
42	Routinely collected data.mp.	144
43	Hospital Records/ or Hospital record*.mp.	362
44	Hospital Information Systems/ or Information Systems/ or Information system*.mp.	6800
45	Discharge data.mp.	88
46	Billing data.mp.	12
47	Billing record*.mp.	6
48	Consultation record*.mp.	19
49	Discharge summary*.mp.	32

50	38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49	9872
51	22 or 37	41330
52	9 and 50 and 51	181

**No limit available for language restrictions in advanced search.
Search time period: 1979 to July 2009. Interface: Ovid. Search method: Advanced. Search strategy: non-MeSH.

Where terms were mapped, the fields used in the search were: [mp=abstract:ab, keyword heading:kw, keyword heading word:kf, original title:ti, subject heading word:sh, text word:tw].

Table A.6 Literature search results from ISI Web of Science

#	Search term	Results
1	TS=Ambulatory care facilit*	690
2	TS=Ambulatory care physician*	2,258
3	TS=Ambulatory care	8,576
4	TS=Family Practice	17,521
5	TS=General practice	45,968
6	TS=Family physician*	14,275
7	TS=Primary Health Care	37,131
8	TS=Primary care	77,487
9	TS=General practitioner*	25,272
10	#9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1	>100,000
11	TS=Accident Prevention	2,211
12	TS=Outcome assessment*	38,867
13	TS=(Outcome and Process assessment*)	2,837
14	TS=Patient outcome*	>100,000
15	TS=Patient care	>100,000
16	TS=Patient safety	32,181
17	TS=Quality assessment*	65,905
18	TS=Quality improvement*	69,766
19	TS=Quality indicator*	22,316
20	TS=Healthcare quality indicator*	492
21	TS=Safety assessment*	24,092
22	TS=Safety improvement*	17,804
23	TS=Safety Management	25,968
24	TS=Safety	>100,000
25	#11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24	>100,000
26	TS=Adverse event*	51,852
27	TS=Avoidable complication*	444
28	TS=Avoidable death*	595
29	TS=Diagnostic error*	6,237
30	TS=Healthcare associated injur*	291
31	TS=Iatrogenic disease*	2,532
32	TS=Medical error*	8,451
33	TS=Medication error*	2,862
34	TS=Patient safety index	1,489
35	TS=Patient safety indicator*	401
36	TS=Patient safety indices	119
37	TS=Preventable complication*	912
38	TS=Sentinel event*	529
39	#26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38	72,419
40	TS=Administrative data	7,719
41	TS=Billing data	1,087
42	TS=Billing record*	590
43	TS=Consultation record*	1,985
44	TS=Discharge data	28,472
45	TS=Discharge summar*	2,282
46	TS=Hospital Information System*	7,551
47	TS=Information system*	>100,000
48	TS=Hospital record*	33,491
49	TS=inpatient data	7,223
50	TS=Medical Record*	47,880
51	TS=Electronic data	52,168

52	TS=Electronic record*	13,837
53	TS=Computer* medical record* system*	2,197
54	TS=Routine data	25,388
55	TS=Routinely collected data	1,880
56	#40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55	>100,000
57	#10 and #25 and #39 and #56	591
58	#10 and (#25 or #39) and #56	7,941
59	#10 and (#25 or #39) and #56 AND Language=(English)	7,618

Databases searched: Science Citation Index Expanded (SCI-EXPANDED)--1970-present, Social Sciences Citation Index (SSCI)--1970-present, Conference Proceedings Citation Index- Science (CPCI-S)--1990-present. Search field: title, abstract or keywords. Search method: advanced. Search strategy: non-MeSH.

Table A.7 Literature search results from Medline

#	Search term	Results
1	Ambulatory care.mp. or Ambulatory Care/	43196
2	"Ambulatory care facilit*".sh,ab,tw,ti,ot,kf,hw,kw.	9269
3	"Ambulatory care physician*".sh,ab,tw,ti,ot,kf,hw,kw.	38
4	Physicians, Family/ or Family physician*.mp.	19899
5	Family practice.mp. or Family Practice/	57405
6	General practice.mp.	26835
7	Physician*, Family.mp.	13421
8	Primary Health Care/ or Primary care*.mp.	70600
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	178575
10	Patient care.mp. or Patient Care/	108521
11	Patient safety.mp.	6889
12	Quality assessment*.mp.	5039
13	Quality improvement*.mp.	9419
14	Quality indicator*.mp.	7461
15	Quality Indicators, Health Care.mp.	6149
16	Safety.mp. or Safety/	205460
17	Safety assessment*.mp.	1969
18	Safety Management/ or Safety Management.mp.	11097
19	Safety improvement*.mp.	201
20	Accident Prevention.mp. or Accident Prevention/	8143
21	"Outcome Assessment (Health Care)"/ or "Outcome and Process Assessment (Health Care)"/ or patient outcome.mp.	56656
22	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	381615
23	Patient safety indicator*.mp.	111
24	Patient safety index.mp.	0
25	Patient safety indices.mp.	0
26	Adverse event*.mp.	43081
27	Medical error*.mp.	9100
28	Medication error*.mp.	8172
29	Sentinel event*.mp.	403
30	Healthcare associated injury.mp.	2
31	Healthcare associated injuries.mp.	0
32	Iatrogenic disease*.mp.	10970
33	Postoperative Complications/ or Preventable complication*.mp. or Foreign Bodies/	263750
34	Avoidable death*.mp.	248
35	Avoidable complication*.mp.	158
36	Diagnostic Errors/ or Diagnostic error*.mp.	26994
37	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	356819
38	Administrative data.mp.	1987
39	Medical Records/ or Electronic data.mp. or Medical Records Systems, Computerized/	46878
40	Inpatient data.mp.	127
41	Routine data.mp.	550
42	Routinely collected data.mp.	350
43	Hospital Records/ or Hospital record*.mp.	7110
44	Hospital Information Systems/ or Information Systems/ or Information system*.mp.	44339
45	Discharge data.mp.	1371
46	Billing data.mp.	293
47	Billing record*.mp.	269
48	Consultation record*.mp.	64
49	Discharge summary*.mp.	278
50	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49	94535
51	22 or 37	704375
52	9 and 50 and 51	1364
53	limit 52 to English language	1280

Search time period: In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1950 to Present (1950 to week 34 2009). Interface: Ovid. Search method: advanced. Search strategy: MeSH and non-MeSH.

Where terms were mapped, the fields used in the search were: [mp=abstract:ab, keyword heading:kw, keyword heading word:kf, original title:ti, subject heading word:sh, text word:tw].

Table A.8 Literature search results from PsycINFO

#	Search term	Results
1	Ambulatory care.mp. or Ambulatory Care/	4791
2	"Ambulatory care facilit*".sh,ab,tw,ti,ot,kf,hw,kw.	6
3	"Ambulatory care physician*".sh,ab,tw,ti,ot,kf,hw,kw.	4
4	Physicians, Family/ or Family physician*.mp.	2073
5	Family practice.mp. or Family Practice/	1355
6	General practice.mp.	2879
7	Physician*, Family.mp.	106
8	Primary Health Care/ or Primary care*.mp.	15757
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	24662
10	Patient care.mp. or Patient Care/	6329
11	Patient safety.mp.	531
12	Quality assessment*.mp.	435
13	Quality improvement*.mp.	1283
14	Quality indicator*.mp.	420
15	Quality Indicators, Health Care.mp.	0
16	Safety.mp. or Safety/	25175
17	Safety assessment*.mp.	150
18	Safety Management/ or Safety Management.mp.	148
19	Safety improvement*.mp.	54
20	Accident Prevention.mp. or Accident Prevention/	1186
21	"Outcome Assessment (Health Care)"/ or "Outcome and Process Assessment (Health Care)"/ or patient outcome.mp.	354
22	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	34132
23	Patient safety indicator*.mp.	11
24	Patient safety index.mp.	0
25	Patient safety indices.mp.	0
26	Adverse event*.mp.	3852
27	Medical error*.mp.	229
28	Medication error*.mp.	154
29	Sentinel event*.mp.	33
30	Healthcare associated injury.mp.	0
31	Healthcare associated injuries.mp.	0
32	Iatrogenic disease*.mp.	33
33	Postoperative Complications/ or Preventable complication*.mp. or Foreign Bodies/	8
34	Avoidable death*.mp.	21
35	Avoidable complication*.mp.	3
36	Diagnostic Errors/ or Diagnostic error*.mp.	162
37	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	4440
38	Administrative data.mp.	466
39	Medical Records/ or Electronic data.mp. or Medical Records Systems, Computerized/	1145
40	Inpatient data.mp.	23
41	Routine data.mp.	57
42	Routinely collected data.mp.	34
43	Hospital Records/ or Hospital record*.mp.	629
44	Hospital Information Systems/ or Information Systems/ or Information system*.mp.	4499
45	Discharge data.mp.	169
46	Billing data.mp.	37
47	Billing record*.mp.	28
48	Consultation record*.mp.	14
49	Discharge summary*.mp.	46
50	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49	7006
51	22 or 37	36972
52	9 and 50 and 51	36
53	limit 52 to English language	36

Search time period: 1806 to August Week 3 2009. Interface: Ovid. Search method: advanced. Search strategy: MeSH and non-MeSH.

Where terms were mapped, the fields used in the search were: [mp=abstract:ab, keyword heading:kw, keyword heading word:kf, original title:ti, subject heading word:sh, text word:tw]

Appendix 3. Adverse event codes used in Chapters 5 and 6

Table A.9 READ codes for adverse events mapped to ICD 10 codes

ICD-10							READ codes	
Chapter	**Blocks**	**Chapter name**	**Subgroups**	**Subgroup name**	**Codes**	**Code name**	**Codes**	**Description**
V	F00-F99	Mental and behavioural disorders	F10-F19	Mental and behavioural disorders due to psychoactive substance use	F10-F19	All code names within subgroups	Eu1..	[X]Mental and behavioural disorders due to psychoactive substance use
XIX	S00-T98	Injury, poisoning and certain other consequences of external causes			T36-T50	Poisoning by drugs, medicaments and biological substances	SL…	Poisoning
					T80-T88	Complications of surgical and medical care, not elsewhere classified	SP…	Surgical and medical complications NEC
					T82-T87	Complications of cardiac and vascular prosthetic devices, implants and grafts - Complications peculiar to reattachment and amputation	SP0..	Complications of certain procedures
						Not available in ICD-10	SP1..	Body system complications NEC
					T81.9	Unspecified complication of procedure	SP2..	Other procedure complication NEC
					T88.9	Complication of surgical and medical care, unspecified	SP3..	Medical care complication NEC
					T88.9	Complication of surgical and medical care, unspecified	SPz..	Medical and surgical care complications NOS
Not applicable, mapped to ICD-9 but not ICD-10.							TA...	Medical accidents to patients during surgical and medical care
							TA0..	Accidental cut, puncture, perforation or haemorrhage during medical care

							TA1..	Foreign object left in body during procedure
							TA2..	Failure of sterile precautions during procedure
							TA3..	Failure in dosage
							TA4..	Mechanical failure of instrument or apparatus during procedure
							TA5..	Administration of contaminated blood, other fluid, drug or biological substance
							TAy..	Other misadventures during medical care
							TAz..	Medical accident to patient NOS
							TB...	Medical and surgical procedures as the cause of abnormal reaction of patient or later complication, without mention of misadventure at the time of procedure
							TJ...	Drugs, medicines and biological substances causing adverse effects in therapeutic use
							TK…	Suicide and self-inflicted injury
							Tz...	Causes of injury and poisoning NOS
XX	V01-Y98	External causes of morbidity and mortality	X60-X84	Intentional self-harm	X60-X84	All code names within subgroups	U2...	[X]Intentional self-harm
			Y10-Y34	Event of undetermined intent	Y10-Y14	Poisoning by and exposure to drugs, medicaments and biological substances, undetermined intent	U40..	[X]Poisoning by and exposure to drugs, medicaments and biological substances, undetermined intent
			Y40-Y84	Complications of medical and surgical care	Y40-Y59	Drugs, medicaments and biological substances causing adverse effects in therapeutic use	U60..	[X]Drugs, medicaments and biological substances causing adverse effects in therapeutic use
					Y60-Y69	Misadventures to patients during surgical and medical care	U61..	[X]Misadventures to patients during surgical and medical care

		Y70-Y82	Medical devices associated with adverse incidents in diagnostic and therapeutic use	U62..	[X]Medical devices associated with adverse incidents in diagnostic and therapeutic use
		Y83	Surgical operation and other surgical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure	U63..	[X]Surgical operation and other surgical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure
		Y84	Other medical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure	U64..	[X]Other medical procedures causing abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure
Y85-Y89	Sequelae of external causes of morbidity and mortality	Y88	Sequelae with surgical and medical care as external cause	U73..	[X]Sequelae with surgical and medical care as external cause
		Y88.0	Sequelae of adverse effects caused by drugs, medicaments and biological substances in therapeutic use	U730.	[X]Sequelae of adverse effects caused by drugs, medicaments and biological substances in therapeutic use
		Y88.1	Sequelae of misadventures to patients during surgical and medical procedures	U731.	[X]Sequelae of misadventures to patients during surgical and medical procedures
		Y88.2	Sequelae of adverse incidents associated with medical devices in diagnostic and therapeutic use	U732.	[X]Sequelae of adverse incidents associated with medical devices in diagnostic and therapeutic use
		Y88.3	Sequelae of surgical and medical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure	U733.	[X]Sequelae of surgical and medical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure

Y90-Y98	Supplementary factors related to causes of morbidity and mortality classified elsewhere	Y95	Nosocomial condition	U82..	[X]Nosocomial condition

Source: Date of consultation as provided in the GPRD dataset. From International Statistical Classification of Diseases and Related Health Problems 10th Revision Version for 2007, Chapter XIX Injury, poisoning and certain other consequences of external causes (S00-T98) and Chapter XX External causes of morbidity and mortality (V01-Y98) - Complications of medical and surgical care (Y40-Y84).

Exclusions

From Chapter XIX:

- Frostbite (T33-T35);
- Toxic effects of substances chiefly nonmedicinal as to source (T51-T65);
- Other and unspecified effects of external causes (T66-T78);
- Sequelae of injuries, of poisoning and of other consequences of external cause (T90-98).

From Chapter XX:

- Accidents (V01-X59);
- Intentional self-harm (X60-X84);
- Assault (X85-Y09);
- Event of undetermined intent (Y10-Y34);
- Legal intervention and operations of war (Y35-Y36);
- Sequelae of external causes of morbidity and mortality (Y85-Y89);

Supplementary factors related to causes of morbidity and mortality classified elsewhere (Y90-Y91, Y96-Y98).

