The epidemiology of hospital admissions in a general population: record linkage of hospital episode statistics to the European Prospective Investigation of Cancer (EPIC-Norfolk) cohort

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Declaration

This thesis is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the Preface and specified in the text. It is not substantially the same as any that I have submitted, or, is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. I further state that no substantial part of my thesis has already been submitted, or, is being concurrently submitted for any such degree, diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. It does not exceed the prescribed word limit for the relevant Degree Committee. It does not exceed the prescribed word limit for the Degree Committee of the School of Clinical Medicine.

Summary

The epidemiology of hospital admissions in a general population: record linkage of hospital episode statistics to the European Prospective Investigation of Cancer (EPIC-Norfolk) cohort

Robert Neil Luben

The UK National Health Service (NHS) is primarily funded by taxation free at the point of delivery. Hospitals account for approximately 50% of overall NHS spending. Two-thirds of people admitted to hospital are over 65 with those over 85 accounting for 25% of bed days. This thesis aims to quantify hospital usage in a general population of middle-aged and older men and women over a 20-year follow-up period and to examine related demographic and behavioural factors. Patterns of hospital usage are described using two main hospital usage measures: admission numbers and length of stay. Socioeconomic factors such as education, occupational social class and residential area deprivation that may predict future hospital usage are examined. I assess the relationships between potentially modifiable factors such as cigarette smoking, the consumption of alcohol, body mass index and physical activity and future hospital usage while the implications for clinical and public health planning, policy and practice are also considered.

The thesis is based on the European Prospective Investigation of Cancer in Norfolk (EPIC-Norfolk), a community-based cohort of 25,639 men and women aged 40-79 at recruitment between 1993-1997 and followed up to the present. Participants completed a lifestyle questionnaire and attended a clinic where measurements and blood were taken at baseline and again at a second time-point after 12 years. All participants were linked to hospital records using their unique NHS numbers and to census data using their postcode. Episode statistics including admission and discharge dates were used to create numbers of admissions and length of stay outcomes. ICD-10 diagnosis codes were used to construct a hospital multimorbidity outcome using the Charlson Comorbidity Index above the level of 3. Logistic regression was the primary statistical model used throughout the analyses. Exposures were examined prospectively, prior to any hospital admission.

The current analyses were conducted on 25,014 participants in the cohort still alive in 1999 when hospital admission data were first available. Over the first 10 years of follow-up, 73% of study participants had at least one admission to hospital, 14% with ≥7 admissions and 20% with >20 hospital days. After 20 years, 90% of participants had a hospital admission, 65% had ≥7 admissions and 59% had >20 hospital days. High numbers of admissions and hospital days were positively associated with male sex, age, manual social class, current cigarette smoking and body mass index (BMI) >30 kg/m^2. The thesis examined levels of deprivation both at individual level, using education

and occupational social class, and residential area level using the Townsend Area Deprivation Index. Compared with those having Townsend Index lower than the average for England and Wales, those with a higher than average deprivation index had a higher likelihood of spending >20 days in hospital. Occupational social class and educational attainment modified the association between area deprivation and hospitalisation; those with manual social class and lower education level were at greater risk of hospitalisation when living in an area with higher deprivation index.

The thesis also examined potentially modifiable behavioural factors. Compared with current non-drinkers, men and women who reported any alcohol drinking had a lower risk of spending >20 days in hospital. Participants with a baseline physical activity score of at least moderately inactive had fewer hospital admissions and fewer days in hospital over 10 years, than those who were inactive. Similar associations were observed over 10 years from time-point two (TP2) and similar but attenuated results were observed for 20-year follow-up. Participants who remained physically active or became active between baseline and TP2 had lower risk of subsequent hospital usage than those who remained inactive or became inactive.

An additional hospital-based outcome measure, hospital admission with multimorbidity (HAWM), was used to examine incident multimorbidity for participants free of the condition at baseline. Baseline 5-year and 10-year incident HAWM were observed in 11% and 21% of participants, respectively. More men had incident HAWM than women and those aged >75 years had the highest proportion of multimorbid conditions with 29% at 5 years and 47% at 10 years. HAWM rates at TP2 were similar to baseline. Longer duration of hospital stay and number of admissions, age, male sex and prevalent diseases, smoking, physical inactivity, high BMI and low fruit and vegetable intake were associated with incident HAWM.

Simple demographic and behavioural indicators are related to the future probability of cumulative hospital admissions, length of stay and hospital admissions with multimorbidity. Increasing age, male sex and modifiable factors such as smoking, body mass index and usual physical activity are all strongly associated with subsequent hospital usage. Modest feasible differences in lifestyles in the general population may potentially mitigate the future impact of long hospital stay and multimorbidity and have a substantial impact on hospital usage and costs. The social determinants of health are well recognised. While some of the socioeconomic gradient in ill health has been attributed to differences in behavioural factors, there is also a socioeconomic gradient in hospital usage for individually measured social class and education and for area level deprivation apparently independently of measured behavioural factors and reported prevalent disease which warrant further exploration.

Acknowledgements

I would like to acknowledge the dedication and professionalism of the staff of EPIC-Norfolk, who devoted their time and energy over many years to making our study a success. Their attention to detail mattered and together we all created something fantastic. It was a real privilege to work with them. I would also like to thank the EPIC participants who never complained when we asked them to complete yet another questionnaire or come to yet another clinic visit. Thanks also goes to the general practitioners without whom we would not have been able to recruit volunteers and establish the cohort.

Contributions

Personal contributions

The EPIC-Norfolk study has represented a large part of my career. I joined the study in 1994 soon after the first participants were recruited, responsible for data management and computing. One of my first tasks was to create a database of participants' personal details such as name, address, telephone number and NHS number held by their GP. I drove to each of the Norfolk GP practices in turn and downloaded the required information onto a floppy disc — a process which may sound rather quaint to a contemporary audience. The early years of EPIC involved establishing an Oracle relational database, creating systems to allow data to be manually entered, designing nutritional modelling systems and automating the sending of vast numbers of letters. By 2006, EPIC-Norfolk was embarking on its third health check, the most ambitious ever undertaken, including detailed eye and cognitive components with each examination taking up to 3 hours. The process was highly automated and paperless with nurses entering information onto laptops and tablets. By this time I was managing a team of applied computer scientists and statistical programmers and we developed the many systems needed for this ambitious venture. I felt it was very important for both me and my team not to be distant from the fieldwork and participants in order to have the best possible understanding of the work. I spent as much time in Norwich as I could in our various clinics and labs working closely with the nurses, lab technicians and research assistants. To stay in touch with study participants I gave regular talks to local community groups and attended EPAP, the EPIC participants lay panel meeting.

Biological and genetic sample management was another important aspect of the study. Multiple blood and urine samples were collected and stored and needed to be tracked when used; DNA was extracted and GWAS databases established. These and other huge databases represented the start of the new discipline of data science. Another important element of the work of a cohort study is linkage. In 1997/98 I made contact with Norfolk Health Authority, later to become a Primary Care Trust (PCT) and asked if it would be possible to link the cohort to hospital episode statistics (HES) records held at that time by the Trust for all Norfolk residents. I linked the HES data each subsequent year until 2009 when organisational changes in PCTs meant this was no longer possible. I became very familiar with HES data and coding systems such as ICD-10 and OPCS-4 and I constructed hospital outcome variables allowing EPIC-Norfolk to publish extensively using hospital-based outcomes many years earlier than most community-based cohorts. As well as linking to HES and to disease registries I also became interested in using postcode to link to area level data. In 2002 I compiled a list of postcodes for the EPIC cohort and was given access to 1991 census data. This enabled me to map the cohort and to link it to area measures such as the Townsend Deprivation Index collected during the census and later to area records held in other databases such as weather data, water companies and air monitoring stations. I was very fortunate to be able to divide my time between technical responsibilities, managing a team and active involvement in numerous research projects. In 2002, I was fortunate to work closely with Professor Nick Day, constructing statistical models for the first paper published on the full European EPIC cohort on the subject of fibre and colorectal cancer. I went on to work closely with collaborators from many disciplines representing the many dimensions of EPIC-Norfolk: eye disease, bone health, cardiovascular disease, breast cancer genetics, nutrition, frailty, thyroid disease, dementia, Parkinson's disease, and many others. I enjoyed working with EPIC-Norfolk PhD students and becoming involved with their projects, and was the first point of contact for the many academic collaborators from the UK and elsewhere.

Contribution of team members, coauthors and others

The EPIC-Norfolk study originated and was conceptualised using the ideas of Nick Day, Sheila Bingham and Kay-Tee Khaw, the original principal investigators who also obtained the necessary funding to sustain the study over 25 years. My colleagues Suzy Oakes and Ailsa Welch were the first study coordinator and nutritionist and Shabina Hayat and Nichola Dalzell subsequently coordinated the study and the fieldwork.

My coauthors have all been closely involved with the study: Angela Mulligan and Marleen Lentjes, members of the core team specialising in nutrition; Nick Wareham principal investigator and Shabina Hayat research coordinator, both fellow members of the steering committee; Anthony Khawaja, closely involved with the eye study and an EPIC PhD student; and Paul Pharoah, a collaborator who works on breast and ovarian cancer genetics. I would like to thank my supervisors Paul Pharoah and Kay-Tee Khaw. I am hugely grateful to Kay-Tee who encouraged me to study, helped me to write papers, taught me many aspects of epidemiology and for her continuing help even after retiring. I would also like to thank Shaun Seaman for his statistical advice.

I have been fortunate to work with a wide group of collaborators from other institutions and universities both in the UK and Europe, some of whom I have known for many years, and I want to thank them for the mutual respect they showed which not only resulted in productive science but also enabled me to learn so much. Thanks to Andy Hart and Max Yates from the University of East Anglia, Phyo Myint from the University of Aberdeen, Matthijs Boekholdt from the University of Amsterdam, Gunter Kuhnle from University of Reading, Anthony Khawaja and Paul Foster from UCL Institute of Ophthalmology, Victoria Keevil from Addenbrookes Hospital, Doug Easton and Carol Brayne from the University of Cambridge, Marc Gunter from Imperial College London, Bertrand Hemon from the International Agency for Research into Cancer and many others.

I am very lucky to have worked with the EPIC-Norfolk group who were so friendly and supportive. It is not possible for epidemiological research to be effective without people from many disciplines working together in a team and supporting each other; the contribution of these team members is not stated often enough. Directly or indirectly, I use their work and their intellect in this thesis and I want to thank all staff, past and present for their work. In particular I would like to thank Joanna Camus, Amit Bhaniani, Carolyn Brechin, Neha Shah and other former colleagues who worked in my data management team. I also want to thank Nichola Dalzell, a colleague and friend whose drive and energy, together with the enthusiasm of her Norwich fieldwork team, made EPIC such a success.

I want to say a special thank you to Shabina for her support and friendship throughout our time as PhD students and while we both strived to finish writing our theses and lastly I want to thank my family, Jayne, Ella and Cleo for giving me time and space to study and my parents Jackie and Michael for their support.

Some chapters in the thesis closely correspond to published papers and sometimes use “we” rather than “I” reflecting the collaborative nature of the work.

Throughout this thesis I have used mathematical bracket notation for intervals. Round brackets are used to denote open intervals (strict inequalities) $<$ and $>$ and square brackets to denote closed intervals (non-strict inequalities) $\geq$ and $\leq$. For example (2,6] means greater than 2 and less than or equal to 6. All diagrams, graphs, maps and tables were created by me unless attributed to others in footnotes. All outcome variables were derived, coded and created by me. All hybrid exposure variables were created using algorithms I developed and coded by me.

Supporting publications

Luben R, Hayat S, Wareham N, Khaw KT. Predicting admissions and time spent in hospital over a decade in a population-based record linkage study: the EPIC-Norfolk cohort. BMJ Open. 2016;6: e009461.
https://doi.org/10.1136/bmjopen-2015-009461

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https://doi.org/10.1371/journal.pone.0200747

Luben R, Hayat S, Khawaja A, Wareham N, Pharoah P, Khaw KT. Residential area deprivation and risk of subsequent hospital admission in a British population: the EPIC-Norfolk cohort. BMJ Open 2019;9:e031251.
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Luben R, Hayat S, Wareham N, Pharoah P, Khaw KT. Usual physical activity and subsequent hospital usage over 19 years in a general population: the EPIC-Norfolk cohort. BMC Geriatr. 2020 May 6;20(1):165.
https://doi.org/10.1186/s12877-020-01573-0

Luben R, Hayat S, Wareham N, Pharoah P, Khaw KT. Sociodemographic and lifestyle predictors of incident hospital admissions with multimorbidity in a general population 1999–2019: the EPIC-Norfolk cohort. BMJ Open 2020;10:e042115.
http://dx.doi.org/10.1136/bmjopen-2020-042115

Conference abstracts, posters and oral presentations

Society of Social Medicine, 2019: Luben R, Hayat S, Wareham N, Pharoah P, Khaw KT. RF30 Residential area deprivation predicts subsequent hospital admission in a British population independently of social class and education status: the EPIC-Norfolk cohort. J Epidemiol Community Health 2019;73:A68–A68.
http://doi.org/10.1136/jech-2019-SSMabstracts.145
Oral presentation

Ageing: Perspectives from Cell to Society, 2020: Luben R, Hayat S, Wareham N, Pharoah P, Khaw KT. Usual physical activity and subsequent hospital usage: the EPIC-Norfolk cohort
Poster presentation.

Society of Social Medicine, 2020: Luben R, Hayat S, Wareham N, Pharoah P, Khaw KT. Sociodemographic and lifestyle predictors of incident hospital admissions with multimorbidity in a general population 1999–2019: the EPIC-Norfolk cohort.
Journal of Epidemiology and Community Health Sep 2020, 74 (Suppl 1) A13
http://dx.doi.org/10.1136/jech-2020-SSMabstracts.27
https://jech.bmj.com/content/74/Suppl_1/A13.1
Oral presentation

Society of Social Medicine, 2020: Luben R, Hayat S, Wareham N, Pharoah P, Khaw KT. Usual physical activity and subsequent hospital usage over 19 years in a general population: the EPIC-Norfolk cohort. Journal of Epidemiology and Community Health Sep 2020, 74 (Suppl 1) A75
http://dx.doi.org/10.1136/jech-2020-SSMabstracts.160
https://jech.bmj.com/content/74/Suppl_1/A75.1
Poster presentation.

Abbreviations and definitions

- AAF - Alcohol-attributable fractions
- Bed Day - A day during which a person is confined to a bed and in which the patient stays overnight in a hospital (OECD)
- BMI - Body Mass Index
- CAD - Coronary Artery Disease
- CI - Confidence Interval
- COPD - Chronic Obstructive Pulmonary Disease
- CPRD - Clinical Practice Research Datalink
- CVD - Cardiovascular Disease
- Day case - Patients admitted for an elective medical procedure or surgery and not expected to remain in hospital overnight
- DEL - Departmental Expenditure Limit
- ED - Enumeration District
- Emergency admission - an unplanned hospital admission, generally unpredictable and at short notice because of clinical need, through self-presentation at an accident or emergency department, an emergency ambulance transfer or by referral from a general practitioner
- Endpoint - See outcome
- Endpoint ascertainment - The process by which endpoints are identified and confirmed in a cohort study
- EPIC - European Prospective Investigation of Cancer
- EPIC-Norfolk - European Prospective Investigation of Cancer in Norfolk
- FCE - Finished Consultant Episode, a continuous period of care under one consultant
- Exposure - Measurements made of participants in a prospective study, usually at baseline and prior to any outcome.
- FAE - Finished Admission Episodes, the first episode in a spell of care
- GDP - Gross Domestic Product
- GP - General Practitioner
- HAWM - Hospital Admissions with Multimorbidity
- HES - Hospital Episode Statistics
- Hospital admission - The start of a spell in hospital, prior to discharge, with a continuous stay in hospital bed under the care of one or more consultants
- Hospital day - An admission to hospital either involving an overnight stay or a discharge on the same day

- Hospital usage / hospitalisation - The amount, pattern or consumption of hospital services used over period of time
- HRG - Health resource Groups
- HSCIC - Health and Social Care Information Centre, later renamed NHS Digital
- IARC - International Agency for Research on Cancer
- ICD10 - International Classification of Diseases, tenth edition
- ICNARC - Intensive Care National Audit and Research Centre
- IHD - Ischaemic Heart Disease
- IMD - Index of Multiple Deprivation
- Incident event - a cohort study outcome where participants are apparently free of the condition at baseline, but develop the condition later, identified during cohort follow-up.
- Inpatient - An NHS hospital patient, admitted for an elective procedure or as an emergency, who occupies bed and remains or is expected to remain overnight
- LEHD - Linked Electronic Healthcare Databases
- Length of stay - The duration in days of time spent in hospital as an inpatient
- LSOA - Lower Layer Super Output Area
- LTC - Long Term Conditions
- MINAP - Myocardial Ischaemia National Audit Project
- Multimorbidity - The presence of multiple diseases or conditions with a cut-off of two or more conditions
- NHS - National Health Service
- NR - Norfolk
- OBS - Office for Budget Responsibility
- OECD - Organisation for Economic Co-operation and Development
- ONS - Office for National Statistics
- OPCS - Office for Population, Censuses and Surveys
- OR - Odds Ratio
- Ordinary admissions - elective admissions with the expectation that a patient will remain in hospital for at least one night
- OSRM - Open Source Routing Machine
- Outcome - Disease or condition of interest in a prospective study, occurring after exposures are measured. Outcomes in this thesis use linked hospital episode statistic records for events occurring after baseline.
- QOF - Quality and Outcomes Framework
- PAS - Patient Administration System
- PCT - Primary Care Trust

- Prevalence / prevalent disease - Participants with a disease at a point in time, generally at study baseline. Prevalent disease in this thesis is defined as the most serious diseases reported on the baseline questionnaire - heart attack, stroke and cancer.
- PEDW - Patient Episode Database for Wales
- RCT - Randomised Controlled Trial
- SD - Standard Deviation
- SOC - Standard occupational classification
- SMR - Scottish Morbidity Record
- TP2 - Time-point two, an additional cohort baseline on a subset of participants

Table of contents

List of tables

List of figures

1 Introduction

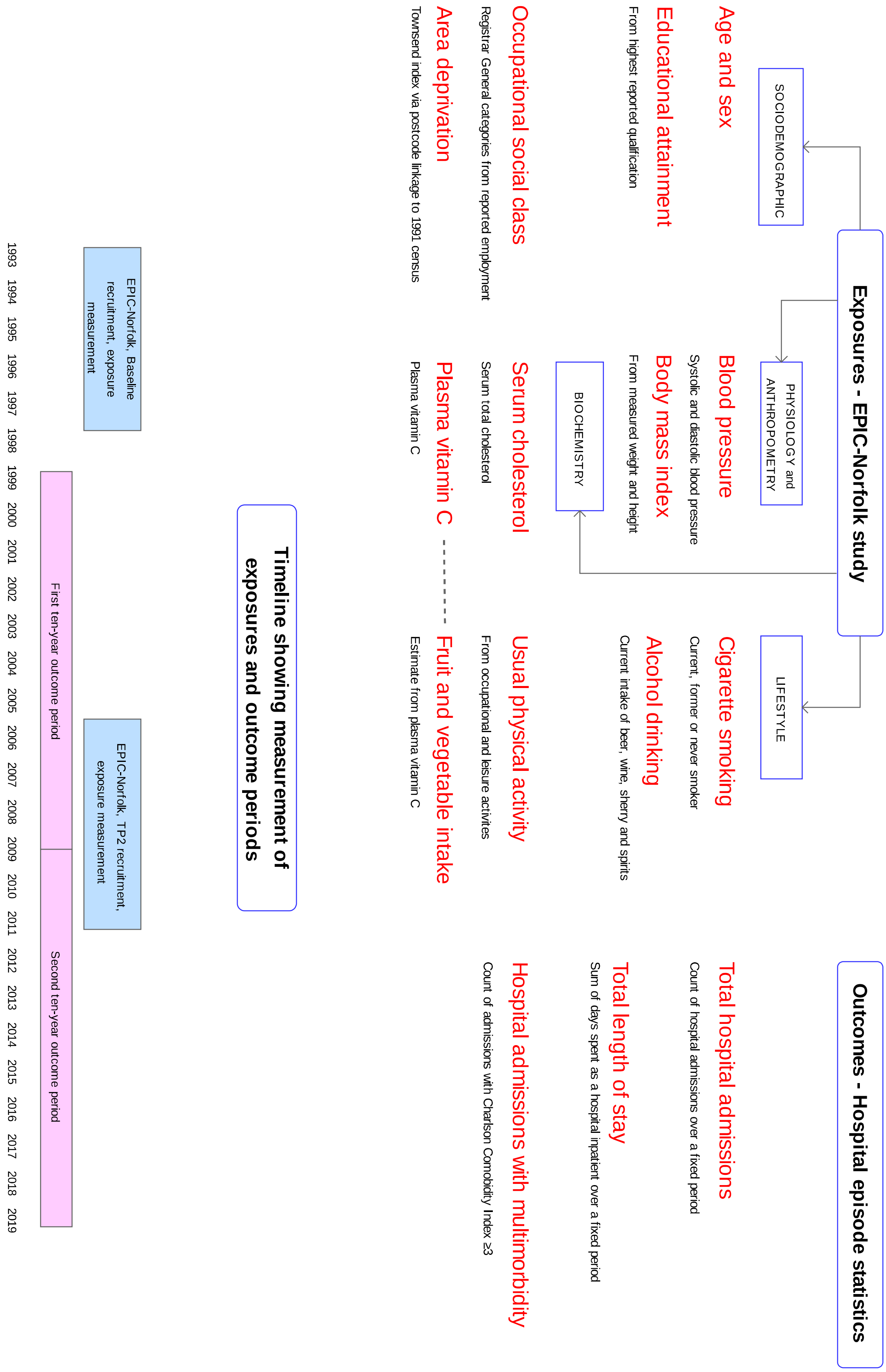
1.1 Overview

UK spending on health outpaces economic growth. Secondary healthcare accounts for the majority of spending. Overnight stays in hospital are the most expensive element of NHS provision but the number of NHS hospital beds has reduced over time. The majority of people admitted to hospital are aged 65 or more and the number in this age group is projected to continue to increase over the next thirty years. In Britain, "Hospital Episode Statistics" (HES) records are collated nationally. There are many factors which may influence hospital usage, not all of which are related to ill health. Common risk factors such as social class, education, smoking habit, low physical activity and obesity are known to influence health, disease risk and mortality but the relationship between such factors and hospital usage is less well studied. Most community-based population cohorts have relied on death certificates or questionnaire-based follow-up and few have been able to link individuals to hospital records. Most studies examining hospital activity start from those hospitalised but are limited with respect to population denominators. This thesis aims to understand the epidemiology of hospital usage in a general UK population to inform clinical and public health planning, policy and practice. Methods were developed to enable linkage to Hospital Episode Statistics, patterns of hospital usage described and risk factors that influence hospital usage established. The research used EPIC-Norfolk, a prospective population-based cohort study. Figure 1.1 shows an overview of exposures, outcomes and a chronology of measurements and outcome periods.

Thesis structure

- Chapter 1, Introduction: Background, rationale, current literature and thesis aims.
- Chapter 2, Methods and methodology: EPIC-Norfolk, exposures, HES acquisition, linkage, outcomes, and analysis plan. Description of methods common to all analyses.
- Chapter 3, Descriptive epidemiology: Comparison of national summary level data to cohort linked HES data, secular trends in EPIC-Norfolk hospital usage, summary of main hospital diagnoses and procedures in EPIC-Norfolk.
- Chapter 4-8, Main analytical sections.
- Chapter 9, Discussion: Key findings, strengths, limitations, comparison with other studies, findings in context, implications for practice and policy, future research, and conclusions.

Figure 1.1 | Overview of exposures, outcomes and study timeline



1.2 Background

The National Health Service (NHS) founded in 1948, is the publicly funded national healthcare system in the United Kingdom, primarily funded by taxation and providing healthcare free at the point of delivery to all those "ordinarily resident" in the United Kingdom [1]. The UK Department of Health oversees the NHS; patient records are maintained by healthcare providers and data centrally collected.

1.2.1 UK government spending on the NHS

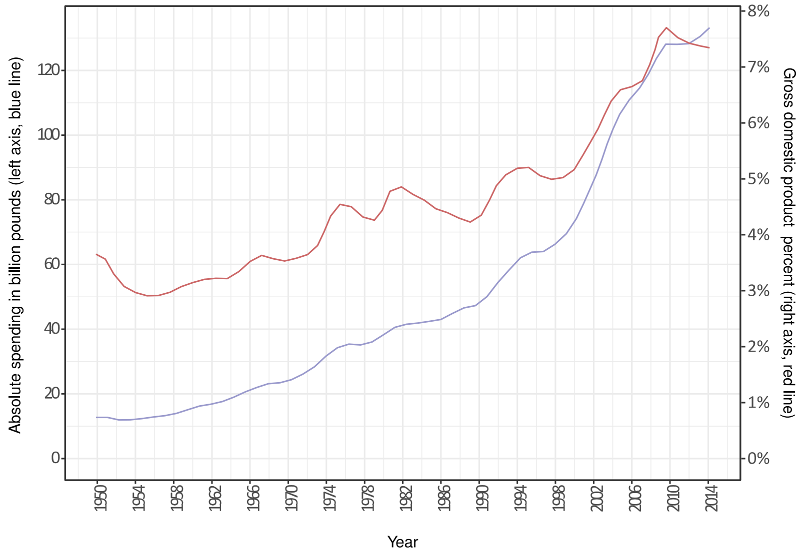
The cost of NHS spending in the UK was £129 billion in 2018/19 and is projected to increase to £134 billion in 2019/20 the highest it has ever been [2]. Historically, spending on health between 1948 and 2017 has risen on average by 3.7% per year, outpacing economic growth over the period [3]. As a result, health as a proportion of UK Gross Domestic Product (GDP) has increased from 3.6% to 7.5% over the same period. Between 1999 and 2005 the rate of increase in health spending was higher than average at 6.3% a year in real terms but has subsequently reduced each year until 2016[4]. The proportion of total UK government spending devoted to health has risen, from 7.7% in the mid-1950s to 17.9% in 2018/19 (figure 1.2 and figure 1.3). This means that healthcare now accounts for almost £1 in every £5 of government spending.

Secondary healthcare accounts for approximately 70%, and general and acute hospital-based services approximately half, of overall NHS spending — £70 billion was spent on secondary care in England in 2013/14 (prior to the abolition of PCTs) with £45 billion being spent on hospital services for NHS providers (figure 1.4) [5]. In contrast, primary care which includes general practitioner (GP) services and prescribed medicines cost £21 billion over the same period. The data presented relate to the period during which these analyses were conducted, but there have been substantial reorganisations to the NHS over this time. The average annual real growth rate between 2014–15 to 2018–19, after the NHS reorganisation and the abolition of PCTs, was 1.6% - a much lower rate of increase than the historical average [5,6]. I have explored, later in the thesis, different follow-up periods to examine whether the associations are consistent over time.

The cost to the NHS in 2017/18 of one hospital day (either an overnight bed day or a day case) was approximately £587 based on total available beds of approximately 129,200 [7]. The reported OECD UK per capita expenditure on health in 2017, was £3,375 [8].

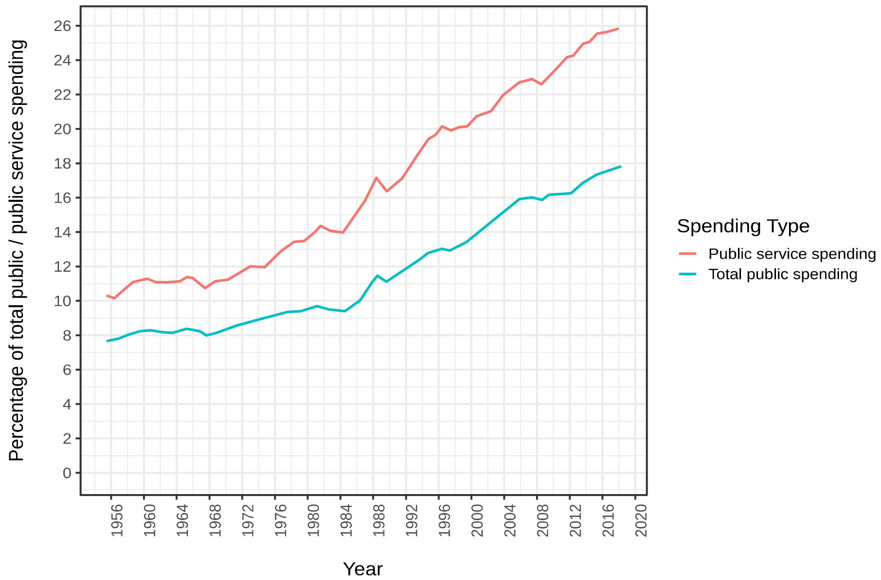
Overnight stays in hospital are considered the most expensive element of hospitalisation and UK hospitals increasingly prefer to limit the number of overnight stays for many types of procedure [7]. The total number of NHS hospital beds in England has more than halved over the past 30 years, despite the number of patients treated having increased significantly [9]. The reduction arises from policy changes resulting in bed closures and medical advances that reduce hospital length of stay. Since 1987/88, the largest percentage reductions in bed numbers have occurred in mental illness and learning disability beds with patients moved from hospitals to be cared for in the community. The number of maternity beds has fallen by 51% over the period due to shorter length of stay [9]. Numbers of acute beds have fallen albeit at a lower rate, mainly due to the closure of beds for long-term care of older people and advances in anaesthetic and surgical techniques, pain control and changes to how recovery is managed, all of which mean that many patients now spend less time in hospital than in the past. For example, 98% of cataract surgery is now conducted as day surgery [9]. The number of day-only beds has grown from around 2,000 in 1987/88 to 12,463 in 2016/17, reflecting the rise in day case surgery. However, the UK has fewer acute beds per capita than almost any other comparable health system and during winter, overnight occupancy is usually between 90 and 95 per cent [9].

Figure 1.2 | Spending on health in real terms and by Gross Domestic Product



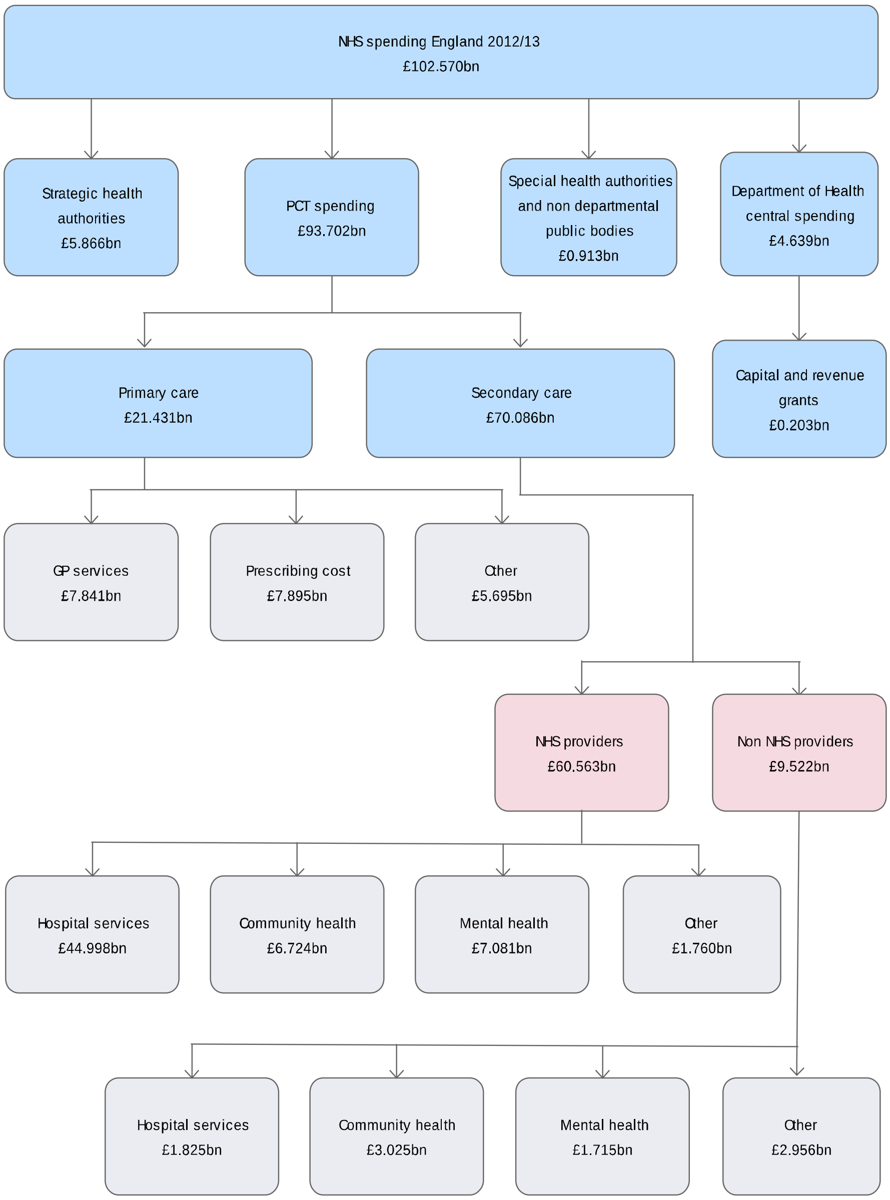
Source: The Health Foundation 2014

Figure 1.3 | UK public spending on health as a percentage of total public and public service spending, 1955-56 to 2018-19



Source: Institute for Fiscal Studies 2019

Figure 1.4 | NHS spending in real terms in England, 2012/13, prior to the abolition of PCTs



Source: The Kings Fund 2012

1.2.2 Changes in population demographics

In the UK, the number of men and women over 65 years of age was 12.2 million in 2018 and is projected to increase to 17.8 million by 2037 with the number of over-85s doubling to 3.6 million [10]. Two-thirds of people admitted to hospital are over 65 years old with those over 85 years accounting for 25% of bed days(figure 1.5) [11–13]. The King's Fund estimated in 2013 that spending on healthcare will double by 2060 to 16% of GDP (figure 1.6) [14,15].

1.2.3 Other pressures driving additional health service spending

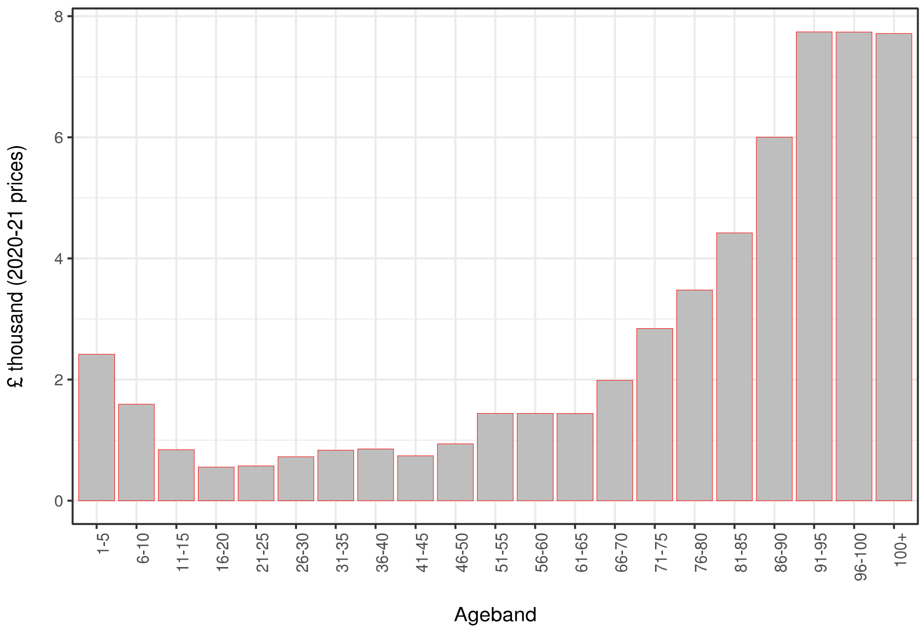
While demographic changes such as the increasingly elderly population as well as overall population growth have a significant impact on NHS budgets, they only account for 1.3% (approximately one-third) of overall annual spending increases. Increased life expectancy results in increased expenditure on general healthcare which is relatively high in older people but only delay the very significant end-of-life healthcare costs which account for 11.6% of hospital expenditure in England [16–18]. Non-demographic factors such as changes in morbidity, new medical technologies and pay are also influential [3,13]. Multimorbidity (individuals having two or more chronic conditions) is reported to increase the risk of long hospital stay [19] while new drugs, medical procedures and medical devices account for a large proportion of the increases in expenditure [20]. Trends in public health, such as obesity and smoking prevalence, also impact on future population health. High income countries may choose to spend more on health over time as their economies grow and as they are able to afford this. This tends to be driven by people's expectations of the level and quality of treatment. In OECD countries between 1995 and 2009 an estimated 42% of health spending growth was explained by income growth. Between 2000 and 2017, overall health spending increased in the 42 countries that experienced the fastest economic growth [3,14,21,22].

1.3 What is known about hospitalisation?

In Britain, "Hospital Episode Statistics" (HES) records are collated nationally in data warehouses by NHS Digital in England, the Scottish Morbidity Record and the Patient Episode Database for Wales, together containing records of all patients admitted to NHS hospitals. The term HES has been broadened to include details of inpatient care, outpatient appointments and accident and emergency records. Inpatient HES records include information on admission dates, one or more hospital consultant episodes within an admission and per-episode coded diagnostic and procedure categories.

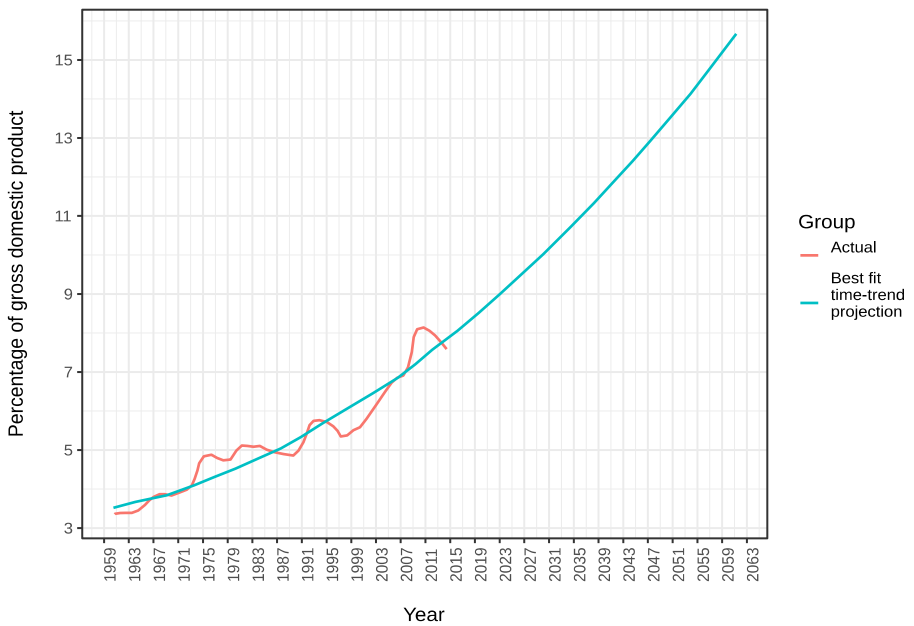
In 2018/19 there were 20.8 million finished consultant episodes in UK hospitals of which 17.1 million were the first episode in an admission (finished admission episodes) [23]. The 70–74 year age group had the highest number of episodes (9.2%, 1.9 million) (figure 1.7). Women accounted for 54% (11.3 million) of episodes. People from more deprived backgrounds accounted for a larger proportion of admissions than those from less deprived backgrounds [24]. The most common diagnoses were diseases of the digestive system and neoplasms.

Figure 1.5 | Hospital and community health service spending in England by age group



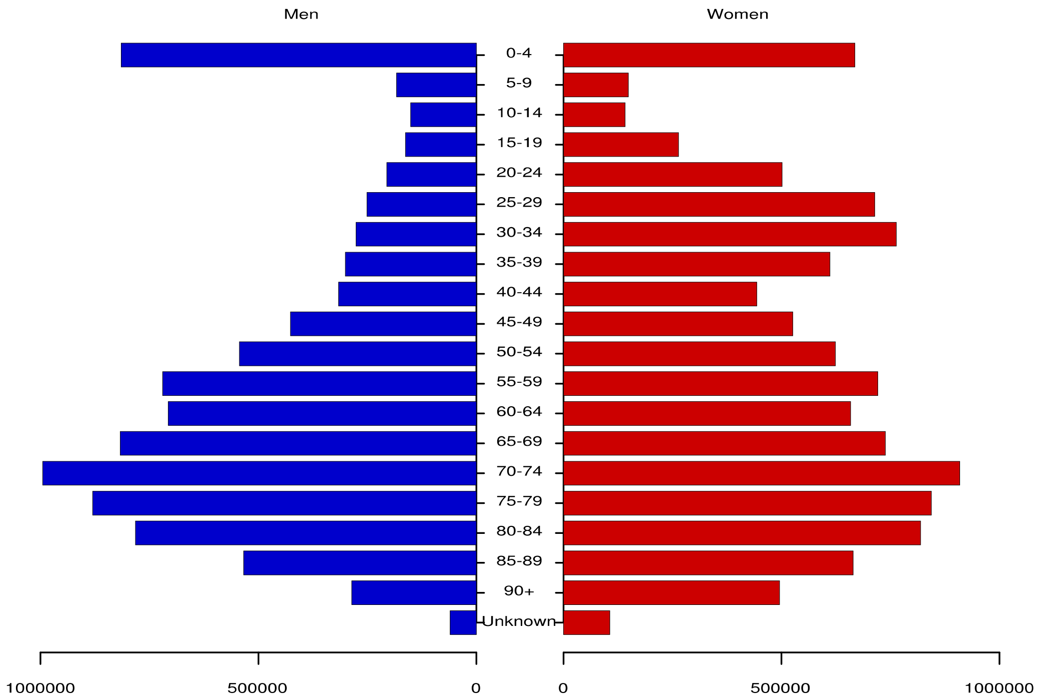
Source: Fiscal sustainability and public spending on health, OBS 2016

Figure 1.6 | Projections of UK healthcare expenditure, 1960–2059



Source: The Kings Fund, A Century of Health Spending

Figure 1.7 | Finished Consultant Episodes in English hospitals 2018/2019



Source: HSCIC 2019

1.4 General influences on UK National Health Service hospitalisation rates

There are many factors which may influence hospital usage, not all of which are related to ill health. These include sociodemographic variables such as social support, accessibility of other services, and cultural factors such as theorised by Anderson and others [25–27] outwith the scope of this thesis. Nevertheless, there are several common risk factors such as social class, education, smoking habit, low physical activity and obesity which are known to influence health, disease risk and mortality in numerous studies [28] and which we have also reported or confirmed in the current population cohort[29–32]. While these associations, are well established, the relationship between such factors and hospital usage is less well studied. Most community-based population cohorts have relied on death certificates or questionnaire-based follow-up and few have been able to link individuals to hospital records.

1.5 Rationale for the study

A few population-based community cohorts have reported on risk factor associations with hospital usage. The Renfrew and Paisley MIDSPAN cohort, whose participants were recruited between 1972 and 1976 and linked to HES data up to 1995, have reported on hospital usage and socioeconomic inequalities, body mass index (BMI) and social deprivation after linking to hospital discharge records in the west of Scotland [33–38]. The Hertfordshire Cohort Study, recruited between 1931 and 1939, obtained a HES extract for the period 1998 to 2010 [39,40] and have reported on poor health behaviours as predictors and differences in admission rates by sex. The Million Women study has also reported on risk factors for hospitalisation [41]. Between 1996 and 2001, around 1.3 million women aged 50 to 64 years old, were recruited into the study through National Health Service (NHS) breast screening clinics [42]. English participants were linked to HES data from 1997 while those living in Scotland were linked to the Scottish Morbidity Record (SMR) from 1981. The UK Biobank study, which recruited its cohort of men and women between 2006 and 2010, has been able to link to HES records since 2014. Investigators using UK Biobank data have reported on numerous individual disease outcomes derived from HES data, but few papers have reported on hospital usage. The relationship between adiposity and inpatient hospital costs was reported by Dixon et al. [43] by constructing Healthcare Resource Groups (HRGs) from hospital length of stay, procedures and diagnoses using the NHS "Grouper" software.

Linked Electronic Healthcare Databases (LEHD) are a form of cohort constructed by taking data from participating GP practices, linking to HES and combining with census data. The decision to participate is made by the practice although patients can opt out of the automatic use of their anonymised data. The Clinical Practice Research Datalink (CPRD) for example, contains computerised primary care records from GPs covering about 9% of the UK population and combines opportunistic capture of lifestyle data in those attending general practice clinics by general practitioners of, for example, smoking status, alcohol use, height and weight [44–46]. Use of patients' home postcodes enables studies that use CPRD data to link to area based measurements such as the Index of Multiple Deprivation (IMD).

1.6 What is known about the risk factors for hospitalisation?

1.6.1 Occupational social class and area deprivation

Social deprivation can be measured using various systems, using information acquired from an individual or using averages in small geographical areas. Occupational social class is a longstanding individual measure of socioeconomic status, used in all UK censuses since 1921 and defined according to the Registrar General's classification (now referred to as Social Class based on Occupation) [47]. Originally created in 1913 by a medical statistician in the UK General Register Office, it enabled all occupations to be categorised into 6 distinct ordered groups, of which 3 refer to manual and 3 to non-manual occupations. The Townsend Area Deprivation Index, a measure of area deprivation, has also been used in UK censuses. It is constructed using four components measuring material resources, current income, current wealth and material living conditions. The index was first described in 1988 by the sociologist Peter Townsend and used in the 1991 UK census. Unlike other related area deprivation indexes such as the Carstairs index, the Townsend index does not include social class as a component. Both individual social class and area-based measures are used to describe social deprivation, but differ in some respects, as described in chapter 5. Newer occupational social class classifications such as NS-SEC (introduced in 2001) [48] have been created to reflect recent changes in labour market positions and employment statuses, but the original Registrar General's classification continues to be widely used [49,50], especially when examining historical cohorts or when estimating social class over the life course. Area based deprivation measures have become more widely used in recent years, possibly because of practicality - they are simpler and quicker to derive than individual measures since they require no manual coding.

Inequalities in health across socioeconomic groups have been increasing since the 1970s [1]. In the UK, successive reports on health inequality over 4 decades [51–54] have highlighted the graded relationship between socioeconomic position and poor health outcomes in later life such as reduced life expectancy, poor health and disability. Differences in life expectancy at birth between unskilled and professional social classes are illustrated in table 1.1 which shows 7.3 and 7.0 year differences among men and women respectively in the period 2002 to 2005. Although life expectancy improved for all classes over this period, the gain in life expectancy at birth for those in social class I exceeded those in social class V for both men and women. The report "Health Equity in England: The Marmot Review 10 years on" [54] noted that increases in life expectancy have slowed since 2010 with the slowdown greatest in more deprived areas of the country. It reported that the difference in life expectancy at birth in 2016–2018 was 7.7 years for women and 9.5 years for men between the highest and lowest area deprivation deciles.

Table 1.1 | Life expectancy at birth by social class and sex in England and Wales, 1976-2005

	Men(years)			Women (years)		
	1972-1976	1987-1991	2002-2005	1972-1976	1987-1991	2002-2005
Professional	71.9	76.2	80.0	79.0	81.1	85.1
Managerial and technical	71.9	75.0	79.4	77.1	80.7	83.2
Skilled non-manual	69.5	74.4	78.4	78.3	80.0	82.4
Skilled manual	70.0	72.7	76.5	75.2	77.9	80.5
Partly skilled	68.3	70.8	75.7	75.3	77.4	79.9
Unskilled	66.5	68.7	72.7	74.2	76.6	78.1

Source: ONS 2007

Social class and the extent to which hospital admissions are socially patterned were examined in 7,049 men and 8,353 women in the Renfrew and Paisley MIDSPAN cohort, reporting its finding in 2013 [55]. All-cause hospital admission rate ratios were not found to be obviously socially patterned comparing social class I and II with social class IV and V. However, time spent in hospital was associated with social class and the likelihood of mental health admissions was significantly higher in those with low social class after adjustment for other risk factors. Socioeconomic deprivation and the incidence of cardiovascular disease were examined in 1.9 million men and women using the CALIBER programme (Cardiovascular disease research using LInked Bespoke studies and Electronic health Records) [41]. Patient electronic medical records were linked across four data sources including the CPRD, the Myocardial Ischaemia National Audit Project (MINAP) and HES. Individual social class was not available in the study but the level of socioeconomic deprivation was instead measured using the IMD 2007 calculated at Lower Layer Super Output Area (LSOA) level using the patient postcode of residence. Findings varied by sex with all except one of the cardiovascular subtypes increasing linearly with higher small-area socioeconomic deprivation in women while in men the results were more heterogeneous.

1.6.2 Education

Level of education has been associated with mortality in numerous studies. A birth cohort from the Netherlands with 32 years of follow-up reported that a "very consistent universal association was observed between educational level and mortality" and this persisted whether analyses were carried out for all-cause mortality or for specific causes of death [56]. The Reykjavík Study also examined the association between mortality and education and reported a 14% reduction in men and a 34% reduction in women for ischaemic heart disease mortality for those having high school education relative to primary school [57]. There is, however, very little in the literature that examines the independent association between level of education and subsequent hospital usage. While education level is frequently used as a covariate in models relating to other risk factors, it has not been studied greatly in its own right. A study that used the Taiwan National Health Interview Survey and linked it to national health insurance data, reported non-significant associations for admissions OR 0.90 (95% CI 0.62–1.30) and bed days OR 0.56 (95% CI 0.30–1.04) in those with ≥7 years of education compared with those with no education [58].

1.6.3 Body mass index and obesity

Between 1993 and 2008 there was a sharp increase in the proportion of both men and women in England who were clinically obese [1]. In 2008, 24% of men and 25% of women in England were classified as obese (BMI >30 kg/m^2) rising to 27% and 30% respectively by 2017. The number of people admitted to hospital in England with a secondary diagnosis of obesity rose steeply between 1996/1997 and 2006/2007, with the number of finished consultant episodes (FCEs) increasing in all age groups from 21,257 to 81,113. In 2017/18 there were approximately 711,000 hospital admissions where obesity was recorded as the primary or a secondary diagnosis.

BMI was measured in the Renfrew and Paisley MIDSPAN cohort [36] and was reported to have a highly significant effect on likelihood of admission for diabetes mellitus, ischaemic heart disease (including acute myocardial infarction) and strokes. The "45 and Up" study of 267,153 men and women aged ≥45, recruited from a random sample of patients held by Medicare, Australia's health insurance provider, also examined the role of BMI on admissions [59]. They observed a dose-response relationship between BMI calculated from self-reported weight and height and bed days per person year of follow-up and a corresponding relationship with costs. Compared with those with BMI [22.5,25) kg/m^2, rates of admissions and bed days in the study were 1.64–2.54 times higher for BMI [40,50) kg/m^2 after adjustment for age, sex, education, smoking and alcohol intake. These same relationships were not evident in those aged 80 years or older. Hospital admissions and their relation to BMI were also examined in a prospective cohort study of UK women — the "Million Women Study". BMI was calculated using baseline self-reported height and weight where available. Results from this study show that overall rates of hospital admission increased with increasing BMI in women. Total admission rates were significantly higher in both overweight and obese women compared with women with a BMI of [22.5, 25) kg/m^2 with a positive association between BMI and the risk of hospitalisation found for 19 of the 25 most common types of hospital admission. However, in women with a BMI of less than 22.5 kg/m^2 the corresponding rate was slightly higher than that in the reference group.

1.6.4 Cigarette smoking

Smoking is the leading cause of preventable illness and premature death in Great Britain [60]. The prevalence of cigarette smoking has reduced significantly in the UK over time, due in part to effective public health interventions and restrictions on advertising. In 1948, when the NHS was founded, 65% of men and 41% of women smoked cigarettes, although the rate was much higher in those below 60 years with 80% of men smoking [61]. By 1974, this had reduced to 51% of men and 41% of women; by 1994 there had been a significant reduction to 27% with a similar proportion of men and women smokers and by 2019 it was 14% [62]. The General Household Survey has consistently shown striking differences in the prevalence of cigarette smoking in relation to socio-economic group, with smoking being considerably more prevalent (by approximately 20%) among those with manual occupations than among those in non-manual occupations. The Renfrew and Paisley MIDSPAN cohort explored relationships between personal, behavioural and biological factors and subsequent admissions. It found that cigarette smoking was highly significantly and independently associated in all models. Current smokers had a relative risk that was an estimated 17% higher for "any admission" to an acute hospital, 29% higher for a "serious admission", and 42% higher for a "serious admission or death" when compared with those who had never smoked [37]. In a further analysis of the link between major risk factors and important categories of admission in an ageing cohort, smoking emerged as the single most important risk factor investigated. Current smokers were almost eight times more likely to be admitted with lung cancer, 31% more likely to be admitted with any malignant neoplasm, 47% more likely to be admitted with ischaemic heart disease, 56% more likely to be admitted with respiratory disease and 38% more likely to be admitted with a stroke (cerebrovascular disease). Ex-smokers carried higher risks of hospital admission from a variety of causes when compared with those who had never smoked, being 2.5 times more likely to be admitted with lung cancer, 43% more likely to be admitted with ischaemic heart disease and 30% more likely to suffer respiratory disease within the period of follow-up [36].

1.6.5 Physical activity

Physical activity is associated with lower rates of mortality from all causes and cardiovascular disease [63–65]. It is also associated with a lower risk of many non-fatal diseases [66–69]. Few studies have examined the physical activity of middle-aged and older men and women and their subsequent healthcare utilisation in free living populations. Peeters et al. [70] reported that in participants of the Australian Longitudinal Study on Women's Health aged 73–78 years, small increases in physical activity could result in substantial cost savings for the health system and reduced hospital admissions. Tran et al. [71] examined potentially preventable hospitalisation and physical activity per week and reported a lower risk of admission in participants with ≥2.5 hours of physical activity per week. There is evidence from studies based on exercise interventions that pre-admission physical activity programmes may lower duration of hospital stay [72–76]. Intervention studies provide evidence that a physically active lifestyle improves health but intervention protocols vary and differences in dropout rates between groups in randomised controlled trials (RCTs) limit generalisability [77]. Intervention studies typically have smaller study size and shorter follow-up time while observational studies are generally larger. Many studies are based on particular population groups or particular disease outcomes and some rely on self-selection to the exercise programs. Some studies have reported on physical activity using objective measurements, such as accelerometry but these have only been developed relatively recently and hence studies with long follow-up have used self-reported activity from questionnaires. However, studies with longer follow-up time are less likely to be affected by reverse causality which is a major limitation in studies examining physical activity. Hence, studies with long follow-up time may be best placed to describe the associations of usual physical activity and subsequent hospital usage.

1.6.6 Alcohol

The direct and indirect costs to the NHS attributable to alcohol misuse have been estimated at approximately 3.5 billion pounds [78,79]. Approximately 1.1 million hospital admissions are reported as wholly or partly attributable to harm from alcohol in England in 2017/18 [80,81]. However, the relationship between alcohol consumption and future hospital usage at lower levels of consumption has not been clearly established in the literature. Many studies have reported inverse associations for ischaemic heart disease and low levels of alcohol intake [82–87] with some reporting evidence for plausible biological mechanisms. Inverse associations with alcohol intake and some diseases have been reported in systematic reviews [83,88–94]. Bell et al. [95] reported that moderate drinking was associated with a lower risk of several cardiovascular diseases in a study of linked electronic UK health records. However, other studies report the risk of alcohol consumption to be a continuum with no safe threshold. A meta-analysis that controlled for quality-related study characteristics found that moderate drinking had no net mortality benefit compared with lifetime abstention or occasional drinking [96].

1.7 Uses of HES data

HES data have generally been used for survival analysis of non-fatal outcomes within cohort studies such as EPIC-Norfolk [97–99]. The techniques I developed involve identifying individuals with a range of diagnosis codes that relate to a particular condition and establishing the earliest possible event date for each person. While some diseases of interest are represented by a single ICD10 code, it is more usual that several codes need to be considered. For example, breast cancer is represented by a single code C50 while ischaemic heart disease (I20.0-I25.9) includes 35 related conditions. The date of admission to hospital containing the earliest episode where one of these codes was mentioned is generally taken to be the date of disease onset for survival analysis.

HES data can also be used to facilitate or validate endpoint ascertainment (the process by which outcomes are identified and confirmed in a cohort study). I developed the techniques in EPIC-Norfolk that use HES records for this purpose [100–102]. EPIC-Norfolk was one of the earliest cohorts to use such hospital record linked data. In some situations, the diagnostic coding recorded in the HES record may not be sufficient to differentiate between closely related diseases. Information may not be available at the time of coding or may be captured in separate hospital database systems. The HES records can be used by researchers to identify a superset of patients which are then narrowed down using information held in other hospital systems or in patient notes [103]. Similarly, conditions which generally require patients only to visit outpatient clinics may be difficult to determine precisely from outpatient records, but these records can be used to identify a broader group of patients for whom additional ascertainment is then necessary. More general validation of common conditions identified from HES data using patient notes has only been rarely attempted in the EPIC-Norfolk cohort and only in small subcohorts since it is very time consuming and generally considered unfeasible where a disease is common [104,105].

The use of HES data to define conditions of interest has been widely used in medical research, in particular the examination of exposure-disease associations in EPIC-Norfolk and other cohort studies. However, it has rarely been used to examine hospital usage per se which is the main focus of the work presented in this thesis.

1.8 Limitations of the current literature and what this thesis adds

Most studies examining hospital activity start from those hospitalised but are limited with respect to population denominators; even those that use general practice record linkage studies can only include people who attended participating general practices while population-based studies that have measured factors prospectively prior to admission are limited.

The Health and Social Care Information Centre (HSCIC), now known as NHS Digital, collects approximately 20 million Finished Consultant Episodes records each year detailing episodes of those admitted to NHS hospitals in England [106]. Standardised data are collected routinely in hospitals and made available to investigators and the data are used to compile detailed reports for the purposes of planning. Given the very large numbers of records, a high level of accuracy is attainable within the context of the data collected. However, the data only relate to people who attend hospital. In order to put NHS data into context, a population denominator is required. Some studies have attempted to use NHS HES data by constructing a denominator from census data and using area-based deprivation measures [107]. This approach necessarily makes several assumptions. It assumes that those attending hospitals within an area are a subset of the chosen denominator population and conversely that the denominator population would necessarily attend the specified hospitals. Such analyses are limited to using area demographics and deprivation measures but lack individual characteristics limiting their ability to adequately characterise the population and explore predictors prospectively.

The CPRD contains computerised primary care records from GPs covering about 9% of the UK population and combines lifestyle data such as smoking status, alcohol use, height and weight using patient postcode to link to census data including area-based measurements [45]. Linked Electronic Healthcare Databases (LEHD) such as CPRD are typically much larger than population-based cohorts but have a number of specific limitations. The decision to join CPRD is made at practice level and collection of lifestyle data is opportunistic unless it relates specifically to a medical condition. The nature and breadth of information considered as lifestyle data may concern some patients who consider it to be private, despite the removal of personal identifiers and therefore some may choose to opt out of anonymised CPRD data collection with considerable variation in opt-out rates by GP practice [108]. This may result in a higher proportion of missing lifestyle data in GP practices where time pressure or workload limit consultation times. Patients may also respond differently in the context of a GP consultation than cohort study participants [109,110]. I use term "lifestyle" here and elsewhere in the thesis to indicate potentially modifiable behavioural factors but this may be a problematic as it has been interpreted as simplistic individual choices rather than reflecting the more complex underlying determinants.

LEHD using data from primary care or secondary care only have lifestyle data for those individuals attending a consultation or admission. In order to examine the population from which those attending GP or hospital are only a subset, LEHDs need to make assumptions about the population in the proximity of the GP or hospital. Using patient postcode enables linkage by area to data collected every 10 years in UK national census. The area measure generally used is the LSOA level of approximately 1500 people [111].

Prospective community-based studies have detailed information about individuals irrespective of their use of hospitals or GPs. Although many cohort studies initially recruit participants through general practice records, once a cohort is established, lifestyle and other measurements are collected independently from all participants irrespective of health service contact. However, most prospective community-based studies lack hospital usage data and have generally relied on mortality data. Prior to the recent centralising and distribution of HES data, it was difficult for cohorts to obtain linked HES since this would often involve approaching multiple NHS institutions.

1.9 Thesis aims

1.9.1 Main aim

To understand the epidemiology of hospital usage in a general UK population to inform clinical and public health planning, policy and practice.

1.9.2 Sub-aims

1. Develop methods to enable linkage of individuals in the general population to Hospital Episode Statistics.

2. To describe patterns of hospital usage in a general community. For example, to estimate absolute rates of hospital usage by age and sex. Specifically

   i. to estimate absolute rates of hospital usage by age and sex,

   ii. to contrast historical variation in national and cohort hospital rates,

   iii. to compare national and cohort admissions by diagnosis and procedure groups.

3. To establish risk factors that predict future hospital usage. Specifically

   i. sociodemographic characteristics,

   ii. behavioural factors, previously documented to be associated with disease outcomes in the literature.

The research will be largely based on the infrastructure of a prospective population-based cohort study, the European Prospective Investigation of Cancer in Norfolk.

2 Methods and methodology

2.1 The EPIC-Norfolk prospective cohort

The European Prospective Investigation of Cancer in Norfolk (EPIC-Norfolk) is a general population cohort of men and women aged 40–79 years living in Norfolk. Recruitment took place between 1993 and 1997 at 35 general practices who agreed to participate with invitations sent to all those registered with the practices within this age range. This cohort was part of a ten country, half a million participant collaboration, the European Prospective Investigation into Cancer and Nutrition, primarily aimed at examining behavioural, particularly dietary factors and cancer. However, from the outset, the scope of the EPIC-Norfolk cohort was broadened to investigate health and chronic diseases beyond cancer. The recruitment strategy was to recruit a sufficient number of participants to detect associations as per the original study power calculations. This was estimated to be 25,000 and the identification of suitable general practices and recruitment from those practices continued until the target was reached. The National Health Service is used by virtually all UK residents throughout their lives and hence general practice registers approximate population registers. The study has ethics committee approval from Norfolk Research Ethics Committee (Rec Ref: 98CN01) and all participants gave informed, signed consent for study participation including access to medical records. The methods used were carried out in accordance with the relevant guidelines and regulations.

The design and recruitment of the study has been previously described in detail [112,113]. Briefly, a total of 77,630 invitations were sent; 30,445 (40%) consented to participate of whom 25,639 men and women completed a lifestyle questionnaire and attended a health examination (often referred to as a “health check”). There followed a further four health checks and seven postal follow-ups but the data presented here uses only the baseline and repeated measurements taken between 2006 and 2011 referred to as time-point two (TP2). A chronology is shown in figure 2.1

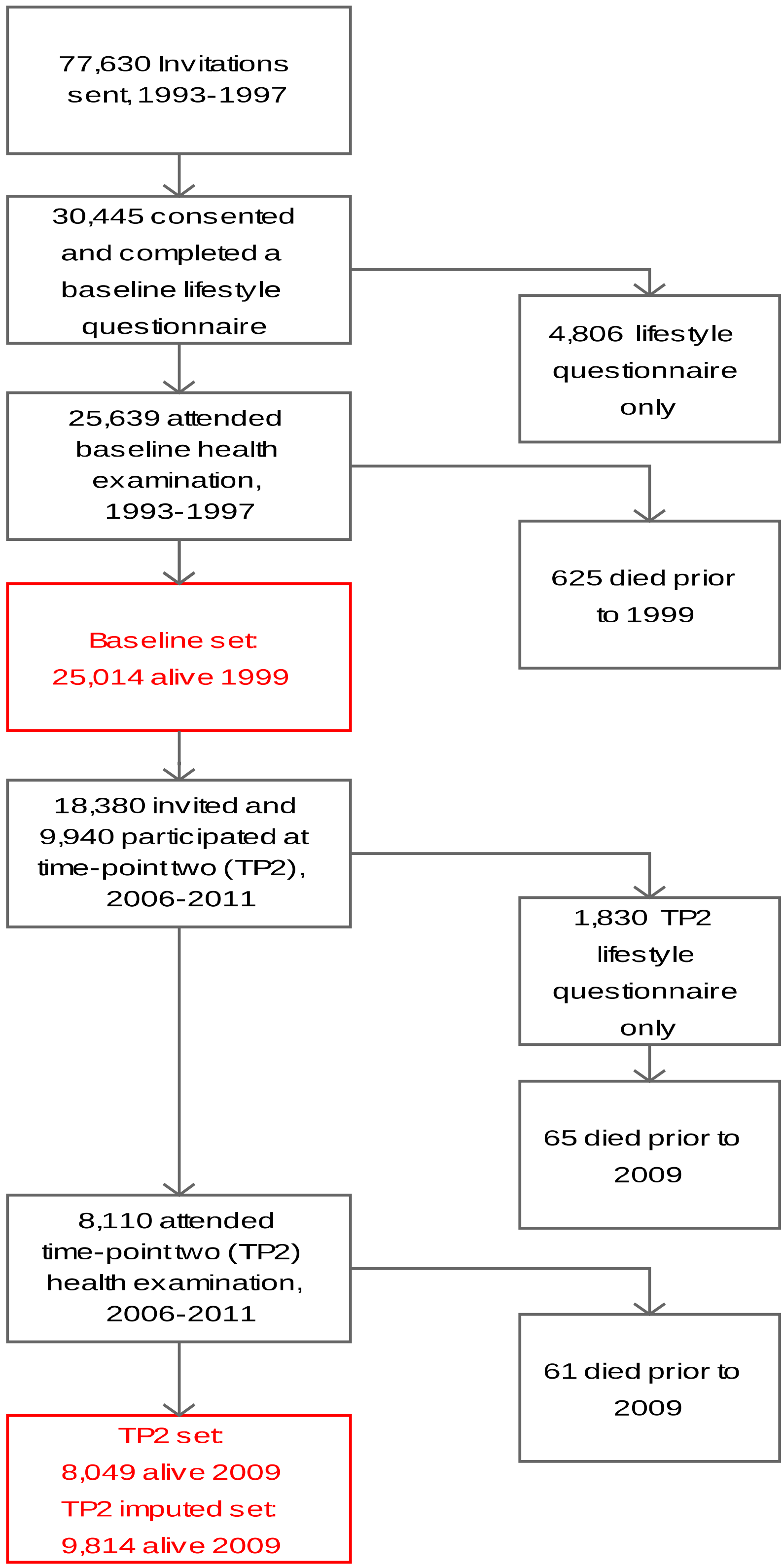
2.2 Exposures measured in EPIC-Norfolk

2.2.1 Socioeconomic status

Participants completed a lifestyle questionnaire at baseline which included questions about their own and their partner’s current and past employment. Standard Occupational Classification (SOC) was derived from semi-automated coding using CASOC [114] which in turn was used to create social classifications. Occupational social class was defined according to the Registrar General’s classification (now referred to as Social Class based on Occupation), as used in the UK 1991 census [47] and dichotomised into non-manual and manual social classes. Professional, managerial and technical and non-manual skilled occupations (codes I, II and IIIa, respectively) were classed as non-manual, while manual skilled, partly skilled and unskilled (codes IIIb, IV and V, respectively) were classed as manual.

Social class for men used (in order of priority) their own current employment, own past employment, partner's current employment or partner's past employment according to whether a social class classification could be defined for a given occupation type. Similarly, social class for women used (in order of priority) their partner's current employment, partner's past employment, own current employment, own past employment. The use of the Registrar General's classification and partner's social class for women in the EPIC-Norfolk cohort born between 1918 and 1957 has been previously discussed [49,115].

Figure 2.1 | Recruitment, participation and attrition: a chronology of the EPIC-Norfolk cohort, 1993-2019



Educational attainment was established at baseline using the question "Do you have any of the following qualifications?" followed by a list of common UK qualifications. Participants were categorised according to the highest qualification attained in four groups: those with no formal qualifications; those with formal qualifications usually associated with a school age between 16 ('O' level or equivalent) or 18 years ('A' level or equivalent); and those with degree level qualifications.

2.2.2 Area deprivation

A snapshot of residential postcode, recorded two years after the end of recruitment, was used to link to the UK 1991 national census data [116]. The Townsend Area Deprivation Index (Townsend Index) is an area deprivation measurement calculated using four components: the percentage unemployed of economically active residents aged over 16 years; the percentage of households with no car; the percentage of households not owner occupied and the percentage of households with more than one person per room. These are respectively: a measure of lack of material resources and insecurity; a proxy for current income; a proxy for current wealth; a measure of material living conditions [116,117]. The index used in this study was constructed using data collected at the 1991 UK census, which takes place every 10 years, with each Townsend component calculated at Enumeration District (ED), a small area containing an average 175 households (420 people) used both as output areas and for data collection [118]. Townsend components were then standardised as Z scores at ED level for England and Wales. Study participants were linked to an ED using their home postcode in the year 2000. The link was then used to establish a residential Townsend Index for each individual.