Appendix 4. Results from analyses in Chapters 6 to 8

Table A.10 Crude associations between comorbidities and risk of having an adverse event, results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic		Patients, n			RR (95% CI)	P-value
		All	≥1 adverse event	(%)		
Disease flags						
Composite Charlson Index measure						<0.0001
	No	59034	921	(1.56)	1	
	Yes	15729	853	(5.42)	3.14 (2.88-3.42)	<0.0001
Cancer						<0.0001
	No	73651	1687	(2.29)	1	
	Yes	1112	87	(7.82)	3.16 (2.58-3.86)	<0.0001
Cerebrovascular disease						<0.0001
	No	73620	1677	(2.28)	1	
	Yes	1143	97	(8.49)	3.81 (3.18-4.57)	<0.0001
Congestive heart disease						<0.0001
	No	65836	1436	(2.18)	1	
	Yes	8927	338	(3.79)	1.46 (1.31-1.63)	<0.0001
Chronic pulmonary disease						<0.0001
	No	73991	1703	(2.30)	1	
	Yes	772	71	(9.20)	4.52 (3.66-5.59)	<0.0001
Dementia						0.001
	No	74449	1760	(2.36)	1	
	Yes	314	14	(4.46)	2.45 (1.54-3.90)	<0.0001
Diabetes without complications						<0.0001
	No	71837	1546	(2.15)	1	
	Yes	2926	228	(7.79)	3.46 (3.06-3.92)	<0.0001
Diabetes with complications						<0.0001
	No	74526	1745	(2.34)	1	
	Yes	237	29	(12.2)	4.95 (3.59-6.82)	<0.0001
Hemiplegia						<0.0001
	No	74693	1765	(2.36)	1	
	Yes	70	9	(12.9)	4.40 (2.36-8.19)	<0.0001
Metastatic tumour						<0.0001
	No	74625	1763	(2.36)	1	
	Yes	138	11	(7.97)	3.36 (1.90-5.92)	<0.0001
Mild liver disease						0.008
	No	74748	1772	(2.37)	1	
	Yes	15	2	(13.3)	7.62 (2.46-23.7)	<0.0001
Moderate liver disease						<0.0001
	No	74186	1712	(2.31)	1	
	Yes	577	62	(10.8)	4.76 (3.82-5.93)	<0.0001
Myocardial infarction						0.314
	No	74669	1770	(2.37)	1	
	Yes	94	4	(4.26)	1.63 (0.68-3.92)	0.276
Peptic ulcer disease						<0.0001
	No	74161	1716	(2.31)	1	

	Yes	602	58	(9.63)	4.08 (3.27-5.09)	<0.0001
Peripheral vascular disease						<0.0001
	No	74103	1685	(2.27)	1	
	Yes	660	89	(13.5)	5.29 (4.35-6.43)	<0.0001
Renal disease						<0.0001
	No	72971	1568	(2.15)	1	
	Yes	1792	206	(11.5)	4.50 (3.95-5.13)	<0.0001
Rheumatological disease						<0.0001
	No	73832	1694	(2.29)	1	
	Yes	931	80	(8.59)	3.26 (2.67-3.98)	<0.0001
Aggregated Disease Groups (ADGs)						
Time Limited: Minor						<0.0001
	No	31868	407	(1.28)	1	
	Yes	39787	1367	(3.44)	2.14 (1.93-2.38)	<0.0001
Time Limited: Minor-Primary						<0.0001
	No	19988	224	(1.12)	1	
	Yes	51667	1550	(3.00)	2.13 (1.87-2.43)	<0.0001
Time Limited: Major						<0.0001
	No	65515	1379	(2.10)	1	
	Yes	6140	395	(6.43)	2.93 (2.64-3.25)	<0.0001
Time Limited: Major-Primary Infections						<0.0001
	No	58658	730	(1.24)	1	
	Yes	12997	1044	(8.03)	5.77 (5.28-6.31)	<0.0001
Allergies						<0.0001
	No	61017	1359	(2.23)	1	
	Yes	10638	415	(3.90)	1.54 (1.39-1.70)	<0.0001
Asthma						<0.0001
	No	63383	1503	(2.37)	1	
	Yes	8272	271	(3.28)	1.28 (1.14-1.45)	<0.0001
Likely to Recur: Discrete						<0.0001
	No	37295	390	(1.05)	1	
	Yes	34360	1384	(4.03)	3.44 (3.09-3.83)	<0.0001
Likely to Recur: Discrete-Infections						<0.0001
	No	41171	687	(1.67)	1	
	Yes	30484	1087	(3.57)	1.79 (1.64-1.96)	<0.0001
Likely to Recur: Progressive						<0.0001
	No	65594	1230	(1.88)	1	
	Yes	6061	544	(8.98)	4.96 (4.53-5.44)	<0.0001
Chronic Medical: Unstable						<0.0001
	No	41567	388	(0.93)	1	
	Yes	30088	1386	(4.61)	4.57 (4.10-5.09)	<0.0001
Chronic Specialty: Stable-Orthopedic						<0.0001
	No	58866	921	(1.56)	1	
	Yes	12789	853	(6.67)	4.24 (3.89-4.63)	<0.0001
Chronic Specialty: Stable-Eye						<0.0001
	No	64724	1353	(2.09)	1	
	Yes	6931	421	(6.07)	2.58 (2.33-2.85)	<0.0001
Chronic Specialty: Stable-Ear, Nose, Throat						<0.0001
	No	69432	1665	(2.40)	1	
	Yes	2223	109	(4.90)	1.75 (1.45-2.09)	<0.0001
Chronic Specialty: Stable-Eye						<0.0001
	No	66500	1468	(2.21)	1	

Yes	5155	306	(5.94)	2.63 (2.36-2.94)	<0.0001
Chronic Specialty: Unstable-Orthopedic					<0.0001
No	69543	1666	(2.40)	1	
Yes	2112	108	(5.11)	1.85 (1.55-2.22)	<0.0001
Chronic Specialty: Unstable-Ear, Nose, Throat					<0.0001
No	71141	1737	(2.44)	1	
Yes	514	37	(7.20)	2.46 (1.82-3.33)	<0.0001
Chronic Specialty: Unstable-Eye					<0.0001
No	66718	1434	(2.15)	1	
Yes	4937	340	(6.89)	2.97 (2.66-3.30)	<0.0001
Dermatologic					<0.0001
No	39540	632	(1.60)	1	
Yes	32115	1142	(3.56)	1.85 (1.69-2.02)	<0.0001
Injuries/Adverse Effects: Minor					<0.0001
No	45948	787	(1.71)	1	
Yes	25707	987	(3.84)	1.82 (1.67-1.99)	<0.0001
Injuries/Adverse Effects: Major					<0.0001
No	53408	880	(1.65)	1	
Yes	18247	894	(4.90)	2.66 (2.44-2.90)	<0.0001
Psychosocial: Time Limited, Minor					<0.0001
No	64468	1345	(2.09)	1	
Yes	7187	429	(5.97)	2.56 (2.32-2.83)	<0.0001
Psychosocial: Recurrent or Persistent, Stable					<0.0001
No	55752	1076	(1.93)	1	
Yes	15903	698	(4.39)	2.13 (1.95-2.32)	<0.0001
Psychosocial: Recurrent or Persistent, Unstable					<0.0001
No	66278	1537	(2.32)	1	
Yes	5377	237	(4.41)	2.00 (1.77-2.27)	<0.0001
Signs/Symptoms: Minor					<0.0001
No	34668	301	(0.87)	1	
Yes	36987	1473	(3.98)	3.81 (3.39-4.29)	<0.0001
Signs/Symptoms: Uncertain					<0.0001
No	30302	225	(0.74)	1	
Yes	41353	1549	(3.75)	4.09 (3.58-4.67)	<0.0001
Signs/Symptoms: Major					<0.0001
No	48093	630	(1.31)	1	
Yes	23562	1144	(4.86)	3.40 (3.10-3.73)	<0.0001
Discretionary					<0.0001
No	46770	641	(1.37)	1	
Yes	24885	1133	(4.55)	2.83 (2.58-3.10)	<0.0001
See and Reassure					<0.0001
No	66255	1409	(2.13)	1	
Yes	5400	365	(6.76)	2.87 (2.59-3.19)	<0.0001
Prevention/Administrative					<0.0001
No	22144	172	(0.78)	1	
Yes	49511	1602	(3.24)	3.43 (2.95-3.99)	<0.0001
Malignancy					<0.0001
No	67767	1486	(2.19)	1	
Yes	3888	288	(7.41)	3.11 (2.77-3.50)	<0.0001
Pregnancy					0.003
No	66008	1579	(2.39)	1	
Yes	5647	195	(3.45)	1.25 (1.09-1.44)	0.002

Dental						<0.0001
	No	68512	1604	(2.34)	1	
	Yes	3143	170	(5.41)	2.06 (1.78-2.37)	<0.0001
Collapsed Aggregated Diagnosis Groups (CADGs)						
Acute Minor						<0.0001
	No	8414	41	(0.49)	1	
	Yes	63241	1733	(2.74)	4.41 (3.25-5.99)	<0.0001
Acute Major						<0.0001
	No	18653	29	(0.16)	1	
	Yes	53002	1745	(3.29)	16.5 (11.6-23.3)	<0.0001
Likely to Recur						<0.0001
	No	13106	63	(0.48)	1	
	Yes	58549	1711	(2.92)	4.65 (3.65-5.91)	<0.0001
Asthma						<0.0001
	No	63383	1503	(2.37)	1	
	Yes	8272	271	(3.28)	1.28 (1.14-1.45)	<0.0001
Chronic Medical: Unstable						<0.0001
	No	54911	719	(1.31)	1	
	Yes	16744	1055	(6.30)	4.72 (4.32-5.16)	<0.0001
Chronic Medical: Stable						<0.0001
	No	39917	347	(0.87)	1	
	Yes	31738	1427	(4.50)	4.72 (4.22-5.29)	<0.0001
Chronic Specialty: Stable						<0.0001
	No	62965	1275	(2.02)	1	
	Yes	8690	499	(5.74)	2.49 (2.27-2.74)	<0.0001
Eye/Dental						<0.0001
	No	63696	1335	(2.10)	1	
	Yes	7959	439	(5.52)	2.46 (2.23-2.71)	<0.0001
Chronic Specialty: Unstable						<0.0001
	No	64477	1341	(2.08)	1	
	Yes	7178	433	(6.03)	2.64 (2.39-2.91)	<0.0001
Psychosocial						<0.0001
	No	49996	831	(1.66)	1	
	Yes	21659	943	(4.35)	2.44 (2.24-2.67)	<0.0001
Preventive/Administrative						<0.0001
	No	22144	172	(0.78)	1	
	Yes	49511	1602	(3.24)	3.43 (2.95-3.99)	<0.0001
Pregnancy						0.003
	No	66008	1579	(2.39)	1	
	Yes	5647	195	(3.45)	1.25 (1.09-1.44)	0.002
Expanded Diagnosis Clusters (EDCs) groups						<0.0001
	Low	23266	43	(0.18)	1	
	Moderate	26506	302	(1.14)	4.10 (3.00-50.6)	<0.0001
	High	24991	1429	(5.72)	17.8 (13.2-23.9)	<0.0001
Major Expanded Diagnosis Clusters (MEDCs)						
Administrative						<0.0001
	No	23563	188	(0.80)	1	
	Yes	48092	1586	(3.30)	3.44 (2.97-3.98)	<0.0001
Allergy						<0.0001
	No	52261	1074	(2.06)	1	
	Yes	19394	700	(3.61)	1.54 (1.40-1.68)	<0.0001
Cardiovascular						<0.0001

	No	55262	732	(1.32)	1	
	Yes	16393	1042	(6.36)	4.62 (4.23-5.05)	<0.0001
Dental						<0.0001
	No	63781	1379	(2.16)	1	
	Yes	7874	395	(5.02)	2.12 (1.92-2.35)	<0.0001
Ear, Nose, Throat						<0.0001
	No	27322	416	(1.52)	1	
	Yes	44333	1358	(3.06)	1.63 (1.47-1.81)	<0.0001
Endocrine						<0.0001
	No	63678	1272	(2.00)	1	
	Yes	7977	502	(6.29)	3.06 (2.78-3.36)	<0.0001
Eye						<0.0001
	No	47267	830	(1.76)	1	
	Yes	24388	944	(3.87)	1.96 (1.80-2.14)	<0.0001
Female reproductive system						<0.0001
	No	50463	1048	(2.08)	1	
	Yes	21192	726	(3.43)	1.42 (1.30-1.55)	<0.0001
Gastrointestinal/hepatic						<0.0001
	No	47191	664	(1.41)	1	
	Yes	24464	1110	(4.54)	2.88 (2.63-3.15)	<0.0001
General signs and symptoms						<0.0001
	No	47845	641	(1.34)	1	
	Yes	23810	1133	(4.76)	3.09 (2.82-3.39)	<0.0001
General surgery						<0.0001
	No	34443	295	(0.86)	1	
	Yes	37212	1479	(3.97)	3.93 (3.48-4.42)	<0.0001
Genetic						0.001
	No	71089	1743	(2.45)	1	
	Yes	566	31	(5.48)	1.86 (1.33-2.61)	<0.0001
Genito-urinary						<0.0001
	No	50155	766	(1.53)	1	
	Yes	21500	1008	(4.69)	2.71 (2.48-2.95)	<0.0001
Hematologic						<0.0001
	No	65363	1384	(2.12)	1	
	Yes	6292	390	(6.20)	2.79 (2.52-3.09)	<0.0001
Infections						<0.0001
	No	54300	1124	(2.07)	1	
	Yes	17355	650	(3.75)	1.64 (1.50-1.79)	<0.0001
Malignancies						<0.0001
	No	67535	1474	(2.18)	1	
	Yes	4120	300	(7.28)	3.08 (2.75-3.46)	<0.0001
Musculoskeletal						<0.0001
	No	26800	207	(0.77)	1	
	Yes	44855	1567	(3.49)	3.67 (3.19-4.22)	<0.0001
Neonatal						0.040
	No	70400	1748	(2.48)	1	
	Yes	1255	26	(2.07)	0.70 (0.48-1.01)	0.054
Neurologic						<0.0001
	No	39311	422	(1.07)	1	
	Yes	32344	1352	(4.18)	3.45 (3.11-3.83)	<0.0001
Nutrition						<0.0001
	No	68873	1614	(2.34)	1	

	Yes	2782	160	(5.75)	2.21 (1.91-2.57)	<0.0001
Psychosocial						<0.0001
	No	50820	880	(1.73)	1	
	Yes	20835	894	(4.29)	2.29 (2.10-2.50)	<0.0001
Reconstructive						<0.0001
	No	63467	1412	(2.22)	1	
	Yes	8188	362	(4.42)	1.83 (1.65-2.03)	<0.0001
Renal						<0.0001
	No	67738	1407	(2.08)	1	
	Yes	3917	367	(9.37)	4.12 (3.71-4.58)	<0.0001
Respiratory						<0.0001
	No	41275	587	(1.42)	1	
	Yes	30380	1187	(3.91)	2.42 (2.20-2.66)	<0.0001
Rheumatologic						<0.0001
	No	66339	1408	(2.12)	1	
	Yes	5316	366	(6.88)	2.95 (2.66-3.28)	<0.0001
Skin						<0.0001
	No	22589	263	(1.16)	1	
	Yes	49066	1511	(3.08)	2.09 (1.85-2.37)	<0.0001
Toxic effects/Adverse events						<0.0001
	No	67679	765	(1.13)	1	
	Yes	3976	1009	(25.4)	20.2 (18.5-22.1)	<0.0001

Table A.11 Crude associations between comorbidities and risk of emergency admission, results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic		Patients with ≥1 admission, n			RR (95% CI)	P-value
		All	≥1 adverse event	(%)		
Disease flags						
Composite Charlson Index measure						<0.0001
	No	11085	402	(3.63)	1	
	Yes	5525	437	(7.91)	2.48 (2.44-2.52)	<0.0001
Cancer						<0.0001
	No	16040	777	(4.84)	1	
	Yes	570	62	(10.9)	5.40 (5.23-5.56)	<0.0001
Cerebrovascular disease						<0.0001
	No	16108	794	(4.93)	1	
	Yes	502	45	(8.96)	2.59 (2.49-2.70)	<0.0001
Congestive heart disease						<0.0001
	No	13904	670	(4.82)	1	
	Yes	2706	169	(6.25)	1.40 (1.37-1.43)	<0.0001
Chronic pulmonary disease						<0.0001
	No	16224	806	(4.97)	1	
	Yes	386	33	(8.55)	4.86 (4.67-5.05)	<0.0001
Dementia						<0.0001
	No	16474	831	(5.04)	1	
	Yes	136	8	(5.88)	2.33 (2.12-2.55)	<0.0001
Diabetes without complications						<0.0001
	No	15469	728	(4.71)	1	
	Yes	1141	111	(9.73)	2.36 (2.30-2.43)	<0.0001
Diabetes with complications						<0.0001
	No	16497	825	(5.00)	1	
	Yes	113	14	(12.4)	3.21 (2.97-3.46)	<0.0001
Hemiplegia						<0.0001
	No	16579	834	(5.03)	1	
	Yes	31	5	(16.1)	10.1 (9.35-11.0)	<0.0001
Metastatic tumour						<0.0001
	No	16536	833	(5.04)	1	
	Yes	74	6	(8.11)	9.64 (9.03-10.3)	<0.0001
Mild liver disease						<0.0001
	No	16599	837	(5.04)	1	
	Yes	11	2	(18.2)	11.3 (9.41-13.5)	<0.0001
Moderate liver disease						<0.0001
	No	16349	814	(4.98)	1	
	Yes	261	25	(9.58)	3.39 (3.23-3.57)	<0.0001
Myocardial infarction						<0.0001
	No	16569	837	(5.05)	1	
	Yes	41	2	(4.88)	3.18 (2.82-3.59)	<0.0001
Peptic ulcer disease						<0.0001
	No	16347	811	(4.96)	1	
	Yes	263	28	(10.7)	2.57 (2.43-2.71)	<0.0001
Peripheral vascular disease						<0.0001
	No	16292	790	(4.85)	1	
	Yes	318	49	(15.4)	3.67 (3.51-3.84)	<0.0001