Travel time and travel distance between participants' home postcode and the Norfolk and Norwich University Hospitals NHS Foundation Trust was calculated using the Open Source Routing Machine (OSRM) [119] which calculates the shortest path between two points over the road network. Postcode of home residence was used to establish if a participant had moved house over the follow-up period. It was available at two points in time: in the year 2000 and the year 2014. Participants whose postcode or house location remained unchanged over the period were classified as not moving house. Urban and rural categories were established using the 1991 census.

2.2.3 Cigarette smoking

Baseline smoking status was derived from two questions each of which could be answered as yes or no: "Have you ever smoked as much as one cigarette a day for as long as a year?" and for those who answered "yes" to the first question "Do you smoke cigarettes now?". At time-point two (TP2), participants were asked "Do you currently smoke cigarettes?" and "If you have stopped smoking, how old were you when you gave up?".

2.2.4 Prevalent disease

Participants were asked in baseline and later questionnaires: "Has the doctor ever told you that you have any of the following?" followed by a list of common conditions including "Heart attack (myocardial infarction)", "Stroke", "Cancer" and "Diabetes". Prevalent history of the disease was defined by a "yes" response. "Prevalent disease" was defined by a positive response to one or more of the three most serious conditions (heart attack, stroke and cancer) since they were most likely to result in a change in behaviour and lifestyle. For analyses using outcome periods starting in 1999, prevalent disease was established using just the baseline questionnaire. At TP2 questions on self-reported disease were not asked and so for analyses using the outcome period starting at 2009, prevalent disease was instead based on the most recent responses to questions in questionnaires prior to TP2; at baseline, 18 months, 3 years and 10 years.

2.2.5 Alcohol exposure definitions

In the baseline lifestyle questionnaire, participants were asked "Are you a non-drinker/teetotaller now?" and "At present, about how many alcoholic drinks do you have each week" for four types of alcohol: beer, cider or lager (pints); wine (glasses), sherry or fortified wines (glasses) and spirits (singles). Current non-drinkers were defined as those who answered "yes" to being a non-drinker now and did not report consuming beer, wine/fortified wine or spirits at present. Similarly, current drinkers were defined as answering "no" to the question or report drinking at present.

Participants were also asked "Have you ever drunk alcohol in the past?" and two similar questions relating to consumption of the four alcohol types when aged 20 and aged 30. Former drinkers were defined as current non-drinkers who answered "yes" to ever drinking alcohol or reported consuming alcohol aged 20 or 30. Lifelong abstainers were defined as participants who were neither current drinkers nor former drinkers.

Current units and past units were calculated from the questionnaire responses with one unit equal to a half pint of beer, one glass of wine or fortified wine or a single measure of spirits. The capacity of a glass was not specified, but assumed to be 125ml for wine and 50ml for fortified wines. An additional category "occasional", representing consumption of less than one drink per week, contributed half a unit when ticked for an alcohol type. Heavy current drinkers were defined as participants currently consuming >35 units per week while heavy former drinkers were defined as participants who consumed >35 units per week in the past. Those with current units greater than zero were divided into four categories: (0,7], (7,14], (14,21] and >21 units per week. Past alcohol consumption was defined as the higher of units reported consumed aged 20 and aged 30.

2.2.6 Physical activity

At recruitment and again at TP2, participants completed a lifestyle questionnaire where they were asked about their occupational and leisure physical activity. Occupational activity was assessed using a four category question ("sedentary", "standing", "moderate physical work" and "heavy manual work") with examples such as office worker, shop assistant, plumber and construction worker respectively. Leisure activity in both summer and winter was assessed from the number of hours per week spent cycling, attending keep fit classes or aerobics and swimming or jogging. Estimated average hours of leisure activity was calculated as the mean of summer and winter activities and categorised using 0, (0,3.5], (3.5,7] and >7. A combined score, divided into four ordered categories, with individuals labelled as "inactive", "moderately inactive", "moderately active" and "active", was created combining leisure and occupational elements. Those who did not complete the activity question were placed in the inactive category. The score was validated against energy expenditure measured by free-living heart rate monitoring with individual calibration [120]. It has been reported to predict all-cause mortality and cardiovascular disease incidence [121].

2.2.7 Anthropometry

Participants attending the baseline and TP2 health checks had their height to the nearest 0.1 cm measured using a stadiometer (Chasemores, UK) and their weight to the nearest 0.1 kg measured in light clothing without shoes (Salter, West Bromwich, UK). All measurements were performed by trained nurses in a clinic setting. BMI was calculated using measured weight in kilograms divided by the square of measured height in square metres.

2.2.8 Blood pressure

Systolic blood pressure was measured at baseline and TP2 using an Accutorr sphygmomanometer (Datascope Medical, Huntington, United Kingdom). Participants sat for three minutes before two measurements were taken with the arm horizontal and held at mid-sternum level. Systolic blood pressure was defined as the average of the two measurements.

2.2.9 Biochemistry

Trained nurses obtained non-fasting blood samples by venepuncture at baseline and TP2 into plain and citrate bottles. Bloods were assayed at the Department of Clinical Biochemistry, University of Cambridge, UK. Serum concentrations of total cholesterol were measured with the RA-1000 Technicon analyser (Bayer Diagnostics, Basingstoke). Plasma was stabilised in a standardised volume of metaphosphoric acid stored at −70 °C and vitamin C concentrations measured using a fluorometric assay within one week [122].

2.2.10 Repeated measurements at time-point two (TP2)

Surviving participants were invited to complete a lifestyle questionnaire and attend a health examination (second time-point, "TP2") between 2006 and 2011 [112]. Questions on physical activity, alcohol and cigarette smoking, similar to those at baseline, were included in a postal questionnaire, completed by a subset of 9,827 of the original cohort. Weight, height, blood pressure were measured and blood taken for cholesterol and vitamin C on 8,094 by clinic staff using protocols similar to those used at baseline described previously.

2.3 Acquisition of hospital episode data: My role

Hospital Episode Statistics (HES) data provide considerable detail for each person attending hospital. While diagnostic and procedure information is available at each time point and can be linked with individuals participating in cohort studies, the frequency of admission and the time spent in hospital irrespective of the reason for admission can also be calculated and individually linked. Linkage of such HES data enables the examination of associations in a well-characterised population between sociodemographic, lifestyle and biological factors and future hospital usage.

The EPIC-Norfolk cohort has been linked to local and national databases held by external organisations such the Office for National Statistics (ONS), NHS Digital, various disease registries and Primary Care Trusts and this has made it possible to investigate predictors of the major chronic diseases of middle and later life. In 1999, the EPIC-Norfolk study became a "flagging study" with the national Health and Social Care Information Centre (HSCIC) by a process of linking every cohort participant to a national population database. A record of flagged participants was held by HSCIC and the study was notified when participants died with coded death certificates provided monthly. However, there was no mechanism at the time to obtain hospital records through national databases.

I initiated the first linkage with hospital records in EPIC-Norfolk participants. Between 1999 and 2009, cohort participants were linked to hospital records held locally using their unique NHS numbers. Databases maintained by the Norfolk Primary Care Trust (PCT) were used rather than hospital databases, an approach with the advantage that all hospital activity for Norfolk residents was captured wherever they were treated. The majority (95%) of admissions were to the Norfolk and Norwich University Hospitals NHS Foundation Trust (formerly Norfolk and Norwich Hospital).

After 2009, Primary Care Trusts were reorganised and later abolished. Responsibility for public health moved from PCTs to local authorities who no longer had access to HES data. In 2017 access to hospital records held nationally became available from HSCIC, later renamed NHS Digital, and HES records from earlier years could be obtained. In addition to HES records from 2009 onwards, records for participants who moved away from the Norfolk area to other parts of England between 1999 and 2009 were obtained from the national database. These records were not available from local PCT databases because once a participant had relocated they were no longer a Norfolk resident.

2.4 Hospital Episode Statistics data structure and linkage

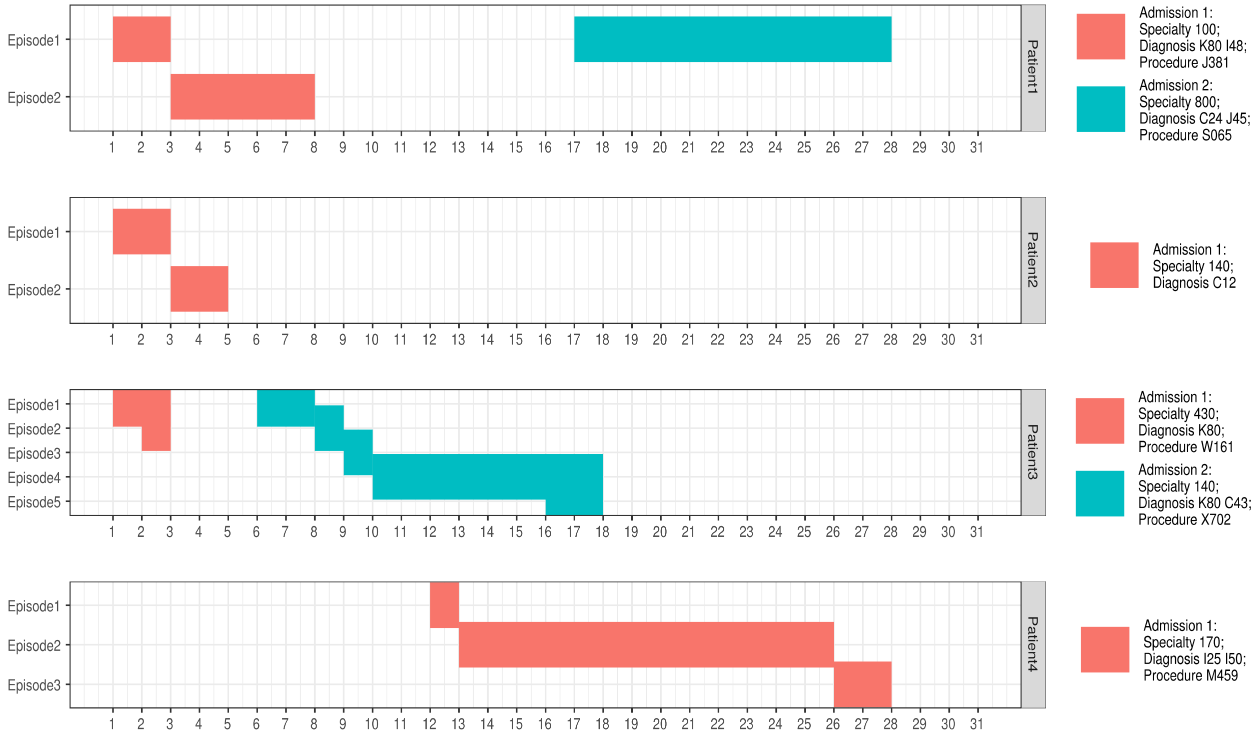
2.4.1 HES data structure

I also derived the summary hospital episode data for each individual. Each record is known as a "Finished Consultant Episode" and represents for an individual, a period of patient time under the care of a consultant. The structure of HES records, illustrated in figure 2.2, can be complex. The diagram presents hospital spells for four fictitious patients, with one or more usually consecutive episodes occurring in an admission spell between admission and discharge. Each episode comprises care under one consultant, corresponding to one specialty code in the HES data. One or more ICD-10 diagnosis and OPCS-4 procedure codes can exist for each episode. Other patterns of stay can occur such as discharge and readmission on the same day and this can affect the way in which admissions are counted. In routine NHS reporting, same day readmissions are generally counted as two admissions but in the analyses presented here, contiguous admissions are counted as a single admission. Episodes may overlap, especially in situations where the transfer between consultants is brief. Incomplete episodes (those with missing admission or discharge date) frequently appear in data at the end of financial years. HES data are organised and distributed in files containing a single financial year and this results in two incomplete episodes for the same individual that need to be joined to create a single finished episode in order to accurately count admission numbers.

2.4.2 Hospital days, inpatients, bed days and day cases

Day cases, where admission and discharge occur on the same day, are generally reported separately from inpatient admissions, admissions involving overnight stays, in routine NHS summary statistics. They do not form part of the Organisation for Economic Co-operation and Development (OECD) definition of bed days. Day cases are, however, an important aspect of hospital usage but since the crude measure of days between admission and discharge is zero, the term "hospital day", defined as 1 plus days between discharge and admission, is used as the primary measure of duration in this thesis. Hospital days can also be considered the sum of bed days (overnight stays) and day cases (admission and discharge on the same day). For some patients, such as those with renal disease requiring regular dialysis, hospital days are predominantly multiple day cases. Others may have many fewer admissions but stay longer in hospital, for example frail, elderly patients with multiple morbidities.

Figure 2.2 | Hospital spell timeline for fictitious patients showing HES data structure



Timeline showing a one month (31 day) period. Only the first two patient admissions are shown with admission 1 coloured red and admission 2 coloured blue. Consultant specialty codes include 100 General medicine 800 clinical oncology 140 oral surgery 430 geriatric medicine 170 cardiothoracic surgery. ICD-10 codes are only displayed to three characters for brevity. All codes were shown for illustrative purposes chosen at random from HES data and bear no relation to actual HES records. Up to 20 diagnosis code and 24 procedure codes can be recorded.

2.4.3 Linkage techniques and identifiers used to link HES data to EPIC-Norfolk

Linking cohort participants to Norfolk PCT databases was achieved mainly by the use of the NHS Number — a unique identifier currently used by most organisations within the UK health service. NHS numbers are assigned at birth or at first contact with the NHS for example when registering with a GP. Consequently, the number acts as a de facto national identifier. The 10-digit "New" NHS Number was introduced in 1996, part way through recruitment of the EPIC-Norfolk cohort. The tenth digit of the New NHS number is a checksum — an arithmetic function of the first nine digits, used to reduce the risk of transcription error. The New NHS number replaced earlier versions that had a variety of formats, mainly consisting of letters and digits but formatted into groups of characters using spaces and strokes. The "Old" NHS number initially used former National Registration Numbers first introduced in September 1939 until the abolition of the national Registration Act in February 1952. In total, the identifier had thirteen format variations introduced at different time-points and different parts of the UK, making it totally unsuitable for computerisation. As a result, the Old NHS number was not used by hospital Patient Administration Systems (PAS), a local computer database system, generally located in larger regional hospitals, which instead adopted a hospital specific identifier known as a "hospital number". Hospital numbers are only unique for a particular hospital PAS but may also be used for associated clinical systems and other nearby affiliated smaller or specialist hospitals. The number does not indicate from which hospital it originates and it is quite possible for the same number to be assigned to different individuals in different UK hospitals. Its use is, therefore, problematic for cohort linkage where participants may have been admitted to more than one hospital. While the large majority of hospitalisations of EPIC-Norfolk participants occurred in one hospital (the Norfolk and Norwich University Hospitals NHS Foundation Trust), hospital activity also occurred at numerous other locations. Adoption of the 10-digit "New" NHS number was slow after its introduction in 1996. This may have been due to the considerable investment made in computer systems prior to its introduction and the significant cost of adapting or replacing them to allow the NHS number to be the primary patient identifier.

Linkage of EPIC-Norfolk participants to NHS systems in Norfolk began in 1997/1998 when incomplete pilot data was obtained and subsequent annual linking was performed from 1999 to 2009, using the NHS number as the primary linkage identifier. Completeness of the NHS number was initially poor, gradually improving over time. Hospital numbers, included in previously matched records, were collated and used in subsequent years as an alternative linkage identifier. Since HES records always included hospital numbers even when NHS numbers were missing, the use of hospital numbers improved the overall matching rate. Hospital numbers were also available from lifestyle questionnaires. Participants were asked to provide their hospital numbers and names of the hospitals they were treated at on the follow-up 3 questionnaire completed in 2004-2006. This information was used to supplement the existing hospital number database in order to maximise linkage. To reduce the risk of mismatch due to non-unique hospital numbers, only Norfolk and Norwich hospital numbers were used for linkage.

Linkage of EPIC-Norfolk participants to hospital records has been validated against medical records in subcohorts [104,105]. Since validation using paper records is a time-consuming manual process, it has only been possible to do this process for a small number of participants. However, these validation studies have reported good agreement between the linkage and the medical records.

2.5 Hospital outcome variables and periods

2.5.1 Definition of the outcome variables

I created two complementary and related outcomes, one based on the number of hospital admissions and the second on the length of time in hospital. The outcomes are both broad measures of hospital usage, the main focus of the work presented in this thesis. The outcomes are designed to represent realistic usage in the population and hence necessarily encompass a broad range of NHS acute hospital activity and patterns of hospital attendance. These variables, unlike those used in survival analysis, were defined over a fixed period of time such as 10 or 20 years. I defined total admissions as the number of times a participant was admitted as an inpatient (staying overnight) or a day case (no overnight stay) to an acute NHS hospital within a fixed period; total length of stay was defined as the sum of the hospital days during spells in NHS hospitals over a fixed period. Hospital spells refer to a period of time in hospital from the date of admission to the date of discharge. Counts of admissions are a metric used in health service planning (although counts of finished consultant episode (FCE) are more commonly used in routine NHS reporting) [123]. Bed days and days cases are also widely used metrics in health service planning, but the outcome variable "length of time in hospital" I created is based on hospital days which combines them. Using length of stay defined in this way simplifies reporting and interpretation. However, it has the limitation that it cannot differentiate between study participants with relatively minor conditions admitted without overnight stay, and those with more serious conditions who stay for longer periods.

Generally, cohort studies considering exposure-outcome associations use survival analysis, censoring participants who become cases at the date of onset of disease. Participants are also censored if they die before the end of follow-up. The hospital usage outcome I have defined for the analyses presented here differs from their survival analysis counterparts since they do not consider time to event. Since the outcomes count total admissions and total hospital days over a time period, participants cannot be censored after an initial event. The effect of differential mortality bias is considered in chapter 9.

Hospital admissions and episodes are defined as finished when an end date has been established. Admissions and episodes may not be finished when data are restricted to a reporting period such as the end of a financial year over which time patients remain in hospital. The hospital time outcome used did not restrict admissions to those that were finished. Instead, any incomplete admissions in annual datasets falling at the end of the period were assigned the date of the end of the period if they could not be matched to an admission in the dataset for the subsequent year. While this artificially shortened the length of stay for some participants it ensured that any hospital usage within the period was accounted for. On occasions, patients are discharged and immediately re-admitted. There may be administrative or clinical reasons for contiguous admissions, but they tend to exaggerate admission numbers by overcounting. The calculation of number of admissions used in these analyses therefore ignores discharge and re-admission on the same day and treats two adjacent admissions as one.

The two outcome variables based on the number of hospital admissions and length of time in hospital were both grouped and dichotomised to make them more suitable outcomes for analysis. The groups consisted of arbitrary cutpoints, based approximately on fifths of the distribution. The original local HES data spanned the 10 years 1999-2009 and the cutpoints chosen for this period were 7 or more admissions and 20 or more hospital days. Subsequently, the HES data was extended to the period 2009–2019. The original cutpoints when considered over the longer 20-year period no longer split the distribution evenly and hence some additional cutpoints were created.

2.5.2 Definition of the outcome periods

The outcome periods used in these analyses reflected the availability of HES data over the five years the work presented here was investigated. Initially, HES data was only available for the 10-year period 1999–2009; later, data became available for a second 10-period 2009–2019. Some thesis chapters use the 10-year follow-up period 1999–2009, some use the combined 20-year period between 1999 and 2019 and some use both 10-year periods with independent measures at TP2 to confirm findings and examine change. HES data from the two periods differs in a number of respects. The period 1999–2009 uses HES data initially acquired locally from Norfolk PCT while the data for the period 2009–2019 was acquired from national databases held by NHS Digital. Since local HES data was limited to Norfolk residents wherever treated, while national data includes all participants wherever treated, the denominator for two datasets differs slightly, for example for participants who relocated outside Norfolk. To address this issue, the 1999–2009 data presented here include, where possible, national data from NHS Digital. Since my earlier publications used locally acquired HES data, small numerical differences may be apparent but make no material difference to the findings.

2.6 Methodological issues arising from differences between data sources

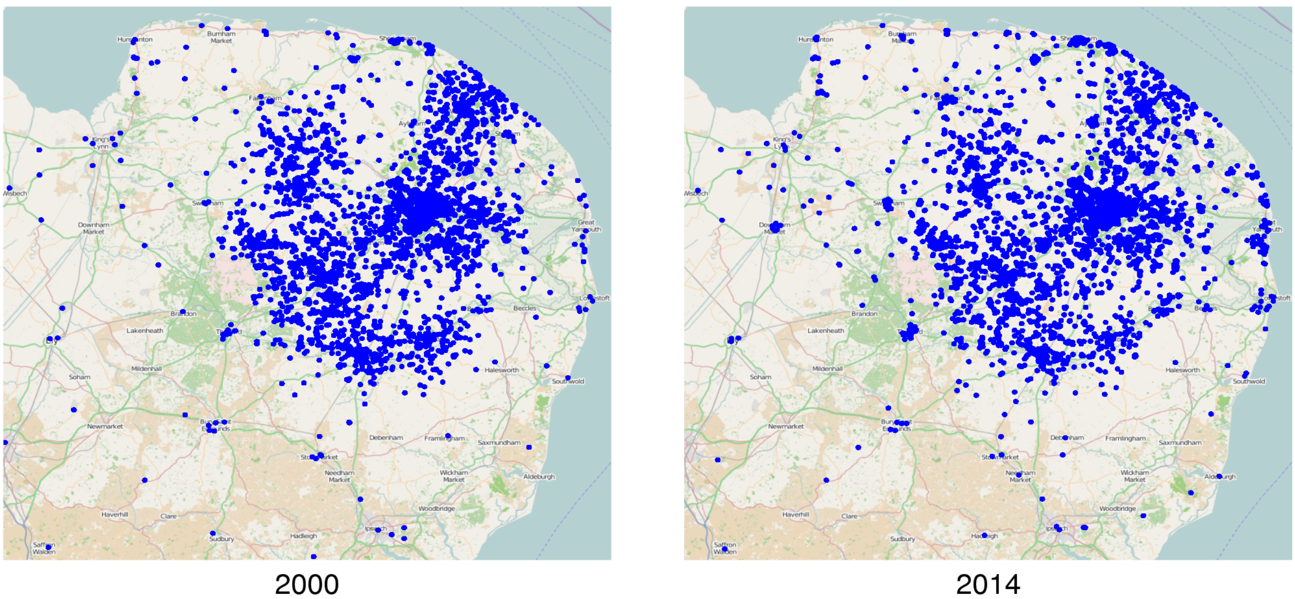
2.6.1 Geographical location and catchment area

Locally acquired HES data differs from national HES data as they were only available for Norfolk residents. All EPIC-Norfolk GP practices are located within the Norfolk area although some participants registered with practices close to county borders lived outside Norfolk. Local HES data was available for these participants. If medical treatment was needed for participants when travelling or during a period spent elsewhere in the UK, this would also be recorded by the Norfolk PCT. However, if a participant decided to move permanently out of area and register with a new GP practice, their hospital records would no longer be available to the PCT. While this may have led initially to some loss to follow-up over the 10-year follow-up period, the missing HES records were later acquired from national databases.

The EPIC-Norfolk cohort was established by recruitment using general practice registers. These computerised databases hold the administrative details of everyone registered with the practice and include details such as date of birth, sex, address and postcode. Prior to 2015, GP practices were only able to register new patients within their boundary area and prior to 2012 this had to be within a catchment area. Hence, the practice registers used by EPIC-Norfolk from 1993–1997 consisted of participants who generally lived very close to their registered GP when recruited. There were a few exceptions however. Some GP practices were close to a county border and had catchment areas that included patients living outside Norfolk — in Suffolk for example. Some patients may have requested referral to a hospital in Suffolk that was closer or more convenient for them. GP registers may have also included people who had moved to a different area but had not yet registered with a new GP.

A snapshot of participants' residential postcode was created in the year 2000, two years after the end of recruitment. An approximate grid reference was established for each postcode using national geographic databases. Figure 2.3 shows a map of the Norfolk area indicating the approximate position of participants residential postcode in the years 2000 and 2014. It is apparent that some participants moved house between their recruitment and the first and second map locations shown, since there are a scatter of points some distance from the main recruitment areas. However, only a very small number of participants moved outside the Norfolk area with a much larger subset of the cohort moving within Norfolk, for example to coastal areas. The 2014 map, which excludes the location of participants who died prior to this date, is remarkably similar to the earlier year 2000 map indicating very low levels of migration.

Figure 2.3 | Map showing participant residential location in the year 2000 and 2014



Map tiles licensed under the Open Data Commons Open Database License (ODbL) by the OpenStreetMap Foundation (OSMF), copyright OpenStreetMap contributors

2.7 Analytical methods and plan

2.7.1 Use of follow-up periods

Participants were followed up for hospital events between 1999 and 2019 but follow-up was used in different ways. Some analyses used the initial 10-year period 1999–2009 to present the main results and the second 10-year period 2009–2019 to check for consistency. In other analyses the full 20-year follow-up period was used to present main results. The second 10-year period was also used to examine change, for example change in physical activity. Sensitivity analyses using baseline exposures but excluding the initial few years of follow-up are also presented to assess reverse causality.

2.7.2 Rationale for categorising hospital admission and duration outcomes

Hospitalisation outcomes are presented in categories but with the continuous relationship also shown. The reason for this approach is that categorical variables are more straightforward to interpret. For the 10-year outcome period (1999-2009), cutpoints were chosen that corresponded approximately to fifths of the distribution. When used in statistical models, these were further collapsed into two categories ("seven or more hospital admissions" for number of admissions and "more than twenty hospital days" for hospital duration). For the longer 20-year outcome period, the same categories were shown for consistency. However, they no longer corresponded to fifths of the distribution and so two further dichotomous outcomes were created to address this. "Twelve or more hospital admissions" and "more than fifty hospital days" were defined corresponding to admissions and duration respectively.

2.7.3 Choice of statistical model

Logistic regression was the primary statistical model used throughout these analyses. Survival analysis techniques such as Cox proportional hazards regression were not used since this would censor participants who died [124]. In order to assess the impact of hospital usage, no distinction was made between not being admitted due to good health and not being admitted because of death. In this important respect, the analyses differ from a standard prospective analysis. Additionally, survival analysis often focuses on the earliest event for a particular disease while hospitalisation techniques take account of all events over a fixed time period. While logistic regression was the primary analytical method used, Cox regression was used to examine differential survival in sensitivity analyses.

Various statistical techniques have been suggested to analyse hospital admission data, highlighting the unsuitability of conventional survival analyses such as Poisson regression and Cox proportional hazards models and may violate assumptions [125]. Studies whose participants include those never hospitalised, may indicate an excess of "zeros" while overdispersion (variance greater than mean), is likely due to the complex patterns of admission and readmission to hospital. Extensions of Poisson and Cox Techniques such as negative binomial regression and Prentice, Williams and Peterson Total Time have been used by some authors [55,126]. However, there was no compelling advantage to using any of these techniques rather than logistic regression in work presented in this thesis, since it was an appropriate analytical technique in the context of the outcomes used.

2.7.4 Handling of missing data

The exposure variables and covariates used for the majority of analyses presented here were collected at EPIC-Norfolk baseline from lifestyle questionnaires and data collected at the initial health examination. In total, 25,014 participants completed a questionnaire, attended a baseline health check and were alive in 1999. Participants did not always complete every question in the lifestyle questionnaire or gave responses that could not be coded such as written comments. Anthropometry and biochemistry were not always available. However, the number of missing values in the exposure variables and covariates represented a very small proportion of the data and so complete case analysis was used in the main analyses. The number of missing values for each of the covariates is stated in each chapter. However, multiple imputation was performed on a number of occasions. At time-point two (TP2) the number of participants completing a lifestyle questionnaire was higher than the number who attended a health examination. Measurements such as body mass index and biochemistry variables such as vitamin C and cholesterol had fewer observations than other questionnaire-based variables and a complete case analysis would have reduced the sample size quite significantly. The baseline cohort included only participants with lifestyle and health check data, but at TP2 multiple imputation was used to maximise sample size and overlap with the baseline. Multiple imputation on baseline exposures was also used in sensitivity analyses for example in chapter 6 on alcohol consumption to check for possible bias in the main results.

2.8 Analytical challenges and limitations

2.8.1 Loss to follow-up

Hospitalisation outcomes were obtained by data linkage mainly using the NHS Number, which is known for all cohort participants. As discussed, two methods were used to obtain HES data. HES data linked annually via local Primary Care Trust databases depended on an NHS Number being stored with the HES record. This was not always the case since the primary identifier used by hospitals at the time was a local hospital number. While the completeness of NHS numbers improved year-on-year and secondary matching by hospital number where known improved the matching rate, there was some loss to follow-up for HES data obtained by the local method. HES data obtained from linkage to national databases held by NHS Digital contained some records previously lost. Comparing local and national HES data for the same year and restricted to participants who did not move house, indicate that the proportion of missing NHS numbers improved over time. However, a small number of local HES records were missing in the national data suggesting anomalies in national data linkage.

Migration of study participants to areas outside England is rare. A few participants moved to areas where capture of HES records was not possible and were lost to follow-up. Some of these participants had transient relocations, spending some time out of the country, occasionally returning to use NHS facilities while in the country.

2.8.2 Alternative denominators

Most analyses presented here use number of admissions and duration of hospital stay over a fixed period of time, initially 10-year follow-up with 20-year follow-up becoming available later. A limitation of this approach, and a potential bias, is differential mortality where cohort participants who die during the follow-up period may be in particular risk groups which might affect results. Participants who died during the follow-up period self-evidently used no hospital resources after their death, however they were included in the denominator. If participants with a particular exposure were more likely to have died earlier than those without, this may have an effect on the associations observed for the exposure. Associations that ignore differential mortality can be useful when used in the context of resource planning in secondary care, but may be problematic in a public health setting. In addition to 10-year and 20-year follow-up periods used for the main analyses presented here, some descriptive presentations showing annual changes use multiple one-year follow-up periods. The denominators for each one-year period are restricted to those surviving to the start of the given year.

2.8.3 Record level coding variations between national and local data

Where local and national HES records were available for the same time periods, it was possible to compare records for the same participant which one would initially assume to be identical. However, the records often differed with respect to coded diagnoses and procedures with many additional codes appearing in the national data. The reason for the additional codes appeared to be the inclusion of chronic conditions recorded for individuals in earlier HES records, being automatically included in subsequent HES records. This contrasts with local HES records which only included diagnoses apparent or relevant to clinicians during the current admission spell. These differences did not affect the main outcome variables used, since numbers of admissions and hospital length of stay were identical in both datasets. However, where diagnosis and procedure codes have been considered over time, statistical algorithms had to take account of the origin of the HES records to mitigate any artificial inflation in frequencies.

3 Descriptive epidemiology of hospital admissions in the EPIC-Norfolk cohort

3.1 Overview

In this chapter, I contrast routinely published NHS summary statistics with similar summaries from HES records linked to EPIC-Norfolk. National annual admission and episode rates per 100 population from census data are compared with rates in EPIC participants alive at the start of each year from 1999/2000 to 2017/2018. Rates by sex and 5-year age groups are presented for two time points, at approximately the start and end of the follow-up. National ordinary admission and day case rates are also compared by financial year between 2007/2008 and 2017/2018. Secular trends in hospitalisation are examined by hospital days, by age within a period and by decade of birth. Reasons for hospital admissions by diagnosis and procedure categories and admission rates by Index of Multiple Deprivation are presented.

3.2 Introduction

Summary data are routinely published by NHS organisations describing many aspects of the UK National Health Service. It is used by the NHS for a number of purposes including monitoring trends and patterns in NHS hospital activity, assessing effective delivery of care, supporting local service planning and revealing health trends over time. National data differ in many ways from linked cohort data. National data most often use finished consultant episodes (generally referred to as “episodes”) to count activity whereas the metric used in this thesis is admissions (more formally described as “finished or unfinished admission episodes”) when describing and modelling hospitalisation. However, the tables presented in this chapter contrast national and cohort hospital records, and counts of both episodes and admissions are used. The hospitalisation outcomes used elsewhere in this thesis count total admissions and duration for individuals over a period of time. This contrasts with the national summary statistics and the tables shown here which compare annual national and cohort events at population level grouped by age, sex or other factors.

3.3 Methods

National summary level data, restricted to the age range 40–75 years, were combined with cohort linked HES data and tabulated. Rates for each year per 100 population were calculated for national data as the ratio of episode or admission counts and census population estimates while for cohort data, cohort participants alive at the given time point were used.

Day case admissions are defined as elective admissions where the intention is that no overnight stay is required. Day cases are reclassified as ordinary admissions in the event that an overnight stay becomes necessary. Ordinary admissions are elective admissions with the expectation that a patient will remain in hospital for at least one night. Ordinary admissions are combined with emergency admissions of any length in the tables presented. Further categories, such as regular day and night admissions for a planned series of treatment are not shown.

The OPCS-4 coding system contains 24 chapters, but this has been reduced to 16 headings when presented. Chapters M, N, P and Q have been combined into a category referred to as “genitourinary” since genital organs/tract procedures are infrequent. Chapter R which relates to pregnancy and childbirth is excluded due to the age of women in the cohort. Chapters V and W have been combined into a category referred to as “bones” since skull and spine procedures are infrequent. Chapters X, Y and Z (miscellaneous operations and subsidiary classifications) have also been excluded since these codes are either rare or used in conjunction with other procedure codes.

3.4 Results

3.4.1 Comparison of national admission rates and study rates

Table 3.1 summarises admission (finished admission episode, FAE) and episode (finished consultant episode, FCE) frequencies combining routinely published national HES data and cohort linked HES data. For the national data, the annual rates per 100 population are the ratio of FAEs or FCEs to the population of England estimated from the 2011 census, which is approximately midway through the period being described. Rates per 100 cohort survivors for the EPIC-Norfolk cohort FAEs and FCEs used the number of participants alive at the start of each year. The cohort denominator never increases, as the cohort was fixed after recruitment was completed and over the period 1999–2017 the number of cohort participants declined as people died.