Renal disease						<0.0001
	No	15829	722	(4.56)	1	
	Yes	781	117	(15.0)	3.05 (2.96-3.14)	<0.0001
Rheumatological disease						<0.0001
	No	16185	791	(4.89)	1	
	Yes	425	48	(11.3)	2.45 (2.34-2.56)	<0.0001
Aggregated Disease Groups (ADGs)						
Time Limited: Minor						<0.0001
	No	5485	167	(3.04)	1	
	Yes	10968	672	(6.13)	1.52 (1.49-1.55)	<0.0001
Time Limited: Minor-Primary						<0.0001
	No	3222	73	(2.27)	1	
	Yes	13231	766	(5.79)	1.47 (1.44-1.50)	<0.0001
Time Limited: Major						<0.0001
	No	14084	624	(4.43)	1	
	Yes	2369	215	(9.08)	2.98 (2.92-3.04)	<0.0001
Time Limited: Major-Primary Infections						<0.0001
	No	11922	305	(2.56)	1	
	Yes	4531	534	(11.8)	2.24 (2.20-2.27)	<0.0001
Allergies						<0.0001
	No	13449	621	(4.62)	1	
	Yes	3004	218	(7.26)	1.21 (1.18-1.23)	<0.0001
Asthma						<0.0001
	No	14179	696	(4.91)	1	
	Yes	2274	143	(6.29)	1.23 (1.20-1.26)	<0.0001
Likely to Recur: Discrete						<0.0001
	No	6133	146	(2.38)	1	
	Yes	10320	693	(6.72)	2.25 (2.21-2.29)	<0.0001
Likely to Recur: Discrete-Infections						<0.0001
	No	7655	278	(3.63)	1	
	Yes	8798	561	(6.38)	1.67 (1.64-1.70)	<0.0001
Likely to Recur: Progressive						<0.0001
	No	13835	555	(4.01)	1	
	Yes	2618	284	(10.9)	3.03 (2.97-3.09)	<0.0001
Chronic Medical: Unstable						<0.0001
	No	6777	143	(2.11)	1	
	Yes	9676	696	(7.19)	2.66 (2.61-2.71)	<0.0001
Chronic Specialty: Stable-Orthopedic						<0.0001
	No	11394	399	(3.50)	1	
	Yes	5059	440	(8.70)	3.27 (3.21-3.32)	<0.0001
Chronic Specialty: Stable-Eye						<0.0001
	No	13979	624	(4.46)	1	
	Yes	2474	215	(8.69)	1.77 (1.73-1.81)	<0.0001
Chronic Specialty: Stable-Ear, Nose, Throat						<0.0001
	No	15719	777	(4.94)	1	
	Yes	734	62	(8.45)	1.51 (1.45-1.56)	<0.0001
Chronic Specialty: Stable-Eye						<0.0001
	No	14554	684	(4.70)	1	
	Yes	1899	155	(8.16)	1.96 (1.91-2.00)	<0.0001
Chronic Specialty: Unstable-Orthopedic						<0.0001
	No	15762	782	(4.96)	1	
	Yes	691	57	(8.25)	1.62 (1.56-1.68)	<0.0001

Chronic Specialty: Unstable-Ear, Nose, Throat						<0.0001
	No	16260	822	(5.06)	1	
	Yes	193	17	(8.81)	1.38 (1.28-1.49)	<0.0001
Chronic Specialty: Unstable-Eye						<0.0001
	No	14514	653	(4.50)	1	
	Yes	1939	186	(9.59)	2.34 (2.28-2.39)	<0.0001
Dermatologic						<0.0001
	No	7820	268	(3.43)	1	
	Yes	8633	571	(6.61)	1.23 (1.21-1.25)	<0.0001
Injuries/Adverse Effects: Minor						<0.0001
	No	9051	343	(3.79)	1	
	Yes	7402	496	(6.70)	1.34 (1.32-1.36)	<0.0001
Injuries/Adverse Effects: Major						<0.0001
	No	10896	388	(3.56)	1	
	Yes	5557	451	(8.12)	1.69 (1.66-1.72)	<0.0001
Psychosocial: Time Limited, Minor						<0.0001
	No	14046	609	(4.34)	1	
	Yes	2407	230	(9.56)	1.89 (1.85-1.93)	<0.0001
Psychosocial: Recurrent or Persistent, Stable						<0.0001
	No	11509	475	(4.13)	1	
	Yes	4944	364	(7.36)	1.69 (1.66-1.72)	<0.0001
Psychosocial: Recurrent or Persistent, Unstable						<0.0001
	No	14563	707	(4.85)	1	
	Yes	1890	132	(6.98)	2.23 (2.17-2.28)	<0.0001
Signs/Symptoms: Minor						<0.0001
	No	5482	111	(2.02)	1	
	Yes	10971	728	(6.64)	2.05 (2.01-2.09)	<0.0001
Signs/Symptoms: Uncertain						<0.0001
	No	4309	70	(1.62)	1	
	Yes	12144	769	(6.33)	2.36 (2.31-2.41)	<0.0001
Signs/Symptoms: Major						<0.0001
	No	8498	263	(3.09)	1	
	Yes	7955	576	(7.24)	2.62 (2.58-2.67)	<0.0001
Discretionary						<0.0001
	No	8487	275	(3.24)	1	
	Yes	7966	564	(7.08)	1.88 (1.85-1.91)	<0.0001
See and Reassure						<0.0001
	No	14466	641	(4.43)	1	
	Yes	1987	198	(9.96)	1.89 (1.85-1.93)	<0.0001
Prevention/Administrative						<0.0001
	No	3125	67	(2.14)	1	
	Yes	13328	772	(5.79)	2.15 (2.10-2.20)	<0.0001
Malignancy						<0.0001
	No	14698	681	(4.63)	1	
	Yes	1755	158	(9.00)	4.16 (4.07-4.24)	<0.0001
Pregnancy						<0.0001
	No	14525	730	(5.03)	1	
	Yes	1928	109	(5.65)	1.51 (1.47-1.55)	<0.0001
Dental						<0.0001

	No	15395	746	(4.85)	1	
	Yes	1058	93	(8.79)	1.51 (1.46-1.55)	<0.0001
Collapsed Aggregated Diagnosis Groups (CADGs)						
Acute Minor						<0.0001
	No	994	11	(1.11)	1	
	Yes	15459	828	(5.36)	1.92 (1.84-2.00)	<0.0001
Acute Major						<0.0001
	No	2025	4	(0.20)	1	
	Yes	14428	835	(5.79)	3.19 (3.09-3.29)	<0.0001
Likely to Recur						<0.0001
	No	1538	17	(1.11)	1	
	Yes	14915	822	(5.51)	2.22 (2.15-2.29)	<0.0001
Asthma						<0.0001
	No	14179	696	(4.91)	1	
	Yes	2274	143	(6.29)	1.23 (1.20-1.26)	<0.0001
Chronic Medical: Unstable						<0.0001
	No	9896	296	(2.99)	1	
	Yes	6557	543	(8.28)	3.78 (3.72-3.85)	<0.0001
Chronic Medical: Stable						<0.0001
	No	6395	124	(1.94)	1	
	Yes	10058	715	(7.11)	2.64 (2.60-2.69)	<0.0001
Chronic Specialty: Stable						<0.0001
	No	13432	578	(4.30)	1	
	Yes	3021	261	(8.64)	1.74 (1.70-1.77)	<0.0001
Eye/Dental						<0.0001
	No	13636	608	(4.46)	1	
	Yes	2817	231	(8.20)	1.85 (1.81-1.88)	<0.0001
Chronic Specialty: Unstable						<0.0001
	No	13821	606	(4.38)	1	
	Yes	2632	233	(8.85)	2.13 (2.08-2.17)	<0.0001
Psychosocial						<0.0001
	No	9701	345	(3.56)	1	
	Yes	6752	494	(7.32)	2.00 (1.96-2.03)	<0.0001
Preventive/Administrative						<0.0001
	No	3125	67	(2.14)	1	
	Yes	13328	772	(5.79)	2.15 (2.10-2.20)	<0.0001
Pregnancy						<0.0001
	No	14525	730	(5.03)	1	
	Yes	1928	109	(5.65)	1.51 (1.47-1.55)	<0.0001
Expanded Diagnosis Clusters (EDCs) groups						<0.0001
	Low	2074	6	(0.29)	1	
	Moderate	5251	112	(2.13)	1.90 (1.83-1.97)	<0.0001
	High	9285	721	(7.77)	4.66 (4.51-4.82)	<0.0001
Major Expanded Diagnosis Clusters (MEDCs)						
Administrative						<0.0001
	No	3436	74	(2.15)	1	
	Yes	13017	765	(5.88)	2.10 (2.05-2.14)	<0.0001
Allergy						<0.0001
	No	11143	483	(4.33)	1	
	Yes	5310	356	(6.70)	1.26 (1.24-1.28)	<0.0001
Cardiovascular						<0.0001
	No	10553	312	(2.96)	1	

	Yes	5900	527	(8.93)	2.62 (2.58-2.67)	<0.0001
Dental						<0.0001
	No	13932	630	(4.52)	1	
	Yes	2521	209	(8.29)	1.52 (1.49-1.55)	<0.0001
Ear, Nose, Throat						<0.0001
	No	4990	170	(3.41)	1	
	Yes	11463	669	(5.84)	1.25 (1.22-1.27)	<0.0001
Endocrine						<0.0001
	No	13509	579	(4.29)	1	
	Yes	2944	260	(8.83)	2.43 (2.39-2.48)	<0.0001
Eye						<0.0001
	No	9243	368	(3.98)	1	
	Yes	7210	471	(6.53)	1.53 (1.51-1.56)	<0.0001
Female reproductive system						<0.0001
	No	10198	472	(4.63)	1	
	Yes	6255	367	(5.87)	1.41 (1.38-1.43)	<0.0001
Gastrointestinal/hepatic						<0.0001
	No	8498	279	(3.28)	1	
	Yes	7955	560	(7.04)	2.33 (2.29-2.37)	<0.0001
General signs and symptoms						<0.0001
	No	8781	256	(2.92)	1	
	Yes	7672	583	(7.60)	2.07 (2.03-2.10)	<0.0001
General surgery						<0.0001
	No	5216	105	(2.01)	1	
	Yes	11237	734	(6.53)	2.33 (2.28-2.37)	<0.0001
Genetic						<0.0001
	No	16239	827	(5.09)	1	
	Yes	214	12	(5.61)	3.98 (3.80-4.16)	<0.0001
Genito-urinary						<0.0001
	No	9434	303	(3.21)	1	
	Yes	7019	536	(7.64)	2.04 (2.00-2.07)	<0.0001
Hematologic						<0.0001
	No	13871	629	(4.53)	1	
	Yes	2582	210	(8.13)	2.95 (2.89-3.01)	<0.0001
Infections						<0.0001
	No	11428	475	(4.16)	1	
	Yes	5025	364	(7.24)	1.45 (1.42-1.47)	<0.0001
Malignancies						<0.0001
	No	14599	672	(4.60)	1	
	Yes	1854	167	(9.01)	4.09 (4.01-4.18)	<0.0001
Musculoskeletal						<0.0001
	No	3999	62	(1.55)	1	
	Yes	12454	777	(6.24)	1.91 (1.87-1.95)	<0.0001
Neonatal						0.053
	No	16138	829	(5.14)	1	
	Yes	315	10	(3.17)	0.94 (0.89-1.00)	0.055
Neurologic						<0.0001
	No	6409	167	(2.61)	1	
	Yes	10044	672	(6.69)	2.25 (2.21-2.29)	<0.0001
Nutrition						<0.0001
	No	15443	753	(4.88)	1	
	Yes	1010	86	(8.51)	1.91 (1.86-1.97)	<0.0001

Psychosocial						<0.0001
	No	9974	369	(3.70)	1	
	Yes	6479	470	(7.25)	1.94 (1.91-1.97)	<0.0001
Reconstructive						<0.0001
	No	13849	651	(4.70)	1	
	Yes	2604	188	(7.22)	1.54 (1.51-1.58)	<0.0001
Renal						<0.0001
	No	14810	640	(4.32)	1	
	Yes	1643	199	(12.1)	2.93 (2.87-3.00)	<0.0001
Respiratory						<0.0001
	No	7282	241	(3.31)	1	
	Yes	9171	598	(6.52)	1.89 (1.86-1.92)	<0.0001
Rheumatologic						<0.0001
	No	14433	646	(4.48)	1	
	Yes	2020	193	(9.55)	2.27 (2.22-2.32)	<0.0001
Skin						<0.0001
	No	3848	96	(2.49)	1	
	Yes	12605	743	(5.89)	1.34 (1.31-1.37)	<0.0001
Toxic effects/Adverse events						<0.0001
	No	14910	322	(2.16)	1	
	Yes	1543	517	(33.5)	2.54 (2.48-2.60)	<0.0001

Table A.12 Crude associations between comorbidities and risk of death, results from log-binomial regression using the generalized estimating equations (GEE) method

Characteristic		Deaths, n			RR (95% CI)	P-value
		All	≥1 adverse event	(%)		
Disease flags						
Composite Charlson Index measure						<0.0001
	No	1723	42	(2.44)	1	
	Yes	2240	136	(6.07)	4.87 (4.58-5.17)	<0.0001
Cancer						<0.0001
	No	3498	149	(4.26)	1	
	Yes	465	29	(6.24)	8.63 (7.99-9.32)	<0.0001
Cerebrovascular disease						<0.0001
	No	3553	157	(4.42)	1	
	Yes	410	21	(5.12)	7.30 (6.72-7.94)	<0.0001
Congestive heart disease						<0.0001
	No	3303	150	(4.54)	1	
	Yes	660	28	(4.24)	1.45 (1.33-1.57)	<0.0001
Chronic pulmonary disease						<0.0001
	No	3528	152	(4.31)	1	
	Yes	435	26	(5.98)	11.6 (10.8-12.5)	<0.0001
Dementia						<0.0001
	No	3793	172	(4.53)	1	
	Yes	170	6	(3.53)	10.4 (9.36-11.6)	<0.0001
Diabetes without complications						<0.0001
	No	3495	142	(4.06)	1	
	Yes	468	36	(7.69)	3.23 (2.95-3.53)	<0.0001
Diabetes with complications						<0.0001
	No	3902	174	(4.46)	1	
	Yes	61	4	(6.56)	4.81 (3.87-5.99)	<0.0001
Hemiplegia						<0.0001
	No	3949	176	(4.46)	1	
	Yes	14	2	(14.2)	3.70 (2.32-5.92)	<0.0001
Metastatic tumour						<0.0001
	No	3867	170	(4.40)	1	
	Yes	96	8	(8.33)	13.2 (11.7-14.8)	<0.0001
Mild liver disease						<0.0001
	No	3941	176	(4.47)	1	
	Yes	22	2	(9.09)	4.34 (3.01-6.27)	<0.0001
Moderate liver disease						<0.0001
	No	3953	176	(4.45)	1	
	Yes	10	2	(20.0)	12.3 (8.62-17.7)	<0.0001
Myocardial infarction						<0.0001
	No	3775	172	(4.56)	1	
	Yes	188	6	(3.19)	6.25 (5.53-7.06)	<0.0001
Peptic ulcer disease						<0.0001
	No	3826	164	(4.29)	1	
	Yes	137	14	(10.2)	4.32 (3.72-5.02)	<0.0001
Peripheral vascular disease						<0.0001
	No	3755	158	(4.21)	1	
	Yes	208	20	(9.62)	6.10 (5.42-6.85)	<0.0001

Renal disease						<0.0001
	No	3737	151	(4.04)	1	
	Yes	226	27	(12.0)	2.41 (2.13-2.74)	<0.0001
Rheumatological disease						<0.0001
	No	3781	165	(4.36)	1	
	Yes	182	13	(7.14)	3.74 (3.27-4.28)	<0.0001
Aggregated Disease Groups (ADGs)						
Time Limited: Minor						0.031
	No	1790	49	(2.74)	1	
	Yes	2089	129	(6.18)	0.94 (0.88-0.99)	0.031
Time Limited: Minor-Primary						<0.0001
	No	1203	32	(2.66)	1	
	Yes	2676	146	(5.46)	0.86 (0.81-0.92)	<0.0001
Time Limited: Major						<0.0001
	No	2890	116	(4.01)	1	
	Yes	989	62	(6.27)	3.65 (3.41-3.91)	<0.0001
Time Limited: Major-Primary Infections						<0.0001
	No	2673	87	(3.25)	1	
	Yes	1206	91	(7.55)	2.04 (1.91-2.17)	<0.0001
Allergies						<0.0001
	No	3479	150	(4.31)	1	
	Yes	400	28	(7.00)	0.66 (0.60-0.73)	<0.0001
Asthma						0.120
	No	3461	155	(4.48)	1	
	Yes	418	23	(5.50)	0.93 (0.84-1.02)	0.124
Likely to Recur: Discrete						<0.0001
	No	1462	37	(2.53)	1	
	Yes	2417	141	(5.83)	1.79 (1.68-1.91)	<0.0001
Likely to Recur: Discrete-Infections						0.021
	No	2298	66	(2.87)	1	
	Yes	1581	112	(7.08)	0.93 (0.87-0.99)	0.021
Likely to Recur: Progressive						<0.0001
	No	2531	90	(3.56)	1	
	Yes	1348	88	(6.53)	5.76 (5.42-6.12)	<0.0001
Chronic Medical: Unstable						<0.0001
	No	1102	17	(1.54)	1	
	Yes	2777	161	(5.80)	3.48 (3.25-3.73)	<0.0001
Chronic Specialty: Stable-Orthopedic						<0.0001
	No	1521	41	(2.70)	1	
	Yes	2358	137	(5.81)	7.14 (6.71-7.59)	<0.0001
Chronic Specialty: Stable-Eye						<0.0001
	No	3214	130	(4.04)	1	
	Yes	665	48	(7.22)	1.93 (1.78-2.09)	<0.0001
Chronic Specialty: Stable-Ear, Nose, Throat						<0.0001
	No	3708	166	(4.48)	1	
	Yes	171	12	(7.02)	1.44 (1.24-1.67)	<0.0001
Chronic Specialty: Stable-Eye						<0.0001
	No	3117	132	(4.23)	1	
	Yes	762	46	(6.04)	3.15 (2.93-3.40)	<0.0001
Chronic Specialty: Unstable-Orthopedic						<0.0001
	No	3715	172	(4.63)	1	
	Yes	164	6	(3.66)	1.45 (1.25-1.69)	<0.0001

Chronic Specialty: Unstable-Ear, Nose, Throat						0.087
	No	3842	177	(4.61)	1	
	Yes	37	1	(2.70)	1.33 (0.98-1.82)	0.071
Chronic Specialty: Unstable-Eye						<0.0001
	No	3094	131	(4.23)	1	
	Yes	785	47	(5.99)	3.43 (3.19-3.69)	<0.0001
Dermatologic						<0.0001
	No	2531	80	(3.16)	1	
	Yes	1348	98	(7.27)	0.66 (0.61-0.70)	<0.0001
Injuries/Adverse Effects: Minor						0.004
	No	2571	91	(3.54)	1	
	Yes	1308	87	(6.65)	0.91 (0.85-0.97)	0.004
Injuries/Adverse Effects: Major						<0.0001
	No	2540	85	(3.35)	1	
	Yes	1339	93	(6.95)	1.54 (1.45-1.64)	<0.0001
Psychosocial: Time Limited, Minor						<0.0001
	No	3202	129	(4.03)	1	
	Yes	677	49	(7.24)	1.90 (1.75-2.05)	<0.0001
Psychosocial: Recurrent or Persistent, Stable						<0.0001
	No	2794	119	(4.26)	1	
	Yes	1085	59	(5.44)	1.36 (1.27-1.46)	<0.0001
Psychosocial: Recurrent or Persistent, Unstable						<0.0001
	No	2972	133	(4.48)	1	
	Yes	907	45	(4.96)	3.76 (3.51-4.03)	<0.0001
Signs/Symptoms: Minor						<0.0001
	No	1444	23	(1.59)	1	
	Yes	2435	155	(6.37)	1.58 (1.48-1.68)	<0.0001
Signs/Symptoms: Uncertain						<0.0001
	No	1141	15	(1.31)	1	
	Yes	2738	163	(5.95)	1.76 (1.64-1.88)	<0.0001
Signs/Symptoms: Major						<0.0001
	No	1674	44	(2.63)	1	
	Yes	2205	134	(6.08)	2.69 (2.53-2.86)	<0.0001
Discretionary						<0.0001
	No	2112	78	(3.69)	1	
	Yes	1767	100	(5.66)	1.57 (1.48-1.67)	<0.0001
See and Reassure						<0.0001
	No	3409	138	(4.05)	1	
	Yes	470	40	(8.51)	1.69 (1.54-1.86)	<0.0001
Prevention/Administrative						<0.0001
	No	957	18	(1.88)	1	
	Yes	2922	160	(5.48)	1.37 (1.27-1.47)	<0.0001
Malignancy						<0.0001
	No	2778	100	(3.60)	1	
	Yes	1101	78	(7.08)	6.91 (6.49-7.35)	<0.0001
Pregnancy						<0.0001
	No	3809	175	(4.59)	1	
	Yes	70	3	(4.29)	0.22 (0.17-0.27)	<0.0001
Dental						0.002
	No	3746	171	(4.56)	1	
	Yes	133	7	(5.26)	0.77 (0.65-0.92)	0.003
Collapsed Aggregated Diagnosis Groups (CADGs)						

Acute Minor						<0.0001
	No	538	3	(0.56)	1	
	Yes	3341	175	(5.24)	0.83 (0.76-0.90)	<0.0001
Acute Major						<0.0001
	No	471	2	(0.42)	1	
	Yes	3408	176	(5.16)	2.55 (2.32-2.80)	<0.0001
Likely to Recur						0.026
	No	658	5	(0.76)	1	
	Yes	3221	173	(5.37)	1.10 (1.01-1.19)	0.028
Asthma						0.120
	No	3461	155	(4.48)	1	
	Yes	418	23	(5.50)	0.93 (0.84-1.02)	0.124
Chronic Medical: Unstable						<0.0001
	No	835	6	(0.72)	1	
	Yes	3044	172	(5.65)	12.0 (11.1-12.9)	<0.0001
Chronic Medical: Stable						<0.0001
	No	1046	14	(1.34)	1	
	Yes	2833	164	(5.79)	3.41 (3.18-3.65)	<0.0001
Chronic Specialty: Stable						<0.0001
	No	3102	122	(3.93)	1	
	Yes	777	56	(7.21)	1.82 (1.68-1.96)	<0.0001
Eye/Dental						<0.0001
	No	3011	129	(4.28)	1	
	Yes	868	49	(5.65)	2.31 (2.15-2.48)	<0.0001
Chronic Specialty: Unstable						<0.0001
	No	2942	127	(4.32)	1	
	Yes	937	51	(5.44)	2.86 (2.67-3.07)	<0.0001
Psychosocial						<0.0001
	No	1991	73	(3.67)	1	
	Yes	1888	105	(5.56)	2.19 (2.06-2.33)	<0.0001
Preventive/Administrative						<0.0001
	No	957	18	(1.88)	1	
	Yes	2922	160	(5.48)	1.37 (1.27-1.47)	<0.0001
Pregnancy						<0.0001
	No	3809	175	(4.59)	1	
	Yes	70	3	(4.29)	0.22 (0.17-0.27)	<0.0001
Expanded Diagnosis Clusters (EDCs) groups						<0.0001
	Low	654		(0)	1	
	Moderate	1181	26	(2.20)	1.58 (1.43-1.74)	<0.0001
	High	2128	152	(7.14)	3.01 (2.75-3.30)	<0.0001
Major Expanded Diagnosis Clusters (MEDCs)						
Administrative						<0.0001
	No	961	16	(1.66)	1	
	Yes	2918	162	(5.55)	1.49 (1.39-1.60)	<0.0001
Allergy						<0.0001
	No	3023	126	(4.17)	1	
	Yes	856	52	(6.07)	0.76 (0.71-0.82)	<0.0001
Cardiovascular						<0.0001
	No	1505	37	(2.46)	1	
	Yes	2374	141	(5.94)	5.32 (5.00-5.66)	<0.0001
Dental						0.017
	No	3407	147	(4.31)	1	

	Yes	472	31	(6.57)	1.12 (1.02-1.23)	0.016
Ear, Nose, Throat						<0.0001
	No	1914	67	(3.50)	1	
	Yes	1965	111	(5.65)	0.63 (0.60-0.67)	<0.0001
Endocrine						<0.0001
	No	2720	97	(3.57)	1	
	Yes	1159	81	(6.99)	3.40 (3.19-3.63)	<0.0001
Eye						<0.0001
	No	2069	79	(3.82)	1	
	Yes	1810	99	(5.47)	1.70 (1.59-1.80)	<0.0001
Female reproductive system						<0.0001
	No	3256	134	(4.12)	1	
	Yes	623	44	(7.06)	0.46 (0.42-0.50)	<0.0001
Gastrointestinal/hepatic						<0.0001
	No	1938	56	(2.89)	1	
	Yes	1941	122	(6.29)	1.93 (1.82-2.05)	<0.0001
General signs and symptoms						<0.0001
	No	1992	55	(2.76)	1	
	Yes	1887	123	(6.52)	1.90 (1.79-2.02)	<0.0001
General surgery						<0.0001
	No	1417	32	(2.26)	1	
	Yes	2462	146	(5.93)	1.61 (1.51-1.71)	<0.0001
Genetic						<0.0001
	No	3813	171	(4.48)	1	
	Yes	66	7	(10.6)	2.17 (1.73-2.73)	<0.0001
Genito-urinary						<0.0001
	No	2174	61	(2.81)	1	
	Yes	1705	117	(6.86)	1.83 (1.72-1.95)	<0.0001
Hematologic						<0.0001
	No	2930	116	(3.96)	1	
	Yes	949	62	(6.53)	3.37 (3.14-3.60)	<0.0001
Infections						<0.0001
	No	3072	122	(3.97)	1	
	Yes	807	56	(6.94)	0.82 (0.76-0.89)	<0.0001
Malignancies						<0.0001
	No	2753	98	(3.56)	1	
	Yes	1126	80	(7.10)	6.70 (6.30-7.13)	<0.0001
Musculoskeletal						<0.0001
	No	997	21	(2.11)	1	
	Yes	2882	157	(5.45)	1.73 (1.61-1.85)	<0.0001
Neonatal						<0.0001
	No	3859	176	(4.56)	1	
	Yes	20	2	(10.0)	0.29 (0.19-0.45)	<0.0001
Neurologic						<0.0001
	No	1164	28	(2.41)	1	
	Yes	2715	150	(5.52)	2.84 (2.65-3.03)	<0.0001
Nutrition						<0.0001
	No	3651	156	(4.27)	1	
	Yes	228	22	(9.65)	1.55 (1.36-1.76)	<0.0001
Psychosocial						<0.0001
	No	2233	88	(3.94)	1	
	Yes	1646	90	(5.47)	1.80 (1.69-1.91)	<0.0001

Reconstructive						<0.0001
	No	3114	127	(4.08)	1	
	Yes	765	51	(6.67)	1.90 (1.77-2.05)	<0.0001
Renal						<0.0001
	No	3292	129	(3.92)	1	
	Yes	587	49	(8.35)	3.08 (2.84-3.35)	<0.0001
Respiratory						<0.0001
	No	1466	41	(2.80)	1	
	Yes	2413	137	(5.68)	2.24 (2.10-2.38)	<0.0001
Rheumatologic						<0.0001
	No	3102	121	(3.90)	1	
	Yes	777	57	(7.34)	3.13 (2.90-3.36)	<0.0001
Skin						<0.0001
	No	1579	42	(2.66)	1	
	Yes	2300	136	(5.91)	0.67 (0.63-0.71)	<0.0001
Toxic effects/Adverse events						<0.0001
	No	3545	88	(2.48)	1	
	Yes	334	90	(27.0)	1.60 (1.44-1.79)	<0.0001

Table A.13 Read coding of diabetes

Code	READ or OXMIS description
C10..	Diabetes mellitus
C100.	Diabetes mellitus with no mention of complication
C1000	Diabetes mellitus, juvenile type, with no mention of complication
C1001	Diabetes mellitus, adult onset, with no mention of complication
C100z	Diabetes mellitus NOS with no mention of complication
C101.	Diabetes mellitus with ketoacidosis
C1010	Diabetes mellitus, juvenile type, with ketoacidosis
C1011	Diabetes mellitus, adult onset, with ketoacidosis
C101y	Other specified diabetes mellitus with ketoacidosis
C101z	Diabetes mellitus NOS with ketoacidosis
C102.	Diabetes mellitus with hyperosmolar coma
C1020	Diabetes mellitus, juvenile type, with hyperosmolar coma
C1021	Diabetes mellitus, adult onset, with hyperosmolar coma
C102z	Diabetes mellitus NOS with hyperosmolar coma
C103.	Diabetes mellitus with ketoacidotic coma
C1030	Diabetes mellitus, juvenile type, with ketoacidotic coma
C1031	Diabetes mellitus, adult onset, with ketoacidotic coma
C103y	Other specified diabetes mellitus with coma
C103z	Diabetes mellitus NOS with ketoacidotic coma
C104.	Diabetes mellitus with renal manifestation
C1040	Diabetes mellitus, juvenile type, with renal manifestation
C1041	Diabetes mellitus, adult onset, with renal manifestation
C104y	Other specified diabetes mellitus with renal complications
C104z	Diabetes mellitus with nephropathy NOS
C105.	Diabetes mellitus with ophthalmic manifestation
C1050	Diabetes mellitus, juvenile type, with ophthalmic manifestation
C1051	Diabetes mellitus, adult onset, with ophthalmic manifestation
C105y	Other specified diabetes mellitus with ophthalmic complications
C105z	Diabetes mellitus NOS with ophthalmic manifestation
C106.	Diabetes mellitus with neurological manifestation
C1060	Diabetes mellitus, juvenile type, with neurological manifestation
C1061	Diabetes mellitus, adult onset, with neurological manifestation
C106y	Other specified diabetes mellitus with neurological complications
C106z	Diabetes mellitus NOS with neurological manifestation
C107.	Diabetes mellitus with peripheral circulatory disorder
C1070	Diabetes mellitus, juvenile type, with peripheral circulatory disorder
C1071	Diabetes mellitus, adult onset, with peripheral circulatory disorder
C1072	Diabetes mellitus, adult with gangrene
C1073	IDDM with peripheral circulatory disorder
C1074	NIDDM with peripheral circulatory disorder
C107y	Other specified diabetes mellitus with peripheral circulatory complications
C107z	Diabetes mellitus NOS with peripheral circulatory disorder
C108.	Insulin dependent diabetes mellitus
C1080	Insulin-dependent diabetes mellitus with renal complications
C1081	Insulin-dependent diabetes mellitus with ophthalmic complications
C1082	Insulin-dependent diabetes mellitus with neurological complications
C1083	Insulin dependent diabetes mellitus with multiple complications
C1084	Unstable insulin dependent diabetes mellitus
C1085	Insulin dependent diabetes mellitus with ulcer
C1086	Insulin dependent diabetes mellitus with gangrene
C1087	Insulin dependent diabetes mellitus with retinopathy
C1088	Insulin dependent diabetes mellitus - poor control

C1089	Insulin dependent diabetes maturity onset
C108A	Insulin-dependent diabetes without complication
C108B	Insulin dependent diabetes mellitus with mononeuropathy
C108C	Insulin dependent diabetes mellitus with polyneuropathy
C108D	Insulin dependent diabetes mellitus with nephropathy
C108E	Insulin dependent diabetes mellitus with hypoglycaemic coma
C108F	Insulin dependent diabetes mellitus with diabetic cataract
C108G	Insulin dependent diabetes mellitus with peripheral angiopathy
C108H	Insulin dependent diabetes mellitus with arthropathy
C108J	Insulin dependent diabetes mellitus with neuropathic arthropathy
C108y	Other specified diabetes mellitus with multiple complications
C108z	Unspecified diabetes mellitus with multiple complications
C109.	Non-insulin dependent diabetes mellitus
C1090	Non-insulin-dependent diabetes mellitus with renal complications
C1091	Non-insulin-dependent diabetes mellitus with ophthalmic complications
C1092	Non-insulin-dependent diabetes mellitus with neurological complications
C1093	Non-insulin-dependent diabetes mellitus with multiple complications
C1094	Non-insulin dependent diabetes mellitus with ulcer
C1095	Non-insulin dependent diabetes mellitus with gangrene
C1096	Non-insulin-dependent diabetes mellitus with retinopathy
C1097	Non-insulin dependent diabetes mellitus - poor control
C1099	Non-insulin-dependent diabetes mellitus without complication
C109A	Non-insulin dependent diabetes mellitus with mononeuropathy
C109B	Non-insulin dependent diabetes mellitus with polyneuropathy
C109C	Non-insulin dependent diabetes mellitus with nephropathy
C109D	Non-insulin dependent diabetes mellitus with hypoglycaemic coma
C109E	Non-insulin dependent diabetes mellitus with diabetic cataract
C109F	Non-insulin-dependent diabetes mellitus with peripheral angiopathy
C109G	Non-insulin dependent diabetes mellitus with arthropathy
C109H	Non-insulin dependent diabetes mellitus with neuropathic arthropathy
C109J	Insulin treated Type 2 diabetes mellitus
C109K	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10A.	Malnutrition-related diabetes mellitus
C10A0	Malnutrition-related diabetes mellitus with coma
C10A1	Malnutrition-related diabetes mellitus with ketoacidosis
C10A2	Malnutrition-related diabetes mellitus with renal complications
C10A3	Malnutrition-related diabetes mellitus with ophthalmic complications
C10A4	Malnutrition-related diabetes mellitus with neurological complications
C10A5	Malnutrition-related diabetes mellitus with peripheral circulatory complications
C10A6	Malnutrition-related diabetes mellitus with multiple complications
C10A7	Malnutrition-related diabetes mellitus without complications
C10AW	Malnutrition-related diabetes mellitus with unspecified complications
C10AX	Malnutrition-related diabetes mellitus with other specified complications
C10B.	Diabetes mellitus induced by steroids
C10B0	Steroid induced diabetes mellitus without complication
C10C.	Diabetes mellitus autosomal dominant
C10D.	Diabetes mellitus autosomal dominant type 2
C10E.	Type 1 diabetes mellitus
C10E0	Type 1 diabetes mellitus with renal complications
C10E1	Type 1 diabetes mellitus with ophthalmic complications
C10E2	Type 1 diabetes mellitus with neurological complications
C10E3	Type 1 diabetes mellitus with multiple complications
C10E4	Unstable type 1 diabetes mellitus
C10E5	Type 1 diabetes mellitus with ulcer