Annual national hospital rates are not directly comparable to cohort data since the cohort denominator diminishes over time while the national population demographic is influenced by increasing longevity and advances in medicine and drugs. The comparatively higher rates observed in cohort participants in 1999/2000 are surprising since recently recruited volunteers in studies are typically more healthy than the general population — the “healthy volunteer effect”. However, the mean age of cohort participants is higher than the national mean. The episode and admission rates increase more rapidly in the cohort participants than in the national data but there are multiple factors driving the increase: the changing denominator due to an ageing cohort is specific to study data; study HES records are prone to the same artefactual increases as national data; national data are influenced by changes in population demography.

Table 3.1 | Historical episode and admission frequency for England and EPIC-Norfolk

	England				EPIC-Norfolk				
	FCE	FCE rate per 100	FAE	FAE rate per 100	FCE	FCE rate	FAE	FAE rate	Cohort alive
1999/2000	12,196,270	23.0	11,149,354	21.0	7,555	30.2	7,443	29.8	24,978
2000/2001	12,264,676	23.1	11,116,160	21.0	8,530	34.5	8,408	34.0	24,710
2001/2002	12,337,724	23.3	11,077,270	20.9	8,790	36.0	8,602	35.3	24,398
2002/2003	12,712,153	24.0	11,372,571	21.5	10,003	41.5	9,834	40.8	24,092
2003/2004	13,295,166	25.1	11,809,017	22.3	10,583	44.6	10,344	43.6	23,738
2004/2005	13,706,450	25.9	12,101,986	22.8	10,729	45.9	10,438	44.6	23,396
2005/2006	14,423,506	27.2	12,678,628	23.9	11,042	48.0	10,725	46.6	23,010
2006/2007	14,784,581	27.9	12,976,273	24.5	11,149	49.3	10,817	47.9	22,594
2007/2008	15,359,062	29.0	13,479,828	25.4	11,059	49.9	10,740	48.5	22,149
2008/2009	16,232,579	30.6	14,152,692	26.7	11,381	52.5	11,049	50.9	21,697
2009/2010	16,806,196	31.7	14,537,712	27.4	11,650	54.9	11,351	53.5	21,233
2010/2011	17,269,882	32.6	14,890,844	28.1	11,990	57.8	11,697	56.4	20,738
2011/2012	17,465,425	32.9	15,019,396	28.3	12,047	59.7	11,746	58.2	20,170
2012/2013	17,715,046	33.4	15,145,633	28.6	11,329	57.7	11,011	56.1	19,618
2013/2014	18,163,101	34.3	15,462,057	29.2	11,318	59.3	11,012	57.7	19,076
2014/2015	18,731,987	35.3	15,892,457	30.0	11,244	60.9	10,900	59.0	18,459
2015/2016	19,239,608	36.3	16,251,841	30.7	10,682	59.9	10,349	58.0	17,829
2016/2017	19,726,907	37.2	16,546,667	31.2	10,508	61.2	10,180	59.3	17,177
2017/2018	20,030,870	37.8	16,622,939	31.4	10,452	63.4	10,106	61.3	16,479

FCE = "finished consultant episode", FAE = "finished admission episode". Population of England: 53,012,456 (2011 census). Cohort linked rates per 100 participants alive at the start of each year uses national HES records from NHS Digital

Table 3.2 shows episode frequencies by age and sex for national data in the 2017/2018 period. Rates per 100 population were again calculated using information from the 2011 census. In EPIC-Norfolk, rates were calculated by age at recruitment and presented for two periods: 1999/2000 just after the end of cohort recruitment and 2017/2018. Rates in the earlier period are more directly comparable with national rates as the mean age of the cohort is only slightly higher than at recruitment. The rates for men and women at all age groups are lower than national rates.

Table 3.2 | Episode frequency for England (2017) and EPIC-Norfolk (1999 and 2017) by age group and sex

	Men FCE rate England 2017/2018	FCE EPIC-Norfolk 1999/2000	FCE EPIC-Norfolk 2017/2018	**Women** FCE rate England 2017/2018	FCE EPIC-Norfolk 1999/2000	FCE EPIC-Norfolk 2017/2018
40 - 44	15.9 (305,705/1,923,441)	7.91 (20/ 253)		22.0 (432,337/1,962,493)	15.3 (54/ 352)	
45 - 49	21.5 (411,980/1,919,758)	8.58 (50/ 583)		26.3 (515,749/1,960,057)	11.9 (96/ 804)	
50 - 54	30.7 (518,028/1,687,729)	16.03 (332/2,071)		34.8 (596,707/1,712,366)	17.5 (481/2,752)	
55 - 59	44.7 (662,390/1,481,745)	21.32 (375/1,759)		43.8 (663,834/1,515,247)	26.2 (589/2,244)	
60 - 64	42.7 (664,856/1,557,140)	25.91 (472/1,822)	27.2 (113/ 415)	38.5 (622,391/1,615,137)	32.8 (700/2,134)	40.3 (231/ 573)
65 - 69	65.5 (798,112/1,217,965)	33.28 (618/1,857)	38.7 (459/1,187)	56.4 (727,291/1,290,189)	41.6 (883/2,122)	48.3 (781/1,617)
70 - 74	96.0 (929,295/ 967,953)	32.67 (575/1,760)	54.7 (1,115/2,037)	78.9 (849,409/1,076,176)	29.1 (570/1,962)	43.7 (1,160/2,652)
75 - 79	110.4 (834,294/ 755,703)	72.04 (1,082/1,502)	48.9 (853/1,744)	87.7 (800,911/ 913,642)	39.6 (658/1,662)	50.6 (1,083/2,141)
80 - 84	142.1 (738,545/ 519,650)		50.8 (927/1,824)	105.1 (776,731/ 739,123)		52.0 (1,098/2,110)
85 - 89	187.1 (515,271/ 275,459)		47.2 (849/1,799)	129.5 (648,726/ 500,852)		38.8 (822/2,116)
90+	255.7 (276,413/ 108,109)		15.4 (397/2,576)	163.8 (484,439/ 295,708)		19.9 (556/2,796)

FCE = "finished consultant episode". England population by age and sex from 2011 census. Cohort linked data uses national HES records from NHS Digital

In table 3.3, national and cohort data are stratified by admission category and by year of admission 2007–2017. The day case rate in the cohort is much higher than the national rate which suggests a much higher rate of elective admissions and lower rate of emergency or unplanned admissions. The proportion of study participants with and without an overnight stay is also shown. This differs from the day case tabulation since it includes emergency admissions where no overnight stay is required.

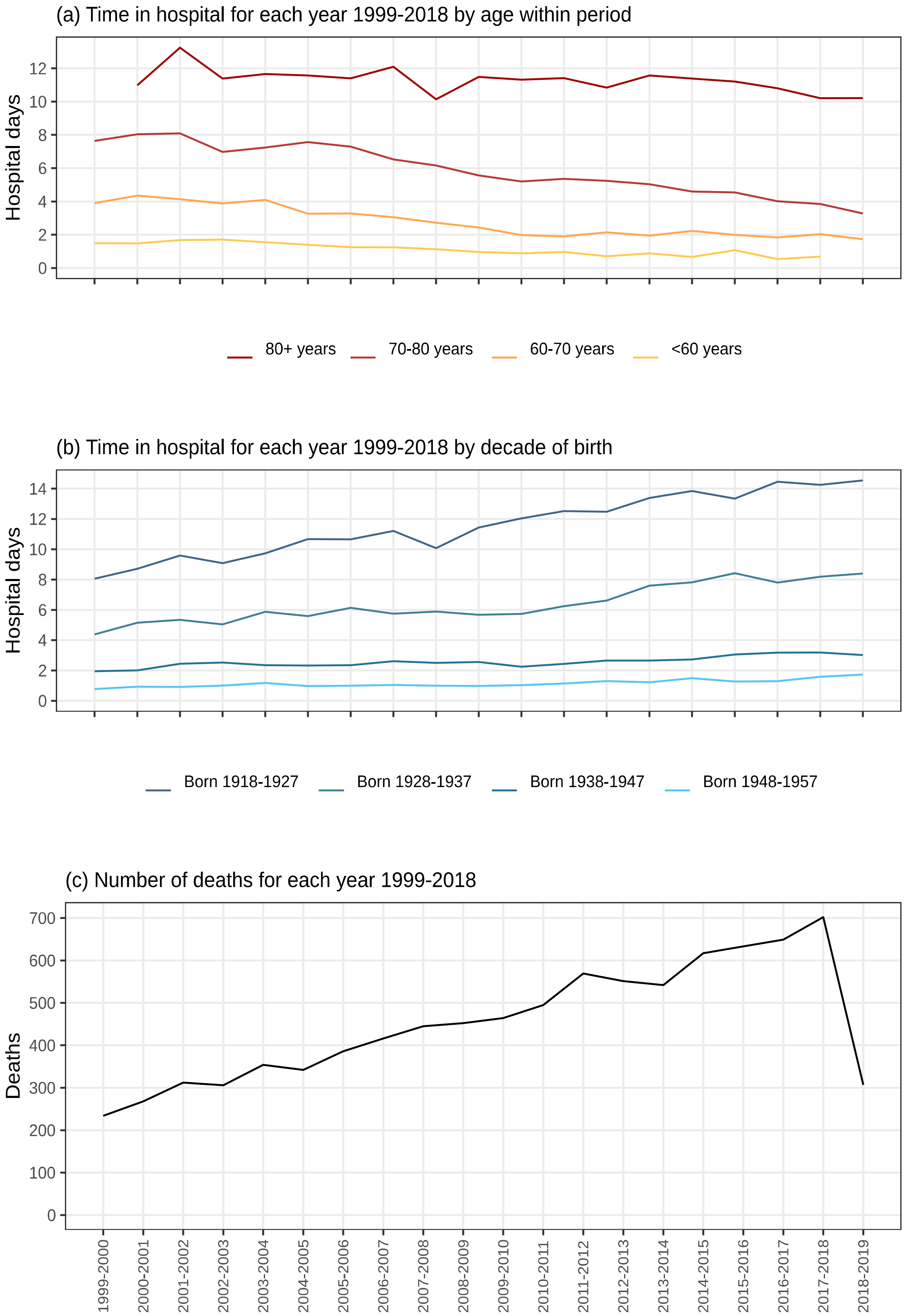
Table 3.3 | National and cohort frequencies for ordinary and day case admissions and overnight stays

	National data Ordinary admissions	Day case	EPIC-Norfolk data Ordinary admissions	Day-case	EPIC-Norfolk data Overnight stay	No overnight stay
2007/2008	10,592,679 (69%)	4,766,383 (31%)	4,581 (49%)	4,792 (51%)	3,967 (36%)	7,092 (64%)
2008/2009	11,012,063 (68%)	5,220,516 (32%)	4,825 (49%)	5,111 (51%)	4,123 (36%)	7,258 (64%)
2009/2010	11,331,307 (67%)	5,474,889 (33%)	4,602 (46%)	5,417 (54%)	3,879 (33%)	7,771 (67%)
2010/2011	11,578,176 (67%)	5,691,706 (33%)	4,877 (46%)	5,669 (54%)	4,137 (35%)	7,853 (65%)
2011/2012	11,541,318 (66%)	5,924,107 (34%)	5,023 (46%)	5,819 (54%)	4,337 (36%)	7,710 (64%)
2012/2013	11,653,256 (66%)	6,061,790 (34%)	4,884 (48%)	5,327 (52%)	4,161 (37%)	7,168 (63%)
2013/2014	11,841,633 (65%)	6,321,468 (35%)	5,136 (47%)	5,719 (53%)	4,413 (39%)	6,905 (61%)
2014/2015	12,158,914 (65%)	6,573,073 (35%)	4,945 (46%)	5,768 (54%)	4,225 (38%)	7,019 (62%)
2015/2016	12,352,627 (64%)	6,886,981 (36%)	4,759 (47%)	5,304 (53%)	4,103 (38%)	6,579 (62%)
2016/2017	12,600,443 (64%)	7,126,464 (36%)	4,654 (48%)	4,943 (52%)	4,070 (39%)	6,438 (61%)
2017/2018	12,905,246 (64%)	7,125,624 (36%)	4,641 (51%)	4,520 (49%)	4,015 (38%)	6,437 (62%)

3.4.2 Secular trends / historical variation in hospitalisation rates

Figure 3.1 (a) shows the hospital days by calendar year for the cohort by various age groups: <60 years, 60–70 years, 70–80 years and 80 years and older. Age and hospital days are calculated for each calendar year separately and exclude participants who died prior to the start of the year. Participant age is defined as age at the start of the year. The plot excludes two points due to small numbers: participants aged ≥80 in 1999–2000 and participants aged <60 years in 2017–2018. The hospital length of stay declines in all of the groups. The largest decline in absolute number of days was observed in the group aged 70–80 years who had on average 4 fewer hospital days in 2017–2018 than in 1999–2000. However, the relative decline in hospital days is similar in all age groups (approximately twofold) except the oldest. Figure 3.1 (b) shows hospital days by calendar year for the cohort by birth cohort: 1918–1927, 1927–1937, 1937–1948 and 1948–1957. Hospital days increase by year for all groups, with the largest absolute change (approximately 6 days) in the 1918–1927 band. Figure 3.1 (c) shows the number of deaths in the cohort occurring in each of the years between 1999 and 2018. The death numbers increase approximately linearly throughout the period even though the denominator cohort is reducing as a consequence. Hence the death rate increases more rapidly as expected in an ageing cohort. The drop in deaths in 2018–2019 is due to incomplete mortality data.

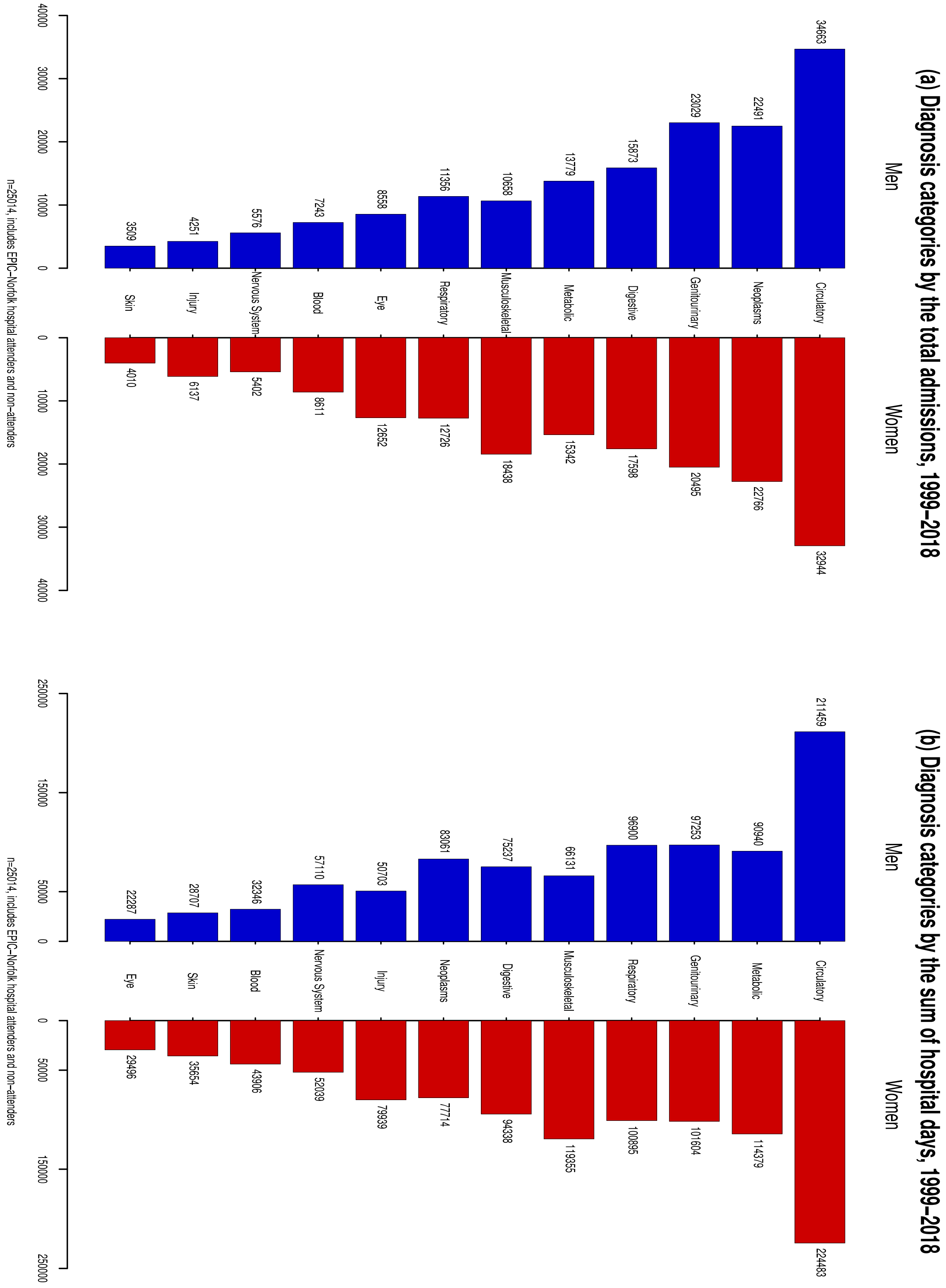
Figure 3.1 | Plots showing hospital days and deaths for each calendar year between 1999 and 2018. In (a) hospital days are shown by age groups; in (b) hospital days by birth cohort in (c) number of deaths occurring in each year



3.4.3 Main causes for hospitalisation

Figure 3.2 (a) shows diagnosis categories using the International Classification of Diseases (ICD) v.10 chapter headings by total admissions for men and women separately. Total admissions were calculated by summing all hospital admissions over the 19-year period 1999–2018 where a participant's discharge diagnoses included a relevant chapter heading. The diagnosis categories are shown in descending order of magnitude for men and women combined. Since patients can have multiple diagnosis codes, the admission counts are not mutually exclusive. Participants who had several hospital visits or were under the care of different consultants while in hospital may have been repeatedly assigned the same code. Similarly, participants with related conditions which fall under the same ICD v.10 chapter headings will also have multiple counts. For these reasons, the numbers shown are not meaningful in themselves but can be used as a metric to compare between disease categories. The circulatory disease category had the highest admission count for both men and women. The category includes common diseases such as ischaemic heart disease and stroke. Figure 3.2 (b) shows ICD v.10 diagnosis categories by total hospital days for men and women. Total hospital days were calculated in a similar way to total admissions. The order of the disease categories is similar to the order for total admissions with some exceptions. The neoplasms category had the third greatest number of hospital days reflecting that cancer patients may need to spend longer periods in hospital while having fewer admissions. In most categories, the pattern of total admissions and hospital days is similar for men and women. However, for the "musculoskeletal", "eye" and "injury" categories, admission and duration is significantly higher for women than men. However, these differences are partly explained by the larger proportion of women in the cohort.

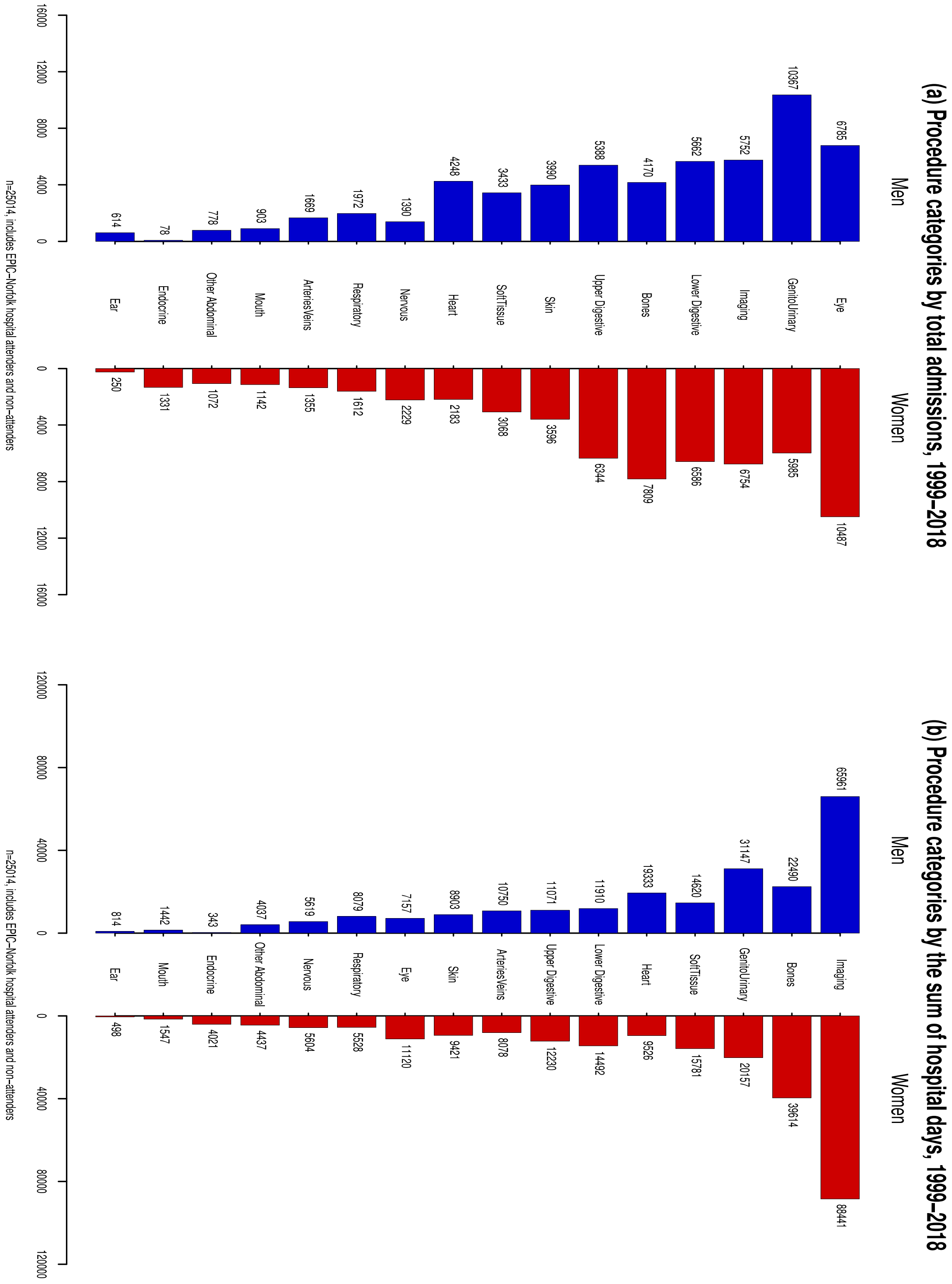
Figure 3.2 | ICD v.10 chapter headings by total admissions (left-hand plot) and total hospital days (right-hand plot) for men and women



Distribution of admissions and length of stay by ICD v.10 category

Figure 3.3 (a) shows procedure categories using the "OPCS Classification of Interventions and Procedures version 4" (OPCS-4) chapter headings by total admissions for men and women separately. Total admissions was calculated by summing all hospital admissions over the 19-year period 1999–2018 where a participant had an operation or procedure classified under an OPCS-4 chapter heading. The procedure categories are shown in descending order of magnitude for men and women combined. As with ICD codes, it is possible to have multiple procedure codes, due to multiple admissions, care under different consultants or several related procedures within the same chapter heading and hence the admission counts are not mutually exclusive. The "eye" procedure category had the highest number of admissions reflecting the large numbers of participants who had cataract surgery. Figure 3.3 (b) shows the procedure categories by the total duration of hospital days for men and women which is calculated in a similar way to total admissions. The pattern differs markedly from the admissions diagram. Imaging represents by far the largest group, however procedures involving diagnostic imaging and testing will often occur with other procedures. Procedures relating to bones and joints also have long hospital duration and are higher in women while genitourinary procedures involve longer hospital stays in men.

Figure 3.3 | OPCS-4 chapter headings by total admissions (left-hand plot) and the sum of hospital days (right-hand plot) for men and women



Distribution of admissions and length of stay by OPCS v.4 category

Table 3.4 shows the national Index of Multiple Deprivation (IMD) and EPIC-Norfolk IMD using decile cutpoints defined by the national distribution and numbers of admissions for period 2017–2018. The cohort data uses IMD in 2007. As described in detail later (chapter 5), the majority of cohort participants live in less deprived areas — those above the national average for deprivation. However, the prevalence of hospital admissions per 100,000 population is higher in cohort participants for all deciles of deprivation.

Table 3.4 | National and cohort admissions by Index of Multiple Deprivation and prevalence per 100,000 population

	National data Admission prevalence	EPIC-Norfolk data Admission prevalence
Most deprived 10%	33,171 (1,842,545/5,554,693)	40,301 (241/598)
More deprived 10-20%	30,505 (1,734,079/5,684,550)	38,473 (262/681)
More deprived 20-30%	29,307 (1,676,684/5,721,120)	46,282 (361/780)
More deprived 30-40%	29,032 (1,643,455/5,660,910)	57,379 (867/1,511)
More deprived 40-50%	29,334 (1,628,059/5,550,165)	31,815 (524/1,647)
Less deprived 40-50%	29,054 (1,609,631/5,540,151)	33,719 (1,050/3,114)
Less deprived 30-40%	28,736 (1,569,104/5,460,477)	45,437 (2,390/5,260)
Less deprived 20-30%	28,238 (1,534,848/5,435,442)	38,404 (2,007/5,226)
Less deprived 10-20%	28,095 (1,516,621/5,398,187)	36,090 (1,571/4,353)
Least deprived 10%	26,770 (1,408,729/5,262,372)	33,994 (823/2,421)

Number of admissions in national and EPIC data in 2017/18

3.5 Discussion

National HES summary data can be contrasted with cohort linked data and while they are not generally directly comparable, similar trends over time are apparent. Rates for both national HES and cohort linked data show increases in admissions and episodes over time but the reason for these increases differs. The population size of England has increased over the period (from 49 million in 1999 to 56 million in 2018) but although national rates were based on the population at the 2011 census, changes in the population can not explain the rapid increase in the rate of hospitalisation by year. The difference in national FCE rates between 1999–2000 and 2017–2018 are larger than the difference in FAE rates. This may indicate an artificial inflation in counting episodes, reflecting changes in the recording of hospital episodes. However, changes in hospital processes over the period may also account for some of the increase. Inflation in admission rates may also be in part artefactual, resulting from the discharge of some patients before their complete recovery and subsequent readmission after a short period. Artefactual explanations for the increase in rates of admissions and episodes do not however explain the considerable increases observed. Changes in the population structure, with an increased proportion of older men and women, are likely to account for a large part of the differences observed. While improvements in medical technology influence hospital usage and costs, it is not clear how this might affect rates of admissions and episodes.

The use of episodes to measure activity can be problematic since this is the mechanism by which hospitals are remunerated and it creates an incentive for episode inflation when submitting data. The historical national HES data over a 19-year period presented here shows higher rates of increase in episodes than admissions. However, both the episode and admission rates per 100 persons increase significantly over the period and there are a number of possible explanations for this. While counts of admissions are less prone to be distorted by financial pressures, discharge of patients who are not fully recovered resulting in rapid readmission may partly explain the increase over time of admission rates.

The higher rate of day cases observed in the cohort compared with the national figures may be due to more effective primary care in Norfolk compared with larger cities where unplanned hospital admissions are more common [127]. The adoption of surgical techniques suitable for day case admissions may also vary by region [128]. However, the lower rate of emergency admissions may also indicate that the cohort is generally more healthy than the national population or has lower rates of deprivation [129,130].

The FCE and FAE rates within the cohort are higher than the national rates reflecting the age distribution of the cohort. However, the rates also increase rapidly year-on-year and there are a number of explanations for this. The decrease in the denominator population due to mortality cause a corresponding rise in the rates. The absolute number of FCEs and FAEs initially increases, but plateaus after a short period. Some further increases are partly due to coding changes, especially in the period 2009-2010. The mean age of cohort participants increased from 62 in 1999 to 77 in 2017. However, the expected increase in the absolute numbers of FCEs and FAEs due to increased age and national trends is masked by the reduction of the denominator.

When hospital episodes are examined by age and sex, the rates for men and women in the EPIC-Norfolk cohort in 1999 are lower than the corresponding national rates, despite the mean age of the cohort being marginally higher than at recruitment. One explanation for this is the “healthy volunteer effect” [107,131], whereby people who choose to join a medical study are typically healthier than the general population. The healthy volunteer effect can also be observed when examining death rates. Another factor influencing the lower rates in EPIC-Norfolk in 1999 is a general increase in the use of hospital services over time as shown in table 3.1, whether artefactual or real, which is not explained by increased longevity. Rates in the cohort in 2017/2018 are much higher than national rates for younger age groups in both men and women mainly because the mean age of the cohort is much higher than at recruitment. However, the rates in the oldest age groups, those 70 years and above, are lower than national rates which may reflect differential selective mortality.

HES records include detailed coded information taken from discharge summaries that classify both patient diagnoses and the procedures used to treat them. Hospitalisation outcomes such as total admissions and length of stay do not take into account the reasons for admission. The purpose of examining these outcomes is to gauge the overall impact to the NHS of various sociodemographic and lifestyle behaviours. However, the pattern of disease experienced by the cohort can be important to put findings into context. Diagnoses are coded using the International Classification of Diseases v.10 which I have presented grouped into chapter headings for men and women separately giving a broad grouping of disease type. The most common diagnosis group in EPIC-Norfolk linked HES records is “Diseases of the circulatory system” in both men and women for both total admissions and the sum of hospital days. HES records also include coded procedures using the OPCS v4. system. These codes can also be grouped by main or related chapter headings and I have presented the frequencies for total admissions and the sum of hospital days for men and women. The most common procedure groups differ by sex and summary method. When summarised by total admissions, eye procedures are most common in women and genitourinary procedures in men. When summarised by total hospital duration, diagnostic imaging, testing and rehabilitation are the most common procedures. Data are also presented comparing area deprivation in the cohort to national area deprivation data by number of admissions in 2017–2018 using deciles of IMD. The comparison is not directly comparable since the measurements of IMD were made at different times and national and cohort age distributions differ, however they show similar trends, with those in more deprived areas having a higher admission rate than those in the least deprived areas.

3.6 Key points

What is already known on this subject

• Comprehensive summary statistics are regularly published by NHS organisations and the Office for National Statistics.

What this study adds

• A comparison of English hospitalisation rates and rates for EPIC-Norfolk linked hospital records show a similar increase in episodes and admissions by year.

• Total hospital duration group decreases year-on-year in all age groups over a 20-year follow-up period.

• Diseases of the circulatory system are the most common diagnoses in cohort participants; procedures relating to eyes, genitourinary and imaging are the most common procedures.

4 Predicting admissions and time spent in hospital

4.1 Overview

In this chapter I examine the relationship between easily understood and simple to measure sociodemographic factors, such as age, sex and social class, modifiable factors such as smoking and body mass index and future hospitalisation. Each of these factors has been reported to be associated with mortality risk in cohort studies but in this chapter, I will investigate whether similar associations are found for hospitalisation outcomes. Participant age was the strongest association and male sex was also a risk factor. However, modifiable factors — such as body mass index and cigarette smoking and sociodemographic factors including having a manual social class and having a low educational attainment — were all strongly and independently associated with future long hospital stay or a high number of admissions.

4.2 Abstract

Luben et al., BMJ Open, 2016

This study quantifies hospital usage in a general population over 10 years follow-up and examines related factors in a general population-based cohort. It uses data from a prospective population-based cohort of men and women living in Norfolk, UK. 11,228 men and 13,786 women aged 40–79 years in 1993–1997 were followed between 1999 and 2009. The number of hospital admissions and total hospital days for individuals over a 10-year follow-up period were identified using record linkage and five categories were defined for admissions (from zero to highest ≥7) and for hospital days (from zero to highest >20 days).

Over a period of 10 years, 18,179 (73%) study participants had at least one admission to hospital, 14% with 7 or more admissions and 20% with >20 days in hospital. In logistic regression models with outcome ≥7 admissions, age per 10-year increase OR 1.75 (95% CI 1.67–1.82), male sex OR 1.32 (95% CI 1.22–1.42), low education level OR 1.14 (95% CI 1.05–1.24), manual social class OR 1.22 (95% CI 1.13–1.32), current cigarette smoker OR 1.53 (95% CI 1.37–1.70) and body mass index >30 kg/m^2 OR 1.41 (95% CI 1.28–1.56) all independently predicted the outcome with $p<0.0001$. Results were similar for those with >20 hospital days. A risk score constructed using male sex, manual social class, no educational qualifications; current smoker and body mass index >30 kg/m^2, estimated percentages of the cohort in the categories of admission numbers and hospital days in stratified age bands with twofold to threefold differences in future hospital usage between those with high-risk and low-risk scores.

The future probability of cumulative hospital admissions and hospital days appears independently related to a range of simple demographic and behavioural indicators. The strongest of these is increasing age with high body mass index and smoking having similar magnitudes for predicting risk of future hospital usage.

4.3 Introduction

In the UK, the number of men and women over 65 years of age was 10.8 million in 2012 and is projected to increase to 17.8 million by 2037 with those over-85s doubling in number to 3.6 million [132]. Two-thirds of people admitted to hospital are over 65 years old with those over 85 years accounting for 25% of bed days [11]. Though increasing age is associated with increased health service usage, other factors may help identify those at greatest risk of admission. Most studies examining hospital activity start from those hospitalised but are limited with respect to population denominators;[41,42,46,133,134] even those that use general practice record linkage studies only include people who attended general practices while population-based studies that have measured factors prospectively prior to admission are limited [35–38,59,135].

In this study I examined the relationship between simple and easily measurable demographic and behavioural factors to predict in a general population cohort resident in Norfolk, the future risk of use of National Health Service (NHS) hospitals over a 10-year period from 1999 to 2009, a period of relative stability for the NHS under Primary Care Trusts [112,113].

4.4 Methods

4.4.1 Statistical analyses

I examined the distribution of hospital admissions by baseline descriptive data. Odds ratios for each of the main outcomes: ≥7 hospital admissions; hospital days >20 and no hospital admissions were calculated using unmatched logistic regression with independent variables age, smoking, BMI >30, manual social class and no educational qualifications. I then created a summary risk score, defined as the sum of five baseline risk factors dichotomised as binary categories each coded one or zero. The categories, each contributing one point, were male sex, manual social class, low education level (those with no qualifications), current smoker and body mass index >30 kg/m^2. Those with scores four and five were combined into a single category as the number with score equal to five was very low.