C10E6 Type 1 diabetes mellitus with gangrene
C10E7 Type 1 diabetes mellitus with retinopathy
C10E8 Type 1 diabetes mellitus - poor control
C10E9 Type 1 diabetes mellitus maturity onset
C10EA Type 1 diabetes mellitus without complication
C10EB Type 1 diabetes mellitus with mononeuropathy
C10EC Type 1 diabetes mellitus with polyneuropathy
C10ED Type 1 diabetes mellitus with nephropathy
C10EE Type 1 diabetes mellitus with hypoglycaemic coma
C10EF Type 1 diabetes mellitus with diabetic cataract
C10EG Type 1 diabetes mellitus with peripheral angiopathy
C10EH Type 1 diabetes mellitus with arthropathy
C10EJ Type 1 diabetes mellitus with neuropathic arthropathy
C10EK Type 1 diabetes mellitus with persistent proteinuria
C10EL Type 1 diabetes mellitus with persistent microalbuminuria
C10EM Type 1 diabetes mellitus with ketoacidosis
C10EN Type 1 diabetes mellitus with ketoacidotic coma
C10EP Type 1 diabetes mellitus with exudative maculopathy
C10EQ Type 1 diabetes mellitus with gastroparesis
C10ER Latent autoimmune diabetes mellitus in adult
C10F. Type 2 diabetes mellitus
C10F0 Type 2 diabetes mellitus with renal complications
C10F1 Type 2 diabetes mellitus with ophthalmic complications
C10F2 Type 2 diabetes mellitus with neurological complications
C10F3 Type 2 diabetes mellitus with multiple complications
C10F4 Type 2 diabetes mellitus with ulcer
C10F5 Type 2 diabetes mellitus with gangrene
C10F6 Type 2 diabetes mellitus with retinopathy
C10F7 Type 2 diabetes mellitus - poor control
C10F9 Type 2 diabetes mellitus without complication
C10FA Type 2 diabetes mellitus with mononeuropathy
C10FB Type 2 diabetes mellitus with polyneuropathy
C10FC Type 2 diabetes mellitus with nephropathy
C10FD Type 2 diabetes mellitus with hypoglycaemic coma
C10FE Type 2 diabetes mellitus with diabetic cataract
C10FF Type 2 diabetes mellitus with peripheral angiopathy
C10FG Type 2 diabetes mellitus with arthropathy
C10FH Type 2 diabetes mellitus with neuropathic arthropathy
C10FJ Insulin treated Type 2 diabetes mellitus
C10FK Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10FL Type 2 diabetes mellitus with persistent proteinuria
C10FM Type 2 diabetes mellitus with persistent microalbuminuria
C10FN Type 2 diabetes mellitus with ketoacidosis
C10FP Type 2 diabetes mellitus with ketoacidotic coma
C10FQ Type 2 diabetes mellitus with exudative maculopathy
C10FR Type 2 diabetes mellitus with gastroparesis
C10FS Maternally inherited diabetes mellitus
C10G. Secondary pancreatic diabetes mellitus
C10G0 Secondary pancreatic diabetes mellitus without complication
C10H. Diabetes mellitus induced by non-steroid drugs
C10H0 Diabetes mellitus induced by non-steroid drugs without complication
C10J. Insulin autoimmune syndrome
C10J0 Insulin autoimmune syndrome without complication
C10K. Type A insulin resistance

C10K0	Type A insulin resistance without complication
C10L.	Fibrocalculous pancreatopathy
C10L0	Fibrocalculous pancreatopathy without complication
C10M.	Lipoatrophic diabetes mellitus
C10M0	Lipoatrophic diabetes mellitus without complication
C10N.	Secondary diabetes mellitus
C10N0	Secondary diabetes mellitus without complication
C10N1	Cystic fibrosis related diabetes mellitus
C10y.	Diabetes mellitus with other specified manifestation
C10y0	Diabetes mellitus, juvenile type, with other specified manifestation
C10y1	Diabetes mellitus, adult onset, with other specified manifestation
C10yy	Other specified diabetes mellitus with other specified complications
C10yz	Diabetes mellitus NOS with other specified manifestation
C10z.	Diabetes mellitus with unspecified complication
C10z0	Diabetes mellitus, juvenile type, with unspecified complication
C10z1	Diabetes mellitus, adult onset, with unspecified complication
C10zy	Other specified diabetes mellitus with unspecified complications
C10zz	Diabetes mellitus NOS with unspecified complication
L180.	Diabetes mellitus during pregnancy, childbirth and the puerperium
L1800	Diabetes mellitus - unspecified whether during pregnancy or the puerperium
L1801	Diabetes mellitus during pregnancy - baby delivered
L1802	Diabetes mellitus in the puerperium - baby delivered during current episode of care
L1803	Diabetes mellitus during pregnancy - baby not yet delivered
L1804	Diabetes mellitus in the pueperium - baby delivered during previous episode of care
L1805	Pre-existing diabetes mellitus, insulin-dependent
L1806	Pre-existing diabetes mellitus, non-insulin-dependent
L1807	Pre-existing malnutrition-related diabetes mellitus
L1808	Diabetes mellitus arising in pregnancy
L1809	Gestational diabetes mellitus
L180X	Pre-existing diabetes mellitus, unspecified
L180z	Diabetes mellitus during pregnancy, childbirth or the puerperium NOS
Q441.	Neonatal diabetes mellitus

Source: NHS Clinical Terminology Browser, 2009.[284]

Table A.14 Codes and terms associated with diabetes, Read codes

Read code	Domain	Read term
9360	Administration	Patient held diabetic record issued
13AB.	History/symptoms	Diabetic lipid lowering diet
13AC.	History/symptoms	Diabetic weight reducing diet
13B1.	History/symptoms	Diabetic diet
13L4.	History/symptoms	Diabetic child
2BBP.	Examination/signs	O/E - right eye background diabetic retinopathy
2BBQ.	Examination/signs	O/E - left eye background diabetic retinopathy
2BBR.	Examination/signs	O/E - right eye preproliferative diabetic retinopathy
2BBS.	Examination/signs	O/E - left eye preproliferative diabetic retinopathy
2BBT.	Examination/signs	O/E - right eye proliferative diabetic retinopathy
2BBV.	Examination/signs	O/E - left eye proliferative diabetic retinopathy
2BBW.	Examination/signs	O/E - right eye diabetic maculopathy
2BBX.	Examination/signs	O/E - left eye diabetic maculopathy
66A..	Preventative procedures	Diabetic monitoring
66A1.	Preventative procedures	Initial diabetic assessment
66A2.	Preventative procedures	Follow-up diabetic assessment
66A3.	Preventative procedures	Diabetic on diet only
66A4.	Preventative procedures	Diabetic on oral treatment
66A5.	Preventative procedures	Diabetic on insulin
66A6.	Preventative procedures	Last hypo. attack
66A7.	Preventative procedures	Frequency of hypo. attacks
66A70	Preventative procedures	Frequency of hospital treated hypoglycaemia
66A71	Preventative procedures	Frequency of GP or paramedic treated hypoglycaemia
66A8.	Preventative procedures	Has seen dietician - diabetes
66A9.	Preventative procedures	Understands diet - diabetes
66AA.	Preventative procedures	Injection sites
66Aa.	Preventative procedures	Diabetic diet - poor compliance
66AB.	Preventative procedures	Urine sugar charts
66Ab.	Preventative procedures	Diabetic foot examination
66AC.	Preventative procedures	Blood sugar charts
66Ac.	Preventative procedures	Diabetic peripheral neuropathy screening
66AD.	Preventative procedures	Fundoscopy - diabetic check
66Ad.	Preventative procedures	Hypoglycaemic attack requiring 3rd party assistance
66AE.	Preventative procedures	Feet examination
66Ae.	Preventative procedures	HBA1c target
66AF.	Preventative procedures	Attends out-patients
66Af.	Preventative procedures	Patient diabetes education review
66AG.	Preventative procedures	Diabetic drug side effects
66Ag.	Preventative procedures	Insulin needles changed daily
66AH.	Preventative procedures	Diabetic treatment changed
66Ah.	Preventative procedures	Insulin needles changed for each injection
66AH0	Preventative procedures	Conversion to insulin
66AI.	Preventative procedures	Diabetic - good control
66Ai.	Preventative procedures	Diabetic 6 month review
66Ai.	Preventative procedures	Diabetic 6 month review
66AJ.	Preventative procedures	Diabetic - poor control
66Aj.	Preventative procedures	Insulin needles changed less than once a day
66AJ0	Preventative procedures	Chronic hyperglycaemia
66AJ1	Preventative procedures	Brittle diabetes

66AJ2	Preventative procedures	Loss of hypoglycaemic warning
66AJ3	Preventative procedures	Recurrent severe hypos
66AJz	Preventative procedures	Diabetic - poor control NOS
66AK.	Preventative procedures	Diabetic - cooperative patient
66Ak.	Preventative procedures	Diabetic monitoring - lower risk albumin excretion
66Ak.	Preventative procedures	Diabetic monitoring - lower risk albumin excretion
66AL.	Preventative procedures	Diabetic-uncooperative patient
66Al.	Preventative procedures	Diabetic monitoring - higher risk albumin excretion
66Al.	Preventative procedures	Diabetic monitoring - higher risk albumin excretion
66AM.	Preventative procedures	Diabetic - follow-up default
66Am.	Preventative procedures	Insulin dose changed
66AN.	Preventative procedures	Date diabetic treatment start
66An.	Preventative procedures	Diabetes type 1 review
66AO.	Preventative procedures	Date diabetic treatment stopp.
66Ao.	Preventative procedures	Diabetes type 2 review
66AP.	Preventative procedures	Diabetes: practice programme
66Ap.	Preventative procedures	Insulin treatment initiated
66AQ.	Preventative procedures	Diabetes: shared care programme
66Aq.	Preventative procedures	Diabetic foot screen
66AR.	Preventative procedures	Diabetes management plan given
66AS.	Preventative procedures	Diabetic annual review
66AT.	Preventative procedures	Annual diabetic blood test
66AU.	Preventative procedures	Diabetes care by hospital only
66AV.	Preventative procedures	Diabetic on insulin and oral treatment
66AW.	Preventative procedures	Diabetic foot risk assessment
66AX.	Preventative procedures	Diabetes: shared care in pregnancy - diabetologist and obstetrician
66AY.	Preventative procedures	Diabetic diet - good compliance
66AZ.	Preventative procedures	Diabetic monitoring NOS
66b1.	Preventative procedures	Diabetic monitoring not required
68A7.	Preventative procedures	Diabetic retinopathy screening
68A8.	Preventative procedures	Digital retinal screening
68A9.	Preventative procedures	Diabetic retinopathy screening offered
68AA.	Preventative procedures	Digital retinal screening offered
68AB.	Preventative procedures	Diabetic digital retinopathy screening offered
8A12.	Other theraputic procedures	Diabetic crisis monitoring
8A13.	Other theraputic procedures	Diabetic stabilisation
8CA41	Other theraputic procedures	Pt advised re diabetic diet
8CE0.	Other theraputic procedures	Diabetic leaflet given
8H2J.	Other theraputic procedures	Admit diabetic emergency
8H3O.	Other theraputic procedures	Non-urgent diabetic admission
8H7C.	Other theraputic procedures	Refer, diabetic liaison nurse
8HBG.	Other theraputic procedures	Diabetic retinopathy 12 month review
8HBG.	Other theraputic procedures	Diabetic retinopathy 12 month review
8HBH.	Other theraputic procedures	Diabetic retinopathy 6 month review
8HHy.	Other theraputic procedures	Referral to diabetic register
8HTk.	Other theraputic procedures	Referral to diabetic eye clinic
8I3X.	Other theraputic procedures	Diabetic retinopathy screening refused
8I57.	Other theraputic procedures	Patient held diabetic record declined
8I6G.	Other theraputic procedures	Diabetic foot examination not indicated
93C4.	Administration	Patient consent given for addition to diabetic register
9N1i.	Administration	Seen in diabetic foot clinic
9N1Q.	Administration	Seen in diabetic clinic

9N1v.	Administration	Seen in diabetic eye clinic
9NND.	Administration	Under care of diabetic foot screener
F3450	Disorders	Diabetic mononeuritis multiplex
F35z0	Disorders	Diabetic mononeuritis NOS
F372.	Disorders	Polyneuropathy in diabetes
F3720	Disorders	Acute painful diabetic neuropathy
F3721	Disorders	Chronic painful diabetic neuropathy
F3722	Disorders	Asymptomatic diabetic neuropathy
F3813	Disorders	Myasthenic syndrome due to diabetic amyotrophy
F3y0.	Disorders	Diabetic mononeuropathy
F420.	Disorders	Diabetic retinopathy
F4200	Disorders	Background diabetic retinopathy
F4201	Disorders	Proliferative diabetic retinopathy
F4202	Disorders	Preproliferative diabetic retinopathy
F4203	Disorders	Advanced diabetic maculopathy
F4204	Disorders	Diabetic maculopathy
F4205	Disorders	Advanced diabetic retinal disease
F4206	Disorders	Non proliferative diabetic retinopathy
F4207	Disorders	High risk proliferative diabetic retinopathy
F4208	Disorders	High risk non proliferative diabetic retinopathy
F420z	Disorders	Diabetic retinopathy NOS
F4407	Disorders	Diabetic iritis
G73y0	Disorders	Diabetic peripheral angiopathy
M0372	Disorders	Cellulitis in diabetic foot
M2710	Disorders	Ischaemic ulcer diabetic foot
M2711	Disorders	Neuropathic diabetic ulcer - foot
M2712	Disorders	Mixed diabetic ulcer - foot
R0542	[D]Symptoms,signs,ill-def.cond	[D]Gangrene of toe in diabetic
R0543	[D]Symptoms,signs,ill-def.cond	[D]Widespread diabetic foot gangrene

Source: NHS Clinical Terminology Browser, 2009.[284]

Table A.15 READ codes for DKA and coma mapped to ICD 10 codes

ICD 10 code	Condition	Read code	Read description
E10.0	**Insulin-dependent diabetes mellitus with coma**	C1030	Diabetes mellitus, juvenile type, with ketoacidotic coma
	Diabetic:	C10EE	
	· coma with or without ketoacidosis		Type 1 diabetes mellitus with
	· hyperosmolar coma	C10EN	hypoglycaemic coma
	· hypoglycaemic coma		
	Hyperglycaemic coma NOS		Type 1 diabetes mellitus with ketoacidotic coma
E10.1	**Insulin-dependent diabetes mellitus with ketoacidosis**	C10EM	Type 1 diabetes mellitus with ketoacidosis
	Diabetic:	C1010	Diabetes mellitus, juvenile type, with ketoacidosis
	· acidosis		
	· ketoacidosis		
	without mention of coma		
E11.0	**Non-insulin-dependent diabetes mellitus with coma**	C1031	Diabetes mellitus, adult onset, with ketoacidotic coma
	Diabetic:	C10FD	
	· coma with or without ketoacidosis		Type 2 diabetes mellitus with
	· hyperosmolar coma	C10FP	hypoglycaemic coma
	· hypoglycaemic coma		
	Hyperglycaemic coma NOS		Type 2 diabetes mellitus with ketoacidotic coma
E11.1	**Non-insulin-dependent diabetes mellitus with ketoacidosis**	C10FN	Type 2 diabetes mellitus with ketoacidosis
	Diabetic:	C1011	Diabetes mellitus, adult onset, with ketoacidosis
	· acidosis		
	· ketoacidosis		
	without mention of coma		
E12.0	**Malnutrition-related diabetes mellitus with coma**	C10A0	Malnutrition-related diabetes mellitus with coma
	Diabetic:		
	· coma with or without ketoacidosis		
	· hyperosmolar coma		
	· hypoglycaemic coma		
	Hyperglycaemic coma NOS		
E12.1	**Malnutrition-related diabetes mellitus with ketoacidosis**	C10A1	Malnutrition-related diabetes mellitus with ketoacidosis
	Diabetic:		
	· acidosis		
	· ketoacidosis		
	without mention of coma		
E13.0	**Other specified diabetes mellitus with coma**	C103y	Other specified diabetes mellitus with coma
	Diabetic:		
	· coma with or without ketoacidosis		
	· hyperosmolar coma		
	· hypoglycaemic coma		
	Hyperglycaemic coma NOS		

E13.1	**Other specified diabetes mellitus with ketoacidosis** Diabetic: · acidosis · ketoacidosis without mention of coma	C101y	Other specified diabetes mellitus with ketoacidosis
E14.0	**Unspecified diabetes mellitus with coma** Diabetic: · coma with or without ketoacidosis · hyperosmolar coma · hypoglycaemic coma Hyperglycaemic coma NOS	C103z	Diabetes mellitus NOS with ketoacidotic coma
E14.1	**Unspecified diabetes mellitus with ketoacidosis** Diabetic: · acidosis · ketoacidosis without mention of coma	C101z	Diabetes mellitus NOS with ketoacidosis

Source: World Health Organization and NHS Clinical Terminology Browser, 2009.[284,424]

Table A.16 Aggregated regions by Strategic Health Authority (SHA) cluster

Original region	Strategic Health Authority cluster
Missing	N/A
North East	NHS North of England
North West	NHS North of England
Yorkshire & The Humber	NHS North of England
East Midlands	NHS Midlands and East
West Midlands	NHS Midlands and East
East of England	NHS Midlands and East
South West	NHS South of England
South Central	NHS South of England
London	NHS London
South East Coast	NHS South of England
Northern Ireland	N/A
Scotland	N/A
Wales	N/A

Source: Department of Health, 2011.[358]

Table A.17 Associations between comorbidities and diabetic emergency admission (DEA) in patients with diabetes, crude results from Poisson regression

Characteristic		Patients with diabetes, n		RR (95% CI)	P-value
		All	≥1 DEA* (%)		
Disease groups					
Chronic pulmonary disease					0.014
	No	1125	27 (2.40)	1	
	Yes	234	2 (0.85)	0.24 (0.06-0.99)	0.048
Congestive heart disease					0.998
	No	1280	27 (2.11)	1	
	Yes	79	2 (2.53)	1.00 (0.24-4.16)	0.998
Dementia					0.270
	No	1348	28 (2.08)	1	
	Yes	11	1 (9.09)	3.90 (0.53-28.4)	0.179
Diabetes with complication					0.016
	No	1249	26 (2.08)	1	
	Yes	110	3 (2.73)	2.91 (1.34-6.33)	0.007
Mild liver disease					0.148
	No	1354	28 (2.07)	1	
	Yes	5	1 (20.9)	6.75 (0.93-49.2)	0.059
Myocardial infarction					0.617
	No	1302	28 (2.15)	1	
	Yes	57	1 (1.75)	0.63 (0.09-4.56)	0.643
Peptic ulcer					0.647
	No	1309	28 (2.14)	1	
	Yes	50	1 (2.00)	0.65 (0.09-4.72)	0.669
Peripheral vascular disease					0.229
	No	1270	28 (2.20)	1	
	Yes	89	1 (1.12)	0.36 (0.05-2.61)	0.312
Aggregated Disease Groups (ADGs)					
Time Limited: Minor					0.166
	No	383	10 (2.61)	1	
	Yes	976	19 (1.95)	0.62 (0.32-1.20)	0.154
Time Limited: Minor-Primary					0.968
	No	255	6 (2.35)	1	
	Yes	1104	23 (2.08)	0.98 (0.41-2.35)	0.968
Time Limited: Major					<0.0001
	No	1054	28 (2.66)	1	
	Yes	305	1 (0.33)	0.09 (0.01-0.67)	0.019
Time Limited: Major-Primary Infections					0.099
	No	856	17 (1.99)	1	
	Yes	503	12 (2.39)	1.70 (0.91-3.19)	0.098
Allergies					0.411
	No	1143	20 (1.75)	1	
	Yes	216	9 (4.17)	1.38 (0.65-2.91)	0.397
Asthma					0.209

*DEA – Diabetic emergency admission refers to admissions for hyperglycaemic or hypoglycaemic emergencies, namely, diabetic ketoacidosis or diabetic coma.

	No	1170	26 (2.22)	1	
	Yes	189	3 (1.59)	0.50 (0.16-1.64)	0.254
Likely to Recur: Discrete					0.004
	No	316	11 (3.48)	1	
	Yes	1043	18 (1.73)	0.37 (0.20-0.71)	0.003
Likely to Recur: Discrete-Infections					0.020
	No	601	14 (2.33)	1	
	Yes	758	15 (1.98)	0.47 (0.25-0.90)	0.022
Likely to Recur: Progressive					0.032
	No	802	13 (1.62)	1	
	Yes	557	16 (2.87)	1.99 (1.05-3.77)	0.034
Chronic Specialty: Stable-Orthopedic					0.375
	No	489	9 (1.84)	1	
	Yes	870	20 (2.30)	1.36 (0.68-2.74)	0.385
Chronic Specialty: Stable-Eye					0.002
	No	1029	26 (2.53)	1	
	Yes	330	3 (0.91)	0.22 (0.07-0.73)	0.013
Chronic Specialty: Stable-Eye					0.004
	No	1085	27 (2.49)	1	
	Yes	274	2 (0.73)	0.20 (0.05-0.83)	0.026
Chronic Specialty: Unstable-Eye					0.364
	No	906	19 (2.10)	1	
	Yes	453	10 (2.21)	1.35 (0.71-2.55)	0.359
Dermatologic					0.482
	No	644	16 (2.48)	1	
	Yes	715	13 (1.82)	0.80 (0.43-1.50)	0.481
Injuries/Adverse Effects: Minor					0.025
	No	711	18 (2.53)	1	
	Yes	648	11 (1.70)	0.48 (0.25-0.93)	0.030
Injuries/Adverse Effects: Major					<0.0001
	No	882	10 (1.13)	1	
	Yes	477	19 (3.98)	4.93 (2.40-10.1)	<0.0001
Psychosocial: Time Limited, Minor					0.111
	No	1016	22 (2.17)	1	
	Yes	343	7 (2.04)	1.71 (0.90-3.27)	0.102
Psychosocial: Recurrent or Persistent, Stable					0.366
	No	879	19 (2.16)	1	
	Yes	480	10 (2.08)	1.34 (0.71-2.53)	0.363
Psychosocial: Recurrent or Persistent, Unstable					0.039
	No	1164	25 (2.15)	1	
	Yes	195	4 (2.05)	2.25 (1.10-4.62)	0.027
Signs/Symptoms: Minor					0.270
	No	326	10 (3.07)	1	
	Yes	1033	19 (1.84)	0.67 (0.33-1.34)	0.255
Signs/Symptoms: Uncertain					0.457
	No	239	4 (1.67)	1	
	Yes	1120	25 (2.23)	1.45 (0.52-4.09)	0.479
Signs/Symptoms: Major					0.743
	No	488	10 (2.05)	1	
	Yes	871	19 (2.18)	1.12 (0.57-2.21)	0.745
Discretionary					0.256
	No	576	13 (2.26)	1	

	Yes	783	16 (2.04)	0.69 (0.37-1.30)	0.254
See and Reassure					0.002
	No	1120	28 (2.50)	1	
	Yes	239	1 (0.42)	0.11 (0.02-0.83)	0.032
Prevention/Administrative					0.528
	No	130	4 (3.08)	1	
	Yes	1229	25 (2.03)	0.71 (0.25-1.98)	0.509
Malignancy					0.130
	No	1136	27 (2.38)	1	
	Yes	223	2 (0.90)	0.44 (0.14-1.44)	0.177
Pregnancy					0.408
	No	1287	28 (2.18)	1	
	Yes	72	1 (1.39)	0.48 (0.07-3.47)	0.464
Dental					0.011
	No	1247	25 (2.00)	1	
	Yes	112	4 (3.57)	2.94 (1.39-6.19)	0.005
Collapsed Aggregated Diagnosis Groups (CADGs)					
Acute Minor					0.123
	No	77	4 (5.19)	1	
	Yes	1282	25 (1.95)	0.40 (0.14-1.12)	0.082
Acute Major					0.398
	No	90	1 (1.11)	1	
	Yes	1269	28 (2.21)	2.13 (0.29-15.5)	0.456
Likely to Recur					0.618
	No	97	3 (3.09)	1	
	Yes	1262	26 (2.06)	0.73 (0.23-2.37)	0.602
Asthma					0.209
	No	1170	26 (2.22)	1	
	Yes	189	3 (1.59)	0.50 (0.16-1.64)	0.254
Chronic Medical: Unstable					0.224
	No	326	6 (1.84)	1	
	Yes	1033	23 (2.23)	1.66 (0.70-3.97)	0.251
Chronic Specialty: Stable					<0.0001
	No	976	26 (2.66)	1	
	Yes	383	3 (0.78)	0.19 (0.06-0.61)	0.005
Eye/Dental					0.906
	No	991	23 (2.32)	1	
	Yes	368	6 (1.63)	0.96 (0.48-1.93)	0.906
Chronic Specialty: Unstable					0.770
	No	846	19 (2.25)	1	
	Yes	513	10 (1.95)	1.10 (0.58-2.08)	0.769
Psychosocial					0.895
	No	618	16 (2.59)	1	
	Yes	741	13 (1.75)	1.04 (0.55-1.96)	0.895
Preventive/Administrative					0.528
	No	130	4 (3.08)	1	
	Yes	1229	25 (2.03)	0.71 (0.25-1.98)	0.509
Pregnancy					0.408
	No	1287	28 (2.18)	1	
	Yes	72	1 (1.39)	0.48 (0.07-3.47)	0.464
Expanded Diagnosis Clusters (EDCs) groups					0.001
	Low	436	9 (2.06)	1	

	Moderate	466	15 (3.22)	1.57 (0.77-3.22)	0.217
	High	457	5 (1.09)	0.31 (0.11-0.89)	0.029
Major Expanded Diagnosis Clusters (MEDCs)					
Administrative					0.802
	No	116	3 (2.59)	1	
	Yes	1243	26 (2.09)	0.86 (0.26-2.78)	0.798
Allergy					0.772
	No	938	17 (1.81)	1	
	Yes	421	12 (2.85)	0.91 (0.46-1.79)	0.773
Cardiovascular					0.002
	No	338	10 (2.96)	1	
	Yes	1021	19 (1.86)	0.35 (0.19-0.66)	0.001
Dental					0.189
	No	1092	22 (2.01)	1	
	Yes	267	7 (2.62)	1.60 (0.81-3.16)	0.174
Ear, Nose, Throat					0.301
	No	449	7 (1.56)	1	
	Yes	910	22 (2.42)	1.49 (0.68-3.23)	0.319
Eye					0.929
	No	518	10 (1.93)	1	
	Yes	841	19 (2.26)	0.97 (0.50-1.87)	0.929
Female reproductive system					0.936
	No	964	19 (1.97)	1	
	Yes	395	10 (2.53)	1.03 (0.52-2.03)	0.936
Gastrointestinal/hepatic					0.339
	No	526	9 (1.71)	1	
	Yes	833	20 (2.40)	1.39 (0.69-2.80)	0.350
General signs and symptoms					<0.0001
	No	541	16 (2.96)	1	
	Yes	818	13 (1.59)	0.29 (0.15-0.56)	<0.0001
General surgery					0.284
	No	300	5 (1.67)	1	
	Yes	1059	24 (2.27)	1.62 (0.63-4.15)	0.312
Genetic					0.001
	No	1307	27 (2.07)	1	
	Yes	52	2 (3.85)	5.30 (2.34-12.0)	<0.0001
Genito-urinary					0.001
	No	631	18 (2.85)	1	
	Yes	728	11 (1.51)	0.35 (0.17-0.68)	0.002
Hematologic					0.003
	No	1011	27 (2.67)	1	
	Yes	348	2 (0.57)	0.24 (0.07-0.77)	0.016
Infections					0.343
	No	932	18 (1.93)	1	
	Yes	427	11 (2.58)	1.37 (0.72-2.59)	0.338
Malignancies					0.096
	No	1123	27 (2.40)	1	
	Yes	236	2 (0.85)	0.41 (0.13-1.34)	0.142
Musculoskeletal					0.007
	No	197	6 (3.05)	1	
	Yes	1162	23 (1.98)	0.35 (0.17-0.70)	0.003
Neonatal					0.342

	No	1349	28 (2.08)	1	
	Yes	10	1 (10.0)	3.12 (0.43-22.7)	0.262
Neurologic					0.320
	No	320	6 (1.88)	1	
	Yes	1039	23 (2.21)	1.52 (0.64-3.63)	0.343
Nutrition					0.054
	No	1166	27 (2.32)	1	
	Yes	193	2 (1.04)	0.31 (0.08-1.29)	0.109
Psychosocial					0.646
	No	663	16 (2.41)	1	
	Yes	696	13 (1.87)	1.16 (0.62-2.18)	0.647
Reconstructive					0.001
	No	1094	19 (1.74)	1	
	Yes	265	10 (3.77)	3.00 (1.60-5.66)	0.001
Renal					0.979
	No	999	22 (2.20)	1	
	Yes	360	7 (1.94)	0.99 (0.49-1.99)	0.979
Respiratory					0.328
	No	469	10 (2.13)	1	
	Yes	890	19 (2.13)	0.72 (0.38-1.37)	0.321
Rheumatologic					0.001
	No	1053	27 (2.56)	1	
	Yes	306	2 (0.65)	0.17 (0.04-0.69)	0.014
Skin					0.264
	No	310	8 (2.58)	1	
	Yes	1049	21 (2.00)	0.65 (0.32-1.34)	0.246
Toxic effects/Adverse events					0.658
	No	1193	26 (2.18)	1	
	Yes	166	3 (1.81)	0.80 (0.28-2.24)	0.667

Table A.18 Associations between comorbidities and diabetic emergency admission (DEA) in patients with diabetes, crude results from Poisson regression using the generalized estimating equations (GEE) method

Characteristic	Crude		Adjusted	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Disease groups				
Chronic pulmonary disease		0.014		0.008
No	1		1	
Yes	0.24 (0.06-0.99)	0.048	0.24 (0.06-0.97)	0.045
Congestive heart disease		0.998		0.998
No	1		1	
Yes	1.00 (0.24-4.16)	0.998	1.00 (0.23-4.28)	0.998
Dementia		0.270		0.448
No	1		1	
Yes	3.90 (0.53-28.4)	0.179	3.90 (0.56-27.0)	0.168
Diabetes with complication		0.016		0.396
No	1		1	
Yes	2.91 (1.34-6.33)	0.007	2.91 (0.60-14.1)	0.185
Mild liver disease		0.148		0.378
No	1		1	
Yes	6.75 (0.93-49.2)	0.059	6.75 (1.19-38.4)	0.031
Myocardial infarction		0.617		0.563
No	1		1	
Yes	0.63 (0.09-4.56)	0.643	0.63 (0.09-4.42)	0.638
Peptic ulcer		0.647		0.607
No	1		1	
Yes	0.65 (0.09-4.72)	0.669	0.65 (0.09-4.70)	0.668
Peripheral vascular disease		0.229		0.136
No	1		1	
Yes	0.36 (0.05-2.61)	0.312	0.36 (0.05-2.61)	0.312
Aggregated Disease Groups (ADGs)				
Time Limited: Minor		0.166		0.367
No	1		1	
Yes	0.62 (0.32-1.20)	0.154	0.62 (0.24-1.58)	0.313
Time Limited: Minor-Primary		0.968		0.969
No	1		1	
Yes	0.98 (0.41-2.35)	0.968	0.98 (0.41-2.38)	0.969
Time Limited: Major		<0.0001		0.001
No	1		1	
Yes	0.09 (0.01-0.67)	0.019	0.09 (0.01-0.70)	0.021
Time Limited: Major-Primary Infections		0.099		0.275
No	1		1	
Yes	1.70 (0.91-3.19)	0.098	1.70 (0.76-3.83)	0.200
Allergies		0.411		0.466
No	1		1	
Yes	1.38 (0.65-2.91)	0.397	1.38 (0.60-3.18)	0.450
Asthma		0.209		0.124
No	1		1	
Yes	0.50 (0.16-1.64)	0.254	0.50 (0.17-1.50)	0.217
Likely to Recur: Discrete		0.004		0.142