I used logistic regression rather than survival analysis to prevent the censoring of participants who had died, since I wished to make no distinction between not being admitted to hospital due to good health and not being admitted because of death. The number of missing values were: 53 body mass index, 218 smoking status, 545 social class, 18 level of education. I examined mortality rates in the cohort by risk score stratified by age over three periods of follow-up time: 1993–1998, 1999–2004; and 1999–2009 to explore the possibility of differential mortality and therefore attrition of the population in the different risk groups which might explain some of the patterns observed. In addition, to explore the possibility of the effect of participant migration during the period under examination a sensitivity analysis was conducted on the subset of the cohort whose postcode area was Norfolk ("NR") at both the start and end of the period. All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria V.3.1.2 with packages knitr, Gmisc and IRanges) and Stata statistical software V.12 (Stata Corporation, College Station, Texas, USA).

4.5 Results

For the current analyses, I excluded the 625 men and women from the baseline cohort who died before 1999 leaving 11,228 men and 13,786 women. Over a period of 10 years, between 1999 and 2009, 8,300 (74%) male and 9,879 (72%) female study participants were admitted to hospital. In total 92% of these admissions were to the Norfolk and Norwich Hospital. Descriptive characteristics of the cohort are shown in table 4.1.

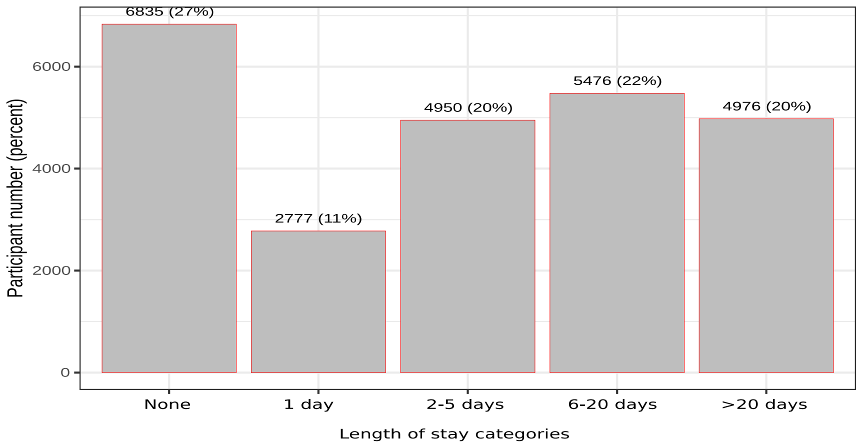
Table 4.1 | Descriptive characteristics at baseline in 25,014 men and women by sex

	Total	Men (n=11,228 44.9%)	Women (n=13,786 55.1%)	P-value
Hospital activity 1999–2009				
No admissions	6,835 (27.3)	2,928 (26.1)	3,907 (28.3)	< 0.0001
One or more admissions	18,179 (72.7)	8,300 (73.9)	9,879 (71.7)	
Time in hospital 1999–2009				
Mean ±SD	16.3 ±46.5	17.1 ±43.4	15.6 ±48.8	< 0.0001
Mean ±SD	22.4 ±53.2	23.2 ±49.1	21.8 ±56.5	< 0.0001
Median (IQR)	3.0 (0.0 - 15.0)	4.0 (0.0 - 17.0)	3.0 (0.0 - 13.0)	< 0.0001
Median (IQR)	8.0 (2.0 - 23.0)	9.0 (3.0 - 25.0)	7.0 (2.0 - 21.0)	< 0.0001
Number of admissions 1999–2009				
Mean ±SD	3.8 ±16.2	4.2 ±16.2	3.6 ±16.3	< 0.0001
Mean ±SD	5.3 ±18.9	5.7 ±18.6	5.0 ±19.0	< 0.0001
Median (IQR)	2.0 (0.0 - 4.0)	2.0 (0.0 - 5.0)	2.0 (0.0 - 4.0)	< 0.0001
Median (IQR)	3.0 (1.0 - 5.0)	3.0 (2.0 - 6.0)	3.0 (1.0 - 5.0)	< 0.0001
Body mass index, kg/m²				
Mean ±SD	26.4 ±3.9	26.5 ±3.3	26.2 ±4.3	< 0.0001
Age, years				
Mean ±SD	59.0 ±9.3	59.3 ±9.2	58.8 ±9.3	< 0.0001
Age band (n (%))				
≤55 years	9,567 (38.2)	4,113 (36.6)	5,454 (39.6)	< 0.0001
(55,65] years	7,805 (31.2)	3,565 (31.8)	4,240 (30.8)	
(65,75] years	6,933 (27.7)	3,216 (28.6)	3,717 (27.0)	
>75 years	709 (2.8)	334 (3.0)	375 (2.7)	
Cigarette smoking (n (%))				
Current	2,904 (11.7)	1,356 (12.2)	1,548 (11.3)	< 0.0001
Former	10,423 (42.0)	6,044 (54.2)	4,379 (32.1)	
Never	11,469 (46.3)	3,748 (33.6)	7,721 (56.6)	
Level of education (n (%))				
Higher level	15,866 (63.5)	7,871 (70.2)	7,995 (58.0)	< 0.0001
Lower level	9,130 (36.5)	3,348 (29.8)	5,782 (42.0)	
Body mass index (n (%))				
≤24 kg/m²	6,985 (28.0)	2,369 (21.1)	4,616 (33.6)	< 0.0001
(24,27] kg/m²	8,608 (34.5)	4,392 (39.2)	4,216 (30.6)	
(27,30] kg/m²	5,565 (22.3)	2,957 (26.4)	2,608 (19.0)	
>30 kg/m²	3,803 (15.2)	1,486 (13.3)	2,317 (16.8)	

p-values use Fisher's exact test for proportions and Wilcoxon rank sum test for continuous values. Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Figure 4.1 shows length of hospital stay categories over 10-year follow-up, 1999–2009. Number and percentage of participants are shown for those who spent no time in hospital, 1, 2–5, 6–20 and >20 hospital days. The second graph shows the same hospital stay categories but further divided by age groups <50, 50–60, 60–70 and >70.

Figure 4.1 | Categories of hospital duration for participants over 10-year follow-up 1999–2009 in 25,014 men and women and additionally grouped by age group



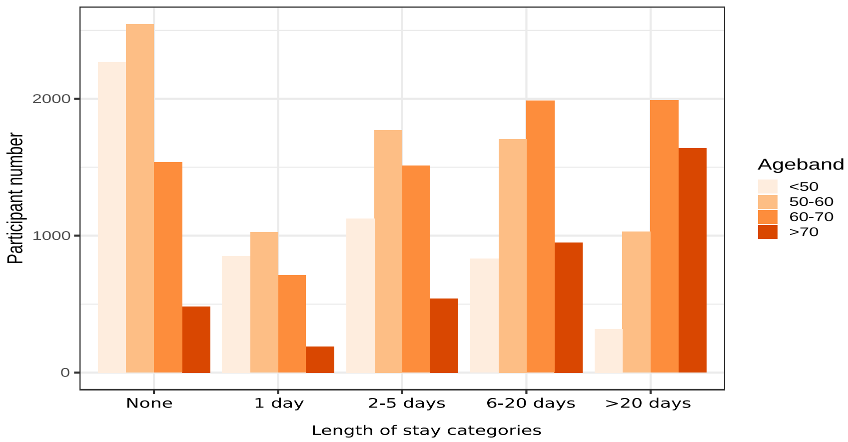


Table 4.2 shows the distribution of characteristics by hospital admission category while table 4.3 shows similar characteristics for categories of hospital duration. The proportion of study participants with no hospital admissions decreased across age groups with the highest proportion in those aged ≤55, while the highest proportion of participants with ≥7 admissions or >20 hospital days were aged >65. The majority of participants with no admissions were never-smokers, while a high proportion of current and former smokers had ≥7 admissions and long duration. Similarly, the frequency of higher educational attainment and non-manual social class was higher in those with fewer admissions and shorter hospital duration and lower in those with more admissions and longer duration. The proportion with BMI >30 was highest in those with ≥7 admissions and >20 hospital days and lowest in those with length of time in hospital ≤1 day.

Table 4.2 | Descriptive characteristics at baseline in 25,014 men and women by admission category

	Total	0 (n=6,835 27.3%)	1 (n=4,582 18.3%)	2–3 (n=6,034 24.1%)	4–6 (n=4,101 16.4%)	≥7 (n=3,462 13.8%)	P-value
Total hospital days, 1999–2009							
Mean ±SD	16.3 ±46.5	0.0 ±0.0	5.4 ±42.1	11.2 ±28.9	24.3 ±39.3	62.2 ±84.0	< 0.0001
Median (IQR)	3.0 (0.0 - 15.0)	0.0 (0.0 - 0.0)	1.0 (1.0 - 3.0)	5.0 (3.0 - 11.0)	13.0 (7.0 - 27.0)	40.0 (22.0 - 73.8)	< 0.0001
Body mass index, kg/m²							
Mean ±SD	26.4 ±3.9	25.9 ±3.7	26.1 ±3.8	26.4 ±3.9	26.8 ±4.0	27.1 ±4.2	< 0.0001
Sex (n (%))							
Men	11,228 (44.9)	2,928 (42.8)	2,012 (43.9)	2,586 (42.9)	1,938 (47.3)	1,764 (51.0)	< 0.0001
Women	13,786 (55.1)	3,907 (57.2)	2,570 (56.1)	3,448 (57.1)	2,163 (52.7)	1,698 (49.0)	
Age, years							
Mean ±SD	59.0 ±9.3	55.4 ±8.6	57.3 ±8.9	59.9 ±9.1	62.4 ±8.9	63.0 ±8.6	< 0.0001
Age band (n (%))							
≤55 years	9,567 (38.2)	3,720 (54.4)	2,063 (45.0)	2,072 (34.3)	986 (24.0)	726 (21.0)	< 0.0001
(55,65] years	7,805 (31.2)	1,973 (28.9)	1,477 (32.2)	1,938 (32.1)	1,289 (31.4)	1,128 (32.6)	
(65,75] years	6,933 (27.7)	1,059 (15.5)	964 (21.0)	1,842 (30.5)	1,614 (39.4)	1,454 (42.0)	
>75 years	709 (2.8)	83 (1.2)	78 (1.7)	182 (3.0)	212 (5.2)	154 (4.4)	
Cigarette smoking (n (%))							
Current	2,904 (11.7)	751 (11.1)	514 (11.3)	665 (11.1)	485 (12.0)	489 (14.3)	< 0.0001
Former	10,423 (42.0)	2,558 (37.7)	1,833 (40.3)	2,549 (42.6)	1,818 (44.8)	1,665 (48.7)	
Never	11,469 (46.3)	3,476 (51.2)	2,199 (48.4)	2,772 (46.3)	1,754 (43.2)	1,268 (37.1)	
Social class (n (%))							
Professional (1)	1,724 (7.0)	599 (8.9)	335 (7.4)	380 (6.4)	234 (5.9)	176 (5.2)	< 0.0001
Technical (2)	8,949 (36.6)	2,754 (41.1)	1,697 (37.7)	2,068 (35.1)	1,348 (33.7)	1,082 (32.0)	
Clerical NM (3.1)	4,044 (16.5)	1,047 (15.6)	732 (16.3)	981 (16.6)	690 (17.3)	594 (17.6)	
Clerical M (3.2)	5,626 (23.0)	1,397 (20.8)	1,039 (23.1)	1,375 (23.3)	961 (24.0)	854 (25.3)	
Semi-skilled (4)	3,266 (13.3)	744 (11.1)	555 (12.3)	868 (14.7)	603 (15.1)	496 (14.7)	
Unskilled (5)	860 (3.5)	163 (2.4)	139 (3.1)	222 (3.8)	160 (4.0)	176 (5.2)	
Level of education (n (%))							
Higher level	15,866 (63.5)	4,922 (72.0)	3,034 (66.3)	3,711 (61.5)	2,280 (55.7)	1,919 (55.5)	< 0.0001
Lower level	9,130 (36.5)	1,910 (28.0)	1,545 (33.7)	2,321 (38.5)	1,815 (44.3)	1,539 (44.5)	
Body mass index (n (%))							
≤24 kg/m²	6,985 (28.0)	2,225 (32.6)	1,365 (29.9)	1,660 (27.6)	969 (23.7)	766 (22.2)	< 0.0001
(24,27] kg/m²	8,608 (34.5)	2,410 (35.3)	1,599 (35.0)	2,105 (35.0)	1,349 (33.0)	1,145 (33.2)	
(27,30] kg/m²	5,565 (22.3)	1,320 (19.3)	1,008 (22.0)	1,327 (22.0)	1,048 (25.6)	862 (25.0)	
>30 kg/m²	3,803 (15.2)	873 (12.8)	600 (13.1)	930 (15.4)	725 (17.7)	675 (19.6)	

p-values use Fisher's exact test for proportions and Wilcoxon rank sum test for continuous values. Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Table 4.3 | Descriptive characteristics at baseline in 25,014 men and women by hospital duration category

	Total	None (n=6,835 27.3%)	Day case (n=2,777 11.1%)	2–5 days (n=4,950 19.8%)	6–20 days (n=5,476 21.9%)	>20 days (n=4,976 19.9%)	P-value
Total hospital days, 1999–2009							
Mean ±SD	16.3 ±46.5	0.0 ±0.0	1.0 ±0.0	3.1 ±1.1	11.4 ±4.2	65.7 ±87.7	< 0.0001
Median (IQR)	3.0 (0.0 - 15.0)	0.0 (0.0 - 0.0)	1.0 (1.0 - 1.0)	3.0 (2.0 - 4.0)	11.0 (8.0 - 14.0)	44.0 (29.0 - 73.0)	< 0.0001
Body mass index, kg/m²							
Mean ±SD	26.4 ±3.9	25.9 ±3.7	25.9 ±3.6	26.1 ±3.8	26.8 ±4.0	27.1 ±4.3	< 0.0001
Sex (n (%))							
Men	11,228 (44.9)	2,928 (42.8)	1,230 (44.3)	2,084 (42.1)	2,572 (47.0)	2,414 (48.5)	< 0.0001
Women	13,786 (55.1)	3,907 (57.2)	1,547 (55.7)	2,866 (57.9)	2,904 (53.0)	2,562 (51.5)	
Age, years							
Mean ±SD	59.0 ±9.3	55.4 ±8.6	56.0 ±8.5	58.1 ±8.8	60.6 ±8.8	64.9 ±8.2	< 0.0001
Age band (n (%))							
≤55 years	9,567 (38.2)	3,720 (54.4)	1,419 (51.1)	2,044 (41.3)	1,632 (29.8)	752 (15.1)	< 0.0001
(55,65] years	7,805 (31.2)	1,973 (28.9)	879 (31.7)	1,625 (32.8)	1,906 (34.8)	1,422 (28.6)	
(65,75] years	6,933 (27.7)	1,059 (15.5)	449 (16.2)	1,197 (24.2)	1,786 (32.6)	2,442 (49.1)	
>75 years	709 (2.8)	83 (1.2)	30 (1.1)	84 (1.7)	152 (2.8)	360 (7.2)	
Cigarette smoking (n (%))							
Current	2,904 (11.7)	751 (11.1)	295 (10.7)	521 (10.6)	684 (12.6)	653 (13.3)	< 0.0001
Former	10,423 (42.0)	2,558 (37.7)	1,118 (40.4)	1,992 (40.6)	2,388 (44.0)	2,367 (48.2)	
Never	11,469 (46.3)	3,476 (51.2)	1,351 (48.9)	2,396 (48.8)	2,354 (43.4)	1,892 (38.5)	
Social class (n (%))							
Professional (1)	1,724 (7.0)	599 (8.9)	210 (7.7)	320 (6.6)	343 (6.4)	252 (5.2)	< 0.0001
Technical (2)	8,949 (36.6)	2,754 (41.1)	1,045 (38.2)	1,753 (36.1)	1,818 (34.0)	1,579 (32.8)	
Clerical NM (3.1)	4,044 (16.5)	1,047 (15.6)	467 (17.1)	797 (16.4)	880 (16.4)	853 (17.7)	
Clerical M (3.2)	5,626 (23.0)	1,397 (20.8)	603 (22.0)	1,130 (23.2)	1,347 (25.2)	1,149 (23.9)	
Semi-skilled (4)	3,266 (13.3)	744 (11.1)	336 (12.3)	695 (14.3)	760 (14.2)	731 (15.2)	
Unskilled (5)	860 (3.5)	163 (2.4)	76 (2.8)	167 (3.4)	204 (3.8)	250 (5.2)	
Level of education (n (%))							
Higher level	15,866 (63.5)	4,922 (72.0)	1,916 (69.0)	3,173 (64.2)	3,235 (59.1)	2,620 (52.7)	< 0.0001
Lower level	9,130 (36.5)	1,910 (28.0)	860 (31.0)	1,773 (35.8)	2,237 (40.9)	2,350 (47.3)	
Body mass index (n (%))							
≤24 kg/m²	6,985 (28.0)	2,225 (32.6)	885 (31.9)	1,460 (29.6)	1,312 (24.0)	1,103 (22.3)	< 0.0001
(24,27] kg/m²	8,608 (34.5)	2,410 (35.3)	978 (35.2)	1,761 (35.7)	1,827 (33.4)	1,632 (32.9)	
(27,30] kg/m²	5,565 (22.3)	1,320 (19.3)	603 (21.7)	1,058 (21.4)	1,366 (25.0)	1,218 (24.6)	
>30 kg/m²	3,803 (15.2)	873 (12.8)	310 (11.2)	658 (13.3)	958 (17.5)	1,004 (20.3)	

p-values use Fisher's exact test for proportions and Wilcoxon rank sum test for continuous values. Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Table 4.4 shows the independent relationships using logistic modelling between demographic and behavioural factors in relation to hospital admissions. High numbers of admissions and hospital days were positively associated with male sex, age, manual social class, smoking and high BMI while no hospital admissions were inversely associated with these factors. The strongest risk factors for more than 7 admissions were age OR 1.75 (95% CI 1.67–1.82) per 10-year increase, being a current cigarette smoker OR 1.53 (95% CI 1.37–1.70) and BMI OR 1.41 (95% CI 1.28–1.56). Age was the strongest risk factor for long hospital duration >20 days OR 2.54 (95% CI 2.44–2.65) per 10 years increase in age. Current smoking OR 1.59 (95% CI 1.44–1.77) and BMI >30 kg/m^2 OR 1.54 (95% CI 1.41–1.68) were also important risk factors.

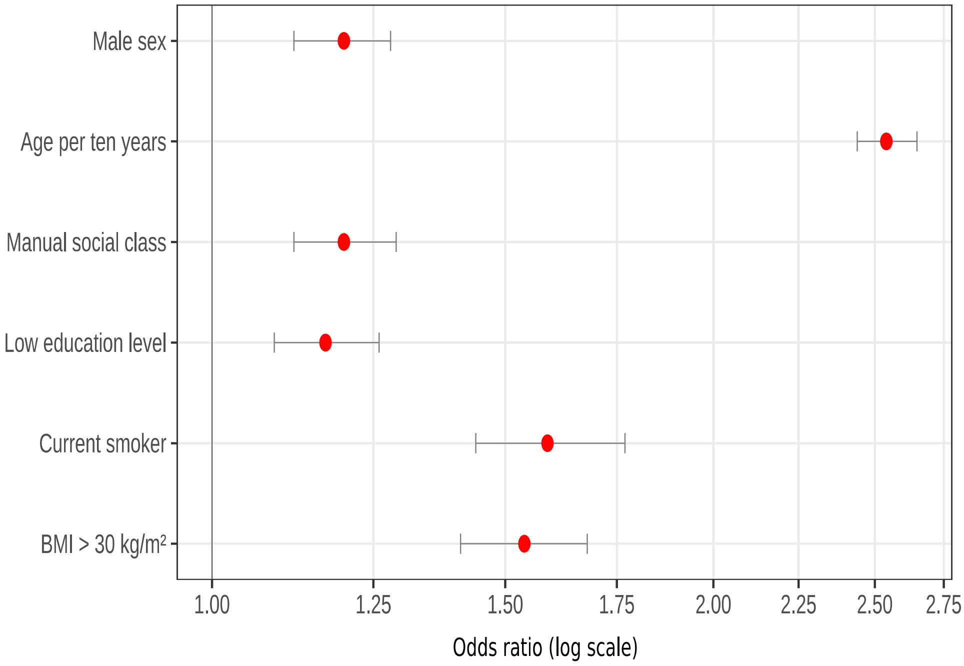
Table 4.4 | Multivariable logistic regression of risk factors for no hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999 to 2009 in 25,014 men and women.

	All subjects OR (95% CI)	p value	Men OR (95% CI)	p value	Women OR (95% CI)	p value
Outcome of no hospital admissions						
Female sex	1.11 (1.05–1.18)	< 0.001				
Age per 10 years	0.56 (0.54–0.57)	< 0.001	0.49 (0.47–0.52)	< 0.001	0.61 (0.58–0.64)	< 0.001
Manual social class	1.29 (1.21–1.38)	< 0.001	1.35 (1.22–1.48)	< 0.001	1.24 (1.14–1.35)	< 0.001
Low education level	1.26 (1.18–1.35)	< 0.001	1.18 (1.06–1.32)	0.003	1.32 (1.21–1.45)	< 0.001
Current smoker	1.23 (1.12–1.35)	< 0.001	1.22 (1.07–1.41)	0.004	1.22 (1.08–1.39)	0.001
BMI>30 kg/m^2	1.25 (1.15–1.37)	< 0.001	1.22 (1.06–1.40)	0.005	1.28 (1.15–1.43)	< 0.001
Outcome of 7 or more hospital admissions						
Male sex	1.32 (1.22–1.42)	< 0.001				
Age per 10 years	1.75 (1.67–1.82)	< 0.001	1.94 (1.82–2.06)	< 0.001	1.58 (1.49–1.68)	< 0.001
Manual social class	1.22 (1.13–1.32)	< 0.001	1.21 (1.09–1.36)	< 0.001	1.23 (1.10–1.37)	< 0.001
Low education level	1.14 (1.05–1.24)	0.002	1.05 (0.93–1.18)	0.407	1.24 (1.11–1.39)	< 0.001
Current smoker	1.53 (1.37–1.70)	< 0.001	1.42 (1.21–1.66)	< 0.001	1.65 (1.41–1.91)	< 0.001
BMI>30 kg/m^2	1.41 (1.28–1.56)	< 0.001	1.43 (1.24–1.65)	< 0.001	1.39 (1.22–1.59)	< 0.001
Outcome of more than 20 hospital days						
Male sex	1.20 (1.12–1.28)	< 0.001				
Age per 10 years	2.54 (2.44–2.65)	< 0.001	2.70 (2.54–2.88)	< 0.001	2.41 (2.28–2.55)	< 0.001
Manual social class	1.20 (1.12–1.29)	< 0.001	1.23 (1.11–1.37)	< 0.001	1.17 (1.06–1.29)	0.003
Low education level	1.17 (1.09–1.26)	< 0.001	1.07 (0.96–1.19)	0.220	1.27 (1.15–1.40)	< 0.001
Current smoker	1.59 (1.44–1.77)	< 0.001	1.64 (1.41–1.89)	< 0.001	1.56 (1.35–1.80)	< 0.001
BMI>30 kg/m^2	1.54 (1.41–1.68)	< 0.001	1.52 (1.33–1.74)	< 0.001	1.56 (1.39–1.74)	< 0.001

Multivariable logistic regression. All models adjusted for age per 10 years, manual social class, low educational level, current smoker and BMI > 30 kg/m^2. All subject models additionally adjusted for female sex (no hospital admissions) and male sex (7 or more hospital admissions and > 20 hospital days)

Figure 4.2 illustrates the multivariable odds ratios of the 6 factors using the outcome of 20 or more hospital days over the 10-year follow-up. Odds ratios, displayed on a log scale, show strong independent associations for all the factors, with age having the strongest association.

Figure 4.2 | Multivariable odds ratios for demographic and behavioural factors having 20 or more hospital days over 10-year follow-up 1999–2009 in 25,014 men and women



Multivariable logistic regression adjusting for age, sex, manual social class, low educational attainment and BMI > 30kg/m²

The demographic and lifestyle factors were used to construct a risk score. Table 4.5 shows the absolute percentage and frequencies by risk score categories of no hospital admissions, 7 or more admissions and more than 20 hospital days. An increase in the absolute rate of admissions and hospital days across risk score categories was observed in all but the oldest age category. Conversely, the percentage not admitted to hospital over 10 years decreased over increasing risk score categories. In the participants <75 years similar increases in the absolute rates of admissions and hospital days were also observed with increasing risk score apart from the highest score categories, though the gradient attenuated with increasing age. Table 4.6 shows mortality rates over different time periods by age group and risk score. There was a mortality gradient by increasing risk score and the gradient was steeper for the shorter follow-up time. Sensitivity analyses (table 4.7) based only on individuals who were at the same postcode throughout the whole duration of this study showed similar results.

Table 4.5 | Absolute percentages and frequencies with no hospital admissions, ≥7 hospital admissions or >20 hospital days by risk score categories during follow-up 1999–2009 in 25,014 men and women 40–79 years in 1993–1997.

	0	1	2	3	4–5;
Outcome of no hospital admissions ***absolute percentage (n/N)***					
≤55 years	43 (913 / 2,112)	42 (1,445 / 3,425)	34 (862 / 2,537)	33 (365 / 1,107)	28 (62 / 222)
(55,65] years	32 (425 / 1,314)	28 (749 / 2,681)	22 (487 / 2,176)	19 (223 / 1,170)	16 (40 / 253)
(65,75] years	23 (229 / 994)	17 (377 / 2,241)	12 (244 / 2,008)	12 (130 / 1,099)	11 (25 / 235)
>75 years	13 (12 / 95)	11 (28 / 254)	13 (25 / 199)	11 (11 / 96)	0 (0 / 14)
Outcome of seven or more hospital admissions ***absolute percentage (n/N)***					
≤55 years	43 (114 / 2,112)	42 (203 / 3,425)	34 (238 / 2,537)	33 (124 / 1,107)	28 (33 / 222)
(55,65] years	32 (133 / 1,314)	28 (350 / 2,681)	22 (328 / 2,176)	19 (225 / 1,170)	16 (54 / 253)
(65,75] years	23 (141 / 994)	17 (427 / 2,241)	12 (452 / 2,008)	12 (294 / 1,099)	11 (73 / 235)
>75 years	13 (20 / 95)	11 (54 / 254)	13 (46 / 199)	11 (21 / 96)	0 (2 / 14)
Outcome of more than twenty hospital days ***absolute percentage (n/N)***					
≤55 years	43 (105 / 2,112)	42 (230 / 3,425)	34 (244 / 2,537)	33 (127 / 1,107)	28 (32 / 222)
(55,65] years	32 (173 / 1,314)	28 (439 / 2,681)	22 (397 / 2,176)	19 (289 / 1,170)	16 (76 / 253)
(65,75] years	23 (262 / 994)	17 (721 / 2,241)	12 (738 / 2,008)	12 (465 / 1,099)	11 (113 / 235)
>75 years	13 (43 / 95)	11 (127 / 254)	13 (102 / 199)	11 (53 / 96)	0 (6 / 14)

Risk score categorised as 0,1,2,3 and 4-5. The 4 and 5 were combined due to small numbers in category 5

Table 4.6 | Mortality rates by risk score and baseline age group for the 5 year recruitment period and 5 and 10 year periods used to examine hospitalisation outcome.

	0	1	2	3	4–5
Mortality rates 1993–1999, 1999–2004 and 1999–2009					
<55 years	1993–1999: 0.3 1999–2004: 1.2 1999–2009: 2.2	1993–1999: 0.6 1999–2004: 1.5 1999–2009: 3.1	1993–1999: 0.5 1999–2004: 2.1 1999–2009: 4.8	1993–1999: 0.7 1999–2004: 2.9 1999–2009: 6.5	1993–1999: 2.2 1999–2004: 4.4 1999–2009: 7.5
55,65 years	1993–1999: 1.0 1999–2004: 2.9 1999–2009: 7.6	1993–1999: 1.3 1999–2004: 4.7 1999–2009: 10.5	1993–1999: 1.2 1999–2004: 5.2 1999–2009: 11.5	1993–1999: 1.8 1999–2004: 6.8 1999–2009: 15.1	1993–1999: 4.2 1999–2004: 12.5 1999–2009: 22.3
65,75 years	1993–1999: 3.8 1999–2004: 8.3 1999–2009: 19.8	1993–1999: 5.1 1999–2004: 11.6 1999–2009: 27.8	1993–1999: 5.1 1999–2004: 13.4 1999–2009: 30.4	1993–1999: 8.0 1999–2004: 17.7 1999–2009: 37.1	1993–1999: 7.8 1999–2004: 25.1 1999–2009: 45.5
>75 years	1993–1999: 3.1 1999–2004: 19.4 1999–2009: 48.0	1993–1999: 3.8 1999–2004: 24.2 1999–2009: 51.5	1993–1999: 5.2 1999–2004: 30.5 1999–2009: 60.5	1993–1999: 20.0 1999–2004: 29.2 1999–2009: 46.7	1993–1999: 22.2 1999–2004: 33.3 1999–2009: 44.4

Risk score categorised as 0,1,2,3 and 4-5. The 4 and 5 were combined due to small numbers in category 5

Table 4.7 | Multivariable logistic regression of risk factors for no hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999 to 2009 in 19,861 men and women who remained at the same postcode over the follow-up period.

	All subjects OR (95% CI)	p value	Men OR (95% CI)	p value	Women OR (95% CI)	p value
Outcome of no hospital admissions						
Female sex	1.12 (1.04–1.20)	0.001				
Age per 10 years	0.53 (0.51–0.55)	< 0.001	0.46 (0.43–0.49)	< 0.001	0.60 (0.57–0.63)	< 0.001
Manual social class	1.26 (1.17–1.35)	< 0.001	1.33 (1.19–1.49)	< 0.001	1.20 (1.09–1.32)	< 0.001
Low education level	1.24 (1.15–1.34)	< 0.001	1.16 (1.02–1.32)	0.023	1.31 (1.19–1.45)	< 0.001
Current smoker	1.30 (1.17–1.45)	< 0.001	1.33 (1.13–1.56)	< 0.001	1.29 (1.12–1.49)	< 0.001
BMI>30 kg/m^2	1.28 (1.16–1.41)	< 0.001	1.30 (1.10–1.53)	0.002	1.27 (1.12–1.44)	< 0.001
Outcome of 7 or more hospital admissions						
Male sex	1.30 (1.19–1.41)	< 0.001				
Age per 10 years	1.76 (1.67–1.84)	< 0.001	1.96 (1.83–2.10)	< 0.001	1.58 (1.48–1.69)	< 0.001
Manual social class	1.21 (1.11–1.32)	< 0.001	1.18 (1.04–1.33)	0.011	1.24 (1.10–1.41)	< 0.001
Low education level	1.15 (1.05–1.26)	0.003	1.06 (0.93–1.21)	0.395	1.25 (1.10–1.41)	< 0.001
Current smoker	1.57 (1.39–1.78)	< 0.001	1.46 (1.22–1.74)	< 0.001	1.70 (1.43–2.00)	< 0.001
BMI>30 kg/m^2	1.46 (1.31–1.63)	< 0.001	1.46 (1.24–1.72)	< 0.001	1.45 (1.26–1.68)	< 0.001
Outcome of more than 20 hospital days						
Male sex	1.22 (1.13–1.31)	< 0.001				
Age per 10 years	2.58 (2.46–2.70)	< 0.001	2.79 (2.60–2.99)	< 0.001	2.41 (2.27–2.57)	< 0.001
Manual social class	1.21 (1.11–1.31)	< 0.001	1.21 (1.08–1.36)	0.001	1.20 (1.08–1.35)	0.001
Low education level	1.17 (1.08–1.27)	< 0.001	1.09 (0.96–1.23)	0.170	1.25 (1.12–1.40)	< 0.001
Current smoker	1.65 (1.47–1.85)	< 0.001	1.72 (1.45–2.03)	< 0.001	1.59 (1.35–1.86)	< 0.001
BMI>30 kg/m^2	1.57 (1.42–1.73)	< 0.001	1.60 (1.38–1.86)	< 0.001	1.54 (1.35–1.75)	< 0.001

Multivariable logistic regression. All models adjusted for age per 10 years, manual social class, low educational level, current smoker and BMI > 30 kg/m^2. All subject models additionally adjusted for female sex (no hospital admissions) and male sex (7 or more hospital admissions and > 20 hospital days)

4.6 Discussion

Our data report on hospital usage patterns measured either by the number of hospital admissions or by total hospital days, over a 10-year follow-up period in a population of middle-aged and older men and women in the UK. I observed that age, male sex, manual social class, low education level, current smoking and BMI >30kg/m^2 independently predicted multiple admissions and extended time in hospital. A simple five-point risk score constructed using male sex, manual social class, no educational qualifications, current smoking and BMI >30 kg/m^2, estimated percentages of the cohort in the categories of admission numbers and hospital days in stratified age bands with twofold to threefold differences in future hospital usage between those with high and low risk scores.

More than half of women under 55 years of age with a risk score of zero will expect one or more hospital admission over the next decade but only 5% would have ≥7 admissions or >20 days in hospital. Up to the age of 75 years the number of hospital admissions one might expect increases with the risk score. For those aged 55–65 years only 13% might expect to spend 20 days in hospital over the next 10 years but this increased to 30% for those with a risk score of four or five. 87% of men and women over 75 years would expect to be admitted to hospital on one or more occasions over 10 years irrespective of their risk score. While the trend for increasing hospital usage with risk score was not consistent in the oldest age group >75 with the highest risk score, numbers in this group were not large. Possible explanations include substantial differential mortality early on in follow-up resulting in attrition as observed in table 4.6 so that fewer individuals were at risk of hospital admissions and bed use over the full 10-year follow-up period.

4.6.1 Comparison with other studies

Most studies examining hospital usage in the UK are based on hospital data but are limited in their capacity to estimate accurately denominator populations or to assess characteristics prior to hospitalisation and how they may relate to relative or absolute risk of hospital usage prospectively [41,42,46,133,134].

The EPIC-Norfolk cohort was recruited from the general population resident in Norfolk and unlike hospital-based studies is able to compare characteristics of hospital attenders and those who did not need to use those services. The period under examination approximately coincides with administrative control by Primary Care Trusts (PCT, 2002–2013) with hospital usage free at the point of delivery under the UK NHS. Health service usage for study participants resident in the Norfolk area was the responsibility of the Norfolk PCT irrespective of where in the country the usage occurred. Linkage to the PCT had the advantage of capturing episodes at any UK hospital, not just those in the area. My study included data from several UK hospitals although the large majority were from Norfolk hospitals. I was able to estimate the probability of hospital admissions and duration over a 10-year period according to how they varied with a range of simple and easily measured demographic and behavioural characteristics generally available in general practice.