No	1		1	
Yes	0.37 (0.20-0.71)	0.003	0.37 (0.15-0.93)	0.035
Likely to Recur: Discrete-Infections		0.020		0.159
No	1		1	
Yes	0.47 (0.25-0.90)	0.022	0.47 (0.20-1.12)	0.087
Likely to Recur: Progressive		0.032		0.176
No	1		1	
Yes	1.99 (1.05-3.77)	0.034	1.99 (0.79-5.02)	0.144
Chronic Specialty: Stable-Orthopedic		0.375		0.474
No	1		1	
Yes	1.36 (0.68-2.74)	0.385	1.36 (0.58-3.19)	0.477
Chronic Specialty: Stable-Eye		0.002		0.009
No	1		1	
Yes	0.22 (0.07-0.73)	0.013	0.22 (0.07-0.77)	0.018
Chronic Specialty: Stable-Eye		0.004		0.003
No	1		1	
Yes	0.20 (0.05-0.83)	0.026	0.20 (0.05-0.80)	0.023
Chronic Specialty: Unstable-Eye		0.364		0.596
No	1		1	
Yes	1.35 (0.71-2.55)	0.359	1.35 (0.49-3.74)	0.566
Dermatologic		0.482		0.621
No	1		1	
Yes	0.80 (0.43-1.50)	0.481	0.80 (0.32-1.97)	0.624
Injuries/Adverse Effects: Minor		0.025		0.139
No	1		1	
Yes	0.48 (0.25-0.93)	0.030	0.48 (0.20-1.13)	0.093
Injuries/Adverse Effects: Major		<0.0001		0.006
No	1		1	
Yes	4.93 (2.4-10.1)	<0.0001	4.93 (2.19-11.1)	<0.0001
Psychosocial: Time Limited, Minor		0.111		0.403
No	1		1	
Yes	1.71 (0.90-3.27)	0.102	1.71 (0.61-4.84)	0.310
Psychosocial: Recurrent or Persistent, Stable		0.366		0.576
No	1		1	
Yes	1.34 (0.71-2.53)	0.363	1.34 (0.52-3.47)	0.544
Psychosocial: Recurrent or Persistent, Unstable		0.039		0.394
No	1		1	
Yes	2.25 (1.10-4.62)	0.027	2.25 (0.59-8.65)	0.237
Signs/Symptoms: Minor		0.270		0.350
No	1		1	
Yes	0.67 (0.33-1.34)	0.255	0.67 (0.30-1.49)	0.322
Signs/Symptoms: Uncertain		0.457		0.408
No	1		1	
Yes	1.45 (0.52-4.09)	0.479	1.45 (0.54-3.89)	0.457
Signs/Symptoms: Major		0.743		0.810
No	1		1	
Yes	1.12 (0.57-2.21)	0.745	1.12 (0.44-2.86)	0.813
Discretionary		0.256		0.443
No	1		1	
Yes	0.69 (0.37-1.30)	0.254	0.69 (0.30-1.63)	0.402
See and Reassure		0.002		0.002
No	1		1	

Yes	0.11 (0.02-0.83)	0.032	0.11 (0.02-0.86)	0.035
Prevention/Administrative		0.528		0.566
No	1		1	
Yes	0.71 (0.25-1.98)	0.509	0.71 (0.24-2.04)	0.520
Malignancy		0.130		0.185
No	1		1	
Yes	0.44 (0.14-1.44)	0.177	0.44 (0.10-2.06)	0.299
Pregnancy		0.408		0.297
No	1		1	
Yes	0.48 (0.07-3.47)	0.464	0.48 (0.07-3.26)	0.450
Dental		0.011		0.344
No	1		1	
Yes	2.94 (1.39-6.19)	0.005	2.94 (0.69-12.4)	0.143
Collapsed Aggregated Diagnosis Groups (CADGs)				
Acute Minor		0.123		0.212
No	1		1	
Yes	0.40 (0.14-1.12)	0.082	0.40 (0.15-1.09)	0.073
Acute Major		0.398		0.258
No	1		1	
Yes	2.13 (0.29-15.5)	0.456	2.13 (0.33-13.7)	0.427
Likely to Recur		0.618		0.632
No	1		1	
Yes	0.73 (0.23-2.37)	0.602	0.73 (0.24-2.25)	0.586
Asthma		0.209		0.124
No	1		1	
Yes	0.50 (0.16-1.64)	0.254	0.50 (0.17-1.50)	0.217
Chronic Medical: Unstable		0.224		0.208
No	1		1	
Yes	1.66 (0.70-3.97)	0.251	1.66 (0.72-3.84)	0.233
Chronic Specialty: Stable		<0.0001		0.005
No	1		1	
Yes	0.19 (0.06-0.61)	0.005	0.19 (0.05-0.64)	0.008
Eye/Dental		0.906		0.945
No	1		1	
Yes	0.96 (0.48-1.93)	0.906	0.96 (0.28-3.23)	0.946
Chronic Specialty: Unstable		0.770		0.859
No	1		1	
Yes	1.10 (0.58-2.08)	0.769	1.10 (0.39-3.07)	0.855
Psychosocial		0.895		0.930
No	1		1	
Yes	1.04 (0.55-1.96)	0.895	1.04 (0.41-2.68)	0.930
Preventive/Administrative		0.528		0.566
No	1		1	
Yes	0.71 (0.25-1.98)	0.509	0.71 (0.24-2.04)	0.520
Pregnancy		0.408		0.297
No	1		1	
Yes	0.48 (0.07-3.47)	0.464	0.48 (0.07-3.26)	0.450
Expanded Diagnosis Clusters (EDCs) groups		0.001		0.039
Low	1		1	
Moderate	1.57 (0.77-3.22)	0.217	1.57 (0.53-4.66)	0.415
High	0.31 (0.11-0.89)	0.029	0.31 (0.09-1.03)	0.055
Major Expanded Diagnosis Clusters (MEDCs)				

Administrative		0.802		0.811
No	1		1	
Yes	0.86 (0.26-2.78)	0.798	0.86 (0.26-2.83)	0.801
Allergy		0.772		0.806
No	1		1	
Yes	0.91 (0.46-1.79)	0.773	0.91 (0.41-2.00)	0.805
Cardiovascular		0.002		0.119
No	1		1	
Yes	0.35 (0.19-0.66)	0.001	0.35 (0.14-0.88)	0.025
Dental		0.189		0.503
No	1		1	
Yes	1.60 (0.81-3.16)	0.174	1.60 (0.50-5.17)	0.430
Ear, Nose, Throat		0.301		0.378
No	1		1	
Yes	1.49 (0.68-3.23)	0.319	1.49 (0.6-3.69)	0.394
Eye		0.929		0.954
No	1		1	
Yes	0.97 (0.50-1.87)	0.929	0.97 (0.35-2.67)	0.954
Female reproductive system		0.936		0.949
No	1		1	
Yes	1.03 (0.52-2.03)	0.936	1.03 (0.44-2.39)	0.949
Gastrointestinal/hepatic		0.339		0.522
No	1		1	
Yes	1.39 (0.69-2.80)	0.350	1.39 (0.48-4.04)	0.540
General signs and symptoms		<0.0001		0.036
No	1		1	
Yes	0.29 (0.15-0.56)	<0.0001	0.29 (0.12-0.68)	0.005
General surgery		0.284		0.248
No	1		1	
Yes	1.62 (0.63-4.15)	0.312	1.62 (0.66-4.01)	0.294
Genetic		0.001		0.343
No	1		1	
Yes	5.30 (2.34-12.0)	<0.0001	5.30 (1.00-28.0)	0.050
Genito-urinary		0.001		0.054
No	1		1	
Yes	0.35 (0.17-0.68)	0.002	0.35 (0.15-0.82)	0.016
Hematologic		0.003		0.018
No	1		1	
Yes	0.24 (0.07-0.77)	0.016	0.24 (0.05-1.12)	0.069
Infections		0.343		0.561
No	1		1	
Yes	1.37 (0.72-2.59)	0.338	1.37 (0.52-3.61)	0.529
Malignancies		0.096		0.144
No	1		1	
Yes	0.41 (0.13-1.34)	0.142	0.41 (0.09-1.92)	0.260
Musculoskeletal		0.007		0.265
No	1		1	
Yes	0.35 (0.17-0.70)	0.003	0.35 (0.11-1.13)	0.080
Neonatal		0.342		0.485
No	1		1	
Yes	3.12 (0.43-22.7)	0.262	3.12 (0.46-21.0)	0.242
Neurologic		0.320		0.291

	No	1		1	
	Yes	1.52 (0.64-3.63)	0.343	1.52 (0.66-3.49)	0.320
Nutrition			0.054		0.023
	No	1		1	
	Yes	0.31 (0.08-1.29)	0.109	0.31 (0.08-1.21)	0.092
Psychosocial			0.646		0.762
	No	1		1	
	Yes	1.16 (0.62-2.18)	0.647	1.16 (0.45-2.96)	0.757
Reconstructive			0.001		0.124
	No	1		1	
	Yes	3.00 (1.60-5.66)	0.001	3.00 (1.12-8.04)	0.028
Renal			0.979		0.984
	No	1		1	
	Yes	0.99 (0.49-1.99)	0.979	0.99 (0.39-2.50)	0.984
Respiratory			0.328		0.545
	No	1		1	
	Yes	0.72 (0.38-1.37)	0.321	0.72 (0.28-1.87)	0.501
Rheumatologic			0.001		0.004
	No	1		1	
	Yes	0.17 (0.04-0.69)	0.014	0.17 (0.04-0.72)	0.016
Skin			0.264		0.490
	No	1		1	
	Yes	0.65 (0.32-1.34)	0.246	0.65 (0.22-1.91)	0.438
Toxic effects/Adverse events			0.658		0.708
	No	1		1	
	Yes	0.80 (0.28-2.24)	0.667	0.80 (0.22-2.86)	0.728

Table A.19 Associations between comorbidities and death in patients with diabetes, crude results from log-binomial regression

Characteristic	Deaths, n			RR (95% CI)	P-value
	All	≥1 DEA*	(%)		
Disease groups					
Chronic pulmonary disease					0.882
No	212	7	(3.30)	1	
Yes	44	0	-	1.01 (0.88 - 1.16)	0.881
Congestive heart disease					0.73
No	214	6	(2.80)	1	
Yes	42	1	(2.38)	1.02 (0.90-1.17)	0.723
Dementia					0.893
No	252	6	(2.38)	1	
Yes	4	1	(25.0)	0.97 (0.62-1.51)	0.898
Diabetes with complication					0.019
No	221	7	(3.17)	1	
Yes	35	0	-	1.17 (1.07-1.29)	0.001
Myocardial infarction					0.054
No	235	7	(2.98)	1	
Yes	21	0	-	1.17 (1.06-1.31)	0.003
Peptic ulcer					0.054
No	243	7	(2.88)	1	
Yes	13	0	-	1.06 (0.86-1.30)	0.003
Peripheral vascular disease					0.864
No	226	7	(3.10)	1	
Yes	30	0	-	1.01 (0.87-1.19)	0.861
Aggregated Disease Groups (ADGs)					
Time Limited: Minor					0.1
No	84	3	(3.57)	1	-
Yes	172	4	(2.33)	0.91 (0.83-1.01)	0.082
Time Limited: Minor-Primary					0.038
No	58	2	(3.45)	1	
Yes	198	5	(2.53)	0.89 (0.80-0.98)	0.017
Time Limited: Major					0.028
No	167	7	(4.19)	1	
Yes	89	0	-	1.12 (1.02-1.24)	0.019
Time Limited: Major-Primary Infections					0.263
No	156	3	(1.92)	1	
Yes	100	4	(4.00)	0.94 (0.84-1.05)	0.274
Allergies					0.681
No	228	7	(3.07)	1	
Yes	28	0	-	1.04 (0.89-1.21)	0.666
Asthma					0.683
No	223	6	(2.69)	1	
Yes	33	1	(3.03)	1.03 (0.89-1.19)	0.669

*DEA – Diabetic emergency admission refers to admissions for hyperglycaemic or hypoglycaemic emergencies, namely, diabetic ketoacidosis or diabetic coma.

Likely to Recur: Discrete				0.912
No	67	1 (1.49)	1	
Yes	189	6 (3.17)	0.99 (0.88-1.12)	0.912
Likely to Recur: Discrete-Infections				0.447
No	112	4 (3.57)	1	
Yes	144	3 (2.08)	0.96 (0.87-1.06)	0.443
Likely to Recur: Progressive				0.61
No	116	4 (3.45)	1	
Yes	140	3 (2.14)	1.03 (0.93-1.14)	0.612
Chronic Medical: Stable				0.748
No	61	3 (4.92)	1	
Yes	195	4 (2.05)	0.98 (0.87-1.10)	0.744
Chronic Specialty: Stable-Orthopedic				0.023
No	205	6 (2.93)	1	
Yes	51	1 (1.96)	0.86 (0.74-1.00)	0.046
Chronic Specialty: Stable-Eye				0.138
No	193	6 (3.11)	1	
Yes	63	1 (1.59)	0.91 (0.80-1.04)	0.167
Chronic Specialty: Unstable-Eye				0.251
No	152	6 (3.95)	1	
Yes	104	1 (0.96)	0.94 (0.84-1.05)	0.26
Dermatologic				0.263
No	156	6 (3.85)	1	
Yes	100	1 (1.00)	0.94 (0.84-1.05)	0.274
Injuries/Adverse Effects: Minor				0.998
No	149	6 (4.03)	1	
Yes	107	1 (0.93)	1.00 (0.90-1.11)	0.998
Injuries/Adverse Effects: Major				0.708
No	156	2 (1.28)	1	
Yes	100	5 (5.00)	1.02 (0.92-1.13)	0.706
Psychosocial: Time Limited, Minor				0.083
No	201	5 (2.49)	1	
Yes	55	2 (3.64)	0.89 (0.77-1.03)	0.115
Psychosocial: Recurrent or Persistent, Stable				0.768
No	182	5 (2.75)	1	
Yes	74	2 (2.70)	0.98 (0.88-1.10)	0.771
Psychosocial: Recurrent or Persistent, Unstable				0.038
No	198	6 (3.03)	1	
Yes	58	1 (1.72)	1.13 (1.02-1.25)	0.017
Signs/Symptoms: Minor				0.784
No	65	3 (4.62)	1	
Yes	191	4 (2.09)	0.98 (0.88-1.10)	0.781
Signs/Symptoms: Uncertain				0.581
No	45	1 (2.22)	1	
Yes	211	6 (2.84)	0.96 (0.85-1.09)	0.564
Signs/Symptoms: Major				0.304
No	83	5 (6.02)	1	
Yes	173	2 (1.16)	0.95 (0.85-1.05)	0.287
Discretionary				0.47
No	116	4 (3.45)	1	
Yes	140	3 (2.14)	0.96 (0.87-1.07)	0.468
See and Reassure				0.724

No	209	7 (3.35)	1	
Yes	47	0 -	1.02 (0.90-1.16)	0.717
Prevention/Administrative				0.955
No	38	0 -	1	
Yes	218	7 (3.21)	1.00 (0.86-1.15)	0.955
Malignancy				0.465
No	176	6 (3.41)	1	
Yes	80	1 (1.25)	0.96 (0.85-1.08)	0.477
Dental				0.714
No	245	7 (2.86)	1	
Yes	11	0 -	0.95 (0.72-1.26)	0.732
Collapsed Aggregated Disease Groups (CADGs)				
Acute Minor				0.14
No	16	2 (12.5)	1	
Yes	240	5 (2.08)	0.87 (0.76-0.99)	0.033
Acute Major				0.613
No	14	1 (7.14)	1	
Yes	242	6 (2.48)	1.06 (0.82-1.37)	0.641
Likely to Recur				0.906
No	22	1 (4.55)	1	
Yes	234	6 (2.56)	1.01 (0.84-1.22)	0.907
Asthma				0.683
No	223	6 (2.69)	1	
Yes	33	1 (3.03)	1.03 (0.89-1.19)	0.669
Chronic Medical: Unstable				0.567
No	30	2 (6.67)	1	
Yes	226	5 (2.21)	0.96 (0.83-1.11)	0.54
Chronic Specialty: Stable				0.006
No	197	6 (3.05)	1	
Yes	59	1 (1.69)	0.84 (0.72-0.97)	0.016
Eye/Dental				0.088
No	184	6 (3.26)	1	
Yes	72	1 (1.39)	0.90 (0.80-1.02)	0.111
Chronic Specialty: Unstable				0.318
No	140	6 (4.29)	1	
Yes	116	1 (0.86)	0.95 (0.85-1.05)	0.322
Psychosocial				0.917
No	123	4 (3.25)	1	
Yes	133	3 (2.26)	1.00 (0.90-1.10)	0.917
Preventive/Administrative				0.955
No	38	0 -	1	
Yes	218	7 (3.21)	1.00 (0.86-1.15)	0.955
Expanded Disease Cluster (EDC) groups				0.134
Low	89	4 (4.49)	1	
Moderate	90	3 (3.33)	0.92 (0.82-1.03)	0.156
High	77	0 -	0.88 (0.78-1.00)	0.055
Major Expanded Disease Clusters (MEDCs)				
Administrative				0.685
No	32	0 -	1	
Yes	224	7 (3.13)	1.03 (0.88-1.22)	0.697
Allergy				0.573
No	191	6 (3.14)	1	