A limitation in my study is the lack of information about non-NHS hospitals and clinics where study participants paid for treatment. This would include common cosmetic procedures such as the removal of varicose veins and other procedures offered as a private service that may be restricted or not available on the NHS. Data on treatment in private hospitals or clinics were not available to us. It is possible that some of the associations I observed between those in higher social class groups and lower hospital usage are explained by private treatment. However, most serious long-term conditions are treated in NHS hospitals. The differences by sex and BMI I observed were independent of social class and education. It is also possible that individuals may have differentially moved away during follow-up. However, the sensitivity analyses table 4.7 based only on those individuals living in the same postcode observed essentially similar results.

The main focus of the study was not to examine the reason for admission and instead was restricted to the number of occasions when hospital services were used. The most common reasons for admission were related to diseases of the circulatory system (essential hypertension and chronic ischaemic heart disease being the most common) and diseases of the digestive system (the most common being gastritis, diaphragmatic hernia and diverticular disease). I have also not looked at the survival of those who did or did not use hospital services. Future exploration of these areas will help give us a clearer and more detailed understanding.

While it is not possible to infer causal links between the lifestyle factors and hospital admissions, differences in social class and education may reflect real differences in health status need or demand. Alternatively, thresholds for admission may vary.

In this study, I have identified a range of simple demographic and behavioural indicators that are related to the future probability of cumulative hospital admissions and hospital days. The strongest of these are increasing age and male sex. However, the modifiable factors examined are all strongly associated with hospital usage. Current cigarette smokers were 59% more likely to have more than 20 days in hospital while those with BMI >30 kg/m^2 are 54% more likely, indicating an important role of potentially modifiable factors for hospital usage. These and the other simple indicators I examined are easy to collect and may assist healthcare providers and those planning services to predict future hospital usage. Small differences in health behaviours appear to be associated with substantial differences in later hospitalisation but while potentially modifiable factors such as smoking and body mass index may predict future hospital usage, these factors are not entirely under the control of individuals. By attempting to understand the structural factors that influence behavioural change, it may be possible to mitigate the impact of future hospitalisation on individuals while also reducing levels expenditure in the health services.

4.7 Replication of earlier findings using the 10-year follow-up period at TP2, 2009–2019

4.7.1 Statistical analyses

Using a new baseline approximately 12 year after the first, hospital outcomes were examined by demographic and lifestyle factors measured on a subset of the main cohort who attended a health check between 2006–2011. Occupational social class was not remeasured but was assumed to be unchanged in a group who predominantly consisted of participants over 65 years, likely to be retired. Education was also not remeasured and assumed to be largely unchanged from childhood or early adulthood. Multiple imputation was used to address missing data for BMI, for participants who completed lifestyle questionnaires at TP2 but did not attend the clinic. Participants who died prior to 2009 were excluded and since there was some overlap between date of health check and the hospitalisation period, hospital events occurring prior to the TP2 heath check were not used.

Linkage to HES records for the follow-up period at TP2 used national disease databases held by NHS Digital and differed from the earlier local PCT-based linkage which was restricted to study participants resident in Norfolk. However, few participants relocated outside the Norfolk area over the period 1999–2009 and results were not materially different.

4.7.2 Results and conclusions

Table 4.8 shows descriptive characteristics of the TP2 cohort for men and women.

Table 4.8 | Descriptive characteristics in 9,722 men and women at TP2 2009–2019, by sex

	Total	Men (n=4,209 43.3%)	Women (n=5,513 56.7%)	P-value
Hospital activity 2009–2019				
No admissions	1,854 (19.1)	693 (16.5)	1,161 (21.1)	< 0.0001
One or more admissions	7,855 (80.9)	3,510 (83.5)	4,345 (78.9)	
Time in hospital 2009–2019				
Mean ±SD	17.5 ±36.0	19.2 ±37.2	16.3 ±35.1	< 0.0001
Mean ±SD	21.7 ±38.9	23.0 ±39.6	20.6 ±38.3	< 0.0001
Median (IQR)	5.0 (1.0 - 18.0)	6.0 (1.0 - 20.0)	4.0 (1.0 - 15.0)	< 0.0001
Median (IQR)	8.0 (3.0 - 24.0)	9.0 (3.0 - 26.0)	7.0 (2.0 - 22.0)	< 0.0001
Number of admissions 2009–2019				
Mean ±SD	4.4 ±7.9	4.8 ±8.3	4.1 ±7.6	< 0.0001
Median (IQR)	2.0 (1.0 - 5.0)	3.0 (1.0 - 6.0)	2.0 (1.0 - 5.0)	< 0.0001
Body mass index at TP2, kg/m²				
Mean ±SD	26.9 ±4.3	27.1 ±3.6	26.7 ±4.7	< 0.0001
Age at TP2, years				
Mean ±SD	69.4 ±8.4	69.9 ±8.4	69.0 ±8.5	< 0.0001
Age band at TP2 (n (%))				
≤55 years	340 (3.5)	139 (3.3)	201 (3.6)	< 0.0001
(55,65] years	3,061 (31.5)	1,213 (28.8)	1,848 (33.5)	

	Total	Men (n=4,209 43.3%)	Women (n=5,513 56.7%)	P-value
(65,75] years	3,652 (37.6)	1,614 (38.3)	2,038 (37.0)	
>75 years	2,669 (27.5)	1,243 (29.5)	1,426 (25.9)	
Cigarette smoking at TP2 (n (%))				
1	440 (4.5)	180 (4.3)	260 (4.7)	< 0.0001
2	4,460 (45.9)	2,465 (58.6)	1,995 (36.2)	
3	4,822 (49.6)	1,564 (37.2)	3,258 (59.1)	
Level of education (n (%))				
Higher level	6,963 (71.6)	3,222 (76.6)	3,741 (67.9)	< 0.0001
Lower level	2,757 (28.4)	986 (23.4)	1,771 (32.1)	
Body mass index at TP2 (n (%))				
≤24 kg/m²	2,429 (25.0)	738 (17.5)	1,691 (30.7)	< 0.0001
(24,27] kg/m²	3,092 (31.8)	1,529 (36.3)	1,563 (28.4)	
(27,30] kg/m²	2,326 (23.9)	1,192 (28.3)	1,134 (20.6)	
>30 kg/m²	1,875 (19.3)	750 (17.8)	1,125 (20.4)	

p-values use Fisher's exact test for proportions and Wilcoxon rank sum test for continuous values. Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

In table 4.9, multivariable logistic regression was used with outcomes of no hospital admissions, ≥7 admissions and >20 hospital days. Associations for age, cigarette smoking and body mass index were similar to those seen in the main study, but education level was attenuated and occupational social class was non-significant.

Table 4.9 | Multivariable logistic regression of risk factors for no hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 2009 to 2019 in 9,722 men and women.

	All subjects OR (95% CI)	p value	Men OR (95% CI)	p value	Women OR (95% CI)	p value
Outcome of no hospital admissions						
Female sex	1.32 (1.18–1.47)	< 0.001				
Age per 10 years	0.45 (0.42–0.48)	< 0.001	0.41 (0.36–0.45)	< 0.001	0.48 (0.44–0.53)	< 0.001
Manual social class	0.95 (0.85–1.07)	0.392	0.87 (0.72–1.04)	0.129	1.00 (0.86–1.16)	0.971
Low education level	1.29 (1.13–1.48)	< 0.001	1.35 (1.07–1.71)	0.011	1.27 (1.08–1.50)	0.003
Current smoker at TP2	1.25 (0.98–1.61)	0.084	1.64 (1.08–2.58)	0.026	1.08 (0.80–1.48)	0.608
BMI>30 kg/m^2 at TP2	1.48 (1.28–1.71)	< 0.001	1.47 (1.16–1.87)	0.002	1.49 (1.25–1.79)	< 0.001
Outcome of 7 or more hospital admissions						
Male sex	1.41 (1.27–1.57)	< 0.001				
Age per 10 years	1.63 (1.53–1.74)	< 0.001	1.71 (1.55–1.88)	< 0.001	1.56 (1.43–1.71)	< 0.001
Manual social class	1.05 (0.93–1.17)	0.428	1.02 (0.86–1.20)	0.840	1.08 (0.92–1.26)	0.358
Low education level	1.16 (1.02–1.30)	0.018	1.29 (1.08–1.54)	0.005	1.06 (0.90–1.24)	0.509
Current smoker at TP2	1.43 (1.11–1.82)	0.005	1.20 (0.81–1.74)	0.348	1.63 (1.17–2.23)	0.003
BMI>30 kg/m^2 at TP2	1.43 (1.26–1.62)	< 0.001	1.43 (1.19–1.72)	< 0.001	1.42 (1.20–1.69)	< 0.001
Outcome of more than 20 hospital days						
Male sex	1.20 (1.08–1.33)	< 0.001				
Age per 10 years	2.83 (2.65–3.03)	< 0.001	2.77 (2.50–3.06)	< 0.001	2.89 (2.64–3.17)	< 0.001
Manual social class	1.06 (0.94–1.18)	0.333	1.09 (0.92–1.28)	0.311	1.03 (0.88–1.20)	0.741
Low education level	1.14 (1.01–1.28)	0.028	1.33 (1.11–1.59)	0.002	1.02 (0.87–1.19)	0.819
Current smoker at TP2	1.53 (1.18–1.96)	< 0.001	1.57 (1.06–2.28)	0.020	1.50 (1.06–2.09)	0.019
BMI>30 kg/m^2 at TP2	1.55 (1.37–1.76)	< 0.001	1.64 (1.35–1.98)	< 0.001	1.49 (1.26–1.76)	< 0.001

Multivariable logistic regression. All models adjusted for age per 10 years, manual social class, low educational level, current smoker and BMI > 30 kg/m². All subject models additionally adjusted for female sex (no hospital admissions) and male sex (7 or more hospital admissions and > 20 hospital days)

In this older sub-cohort with mean age 69, the majority of participants were retired from their main occupation. There are a number of reasons why occupational social class no longer predicts subsequent hospital usage in this group. Participants with a manual social class may be more likely to use hospital services due to accident or injury at work. However, the majority of admissions recorded were for chronic disease and it is unlikely that accidents could account for the change alone. In retirement, there may be less disparity in income than for working age participants [136]. It is also possible that differential mortality in the cohort and a healthy volunteer effect reduced the heterogeneity of the participants at TP2.

4.8 Key points

What is already known on this subject

• Many observational studies have reported associations between age, body mass index and smoking status with hospital usage but most are based on data from people attending hospital or GP clinics and are therefore limited with respect to population denominators from the general population.

What this study adds

• I was able to estimate absolute rates of hospital usage by age and sex in a general community-based population of men and women in the National Health Service where care is free at the point of delivery.

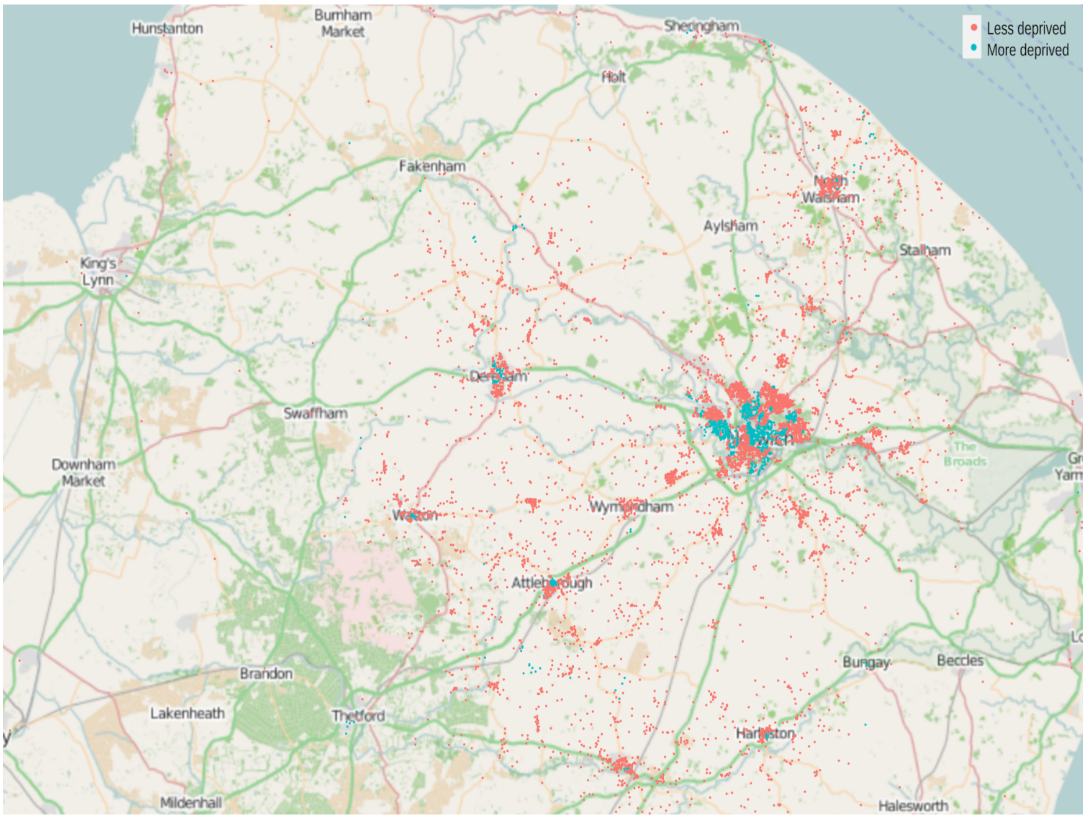
• Age was the strongest predictor of hospital usage. In addition, I observed strong independent associations between male sex, educational status, occupational social class, smoking and high body mass index. In particular, those with body mass index >30 kg/m^2 had a similar likelihood of >20 hospital days to current smokers.

5 Residential area deprivation and risk of subsequent hospital admission in a British population: the EPIC-Norfolk cohort

5.1 Overview

In this chapter, residential area deprivation using the Townsend Area Deprivation Index is examined. The Townsend Index and individual occupational social class discussed in the previous chapter are both measures of deprivation, but differ in a number of important respects. It is known that low social economic position is linked to higher rates of mortality and morbidity and that socioeconomic factors are reported to predict admission to hospital for many conditions. It is less clear if residential area deprivation index predicts hospital usage independently of individual social class and lifestyle factors. EPIC-Norfolk has both area-based census measures and individual social class and education level from questionnaires. The map below shows the location of participant postcodes by area deprivation category. Locations marked "less deprived" are below the national average while those marked "more deprived" are above the national average. Figure 5.1 shows a map of East Anglia which has points overlaid at participant postcode locations at the end of recruitment. The points are coloured red for postcodes in less deprived areas, with Townsend Index above the national average, while blue dots are shown for postcodes with Townsend Index below the national average.

Figure 5.1 | Location of participant postcode in Norfolk by deprivation category



Map tiles licensed under the Open Data Commons Open Database License (ODbL) by the OpenStreetMap Foundation (OSMF), copyright OpenStreetMap contributors

5.2 Abstract

Luben et al., BMJ Open, 2019

I investigated whether residential area deprivation index predicts subsequent admissions to hospital and time spent in hospital independently of individual social class and lifestyle factors using the European Prospective Investigation of Cancer in Norfolk. EPIC-Norfolk is a prospective population-based study of 11,214 men and 13,763 women in the general population, aged 40–79 years at recruitment (1993–1997), alive in 1999. The main outcome measure was total admissions to hospital and time spent in hospital during a 20-year time period (1999–2019).

Compared with those with residential Townsend Area Deprivation Index lower than the average for England and Wales, those with a higher than average deprivation index had a higher likelihood of spending more than twenty days in hospital multivariable-adjusted OR 1.17 (95% CI 1.07 to 1.28) and having 7 or more admissions OR 1.11 (95% CI 1.02 to 1.21) after adjustment for age, sex, smoking status, education, social class, and body mass index. Occupational social class and educational attainment modified the association between area deprivation and hospitalisation; those with manual social class and lower education level were at greater risk of hospitalisation when living in an area with higher deprivation index ($p_{interaction}$=0.02 and 0.01, respectively), while the risk for non-manual and more highly educated participants did not vary greatly by area of residence.

Residential area deprivation predicts future hospitalisations, time spent in hospital and number of admissions, independently of individual social class and education level and other behavioural factors. There are significant interactions such that residential area deprivation has greater impact in those with low education level or manual social class. Conversely, higher education level and social class mitigated the association of area deprivation with hospital usage.

5.3 Introduction

The considerable differences in mortality by social class are well documented [51,52,137,138] with those in higher social classes having a typical life expectancy several years longer than those with the lowest. Similarly, life expectancy and health expectancy vary between UK cities and regions with large variations in expected years of life in good health [139,140]. Despite increasing overall life expectancy, inequality remains with lower life and health expectancy observed more often in disadvantaged groups. While lifestyle factors may account for some part of this, the reported differences in death rates cannot be explained by individual behaviour alone [141,142]. Material deprivation was defined by Townsend as "a state of observable and demonstrable disadvantage relative to the local community or wider society … to which an individual, family or group belongs". Deprivation indices use factors such as unemployment, the standard of housing, overcrowding and rates of car ownership which together can assess the level of deprivation within a neighbourhood [143].

Hospitalisation can be measured using the frequency of admission or the length of stay. When measured in a community-based setting, such as EPIC-Norfolk, over a period of time, these two measures can be used to estimate the resources that might be required in the general population. Inequality in healthcare utilisation favouring patients who are better off is apparent in half of the OECD countries [144–146]. The UK National Health Service is free at the point of use and consequently should provide equitable healthcare not constrained by ability to pay. However, equity of access, while better than health systems in many countries, is not always consistent in the UK, and those in more deprived areas may find it harder to obtain the services they need than people who live in more affluent areas [147].

Socioeconomic predictors of hospitalisation have been examined using individual level exposures such as occupational social class, income and education and at area level using various deprivation indices, but few studies have both individual and area-based measures. Individual occupational social class, income and level of education have all been reported to be associated with chronic disease risk [148,149]. I previously reported that a range of simple demographic and behavioural indicators are related to the future probability of cumulative hospital admissions and duration [150]. Increasing age and male sex, the modifiable lifestyle factors current cigarette smoking and body mass index (BMI) >30 kg/m^2 and manual social class and low education level (albeit less frequently modified in middle-aged and older people) were all associated with higher future hospital usage over a 10-year period. Area-based deprivation measures, available routinely in the UK using postal code linkage, have also reported associations with hospital usage [130,151–154]. However, the participants in such studies are often limited to those attending hospital and so a suitable population denominator is lacking. Studies reporting health associations for both individual and area measures are less common [29,33,155] and I am unaware of any studies examining the independent association of residential area deprivation on subsequent hospital usage.

In this chapter, I examine residential area deprivation using the Townsend Area Deprivation Index (Townsend Index) with subsequent hospital usage over a 20-year period. I explore the independent contribution of residential area deprivation in men and women participants of the EPIC-Norfolk study and its association with future hospitalisation after allowing for the individual level factors previously shown to be associated. I also examine possible interactions between area and individual deprivation measures - social class and education. The aim is to assess whether factors such as material living conditions, poor quality housing and poor infrastructure are associated with subsequent hospitalisation in a setting where access to healthcare is unconstrained by ability to pay.

5.4 Methods

The data used was collected as part of the European Prospective Investigation of Cancer in Norfolk (EPIC-Norfolk), a general population cohort.

5.4.1 Statistical analysis

For the current analyses, I excluded the 625 men and women from the baseline cohort who died before 1999. A further 37 who did not have a valid UK postcode were excluded leaving 24,977 participants. Dichotomous variables were created for the three socioeconomic status variables. Occupational social class was categorised into non-manual and manual: social classes I, II, and III non-manual were classified as “non-manual”, while social classes III manual, IV, and V were classified as “manual”. Educational level was categorised into “Higher level” (which includes those with qualifications at secondary level or above) and “Lower level” (those with no qualifications). Townsend Index was divided into quintiles. Lower Townsend scores correspond to lower levels of deprivation. Quintiles 1–4 are all below zero and hence below (less deprived than) the national average for England and Wales. Quintile 5 (-0.64, 6.99] corresponds to Townsend scores close to or above the national average (more deprived). Overall Townsend score and components were also dichotomised with scores below zero defined as “less deprived” and scores above 0 as “more deprived”. Hospital admissions were categorised into five groups: 0, 1, 2–3, 4–6, and ≥7 while time in hospital was divided into categories: none, day case, 2–5 days, 6–20 days, and >20 days. The cutpoints were chosen to be consistent with earlier work [150]. Since time in hospital was skewed with some people remaining in hospital for extended periods, length of stay longer than 365 days was truncated for graphical presentation. A dichotomous urban/rural variable was defined with “urban” and “urban sparse” as urban and “town”, “village” or “hamlet” as rural. Three dichotomous outcome categories were calculated: any hospital admissions (vs no admissions), 7 or more admissions (vs fewer than 7) using total admissions and >20 hospital days (vs 20 or fewer) using total bed days (overnight stays) and day cases. Multivariable logistic regression was used for all models. All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria version 3.5.3 with packages knitr, Gmisc, ggplot2, tidyverse, intubate)

5.5 Results

Table 5.1 shows descriptive characteristics by quintiles of residential Townsend Index for 11,214 men and 13,763 women. The majority (n=20,996) of study participants had deprivation index below zero while n=3,981, approximately corresponding to those in quintile 5, had levels above the national average. Participants in quintile 5 were much more likely to live in an urban setting (70.2%) while those in quintiles 2, 3 and 4 were more likely to live in a rural location. Travel distance was lowest for participants in quintile 1 and 5, perhaps due to a higher proportion living in cities and travel times followed a similar pattern. Participants in quintile 5 were the most likely to move house (26.1% between 2000 and 2014). Hospital admissions and time in hospital are shown for both the full cohort and restricted to those who attended hospital; 9.9% of study participants had no admissions over the 20 years from 1999 to 2019.

Table 5.1 | Descriptive characteristics by quintiles of Townsend Area Deprivation Index in 24,977 men and women

	Total	Quintile 1 [-6.74,-3.81]	Quintile 2 (-3.81,-2.94]	Quintile 3 (-2.94,-2.09]	Quintile 4 (-2.09,-0.64]	Quintile 5 (-0.64, 6.99]	P-value
Sex (n (%))							
Men	11,214 (44.9)	2,271 (45.2)	2,262 (45.4)	2,280 (45.2)	2,226 (45.0)	2,175 (43.7)	0.41
Women	13,763 (55.1)	2,752 (54.8)	2,723 (54.6)	2,760 (54.8)	2,722 (55.0)	2,806 (56.3)	
Age, years							
Mean ±SD	59.0 ±9.3	58.8 ±9.0	59.0 ±9.2	58.8 ±9.2	59.2 ±9.4	59.4 ±9.5	0.002
Body mass index, kg/m²							
Mean ±SD	26.4 ±3.9	26.1 ±3.8	26.3 ±3.8	26.4 ±3.9	26.5 ±4.0	26.5 ±4.1	< 0.001
Cigarette smoking (n (%))							
Current	2,895 (11.7)	457 (9.2)	501 (10.1)	569 (11.4)	575 (11.7)	793 (16.1)	< 0.001
Former	10,411 (42.0)	2,033 (40.7)	2,083 (42.1)	2,044 (41.0)	2,132 (43.4)	2,119 (43.1)	
Never	11,453 (46.3)	2,502 (50.1)	2,361 (47.7)	2,378 (47.6)	2,203 (44.9)	2,009 (40.8)	
Social class dichotomised (n (%))							
Non-manual	14,691 (60.1)	3,336 (67.4)	3,170 (64.8)	2,950 (59.8)	2,840 (58.9)	2,395 (49.5)	< 0.001
Manual	9,741 (39.9)	1,610 (32.6)	1,722 (35.2)	1,985 (40.2)	1,982 (41.1)	2,442 (50.5)	
Level of education (n (%))							
Higher level	15,841 (63.5)	3,439 (68.5)	3,373 (67.7)	3,218 (63.9)	3,084 (62.4)	2,727 (54.8)	< 0.001
Lower level	9,118 (36.5)	1,584 (31.5)	1,611 (32.3)	1,819 (36.1)	1,858 (37.6)	2,246 (45.2)	
Travel distance to hospital, km							
Mean ±SD	20.4 ±13.1	16.5 ±11.3	20.6 ±12.1	22.0 ±12.2	25.2 ±13.2	17.5 ±14.5	< 0.001
Travel time to hospital, minutes							
Mean ±SD	20.8 ±10.3	18.0 ±8.9	20.8 ±9.5	21.9 ±9.4	24.4 ±10.6	19.0 ±11.6	< 0.001
Urban or rural location (n (%))							
Urban	11,214 (44.9)	2,500 (49.8)	1,832 (36.8)	1,810 (35.9)	1,575 (31.8)	3,497 (70.2)	< 0.001
Rural	13,763 (55.1)	2,523 (50.2)	3,153 (63.2)	3,230 (64.1)	3,373 (68.2)	1,484 (29.8)	
Moved house between 2000 and 2014 (n (%))							
Moved house	5,355 (22.2)	963 (19.8)	972 (20.4)	1,091 (22.4)	1,060 (22.4)	1,269 (26.1)	< 0.001
Did not move house	18,728 (77.8)	3,903 (80.2)	3,799 (79.6)	3,774 (77.6)	3,662 (77.6)	3,590 (73.9)	
Deaths prior to March 2019 (n (%))							
Dead	9,038 (36.3)	1,691 (33.7)	1,774 (35.7)	1,768 (35.1)	1,839 (37.3)	1,966 (39.6)	< 0.001
Alive	15,887 (63.7)	3,325 (66.3)	3,200 (64.3)	3,262 (64.9)	3,097 (62.7)	3,003 (60.4)	
Hospital activity 1999-2019							
No admissions	2,471 (9.9)	510 (10.2)	504 (10.1)	502 (10.0)	522 (10.6)	433 (8.7)	0.023
One or more admissions	22,473 (90.1)	4,509 (89.8)	4,473 (89.9)	4,531 (90.0)	4,420 (89.4)	4,540 (91.3)	
7 or more admissions	16,102 (64.6)	3,340 (66.5)	3,220 (64.7)	3,256 (64.7)	3,197 (64.7)	3,089 (62.1)	< 0.001
>20 hospital days	14,780 (59.3)	3,114 (62.0)	2,975 (59.8)	3,027 (60.1)	2,882 (58.3)	2,782 (55.9)	< 0.001
Time spent in hospital 1999-2019, days							
Full cohort 1999-2019, mean ±SD	34.0 ±63.7	31.5 ±55.8	34.2 ±69.5	32.4 ±57.9	33.5 ±63.3	38.3 ±70.7	< 0.001
Hospital attenders 1999-2019, mean ±SD	37.7 ±66.1	35.1 ±57.8	38.0 ±72.3	35.9 ±60.0	37.5 ±65.8	42.0 ±73.0	< 0.001
Number of inpatient admissions 1999-2019							
Full cohort 1999-2019, mean ±SD	7.8 ±26.5	7.6 ±23.7	8.4 ±36.1	7.9 ±30.9	6.9 ±11.9	7.9 ±23.4	0.079
Hospital attenders 1999-2019, mean ±SD	8.6 ±27.8	8.5 ±24.9	9.4 ±38.0	8.8 ±32.5	7.8 ±12.3	8.7 ±24.3	0.099

p-values use Fisher's exact test for proportions and Wilcoxon rank sum test for continuous values. Round brackets in intervals denote strict inequalities (> or <); square brackets denote non-strict inequalities (≥ or ≤)

Table 5.2 shows the multivariable logistic regression for quintiles of Townsend Index and three outcomes: any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay between 1999 and 2019. Model 1 is adjusted for age and sex while model 2 is additionally adjusted for manual social class, lower education level, current cigarette smoking and BMI >30 kg/m^2. Additionally, each model is repeated in the subset of participants who survived to the end of the follow-up period. Compared with those with Townsend Index quintiles 1 to 4 (lower than the average for England and

Wales), those with a deprivation index in quintile 5 had a higher risk of spending more than 20 days in hospital multivariable-adjusted odds ratio (OR) 1.17 (95% confidence interval (CI) 1.07–1.28) and for 7 or more hospital admissions OR 1.11 (95% CI 1.02–1.21). There was no association for the outcome of any (1 or more) hospital admissions, compared with those who had no admissions over the period. The multivariable regression models only modestly attenuated the area deprivation associations. The multivariable-adjusted p value for trend across quintiles of Townsend Index was 0.002 for more than 20 hospital days and 0.084 for 7 or more admissions. Associations in the subset of participants surviving to March 2019 (n=15,889) were higher than those for the full cohort.

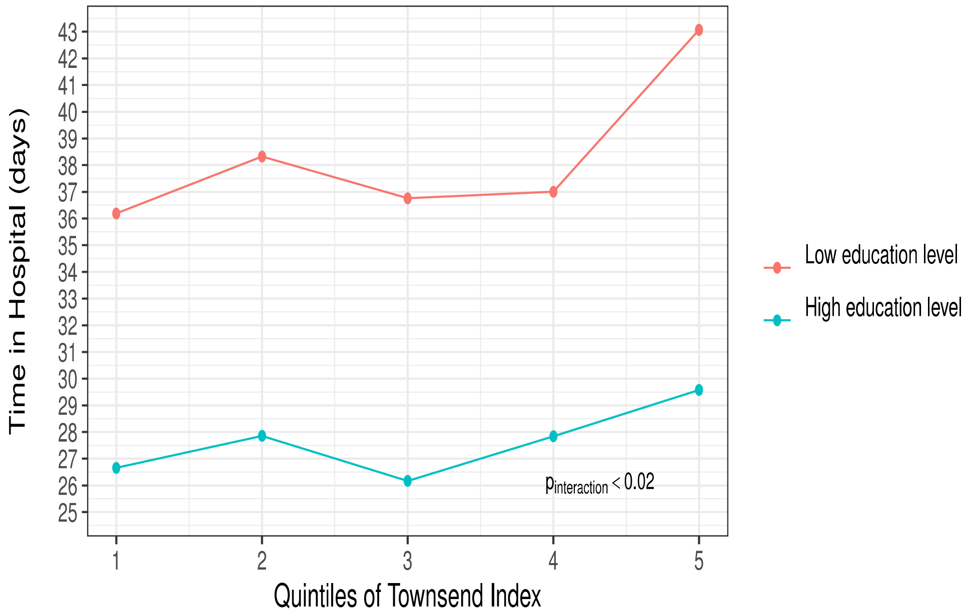
Table 5.2 | Multivariable logistic regression of risk factors by quintiles of Townsend Index for any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999 to 2019 in 24,977 men and women and in a subset of 15,889 men and women alive in March 2019)

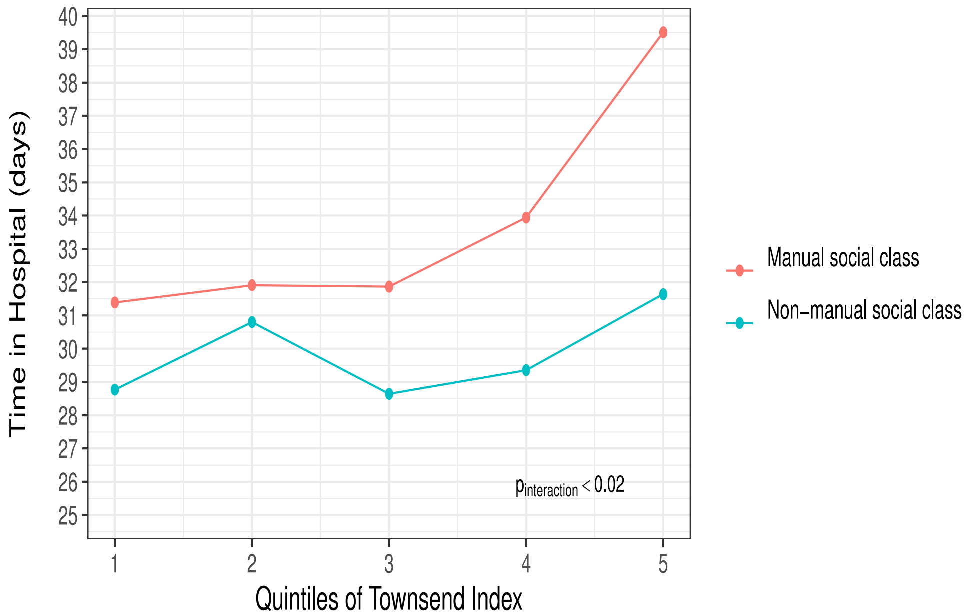
	Quintile 1 [-6.74,-3.81]	Quintile 2 (-3.81,-2.94]	Quintile 3 (-2.94,-2.09]	Quintile 4 (-2.09,-0.64]	Quintile 5 (-0.64, 6.99]	p (trend)
Outcome of any hospital admissions						
Model 1	1.00	1.00 (0.87–1.14)	1.02 (0.90–1.17)	0.93 (0.82–1.07)	1.16 (1.01–1.33)	0.156
Model 1†	1.00	1.02 (0.89–1.18)	1.04 (0.90–1.20)	0.96 (0.83–1.11)	1.25 (1.08–1.46)	0.036
Model 2	1.00	0.98 (0.86–1.12)	1.01 (0.88–1.15)	0.91 (0.79–1.04)	1.08 (0.94–1.25)	0.704
Model 2†	1.00	1.02 (0.88–1.18)	1.02 (0.88–1.18)	0.92 (0.80–1.07)	1.18 (1.01–1.37)	0.266
Outcome of 7 or more hospital admissions						
Model 1	1.00	1.08 (0.99–1.17)	1.09 (1.00–1.18)	1.07 (0.98–1.16)	1.19 (1.10–1.30)	< 0.001
Model 1†	1.00	1.05 (0.93–1.17)	1.16 (1.04–1.29)	1.18 (1.06–1.32)	1.39 (1.25–1.56)	< 0.001
Model 2	1.00	1.06 (0.98–1.16)	1.05 (0.96–1.14)	1.02 (0.94–1.12)	1.11 (1.02–1.21)	0.084
Model 2†	1.00	1.04 (0.92–1.16)	1.12 (1.00–1.25)	1.13 (1.00–1.26)	1.28 (1.15–1.44)	< 0.001
Outcome of more than 20 hospital days						
Model 1	1.00	1.10 (1.01–1.20)	1.09 (1.00–1.19)	1.15 (1.05–1.25)	1.27 (1.16–1.38)	< 0.001
Model 1†	1.00	1.07 (0.94–1.21)	1.14 (1.01–1.29)	1.24 (1.10–1.41)	1.44 (1.28–1.63)	< 0.001
Model 2	1.00	1.09 (0.99–1.19)	1.05 (0.96–1.15)	1.10 (1.01–1.20)	1.17 (1.07–1.28)	0.002
Model 2†	1.00	1.05 (0.93–1.19)	1.09 (0.96–1.23)	1.18 (1.04–1.34)	1.33 (1.17–1.50)	< 0.001

Model 1: Adjusted for age and sex. Model 2: Adjusted for age, sex, manual social class, low education, current cigarette smoker, body mass index > 30kg/m^2 † Excluding participants who died prior to April 2019

Figure 5.2 shows graphs of length of hospital stay by quintiles of Townsend Index and demonstrates the disparity between individual socioeconomic factors and hospital stay, after multivariable adjustment, when area deprivation index is also considered. In the first plot, results are stratified by higher and lower educational attainment. The difference in days between the least deprived (quintile 1) and the most deprived (quintile 5) is 6 days for those with lower educational attainment and 3 days for those with higher educational attainment. The second plot shows results stratified by manual and non-manual social class. The difference in days between the least deprived and the most deprived is 8 days for those with a manual social class and 3 days for those with a non-manual social class. Significant interactions were observed between social class, level of education and Townsend Index ($p_{interaction}$=0.0187 and 0.0119, respectively).

Figure 5.2 | Time spent in hospital 1999-2019, for 24,977 men and women, by quintiles of Townsend Area Deprivation Index, stratified by education level (high/low, first graph) and social class (manual/non-manual, second graph)





Length of hospital stay over 20 years of follow-up by quintiles of Townsend Index grouped by categories of education level and categories of social class. Low education level is defined as those having no qualifications and high education as those with at least some qualifications at secondary level or above. Length of stay is truncated to 365 days for those staying longer than 365 days. Interaction tested using multivariable adjusted linear regression with covariables age, sex, education level (higher/lower), body mass index (≤30/>30) smoking status (current/non-current)

Table 5.3 shows the multivariable logistic regression for risk factors for outcomes of any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay between 1999 and 2018. Models are presented for all participants, men and women and each risk factor is adjusted for all others for the nine models. Male sex is only included in the models for all participants. As well as age, social class, education and body mass index, the four individual components of Townsend Index are modelled. As previously reported, age, male sex, lower education level, manual social class, current cigarette smoking and a body mass index >30 kg/m^2 were all associated with increased hospitalisation. No single component of the Townsend Index was more strongly associated for all outcomes for both men and women. However, the unemployment component was associated with seven or more hospital admissions. Areas with low car ownership appeared to have a greater association in women than men.

Table 5.3 | Multivariable logistic regression of risk factors for any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999 to 2019 in 24,977 men and women. Townsend Index components using the UK 1991 census

	All subjects OR (95% CI)	p value	Men OR (95% CI)	p value	Women OR (95% CI)	p value
Outcome of any hospital admissions						
Male sex	1.13 (1.04–1.24)	0.006				
Age per 10 years	2.05 (1.95–2.17)	< 0.001	2.13 (1.96–2.31)	< 0.001	2.00 (1.86–2.14)	< 0.001
Unemployment Z-Score >0	1.02 (0.89–1.18)	0.739	1.05 (0.85–1.30)	0.651	1.00 (0.83–1.20)	0.993
Households with no car Z-Score >0	1.03 (0.88–1.21)	0.730	0.92 (0.72–1.17)	0.491	1.12 (0.91–1.40)	0.294
Households not owner-occupied Z-Score >0	1.06 (0.93–1.23)	0.386	1.02 (0.83–1.27)	0.856	1.10 (0.92–1.33)	0.311
Household overcrowding Z-Score >0	0.98 (0.88–1.11)	0.784	1.03 (0.86–1.23)	0.765	0.95 (0.82–1.11)	0.548
Manual social class	1.15 (1.05–1.27)	0.004	1.19 (1.04–1.38)	0.015	1.12 (0.99–1.27)	0.076
Low education level	1.41 (1.27–1.57)	< 0.001	1.23 (1.04–1.47)	0.017	1.53 (1.34–1.76)	< 0.001
Current smoker	1.17 (1.03–1.35)	0.021	1.15 (0.94–1.42)	0.180	1.20 (1.00–1.44)	0.056
BMI>30 kg/m^2	1.28 (1.12–1.46)	< 0.001	1.17 (0.96–1.45)	0.133	1.35 (1.14–1.61)	< 0.001
Outcome of 7 or more hospital admissions						
Male sex	1.21 (1.15–1.28)	< 0.001				
Age per 10 years	1.45 (1.41–1.50)	< 0.001	1.45 (1.38–1.51)	< 0.001	1.46 (1.40–1.52)	< 0.001
Unemployment Z-Score >0	1.16 (1.07–1.26)	< 0.001	1.16 (1.03–1.32)	0.015	1.16 (1.04–1.30)	0.010
Households with no car Z-Score >0	0.96 (0.87–1.06)	0.438	0.88 (0.76–1.02)	0.095	1.03 (0.90–1.18)	0.651
Households not owner-occupied Z-Score >0	0.95 (0.87–1.04)	0.245	0.95 (0.84–1.08)	0.430	0.95 (0.84–1.07)	0.383
Household overcrowding Z-Score >0	1.09 (1.01–1.17)	0.026	1.06 (0.96–1.18)	0.258	1.11 (1.00–1.22)	0.046
Manual social class	1.15 (1.08–1.22)	< 0.001	1.15 (1.06–1.25)	0.001	1.15 (1.06–1.25)	< 0.001
Low education level	1.13 (1.07–1.20)	< 0.001	1.12 (1.03–1.23)	0.012	1.14 (1.05–1.23)	0.002
Current smoker	1.33 (1.22–1.44)	< 0.001	1.25 (1.11–1.41)	< 0.001	1.40 (1.25–1.57)	< 0.001
BMI>30 kg/m^2	1.39 (1.29–1.49)	< 0.001	1.39 (1.24–1.56)	< 0.001	1.38 (1.25–1.52)	< 0.001
Outcome of more than 20 hospital days						
Male sex	1.15 (1.08–1.22)	< 0.001				
Age per 10 years	2.64 (2.55–2.73)	< 0.001	2.55 (2.43–2.69)	< 0.001	2.71 (2.59–2.84)	< 0.001
Unemployment Z-Score >0	1.12 (1.02–1.22)	0.014	1.13 (0.99–1.28)	0.069	1.11 (0.98–1.25)	0.096
Households with no car Z-Score >0	0.99 (0.89–1.09)	0.778	0.92 (0.79–1.07)	0.277	1.04 (0.91–1.19)	0.577
Households not owner-occupied Z-Score >0	1.00 (0.91–1.09)	0.969	1.01 (0.88–1.15)	0.893	0.99 (0.87–1.12)	0.840
Household overcrowding Z-Score >0	1.08 (1.00–1.17)	0.049	1.04 (0.93–1.17)	0.480	1.11 (1.00–1.24)	0.041
Manual social class	1.17 (1.10–1.24)	< 0.001	1.19 (1.09–1.30)	< 0.001	1.16 (1.07–1.26)	< 0.001
Low education level	1.16 (1.09–1.23)	< 0.001	1.18 (1.08–1.30)	< 0.001	1.13 (1.04–1.23)	0.003
Current smoker	1.55 (1.42–1.69)	< 0.001	1.54 (1.35–1.75)	< 0.001	1.56 (1.38–1.76)	< 0.001
BMI>30 kg/m^2	1.59 (1.47–1.72)	< 0.001	1.56 (1.38–1.76)	< 0.001	1.62 (1.46–1.79)	< 0.001

Table 5.4 displays logistic regression models for the outcome of >20 hospital days for Townsend Index in various subgroups. Models are stratified by a dichotomised subgroup: men and women, age above or below 65 years, manual and non-manual social class, lower or higher education level, smoking status, BMI above and below 30 kg/m^2, urban or rural home postcode, and moved house between the year 2000 and 2014. ORs within all strata were in consistent directions with no interaction by age, smoking status or BMI.

Table 5.4 | Multivariable logistic regression of Townsend Index and more than twenty hospital days in subgroups

	Townsend Index OR (95% CI)†
Men and women	
Men (n=11214)	1.01 (0.99–1.03)
Women (n=13763)	1.03 (1.01–1.05)
By age above and below 65 years	
Less than 65 years (n=17343)	1.03 (1.01–1.05)
65 years and above (n=7634)	1.01 (0.98–1.03)
Manual and non-manual social class	
Non-manual (n=14691)	1.02 (1.00–1.03)
Manual (n=9741)	1.03 (1.01–1.05)
By level of education	
Higher level (n=15841)	1.01 (0.99–1.03)
Lower level (n=9118)	1.04 (1.02–1.06)
By smoking status	
Former or never smoker (n=21864)	1.02 (1.01–1.04)
Current smoker (n=2895)	1.01 (0.97–1.04)
By level of body mass index	
BMI ≤ 30 kg/m^2 (n=21124)	1.02 (1.01–1.04)
BMI > 30 kg/m^2 (n=3800)	1.01 (0.97–1.04)
Urban or rural home postcode	
Urban (n=11214)	1.02 (1.00–1.03)
Rural (n=13763)	1.03 (1.00–1.05)
Moved house between 2000 and 2014	
Moved house (n=5355)	1.04 (1.01–1.07)
Did not move house (n=18728)	1.01 (1.00–1.03)

Logistic regression per unit Townsend Index. † Adjusted for age, current smoking, BMI (categories)

The numbers of individuals with missing values for covariates were: 53 BMI, 218 smoking status, 545 social class, 18 education level.

5.6 Discussion

Residential area deprivation was associated with future hospital usage independently of individual sociodemographic factors, in particular age, sex, social class and education as well as lifestyle factors including smoking and BMI in this cohort of middle-aged and older men and women. Study participants in the highest fifth of the Townsend Index — those living in the most deprived areas, at or below the national average, were more likely to spend >20 days in hospital or be admitted to hospital on ≥7 occasions. There were also significant interactions between residential area deprivation and individual social class and education level. Participants with a manual social class living in an area with higher deprivation index spent longer in hospital than those with manual occupations living in less deprived areas. Similarly, those with lower education level living in more deprived areas had the greatest risk of hospitalisation. This suggests that hospitalisation is greatest when those with poorer individual socioeconomic factors are combined with residential deprivation. I considered a number of possible explanations for these findings, which are described below.

5.6.1 Strengths and limitations of the study

The EPIC-Norfolk cohort is very well characterised. This enabled us to take into account many potentially confounding variables understood to be related to hospital usage and disease. The UK National Health Service is free at the point of use and consequently income has less influence on hospital admissions when compared with health systems in other countries, although it may influence hospital usage in the UK indirectly through loss of pay or transport costs. Despite this, social class, education and residential deprivation were all independently related to hospital usage. My study examines hospital activity using a prospective cohort design in a population of community-dwelling participants with clearly defined population denominators. It uses a large cohort of middle-aged and older men and women with 20 years of follow-up time having both area-based census measures and individual social class and education level from questionnaires available.

Townsend Area Deprivation Index is associated with individual sociodemographic factors such as occupational social class and education and other factors including age, sex and BMI. Since all these factors are also related to hospital usage, some level of confounding will be present. However, multivariable regression models adjusting for all these variables only modestly attenuated the area deprivation associations. In table 5.4, I stratified by the main confounders and the results remained consistent in the subgroups. The accuracy of the measurement might not be sufficient to ensure adequate adjustment, so I cannot exclude the possibility of residual confounding with known or other unknown factors associated with both Townsend Index and hospital usage. These unknown factors may either attenuate or strengthen the associations. Interactions between area deprivation and individual sociodemographic factors highlighted stronger associations among more deprived groups.

The use of area-based measurements has some limitations. The factors used in the Townsend score may vary in their ability to assess deprivation according to setting. In urban areas, lower car ownership rates may reflect the availability of other transport options and closer proximity of work places and facilities such as shops. In rural areas, overcrowding may be less common while car ownership may be more of a necessity while simultaneously a drain on resources [156–158]. The deprivation index is based on data from the UK census that only takes place every 10 years and over the period under examination, areas may change becoming more or less deprived.

Area deprivation was determined by postcode of residence in the year 2000. Study participants who moved house may have been misclassified for some of the period over which hospitalisation was assessed. However, while 22% of the cohort moved house between the years 2000 and 2014, the large majority of participants relocated locally in Norfolk, with others moving elsewhere in England. Since the Townsend Index was not measured at enumeration district level in the UK census beyond 1991, no directly comparable measure was available at later time points to examine change. However, a sensitivity analysis of non-movers found very similar results to the main analyses and any misclassification due to moves or changes over time in residential area deprivation scoring and resultant measurement error would only be likely to attenuate associations with the residential area score. HES records were available for participants who relocated within England and hence there was virtually no loss to follow-up.

Differential misclassification in hospital usage may be explained by early death rates. Study participants living in more deprived areas may have died earlier and not used hospital services for the full period. However, while the death rate was higher among those living in the most deprived areas, 64% of the cohort survived beyond 2019 and models restricted to survivors were more strongly associated with outcome measures than those in the main analysis. Sociodemographic factors may be less relevant for the very seriously ill who require hospital treatment at the end of life.

It may also be possible that individuals did not use NHS facilities but private hospitals differently by socioeconomic status which might explain lower use in the higher sociodemographic groups. However, the use of private hospitals in the Norfolk area over this time period was minimal [1] and hence record linkage of routinely collected hospital episode data gave virtually complete ascertainment. Reverse causation is also possible whereby those in poor health at recruitment may have lower occupational social class increasing the chance of them living in a more deprived area. However, hospitalisation rates were low in the period directly after recruitment.

5.6.2 Comparison with other studies

Inequality in healthcare favouring the better off has been observed in many countries [144–146] and healthcare insurance and eligibility for government healthcare based on income thresholds may influence the associations observed. NHS healthcare is not constrained by ability to pay and hence I was able to examine the independent association of residential area deprivation — material living conditions, poor quality housing and poor infrastructure — and its association with subsequent hospitalisation. The Commonwealth Fund, which assesses the medical care system in 11 high income countries, regularly scores the NHS highest on equity of access to care and it ranks first overall [159]. However, Julian Tudor Hart's inverse care law paper still has contemporary relevance [147]. Tudor Hart stated that "medical services are not the main determinant of mortality or morbidity; these depend most upon standards of nutrition, housing, working environment, and education, and the presence or absence of war.". He believed that the inverse care law is mainly attributed to operation of the market for medical care — something which the creation of the NHS helped to counteract. However, equity of access remains inconsistent, with people in some parts of the UK, generally the more deprived areas, finding it harder to obtain the services they need than people who live elsewhere, generally the more affluent areas.

There is some evidence to suggest that travel time is associated with hospital usage [160,161] but there was no strong association in this study. Study participants were approximately evenly divided into those living in urban and those in rural areas. The moderately deprived (those with Townsend quintile 2-4) were more likely to live in rural areas while the most deprived (Townsend quintile 5) were predominantly urban dwellers. Study participants in Townsend quintiles 1 and 5 were closer by road from their home to the Norfolk and Norwich hospital but the time taken for the journey did not vary greatly. Neither distance from hospital nor urban or rural location explained my findings, since those in the lowest deprivation areas are mainly urban with the shortest travel time to hospital. Studies examining urban/rural populations and car ownership have noted differences in deprivation characteristics [156,157]. However, irrespective of travel distance or time, owning or having access to a car would make a considerable difference in being able to access local facilities. Although there may be more regular public transport services in cities, this will vary and cost and limited travel options may restrict access not only to hospital but also to friends and relatives, to better quality supermarkets and to parks and recreational facilities [111,162–165].

Most studies examining deprivation in the context of health, disease and mortality either rely on area-based measures collected, for example, from census data [130,151–154] or from individual level data from questionnaires [148,149]. I had access to both forms of information, having derived individual social class and education level from self-reported questionnaires and area level measures from residential postcode linkage. Hospital-based studies using patients as study participants do not have a reliable population-based denominator and cannot estimate overall risk in the population. Studies often attempt to define a denominator using separate population estimates while not individually linking [129,151,166]. I was able to examine hospital usage over 20 years in a clearly defined community-based population using a prospective cohort design.

Norfolk is an area of generally low deprivation with >80% of the study population living in areas with deprivation levels below the national average. Few participants live in areas of high deprivation such as those found in some larger cities in other parts of the country. Those living in more deprived cities or regions have a socioeconomic gradient in hospital usage more extreme than I was able to observe [163] but while my study does not provide any information on the most extreme forms of deprivation, there was sufficient heterogeneity to observe large differences in hospital usage.

Our results provide further evidence adding to the substantial literature linking deprivation to health. Unlike many studies, I used overall measures of hospital activity, including both elective and emergency admissions and found evidence of an independent association of residential area deprivation not accounted for by known individual factors such as social class and education. My results also demonstrate that the combination of residential area deprivation with lower levels of education or manual social class result in the highest levels of hospitalisation.

The report "Health Equity in England: The Marmot Review 10 years on" [54], published in 2020, noted that increases in life expectancy have slowed since 2010 with the slowdown greatest in more deprived areas of the country. It recommended policies to reduce both health inequalities and mitigate climate change, by improving active travel, green spaces, the food environment, transport and the energy efficiency of housing, across the social gradient. The 1998 Acheson report "Inequalities in Health" [52] made several recommendations regarding education, housing and transport and policies to promote the material well being of older people. The Black report [51] concluded that health inequalities were not mainly attributable to failings in the NHS, but rather to many other social inequalities influencing health: income, education, housing, diet, employment, and conditions of work. It suggested two mechanisms for how social risk factors influence health: cultural/behavioural and materialist/structuralist. Some authors have pointed out that research on the predictors of health are generally focused on the individual, but patterns of population health are unclear without examining structural risk factors at the societal level [167]. Townsend's residential deprivation index uses aggregate measures of particular characteristics for people living in an area. It has been used mainly as a surrogate for individual measures of deprivation in many studies [155]. I was not able to examine physical features of the environment in this study. Ecological measurements such as the quality of housing, access to recreational facilities, local services provided, community support and levels of crime may affect health and hospital usage. However, I was able to examine both individual and area level deprivation in the same study participants, and the interaction I observed suggests that there is a higher risk of hospitalisation in more deprived areas of residence disproportionately for those with lower individual social class and education. Conversely, individuals with non-manual social class and higher levels of education appear more resilient to hospitalisation irrespective of the level of deprivation of their residence.

5.7 Conclusions and policy implications

There is a socioeconomic gradient in hospital usage for factors measured both individually and at area level. Residential area deprivation predicts future hospitalisations, time spent in hospital and number of admissions, independently of individual social class and education level and other behavioural factors. There are significant interactions such that residential area deprivation has greater impact in those with low education level or manual social class. Conversely, higher education level and social class mitigated the association of area deprivation with hospital usage. Effective NHS and government policy should therefore involve addressing deprivation both at the individual and infrastructural levels to identify and target those most at risk within the community. There is evidence that interventions, such as the English health inequalities strategy, can reduce geographical health inequalities in life expectancy [168]. NHS policies focused on reducing health inequalities in older people need to work alongside wider government initiatives to improve the quality of housing, transport and infrastructure and access to recreation and green space.

5.8 Key points

What is already known on this subject

• Low social economic position is linked to higher rates of mortality and morbidity. Socioeconomic factors are reported to predict admission to hospital for many conditions. It is less clear if residential area deprivation index predicts hospital usage independently of individual social class and lifestyle factors.

What this study adds

• I observed an association of residential deprivation independent of individual social class and education with subsequent hospital usage in NHS hospitals over 20 years of follow-up using a well characterised and clearly defined population denominator.

• Additionally, I observed an interaction suggesting that residential deprivation was associated with longer or more frequent hospitalisation in those in manual social classes and with low education levels.

6 Alcohol consumption and future hospital usage

6.1 Overview

The chapter describes the relationship between current alcohol consumption in the EPIC-Norfolk cohort and the participants' subsequent hospital usage over a period of 10 years. The results are somewhat unexpected in the light of current beliefs about alcohol intake in the general population and hospital usage. The many diseases related to the high consumption of alcohol would lead one to expect a positive association between hospital usage and alcohol intake. However, cardiovascular disease is a predominant reason for hospital admissions in EPIC-Norfolk and my results might reflect the balance between positive and negative health effects in an older cohort of moderate drinkers. Evidence from a substantial number of observational studies has suggested there is a non-linear J-shaped association of alcohol with all-cause mortality and cardiovascular diseases. However, some recent studies using techniques such as Mendelian Randomisation, have not identified these inverse associations and suggested the findings in the earlier literature were as a result of well known biases. To further examine this issue data modelled using alternative reference groups is presented and the conclusions also acknowledge that the associations observed may in part be due to the choice of reference group. By examining both current non-drinkers and those who never consumed alcohol, I was able to investigate associations using different reference groups and explore various commonly reported biases.

6.2 Abstract

Luben et al., PLOS ONE, 2018

Heavy drinkers of alcohol are reported to use hospitals more than non-drinkers, but it is unclear whether light-to-moderate drinkers use hospitals more than non-drinkers. I examined the relationship between alcohol consumption and subsequent admissions to hospital and time spent in hospital. Participants from the EPIC-Norfolk prospective population-based study were followed for 10 years (1999–2009) using record linkage.

Compared with current non-drinkers, men who reported any alcohol drinking had a lower risk of spending more than twenty days in hospital after adjusting for age, smoking status, education, social class, body mass index and prevalent diseases. Women who were current drinkers were less likely to have any hospital admissions, seven or more admissions or more than twenty hospital days. However, compared with lifelong abstainers, men who were former drinkers had higher risk of any hospital admissions and women former drinkers had higher risk of seven or more admissions.

Current alcohol consumption was associated with lower risk of future hospital usage compared with non-drinkers in this middle-aged and older population. In men, this association may in part be due to whether former drinkers are included in the non-drinker reference group but in women, the association was consistent irrespective of the choice of reference group. In addition, there were few participants in this cohort with very high current alcohol intake (>30 units per week). The measurement of past drinking, the separation of non-drinkers into former drinkers and lifelong abstainers and the choice of reference group are all influential in interpreting the risk of alcohol consumption on future hospitalisation.

6.3 Introduction

Alcohol misuse and its consequences continue to have a profound effect on society in general and on health services in particular. In 2015 there were 8,758 alcohol-related deaths in the UK [169] but a much higher estimate of 21,162 deaths and 914,929 hospital admissions wholly or partly attributable to harm from alcohol in England in 2010/11 has been calculated [170]. The direct and indirect costs to the NHS attributable to alcohol misuse have been estimated at approximately 3.5 billion pounds every year with estimates placing the overall economic burden to be between 1.3% and 2.7% of UK annual GDP [78,79]. Alcohol has been linked to 230 disease and injury categories in systematic reviews and for the majority of these, higher consumption is associated with a greater likelihood of disease. However, the level and pattern of alcohol drinking that constitutes misuse or excess varies by condition. National drinking guidelines also vary widely [171–173], suggesting lack of agreement on the levels of consumption considered acceptable. Alcohol-attributable fractions (AAF), the proportion of a disease or outcome that is attributed to excess alcohol consumption, vary greatly by condition [83]. Liver disease for example, constitutes the third commonest cause of premature death in the UK and three-quarters of deaths from liver disease are the result of excess alcohol consumption [174]. Alcoholic beverages were classified as carcinogenic by the International Agency for Research on Cancer (IARC) and many cancers are partly attributable to alcohol with monotonic increasing risk albeit with AAF at much lower levels [175].

The relationship between alcohol consumption and future hospital usage at lower levels of consumption are less clear. Whether alcohol has a cardioprotective effect has been the subject of considerable debate over many years [82–87]. A large body of epidemiological evidence together with evidence for plausible biological mechanisms, have reported beneficial associations for ischaemic heart disease (IHD) and diabetes at moderate levels of alcohol intake. Associations with other diseases such as Alzheimer's disease and gall bladder disease have also been reported to be mainly beneficial in systematic reviews [83,88–94].

The UK Health Education Council's guidance on alcohol drinking limits, first introduced in 1984, suggested limits considerably higher than those now recommended [171]. Recent public health guidelines in the UK examining lifetime risk associated with alcohol intake recommended a maximum weekly consumption of 14 units or 112 grams (1 UK unit = 8 grams of alcohol) for both men and women. This is based on modelling of the chronic and acute effects of alcohol using published systematic reviews and meta-analysis as the evidence base [172]. However, drinking guidelines vary widely by country, and while this may reflect cultural norms it also suggests a lack of agreement on the level at which consumption becomes harmful [173].

I have previously reported that age, body mass index (BMI) and smoking status predict future hospital usage in a community-based population of middle-aged and older men and women over a 10-year period of follow-up [150]. In the analyses presented here, I examined the relationship between current alcohol consumption in this cohort and their subsequent hospital usage over a period of 10 years. This chapter examines whether current drinking behaviour predicts the frequency or total days of future hospital usage from any cause over a fixed 10-year period. Attendance at an accident and emergency department, while a prominent feature of hospital provision related to alcohol misuse, is not the main focus, although the most serious events are likely to result in emergency admission. Though I did not aim to describe the numerous pathological mechanisms that might be involved, I explored how conditions commonly found in older people might influence the overall relationship between alcohol consumption and future hospital usage. My study is not designed to derive a prognostic model for predicting hospital usage but rather to examine the relationship between usual alcohol consumption patterns at the more moderate levels generally observed in middle-aged and older men and women living in the community and subsequent hospital usage.

6.4 Methods

6.4.1 Statistical analysis

For the analyses presented here, I excluded 625 men and women from the baseline cohort who died before 1999 and excluded 1,274 for whom alcohol intake was not known or inconsistent leaving 23,740 individuals. Men and women were examined separately recognising the different alcohol consumption patterns and conditions between the sexes. Logistic regression models were used to examine associations between alcohol intake and hospital usage outcome categories for total admissions, and in exploratory analyses for various diagnostic codes. The terms "beneficial" and "detrimental" used in table 6.8 and table 6.9 were defined by Rehm and colleagues in their systematic reviews of disease burden [83,93] and approximated by the lists of ICD version 10 codes shown. Logistic regression was used rather than survival analysis since the outcomes under examination are the total number of admissions and total bed days and day cases occurring over a fixed period of 10 years. The numbers of individuals with missing values for covariates were: 51 BMI, 180 smoking status, 466 social class. Logistic regression was also used to examine the risk of death in alcohol drinkers compared with non-alcohol drinkers over the period under examination. Three sensitivity analyses were conducted: using the Random Forest non-parametric algorithm for multiple imputation; using the value of 1.8 units per glass of wine instead of 1 unit per glass; admissions limited to those after March 2004. All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria version 3.4.0 with packages knitr, Gmisc, missForest) and Stata statistical software version 14 (Stata Corporation, College Station, Texas, USA).

6.5 Results

Descriptive characteristics of the 10,883 men and 12,857 women by categories of alcohol intake are shown in table 6.1 (for men) and table 6.2 (for women). Those reporting no current alcohol intake are divided into lifelong abstainers and former drinkers, while those with intake greater than zero are divided into four categories (0,7], (7,14], (14,21] and >21 units per week. Hospital activity is shown in three categories: any hospital admissions; 7 or more admissions; >20 hospital days. Mean and median hospital admissions and duration are shown for all cohort participants and for the subgroup who had attended hospital during the period under examination. This shows the contrast between averages in a population-based denominator and those in a hospital-based denominator; means and medians calculated using the cohort denominator are lower since they include non-attenders. Men and women currently drinking more than 21 units per week tended to be younger, more likely to be current smokers and more likely to have drunk >21 units per week in their 20s and 30s. Current heavy drinkers (those consuming more than 35 units per week) comprised 448 (4.1%) men and 24 (0.2%) women, while 89 men and 1 women drank heavily in the past but were current non-drinkers.

Table 6.1 | Descriptive characteristics by alcohol category for men in the EPIC-Norfolk cohort 1993–1997 and hospital admission 1999–2009

	All (n=10,883)	Lifelong abstainer (n=207 1.9%)	Former drinker (n=701 6.4%)	(0,7] units per week (n=4,873 44.8%)	(7,14] units per week (n=2,346 21.6%)	(14,21] units per week (n=1,237 11.4%)	>21 units per week (n=1,519 14.0%)
Hospital activity, 1999–2009 (n(%))							
Any hospital admissions	8,025 (73.7)	149 (72.0)	584 (83.3)	3,671 (75.3)	1,700 (72.5)	867 (70.1)	1,054 (69.4)
7 or more admissions	1,688 (15.5)	30 (14.5)	156 (22.3)	783 (16.1)	336 (14.3)	175 (14.1)	208 (13.7)
More than 20 hospital days	2,316 (21.3)	53 (25.6)	229 (32.7)	1,072 (22.0)	452 (19.3)	224 (18.1)	286 (18.8)
Total hospital days, 1999–2009							
Mean ±SD, cohort	16.9 ±43.3	17.8 ±38.4	24.9 ±44.3	17.2 ±43.4	15.6 ±40.1	15.0 ±39.2	16.0 ±50.2
Mean ±SD, hospital attenders†	23.0 ±49.0	24.8 ±43.3	29.9 ±46.9	22.8 ±48.7	21.5 ±45.7	21.4 ±45.4	23.1 ±58.9
Median(IQR), cohort	4.0 (0.0 - 16.0)	6.0 (0.0 - 21.0)	9.0 (2.0 - 30.0)	4.0 (1.0 - 17.0)	3.0 (0.0 - 15.0)	3.0 (0.0 - 14.0)	3.0 (0.0 - 13.0)
Median(IQR), hospital attenders†	9.0 (3.0 - 25.0)	12.0 (4.0 - 28.0)	14.0 (4.0 - 39.0)	9.0 (3.0 - 25.0)	8.0 (2.0 - 22.0)	7.0 (2.0 - 21.0)	8.0 (2.0 - 23.0)
Number of admissions, 1999–2009							
Mean ±SD, cohort	4.2 ±16.2	3.7 ±5.0	5.5 ±17.5	4.1 ±11.7	4.0 ±19.5	4.0 ±19.8	4.0 ±19.9
Mean ±SD, hospital attenders†	5.6 ±18.7	5.1 ±5.3	6.6 ±19.0	5.5 ±13.2	5.5 ±22.7	5.7 ±23.4	5.8 ±23.7
Median(IQR), cohort	2.0 (0.0 - 5.0)	2.0 (0.0 - 5.0)	3.0 (1.0 - 6.0)	2.0 (1.0 - 5.0)	2.0 (0.0 - 4.0)	2.0 (0.0 - 4.0)	2.0 (0.0 - 4.0)
Median(IQR), hospital attenders†	3.0 (2.0 - 6.0)	3.0 (2.0 - 6.0)	4.0 (2.0 - 7.0)	3.0 (2.0 - 6.0)	3.0 (1.0 - 6.0)	3.0 (1.0 - 5.0)	3.0 (1.0 - 5.8)
Alcohol intake, units per week							
Mean ±SD	10.2 ±11.9	0.0 ±0.0	0.0 ±0.0	3.0 ±2.0	10.5 ±2.0	17.7 ±2.1	33.4 ±13.1
Age, years							
Mean ±SD	59.2 ±9.2	63.6 ±8.2	62.1 ±9.3	59.7 ±9.1	58.8 ±9.3	57.9 ±9.2	57.4 ±9.0
Prevalent disease (n(%))							
Prevalent heart disease or stroke	691 (6)	11 (5)	65 (9)	347 (7)	146 (6)	53 (4)	69 (5)
Prevalent cancer	398 (4)	10 (5)	32 (5)	168 (3)	85 (4)	49 (4)	54 (4)
Prevalent diabetes	323 (3)	10 (5)	47 (7)	151 (3)	57 (2)	30 (2)	28 (2)
Smoking status (n(%))							
Current	1,308 (12)	11 (5)	107 (15)	552 (11)	236 (10)	144 (12)	258 (17)
Former	5,881 (54)	41 (20)	401 (58)	2,449 (51)	1,287 (55)	725 (59)	978 (65)
Never	3,628 (34)	152 (75)	189 (27)	1,836 (38)	812 (35)	363 (29)	276 (18)
Body mass index, kg/m²							
Mean ±SD	26.5 ±3.3	26.5 ±3.2	26.7 ±3.8	26.4 ±3.3	26.3 ±3.1	26.7 ±3.2	27.0 ±3.4
Level of education (n(%))							
Low	3,190 (29)	92 (44)	302 (43)	1,632 (33)	555 (24)	284 (23)	325 (21)
'O' level or equivalent	948 (9)	17 (8)	48 (7)	394 (8)	216 (9)	118 (10)	155 (10)
'A' level or equivalent	5,037 (46)	69 (33)	294 (42)	2,223 (46)	1,123 (48)	577 (47)	751 (49)
Degree	1,708 (16)	29 (14)	57 (8)	624 (13)	452 (19)	258 (21)	288 (19)
Social class (n(%))							
Professional (1)	828 (8)	23 (11)	33 (5)	311 (6)	209 (9)	126 (10)	126 (8)
Technical (2)	4,126 (39)	56 (28)	190 (28)	1,641 (34)	964 (42)	566 (46)	709 (48)
Clerical NM (3.1)	1,345 (13)	32 (16)	78 (11)	612 (13)	319 (14)	136 (11)	168 (11)
Clerical M (3.2)	2,697 (25)	35 (17)	220 (32)	1,361 (28)	549 (24)	247 (20)	285 (19)
Semi-skilled (4)	1,404 (13)	45 (22)	129 (19)	715 (15)	226 (10)	117 (10)	172 (12)
Unskilled (5)	305 (3)	11 (5)	35 (5)	153 (3)	47 (2)	30 (2)	29 (2)
Past alcohol consumption‡ (n(%))							
(0,7] units per week	3,824 (36)	-	356 (51)	2,487 (51)	644 (27)	195 (16)	142 (9)
(7,14] units per week	2,299 (22)	-	128 (18)	1,039 (21)	647 (28)	280 (23)	205 (14)
(14,21] units per week	1,547 (15)	-	68 (10)	535 (11)	433 (18)	273 (22)	238 (16)
>21 units per week	2,981 (28)	-	149 (21)	792 (16)	619 (26)	488 (39)	933 (61)

† Denominator restricted to cohort participants who attended hospital during the period under examination
‡Past alcohol consumption is defined as the higher of units reported consumed aged 20 and aged 30
Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Table 6.2 | Descriptive characteristics by alcohol category for women in the EPIC-Norfolk cohort 1993–1997 and hospital admission 1999–2009