Yes	65	1 (1.54)	1.03 (0.92-1.16)	0.562
Cardiovascular				0.605
No	48	2 (4.17)	1	
Yes	208	5 (2.40)	1.04 (0.90-1.19)	0.618
Dental				0.492
No	219	7 (3.20)	1	
Yes	37	0 -	0.95 (0.81-1.11)	0.517
Ear, Nose, Throat				0.016
No	114	3 (2.63)	1	
Yes	142	4 (2.82)	0.88 (0.80-0.98)	0.014
Eye				0.255
No	80	4 (5.00)	1	
Yes	176	3 (1.70)	0.94 (0.85-1.04)	0.234
Female reproductive system				0.817
No	206	5 (2.43)	1	
Yes	50	2 (4.00)	1.02 (0.89-1.15)	0.814
Gastrointestinal/hepatic				0.343
No	106	5 (4.72)	1	
Yes	150	2 (1.33)	0.95 (0.86-1.05)	0.336
General signs and symptoms				0.968
No	97	5 (5.15)	1	
Yes	159	2 (1.26)	1.00 (0.90-1.11)	0.968
General surgery				0.175
No	63	2 (3.17)	1	
Yes	193	5 (2.59)	0.92 (0.83-1.03)	0.142
Genito-urinary				0.016
No	129	4 (3.10)	1	
Yes	127	3 (2.36)	0.88 (0.80-0.98)	0.017
Hematologic				0.994
No	177	7 (3.95)	1	
Yes	79	0 -	1.00 (0.89-1.12)	0.994
Infections				0.564
No	181	5 (2.76)	1	
Yes	75	2 (2.67)	1.03 (0.93-1.15)	0.554
Malignancies				0.677
No	175	6 (3.43)	1	
Yes	81	1 (1.23)	0.98 (0.87-1.09)	0.682
Musculoskeletal				0.581
No	50	1 (2.00)	1	
Yes	206	6 (2.91)	0.97 (0.85-1.09)	0.566
Neurologic				0.555
No	34	1 (2.94)	1	
Yes	222	6 (2.7)	1.05 (0.89-1.23)	0.576
Nutrition				0.009
No	226	6 (2.65)	1	
Yes	30	1 (3.33)	1.20 (1.10-1.31)	<0.0001
Psychosocial				0.334
No	144	4 (2.78)	1	
Yes	112	3 (2.68)	0.95 (0.86-1.06)	0.339
Reconstructive				0.992
No	191	4 (2.09)	1	
Yes	65	3 (4.62)	1.00 (0.89-1.13)	0.992

Renal				0.001
No	185	6 (3.24)	1	
Yes	71	1 (1.41)	0.82 (0.72-0.94)	0.004
Respiratory				0.097
No	79	3 (3.8)	1	
Yes	177	4 (2.26)	0.91 (0.82-1.01)	0.076
Rheumatologic				0.536
No	195	6 (3.08)	1	
Yes	61	1 (1.64)	1.04 (0.93-1.17)	0.521
Skin				0.005
No	83	4 (4.82)	1	
Yes	173	3 (1.73)	0.86 (0.78-0.95)	0.002
Toxic effects/Adverse events				0.567
No	226	4 (1.77)	1	
Yes	30	3 (10.0)	1.05 (0.90-1.21)	0.54

Table A.20 Associations between comorbidities and death in patients with diabetes, crude results from log-binomial regression using the generalized estimating equations (GEE) method

Characteristic	Crude		Adjusted	
	RR (95% CI)	P-value	RR (95% CI)	P-value
Disease groups				
Chronic pulmonary disease		0.882		0.888
No	1		1	
Yes	1.01 (0.88-1.16)	0.881	1.01 (0.88-1.17)	0.888
Congestive heart disease		0.730		0.707
No	1		1	
Yes	1.02 (0.90-1.17)	0.723	1.02 (0.90-1.16)	0.704
Dementia		0.893		0.896
No	1		1	
Yes	0.97 (0.62-1.51)	0.898	0.97 (0.62-1.51)	0.898
Diabetes with complication		0.019		0.006
No	1		1	
Yes	1.17 (1.07-1.29)	0.001	1.17 (1.06-1.29)	0.001
Myocardial infarction		0.054		0.016
No	1		1	
Yes	1.17 (1.06-1.31)	0.003	1.17 (1.05-1.31)	0.004
Peptic ulcer		0.639		0.623
No	1		1	
Yes	1.06 (0.86-1.30)	0.605	1.06 (0.86-1.30)	0.610
Peripheral vascular disease		0.864		0.860
No	1		1	
Yes	1.01 (0.87-1.19)	0.861	1.01 (0.87-1.18)	0.859
Aggregated Disease Groups (ADGs)				
Time Limited: Minor		0.100		0.076
No	1		1	
Yes	0.91 (0.83-1.01)	0.082	0.91 (0.83-1.01)	0.069
Time Limited: Minor-Primary		0.038		0.031
No	1		1	
Yes	0.89 (0.80-0.98)	0.017	0.89 (0.80-0.98)	0.018
Time Limited: Major		0.028		0.020
No	1		1	
Yes	1.12 (1.02-1.24)	0.019	1.12 (1.02-1.24)	0.016
Time Limited: Major-Primary Infections		0.263		0.243
No	1		1	
Yes	0.94 (0.84-1.05)	0.274	0.94 (0.85-1.04)	0.250
Allergies		0.681		0.670
No	1		1	
Yes	1.04 (0.89-1.21)	0.666	1.04 (0.89-1.21)	0.663
Asthma		0.683		0.661
No	1		1	
Yes	1.03 (0.89-1.19)	0.669	1.03 (0.90-1.19)	0.659
Likely to Recur: Discrete		0.912		0.913
No	1		1	
Yes	0.99 (0.88-1.12)	0.912	0.99 (0.88-1.12)	0.913
Likely to Recur: Discrete-Infections		0.447		0.485
No	1		1	
Yes	0.96 (0.87-1.06)	0.443	0.96 (0.86-1.08)	0.485

Likely to Recur: Progressive		0.610		0.595
No	1		1	
Yes	1.03 (0.93-1.14)	0.612	1.03 (0.93-1.13)	0.596
Chronic Medical: Unstable		0.748		0.752
No	1		1	
Yes	0.98 (0.87-1.10)	0.744	0.98 (0.87-1.11)	0.750
Chronic Specialty: Stable-Orthopedic		0.023		0.063
No	1		1	
Yes	0.86 (0.74-1.00)	0.046	0.86 (0.72-1.01)	0.072
Chronic Specialty: Stable-Eye		0.138		0.160
No	1		1	
Yes	0.91 (0.8-1.04)	0.167	0.91 (0.80-1.04)	0.173
Chronic Specialty: Unstable-Eye		0.251		0.242
No	1		1	
Yes	0.94 (0.84-1.05)	0.260	0.94 (0.85-1.04)	0.241
Dermatologic		0.263		0.260
No	1		1	
Yes	0.94 (0.84-1.05)	0.274	0.94 (0.85-1.04)	0.256
Injuries/Adverse Effects: Minor		0.998		0.998
No	1		1	
Yes	1.00 (0.90-1.11)	0.998	1.00 (0.90-1.12)	0.998
Injuries/Adverse Effects: Major		0.708		0.703
No	1		1	
Yes	1.02 (0.92-1.13)	0.706	1.02 (0.92-1.13)	0.702
Psychosocial: Time Limited, Minor		0.083		0.101
No	1		1	
Yes	0.89 (0.77-1.03)	0.115	0.89 (0.78-1.03)	0.110
Psychosocial: Recurrent or Persistent, Stable		0.768		0.756
No	1		1	
Yes	0.98 (0.88-1.10)	0.771	0.98 (0.88-1.10)	0.756
Psychosocial: Recurrent or Persistent, Unstable		0.038		0.029
No	1		1	
Yes	1.13 (1.02-1.25)	0.017	1.13 (1.02-1.26)	0.021
Signs/Symptoms: Minor		0.784		0.769
No	1		1	
Yes	0.98 (0.88-1.10)	0.781	0.98 (0.88-1.10)	0.767
Signs/Symptoms: Uncertain		0.581		0.624
No	1		1	
Yes	0.96 (0.85-1.09)	0.564	0.96 (0.83-1.12)	0.620
Signs/Symptoms: Major		0.304		0.265
No	1		1	
Yes	0.95 (0.85-1.05)	0.287	0.95 (0.86-1.04)	0.259
Discretionary		0.470		0.450
No	1		1	
Yes	0.96 (0.87-1.07)	0.468	0.96 (0.87-1.06)	0.448
See and Reassure		0.724		0.720
No	1		1	
Yes	1.02 (0.90-1.16)	0.717	1.02 (0.90-1.17)	0.719
Prevention/Administrative		0.955		0.955
No	1		1	
Yes	1.00 (0.86-1.15)	0.955	1.00 (0.86-1.15)	0.955
Malignancy		0.465		0.506

No	1		1	
Yes	0.96 (0.85-1.08)	0.477	0.96 (0.85-1.09)	0.511
Dental		0.714		0.713
No	1		1	
Yes	0.95 (0.72-1.26)	0.732	0.95 (0.73-1.24)	0.715
Collapsed Aggregated Disease Groups (CADGs)				
Acute Minor		0.140		0.068
No	1		1	
Yes	0.87 (0.76-0.99)	0.033	0.87 (0.76-0.99)	0.034
Acute Major		0.613		0.625
No	1		1	
Yes	1.06 (0.82-1.37)	0.641	1.06 (0.83-1.36)	0.633
Likely to Recur		0.906		0.901
No	1		1	
Yes	1.01 (0.84-1.22)	0.907	1.01 (0.85-1.21)	0.901
Asthma		0.683		0.661
No	1		1	
Yes	1.03 (0.89-1.19)	0.669	1.03 (0.90-1.19)	0.659
Chronic Medical: Unstable		0.567		0.559
No	1		1	
Yes	0.96 (0.83-1.11)	0.540	0.96 (0.82-1.11)	0.548
Chronic Specialty: Stable		0.006		0.042
No	1		1	
Yes	0.84 (0.72-0.97)	0.016	0.84 (0.70-1.00)	0.048
Eye/Dental		0.088		0.106
No	1		1	
Yes	0.90 (0.80-1.02)	0.111	0.90 (0.80-1.03)	0.117
Chronic Specialty: Unstable		0.318		0.331
No	1		1	
Yes	0.95 (0.85-1.05)	0.322	0.95 (0.85-1.06)	0.331
Psychosocial		0.917		0.910
No	1		1	
Yes	1.00 (0.90-1.10)	0.917	1.00 (0.90-1.09)	0.910
Preventive/Administrative		0.955		0.955
No	1		1	
Yes	1.00 (0.86-1.15)	0.955	1.00 (0.86-1.15)	0.955
Expanded Disease Cluster (EDC) groups		0.134		0.140
Low	1		1	
Moderate	0.92 (0.82-1.03)	0.156	0.92 (0.80-1.05)	0.223
High	0.88 (0.78-1.00)	0.055	0.88 (0.78-1.00)	0.050
Major Expanded Disease Clusters (MEDCs)				
Administrative		0.685		0.703
No	1		1	
Yes	1.03 (0.88-1.22)	0.697	1.03 (0.87-1.22)	0.706
Allergy		0.573		0.555
No	1		1	
Yes	1.03 (0.92-1.16)	0.562	1.03 (0.93-1.16)	0.552
Cardiovascular		0.605		0.590
No	1		1	
Yes	1.04 (0.90-1.19)	0.618	1.04 (0.91-1.18)	0.594
Dental		0.492		0.511
No	1		1	

Yes	0.95 (0.81-1.11)	0.517	0.95 (0.81-1.11)	0.515
Ear, Nose, Throat		0.016		0.031
No	1		1	
Yes	0.88 (0.80-0.98)	0.014	0.88 (0.79-0.99)	0.028
Eye		0.255		0.275
No	1		1	
Yes	0.94 (0.85-1.04)	0.234	0.94 (0.84-1.05)	0.267
Female reproductive system		0.817		0.826
No	1		1	
Yes	1.02 (0.89-1.15)	0.814	1.02 (0.89-1.16)	0.826
Gastrointestinal/hepatic		0.343		0.337
No	1		1	
Yes	0.95 (0.86-1.05)	0.336	0.95 (0.86-1.05)	0.332
General signs and symptoms		0.968		0.968
No	1		1	
Yes	1.00 (0.90-1.11)	0.968	1.00 (0.90-1.11)	0.968
General surgery		0.175		0.116
No	1		1	
Yes	0.92 (0.83-1.03)	0.142	0.92 (0.84-1.02)	0.106
Genito-urinary		0.016		0.012
No	1		1	
Yes	0.88 (0.80-0.98)	0.017	0.88 (0.80-0.97)	0.013
Hematologic		0.994		0.994
No	1		1	
Yes	1.00 (0.89-1.12)	0.994	1.00 (0.90-1.11)	0.994
Infections		0.564		0.555
No	1		1	
Yes	1.03 (0.93-1.15)	0.554	1.03 (0.93-1.15)	0.552
Malignancies		0.677		0.701
No	1		1	
Yes	0.98 (0.87-1.09)	0.682	0.98 (0.86-1.10)	0.703
Musculoskeletal		0.581		0.618
No	1		1	
Yes	0.97 (0.85-1.09)	0.566	0.97 (0.84-1.11)	0.614
Neurologic		0.555		0.553
No	1		1	
Yes	1.05 (0.89-1.23)	0.576	1.05 (0.90-1.22)	0.556
Nutrition		0.009		0.002
No	1		1	
Yes	1.20 (1.10-1.31)	<<0.00011	1.20 (1.09-1.31)	<0.0001
Psychosocial		0.334		0.307
No	1		1	
Yes	0.95 (0.86-1.06)	0.339	0.95 (0.86-1.05)	0.307
Reconstructive		0.992		0.992
No	1		1	
Yes	1.00 (0.89-1.13)	0.992	1.00 (0.88-1.13)	0.992
Renal		0.001		0.003
No	1		1	
Yes	0.82 (0.72-0.94)	0.004	0.82 (0.72-0.94)	0.003
Respiratory		0.097		0.069
No	1		1	
Yes	0.91 (0.82-1.01)	0.076	0.91 (0.83-1.00)	0.055

Rheumatologic		0.536		0.558
No	1		1	
Yes	1.04 (0.93-1.17)	0.521	1.04 (0.92-1.18)	0.556
Skin		0.005		0.002
No	1		1	
Yes	0.86 (0.78-0.95)	0.002	0.86 (0.79-0.94)	0.001
Toxic effects/Adverse events		0.567		0.508
No	1		1	
Yes	1.05 (0.90-1.21)	0.540	1.05 (0.92-1.19)	0.491

Table A.21 ICD-10 codes for cancer mapped to Read codes

ICD-10 code	ICD-10 term	Read code	Read term
C00-C14	Malignant neoplasms of lip, oral cavity and pharynx	B0…	Malignant neoplasm of lip, oral cavity and pharynx
C15-C26	Malignant neoplasms of digestive organs	B1…	Malignant neoplasm of digestive organs and peritoneum
C30-C39	Malignant neoplasms of respiratory and intrathoracic organs	B2...	Malignant neoplasm of respiratory tract and intrathoracic organs
C40-C41	Malignant neoplasms of bone and articular cartilage	B3...	Malignant neoplasm of bone, connective tissue, skin and breast
C43-C44	Melanoma and other malignant neoplasms of skin	B3...	Malignant neoplasm of bone, connective tissue, skin and breast
C45-C49	Malignant neoplasms of mesothelial and soft tissue	B3...	Malignant neoplasm of bone, connective tissue, skin and breast
C50-C50	Malignant neoplasm of breast	B3...	Malignant neoplasm of bone, connective tissue, skin and breast
C51-C58	Malignant neoplasms of female genital organs	B4...	Malignant neoplasm of genitourinary organ
C60-C63	Malignant neoplasms of male genital organs	B4...	Malignant neoplasm of genitourinary organ
C64-C68	Malignant neoplasms of urinary tract	B4...	Malignant neoplasm of genitourinary organ
C69-C72	Malignant neoplasms of eye, brain and other parts of central nervous system	B5...	Malignant neoplasm of other and unspecified sites
C73-C75	Malignant neoplasms of thyroid and other endocrine glands	B6...	Malignant neoplasm of lymphatic and haemopoietic tissue
C76-C80	Malignant neoplasms of ill-defined, secondary and unspecified sites	B5...	Malignant neoplasm of other and unspecified sites
C81-C96	Malignant neoplasms, stated or presumed to be primary, of lymphoid,	B6...	Malignant neoplasm of lymphatic and haemopoietic tissue

Table A.22 Excluded diagnoses, ICD-10 codes mapped to Read codes

ICD-10 category	Read category	Cancer type
C44	B33..	Other malignant neoplasms of skin
C97-C97	ByuE	Malignant neoplasms of independent (primary) multiple sites
D00-D09	*B8…, ByuF.*	*In situ neoplasms*
D10-D36	*B7…, ByuG.*	*Benign neoplasms*
D37-D48	*B9…, BA…, ByuH.*	*Neoplasms of uncertain or unknown behaviour*

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