	All (n=12,857)	Lifelong abstainer (n=873 6.8%)	Former drinker (n=1,086 8.4%)	(0,7] units per week (n=8,121 63.2%)	(7,14] units per week (n=1,911 14.9%)	(14,21] units per week (n=615 4.8%)	>21 units per week (n=251 2.0%)
Hospital activity, 1999–2009 (n(%))							
Any hospital admissions	9,168 (71.3)	691 (79.2)	843 (77.6)	5,769 (71.0)	1,295 (67.8)	405 (65.9)	165 (65.7)
7 or more admissions	1,562 (12.1)	140 (16.0)	203 (18.7)	963 (11.9)	178 (9.3)	57 (9.3)	21 (8.4)
More than 20 hospital days	2,329 (18.1)	257 (29.4)	291 (26.8)	1,412 (17.4)	251 (13.1)	83 (13.5)	35 (13.9)
Total hospital days, 1999–2009							
Mean ±SD, cohort	15.2 ±48.9	22.5 ±43.0	23.8 ±64.7	14.3 ±46.3	11.7 ±53.4	12.8 ±46.6	10.9 ±25.9
Mean ±SD, hospital attenders †	21.3 ±56.7	28.5 ±46.5	30.7 ±72.0	20.2 ±53.9	17.2 ±64.2	19.4 ±56.3	16.6 ±30.5
Median(IQR), cohort	3.0 (0.0 - 13.0)	6.0 (1.0 - 25.0)	6.0 (1.0 - 23.0)	3.0 (0.0 - 12.0)	2.0 (0.0 - 9.0)	2.0 (0.0 - 9.0)	2.0 (0.0 - 10.0)
Median(IQR), hospital attenders†	7.0 (2.0 - 21.0)	11.0 (3.0 - 32.0)	11.0 (3.0 - 33.0)	6.0 (2.0 - 20.0)	5.0 (2.0 - 15.0)	6.0 (2.0 - 16.0)	5.0 (2.0 - 16.0)
Number of admissions, 1999–2009							
Mean ±SD, cohort	3.5 ±16.3	4.1 ±7.6	5.3 ±34.0	3.3 ±8.4	3.3 ±23.5	3.8 ±27.8	2.3 ±3.6
Mean ±SD, hospital attenders†	4.9 ±19.1	5.1 ±8.2	6.9 ±38.5	4.6 ±9.7	4.9 ±28.4	5.8 ±34.2	3.6 ±4.0
Median(IQR), cohort	2.0 (0.0 - 4.0)	2.0 (1.0 - 5.0)	2.0 (1.0 - 5.0)	2.0 (0.0 - 4.0)	1.0 (0.0 - 3.0)	1.0 (0.0 - 3.0)	1.0 (0.0 - 3.0)
Median(IQR), hospital attenders†	3.0 (1.0 - 5.0)	3.0 (2.0 - 6.0)	3.0 (2.0 - 6.0)	3.0 (1.0 - 5.0)	2.0 (1.0 - 4.0)	2.0 (1.0 - 5.0)	2.0 (1.0 - 5.0)
Alcohol intake, units per week							
Mean ±SD	4.4 ±5.7	0.0 ±0.0	0.0 ±0.0	2.5 ±1.9	10.1 ±2.0	17.0 ±2.2	27.8 ±7.1
Age, years							
Mean ±SD	58.5 ±9.2	63.0 ±8.6	60.5 ±9.1	58.2 ±9.1	57.1 ±9.1	57.4 ±9.4	55.4 ±9.2
Prevalent disease (n(%))							
Prevalent heart disease or stroke	272 (2)	35 (4)	48 (4)	152 (2)	28 (1)	8 (1)	1 (0)
Prevalent cancer	838 (7)	58 (7)	71 (7)	527 (6)	117 (6)	44 (7)	21 (8)
Prevalent diabetes	186 (1)	26 (3)	33 (3)	107 (1)	15 (1)	2 (0)	3 (1)
Smoking status (n(%))							
Current	1,449 (11)	52 (6)	156 (15)	831 (10)	242 (13)	106 (17)	62 (25)
Former	4,152 (33)	110 (13)	375 (35)	2,472 (31)	790 (42)	291 (47)	114 (46)
Never	7,142 (56)	692 (81)	541 (50)	4,753 (59)	865 (46)	217 (35)	74 (30)
Body mass index, kg/m²							
Mean ±SD	26.2 ±4.3	26.8 ±4.7	26.7 ±4.9	26.2 ±4.4	25.6 ±3.8	25.4 ±3.9	25.7 ±3.7
Level of education (n(%))							
Low	5,253 (41)	531 (61)	610 (56)	3,371 (42)	534 (28)	149 (24)	58 (23)
'O' level or equivalent	1,518 (12)	69 (8)	111 (10)	1,008 (12)	228 (12)	69 (11)	33 (13)
'A' level or equivalent	4,658 (36)	219 (25)	303 (28)	2,943 (36)	821 (43)	268 (44)	104 (41)
Degree	1,428 (11)	54 (6)	62 (6)	799 (10)	328 (17)	129 (21)	56 (22)
Social class (n(%))							
Professional (1)	830 (7)	35 (4)	37 (4)	486 (6)	171 (9)	65 (11)	36 (15)
Technical (2)	4,475 (36)	237 (28)	268 (25)	2,670 (34)	864 (46)	314 (51)	122 (50)
Clerical NM (3.1)	2,490 (20)	129 (15)	232 (22)	1,626 (20)	361 (19)	105 (17)	37 (15)
Clerical M (3.2)	2,655 (21)	213 (25)	267 (25)	1,772 (22)	301 (16)	71 (12)	31 (13)
Semi-skilled (4)	1,637 (13)	159 (19)	181 (17)	1,079 (14)	152 (8)	52 (9)	14 (6)
Unskilled (5)	482 (4)	63 (8)	71 (7)	310 (4)	29 (2)	4 (1)	5 (2)
Past alcohol consumption‡ (n(%))							
(0,7] units per week	9,875 (83)	-	976 (90)	7,185 (90)	1,304 (68)	322 (52)	88 (35)
(7,14] units per week	1,351 (11)	-	77 (7)	612 (8)	435 (23)	160 (26)	67 (27)
(14,21] units per week	384 (3)	-	18 (2)	135 (2)	103 (5)	83 (14)	45 (18)
>21 units per week	248 (2)	-	15 (1)	68 (1)	65 (3)	49 (8)	51 (20)

† Denominator restricted to cohort participants who attended hospital during the period under examination
‡Past alcohol consumption is defined as the higher of units reported consumed aged 20 and aged 30
Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Table 6.3 shows the relationships between dichotomous and grouped alcohol categories and hospital usage for men and women separately. In table 6.3, model 1 (age-adjusted) and model 2 (multivariable-adjusted) compare non-drinkers with current drinkers while model 3 (multivariable-adjusted) compares non-drinkers with intake in four bands. Compared with non-drinkers, men who currently drink had a lower risk of spending more than twenty days in hospital with multivariable-adjusted OR 0.80 (95% CI 0.68–0.94). Women who currently drink were also less likely to have any hospital admissions, multivariable-adjusted OR 0.84 (95% CI 0.74–0.95), seven or more admissions OR 0.77 (95% CI 0.66–0.88) or more than twenty hospital days OR 0.70 (95% CI 0.62–0.80). I did not observe a higher risk of hospitalisation at any level of intake including those consuming 21 units or more per week. Figure 6.1 illustrates the relationship between current non-drinking and subsequent hospital stay of 20 or more days contrasting men and women. Table 6.4 differs from table 6.3 by the use of lifelong abstainers as the reference category. Compared with lifelong abstainers, men who currently drink had a higher risk of any hospital admissions OR 1.53 (95% CI 1.10–2.13) while in women the association was inverse OR 0.84 (95% CI 0.70–1.01) . Men who were former drinkers had a higher risk than lifelong abstainers OR 2.22 (95% CI 1.51–3.28) while former drinking women showed no difference OR 1.01 (95% CI 0.80–1.27). The associations were similar in all categories of intake. Figure 6.2 illustrates the relationship in women of lifelong non-drinking and subsequent hospital stay of 20 or more days.

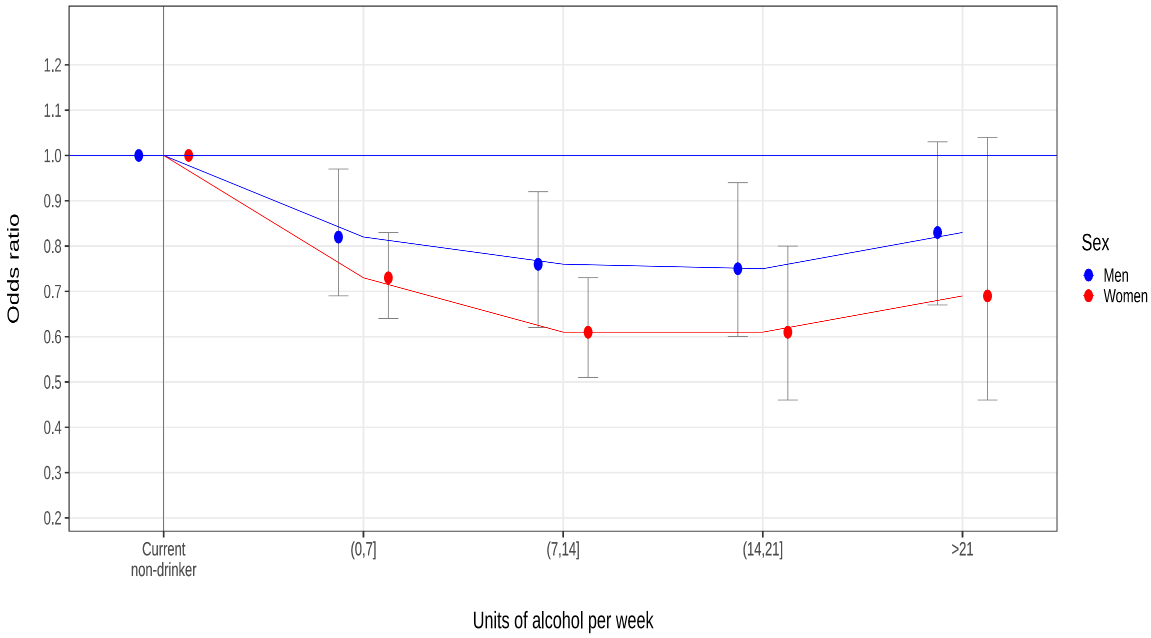
Table 6.3 | Age-adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 hospital admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
Current drinker	9,975	7,292	0.81 (0.68–0.97)	0.021	1502	0.84 (0.71–1.00)	0.052	2034	0.74 (0.63–0.87)	<0.001
Men ‡										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
Current drinker	9,975	7,292	0.85 (0.71–1.02)	0.083	1502	0.88 (0.73–1.05)	0.162	2034	0.80 (0.68–0.94)	0.008
Men ‡										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
(0,7] units per week	4,873	3,671	0.89 (0.74–1.08)	0.231	783	0.90 (0.74–1.09)	0.266	1072	0.82 (0.69–0.97)	0.024
(7,14] units per week	2,346	1,700	0.85 (0.69–1.04)	0.106	336	0.85 (0.68–1.04)	0.120	452	0.76 (0.62–0.92)	0.005
(14,21] units per week	1,237	867	0.79 (0.64–0.99)	0.037	175	0.88 (0.69–1.12)	0.284	224	0.75 (0.60–0.94)	0.012
>21 units per week	1,519	1,054	0.78 (0.63–0.96)	0.020	208	0.85 (0.68–1.08)	0.187	286	0.83 (0.67–1.03)	0.095
Women †										
Current non-drinker	1,959	1,534	1	–	343	1	–	548	1	–
Current drinker	10,898	7,634	0.77 (0.69–0.87)	<0.001	1219	0.69 (0.61–0.79)	<0.001	1781	0.65 (0.57–0.73)	<0.001
Women ‡										
Current non-drinker	1,959	1,534	1	–	343	1	–	548	1	–
Current drinker	10,898	7,634	0.84 (0.74–0.95)	0.005	1219	0.77 (0.66–0.88)	<0.001	1781	0.70 (0.62–0.80)	<0.001
Women ‡										
Current non-drinker	1,959	1,534	1	–	343	1	–	548	1	–
(0,7] units per week	8,121	5,769	0.85 (0.75–0.96)	0.010	963	0.79 (0.68–0.91)	0.001	1412	0.73 (0.64–0.83)	<0.001
(7,14] units per week	1,911	1,295	0.82 (0.70–0.96)	0.012	178	0.69 (0.56–0.85)	<0.001	251	0.61 (0.51–0.73)	<0.001
(14,21] units per week	615	405	0.75 (0.61–0.93)	0.008	57	0.67 (0.49–0.91)	0.011	83	0.61 (0.46–0.80)	<0.001
>21 units per week	251	165	0.79 (0.59–1.07)	0.124	21	0.63 (0.39–1.01)	0.054	35	0.69 (0.46–1.04)	0.078

OR = Odds ratio, CI = Confidence intervals. Comparison group: Current non-drinker †Adjusted for age ‡ Adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Figure 6.1 | The relationship between current non-drinkers and future risk of 20 or more hospital days over 10-year follow-up 1999–2009 in 23,740 men and women



Multiple logistic odds ratio and 95% confidence interval adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes
Round brackets in intervals denote strict inequalities

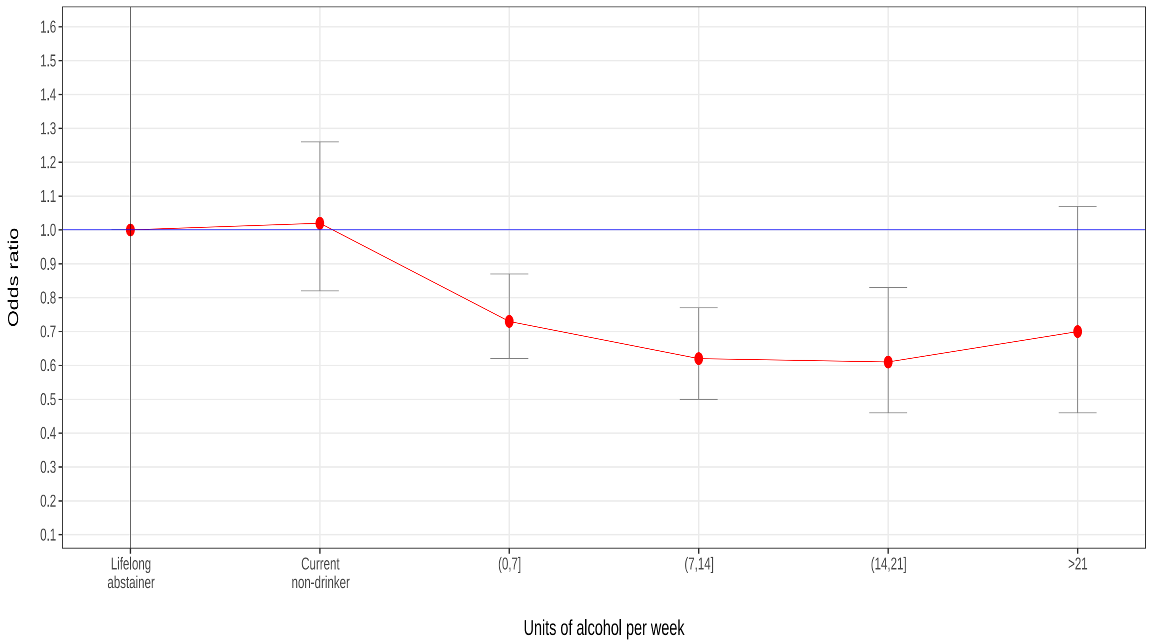
Table 6.4 | Age-adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 hospital admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Lifelong abstainer	207	149	1	–	30	1	–	53	1	–
Former drinker	701	584	2.33 (1.60–3.40)	<0.001	156	1.84 (1.20–2.84)	0.006	229	1.63 (1.13–2.36)	0.009
Current drinker	9,975	7,292	1.52 (1.11–2.10)	0.010	1502	1.37 (0.92–2.03)	0.123	2034	1.08 (0.78–1.51)	0.632
Men ‡										
Lifelong abstainer	207	149	1	–	30	1	–	53	1	–
Former drinker	701	584	2.22 (1.51–3.28)	<0.001	156	1.70 (1.08–2.65)	0.021	229	1.47 (1.00–2.16)	0.051
Current drinker	9,975	7,292	1.53 (1.10–2.13)	0.011	1502	1.34 (0.89–2.02)	0.163	2034	1.08 (0.76–1.52)	0.676
Men ‡										
Lifelong abstainer	207	149	1	–	30	1	–	53	1	–
Former drinker	701	584	2.22 (1.51–3.27)	<0.001	156	1.70 (1.08–2.65)	0.021	229	1.47 (1.00–2.16)	0.051
(0,7] units per week	4,873	3,671	1.61 (1.15–2.24)	0.005	783	1.37 (0.90–2.07)	0.137	1072	1.10 (0.78–1.57)	0.578
(7,14] units per week	2,346	1,700	1.53 (1.09–2.14)	0.015	336	1.29 (0.84–1.97)	0.241	452	1.02 (0.71–1.46)	0.917
(14,21] units per week	1,237	867	1.43 (1.00–2.02)	0.047	175	1.34 (0.86–2.08)	0.197	224	1.01 (0.69–1.48)	0.952
>21 units per week	1,519	1,054	1.40 (0.99–1.98)	0.056	208	1.30 (0.84–2.02)	0.233	286	1.13 (0.78–1.63)	0.533
Women †										
Lifelong abstainer	873	691	1	–	140	1	–	257	1	–
Former drinker	1,086	843	1.04 (0.83–1.30)	0.733	203	1.34 (1.06–1.71)	0.016	291	1.06 (0.86–1.31)	0.569
Current drinker	10,898	7,634	0.79 (0.66–0.94)	0.007	1219	0.82 (0.67–0.99)	0.042	1781	0.67 (0.57–0.79)	<0.001
Women ‡										
Lifelong abstainer	873	691	1	–	140	1	–	257	1	–
Former drinker	1,086	843	1.01 (0.80–1.27)	0.924	203	1.30 (1.01–1.67)	0.042	291	1.02 (0.82–1.27)	0.884
Current drinker	10,898	7,634	0.84 (0.70–1.01)	0.063	1219	0.89 (0.72–1.09)	0.263	1781	0.71 (0.60–0.84)	<0.001
Women ‡										
Lifelong abstainer	873	691	1	–	140	1	–	257	1	–
Former drinker	1,086	843	1.01 (0.80–1.27)	0.932	203	1.30 (1.01–1.67)	0.043	291	1.02 (0.82–1.26)	0.891
(0,7] units per week	8,121	5,769	0.85 (0.71–1.02)	0.088	963	0.91 (0.74–1.13)	0.397	1412	0.73 (0.62–0.87)	<0.001
(7,14] units per week	1,911	1,295	0.82 (0.67–1.01)	0.063	178	0.80 (0.62–1.03)	0.089	251	0.62 (0.50–0.77)	<0.001
(14,21] units per week	615	405	0.76 (0.59–0.97)	0.028	57	0.78 (0.55–1.10)	0.156	83	0.61 (0.46–0.83)	0.001
>21 units per week	251	165	0.80 (0.58–1.10)	0.171	21	0.73 (0.44–1.20)	0.215	35	0.70 (0.46–1.07)	0.099

OR = Odds ratio, CI = Confidence intervals. Comparison group: Lifelong abstainer †Adjusted for age ‡ Adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Figure 6.2 | The relationship between women lifelong non-drinkers and future risk of 20 or more hospital days over 10-year follow-up 1999–2009 in 23,740 men and women



Multiple logistic odds ratio and 95% confidence interval adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes Round brackets in intervals denote strict inequalities

Table 6.5 displays logistic regression models for the outcome of any hospital admissions comparing non-drinkers with current drinkers in various subgroups. Separate models for men and women are stratified by a dichotomised subgroup: age above or below 65 years; smoking status; BMI above and below 30kg/m^2; manual and non-manual social class; low or other education level; prevalent disease (heart disease, cancer or diabetes). Odds ratios (OR) within all strata were in consistent directions with no interaction by age, smoking status or BMI.

Table 6.5 | Logistic regression models for any hospital admissions comparing non-drinkers with current drinkers in subgroups in 23,740 men and women aged 40–79 years 1993–1997

	Men non-drinker (ref)	Men current drinker OR (95% CI)	Women non-drinker (ref)	Women current drinker OR (95% CI)
By age above and below 65 years				
Less than 65 years	1	0.89 (0.72–1.11)	1	0.79 (0.68–0.92)
65 years and above	1	0.79 (0.56–1.12)	1	0.94 (0.75–1.19)
By smoking status				
Current smoker	1	0.85 (0.70–1.03)	1	0.85 (0.74–0.96)
Non-smoker	1	0.87 (0.52–1.45)	1	0.64 (0.43–0.96)
By BMI				
BMI>30	1	0.92 (0.76–1.11)	1	0.81 (0.70–0.92)
BMI≤30	1	0.50 (0.28–0.90)	1	0.91 (0.68–1.22)
By social class				
Manual social class	1	0.90 (0.70–1.16)	1	0.78 (0.66–0.92)
Non-manual social class	1	0.81 (0.62–1.05)	1	0.89 (0.74–1.06)
By education				
Low education level	1	0.88 (0.71–1.11)	1	0.77 (0.65–0.91)
Other education level	1	0.80 (0.59–1.10)	1	0.89 (0.75–1.07)
By prevalent disease				
No reported disease	1	0.82 (0.68–0.99)	1	0.81 (0.72–0.92)
Pre-existing heart disease, cancer or diabetes	1	1.22 (0.55–2.72)	1	0.70 (0.28–1.72)

OR = Odds ratio, CI = Confidence intervals. Comparison group: Current non-drinker . All models adjusted for age, smoking status, education level(low/others), social class (manual/non-manual) and body mass index (continuous) except where a dichotomous adjustment variable was the subgroup being examined

Table 6.6 and table 6.7 show age and mean current intake by categories of admissions and hospital days respectively for men and women separately. Admissions are grouped as: zero, 1, 2–3, 4–6 and ≥7 while hospital days are grouped as none, 1, 2–5, 6–20 and >20.

Table 6.8 shows relationships between dichotomous and grouped alcohol categories and hospital usage but uses modified admission and hospital day counts containing only admissions that include discharge codes entirely attributable to alcohol intake or partly attributable and considered "detrimental" (alcohol intake positively associated with disease) according to previous systematic reviews of the literature. Table 6.9 shows similar relationships for discharge codes considered "beneficial" (alcohol intake inversely associated with disease) [83]. In both sub-classifications, men and women who currently drink have a lower risk of admission compared with non-drinkers.

Sensitivity analyses using 1.8 units per glass of wine instead of 1 unit (table 6.10) [176] and using multiple imputation (table 6.11) gave similar results to those presented in the main tables. A sensitivity analysis (table 6.12) with admissions limited to those after March 2004 gave similar results for women but attenuated results for men. Participants excluded due to missing alcohol intake (n=1274) were older and predominantly women (73%) with a lower proportion having non-manual social classes and education to age 16 or above.

Table 6.6 | Distribution of characteristics of 23,740 men and women in 1993–1997 by category of number of hospital admissions 1999–2009 †

	0 (n=6,547 27.6%)	1 (n=4,389 18.5%)	2–3 (n=5,695 24.0%)	4–6 (n=3,859 16.3%)	≥7 (n=3,250 13.7%)
Alcohol intake, men, units per week					
Mean ±SD	11.2 ±12.1	10.4 ±11.6	10.1 ±11.9	9.5 ±11.9	9.4 ±11.7
Alcohol intake, women, units per week					
Mean ±SD	5.0 ±6.0	4.8 ±5.9	4.2 ±5.6	4.0 ±5.4	3.6 ±5.1
Age, men, years					
Mean ±SD	55.0 ±8.5	57.3 ±8.8	60.2 ±9.0	62.5 ±8.7	63.6 ±8.2
Age, women, years					
Mean ±SD	55.5 ±8.5	56.9 ±8.9	59.4 ±9.2	61.9 ±9.0	62.0 ±9.0

† Includes day cases where admission and discharge are on the same day

Table 6.7 | Distribution of characteristics of 23,740 men and women in 1993–1997 by category of total hospital days 1999–2009 †

	None (n=6,547 27.6%)	1 day (n=2,676 11.3%)	2–5 days (n=4,707 19.8%)	6–20 days (n=5,165 21.8%)	>20 days (n=4,645 19.6%)
Alcohol intake, men, units per week					
Mean ±SD	11.2 ±12.1	10.2 ±11.2	10.5 ±11.9	9.7 ±11.6	9.4 ±12.2
Alcohol intake, women, units per week					
Mean ±SD	5.0 ±6.0	4.8 ±5.5	4.5 ±6.0	4.2 ±5.5	3.5 ±5.1
Age, men, years					
Mean ±SD	55.0 ±8.5	56.1 ±8.2	58.2 ±8.7	60.9 ±8.7	65.1 ±8.0
Age, women, years					
Mean ±SD	55.5 ±8.5	55.5 ±8.6	57.7 ±8.8	59.9 ±8.9	64.4 ±8.5

† Includes day cases where admission and discharge are on the same day

Table 6.8 | Age-adjusted and multivariable logistic regression of risk factors restricted to "detrimental" hospital admissions (those directly associated to alcohol intake in systematic reviews) for any hospital admissions (compared to none), ≥7 admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Current non-drinker	908	438	1	–	34	1	–	117	1	–
Current drinker	9,975	3,752	0.77 (0.67–0.89)	<0.001	298	0.92 (0.64–1.32)	0.642	841	0.82 (0.66–1.01)	0.063
Men ‡										
Current non-drinker	908	438	1	–	34	1	–	117	1	–
Current drinker	9,975	3,752	0.78 (0.67–0.90)	<0.001	298	0.98 (0.67–1.43)	0.926	841	0.85 (0.68–1.06)	0.154
Men ‡										
Current non-drinker	908	438	1	–	34	1	–	117	1	–
(0,7] units per week	4,873	1,891	0.78 (0.67–0.91)	0.001	164	1.05 (0.71–1.55)	0.813	432	0.83 (0.66–1.05)	0.123
(7,14] units per week	2,346	855	0.75 (0.64–0.89)	<0.001	69	1.01 (0.65–1.56)	0.966	187	0.82 (0.63–1.07)	0.146
(14,21] units per week	1,237	426	0.72 (0.60–0.87)	<0.001	26	0.74 (0.43–1.26)	0.261	92	0.83 (0.61–1.12)	0.221
>21 units per week	1,519	580	0.86 (0.72–1.03)	0.099	39	0.87 (0.54–1.43)	0.591	130	1.02 (0.76–1.35)	0.913
Women †										
Current non-drinker	1,959	937	1	–	65	1	–	248	1	–
Current drinker	10,898	3,929	0.69 (0.62–0.76)	<0.001	262	0.76 (0.58–1.01)	0.060	718	0.64 (0.54–0.74)	<0.001
Women ‡										
Current non-drinker	1,959	937	1	–	65	1	–	248	1	–
Current drinker	10,898	3,929	0.74 (0.67–0.82)	<0.001	262	0.85 (0.64–1.14)	0.281	718	0.70 (0.59–0.83)	<0.001
Women ‡										
Current non-drinker	1,959	937	1	–	65	1	–	248	1	–
(0,7] units per week	8,121	2,993	0.75 (0.67–0.83)	<0.001	211	0.89 (0.66–1.20)	0.437	571	0.72 (0.60–0.85)	<0.001
(7,14] units per week	1,911	652	0.72 (0.63–0.83)	<0.001	33	0.67 (0.43–1.04)	0.076	91	0.57 (0.44–0.74)	<0.001
(14,21] units per week	615	200	0.67 (0.55–0.82)	<0.001	13	0.80 (0.43–1.49)	0.482	36	0.67 (0.45–0.98)	0.038
>21 units per week	251	84	0.72 (0.54–0.96)	0.024	5	0.75 (0.30–1.92)	0.551	20	1.04 (0.62–1.73)	0.893

OR = Odds ratio, CI = Confidence intervals. Comparison group: Current non-drinker †Adjusted for age ‡ Adjusted for age, smoking status, education level(low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes
Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities
Restricted to hospital admissions with following ICD-10 codes: A15, A16, A17, A18, A19, B20, B21, B22, B23, B24, B90, C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C15, C18, C19, C20, C21, C22, C32, C33, C34, C50, D00, D01, D02, D03, D04, D05, D06, D07, D08, D09, D10, D11, D12, D13, D14, D15, D16, D17, D18, D19, D20, D21, D22, D23, D24, D25, D26, D27, D28, D29, D30, D31, D32, D33, D34, D35, D36, D37, D38, D39, D40, D41, D42, D43, D44, D45, D46, D47, D48, E24, F10, F32, F33, F34, G31, G40, G41, G62, G72, I11, I12, I13, I42, I47, I48, I60, I61, I62, I85, J09, J10, J11, J12, J13, J14, J15, J16, J17, J18, J19, J20, J21, J22, J85, K20, K21, K22, K28, K29, K30, K31, K38, K57, K58, K59, K60, K61, K62, K63, K70, K73, K74, K75, K76, K77, K80, K81, K82, K83, K85, K86, K90, K91, K92, L40, L41, O00, O01, O02, O03, O04, O05, O06, O07, O35, O08, P04, P05, P06, P07, P22, P25, P26, P27, P28, Q86, R78, T51, X45, X65, Y15, Y90, V01, V02, V03, V04, V09, V10, V11, V12, V13, V14, V15, V16, V17, V18, V19, V20, V21, V22, V23, V24, V25, V26, V27, V28, V29, V30, V31, V32, V33, V34, V35, V36, V37, V38, V39, V40, V41, V42, V43, V44, V45, V46, V47, V48, V49, V50, V51, V52, V53, V54, V55, V56, V57, V58, V59, V60, V61, V62, V63, V64, V65, V66, V67, V68, V69, V70, V71, V72, V73, V74, V75, V76, V77, V78, V79, V80, V81, V82, V83, V84, V85, V86, V87, V88, V89, V90, V91, V92, V93, V94, V95, V96, V97, V98, V99

Table 6.9 | Age-adjusted and multivariable logistic regression of risk factors restricted to "beneficial" hospital admissions (those inversely associated to alcohol intake in systematic reviews) for any hospital admissions (compared to none), ≥7 admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Current non-drinker	908	318	1	–	37	1	–	117	1	–
Current drinker	9,975	2,433	0.75 (0.64–0.87)	<0.001	212	0.63 (0.44–0.91)	0.013	742	0.73 (0.59–0.90)	0.004
Men ‡										
Current non-drinker	908	318	1	–	37	1	–	117	1	–
Current drinker	9,975	2,433	0.81 (0.69–0.96)	0.013	212	0.77 (0.52–1.13)	0.180	742	0.82 (0.65–1.03)	0.091
Men ‡										
Current non-drinker	908	318	1	–	37	1	–	117	1	–
(0,7] units per week	4,873	1,320	0.88 (0.74–1.04)	0.135	119	0.79 (0.52–1.19)	0.252	408	0.85 (0.66–1.08)	0.177
(7,14] units per week	2,346	541	0.78 (0.64–0.94)	0.010	45	0.76 (0.47–1.22)	0.253	170	0.85 (0.64–1.12)	0.239
(14,21] units per week	1,237	256	0.70 (0.56–0.87)	0.001	30	0.98 (0.57–1.67)	0.936	79	0.75 (0.54–1.05)	0.094
>21 units per week	1,519	316	0.71 (0.58–0.88)	0.002	18	0.49 (0.27–0.91)	0.022	85	0.70 (0.51–0.97)	0.031
Women †										
Current non-drinker	1,959	525	1	–	32	1	–	180	1	–
Current drinker	10,898	1,615	0.60 (0.53–0.68)	<0.001	79	0.56 (0.37–0.86)	0.008	428	0.57 (0.47–0.69)	<0.001
Women ‡										
Current non-drinker	1,959	525	1	–	32	1	–	180	1	–
Current drinker	10,898	1,615	0.67 (0.59–0.77)	<0.001	79	0.87 (0.55–1.37)	0.543	428	0.66 (0.54–0.81)	<0.001
Women ‡										
Current non-drinker	1,959	525	1	–	32	1	–	180	1	–
(0,7] units per week	8,121	1,278	0.69 (0.60–0.78)	<0.001	67	0.89 (0.56–1.42)	0.626	354	0.69 (0.56–0.85)	<0.001
(7,14] units per week	1,911	238	0.64 (0.53–0.77)	<0.001	9	0.79 (0.36–1.73)	0.551	45	0.47 (0.33–0.67)	<0.001
(14,21] units per week	615	71	0.58 (0.43–0.77)	<0.001	1	0.30 (0.04–2.23)	0.239	21	0.74 (0.46–1.21)	0.237
>21 units per week	251	28	0.60 (0.39–0.94)	0.026	2	1.38 (0.31–6.17)	0.677	8	0.79 (0.37–1.70)	0.546

OR = Odds ratio, CI = Confidence intervals. Comparison group: Current non-drinker †Adjusted for age ‡ Adjusted for age, smoking status, education level(low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Restricted to hospital admissions with following ICD-10 codes: E10, E11, E12, E13, F01, F02, F03, G30, G31, I20, I21, I22, I23, I24, I25, I63, I64, I65, I66, I67, K80, K81, K82, K83

Table 6.10 | Sensitivity analysis for wine strength 1.8 units per glass. Age-adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 hospital admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
Current drinker	9,975	7,292	0.81 (0.68–0.97)	0.021	1502	0.84 (0.71–1.00)	0.052	2034	0.74 (0.63–0.87)	<0.001
Men ‡										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
Current drinker	9,975	7,292	0.85 (0.71–1.02)	0.083	1502	0.88 (0.73–1.05)	0.162	2034	0.80 (0.68–0.94)	0.008
Men ‡										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
(0,7] units per week	4,466	3,377	0.90 (0.74–1.09)	0.271	728	0.91 (0.75–1.10)	0.313	995	0.83 (0.69–0.98)	0.032
(7,14] units per week	2,338	1,695	0.83 (0.68–1.01)	0.068	348	0.87 (0.71–1.08)	0.200	458	0.75 (0.62–0.91)	0.004
(14,21] units per week	1,321	946	0.86 (0.69–1.07)	0.175	182	0.85 (0.67–1.08)	0.195	240	0.76 (0.61–0.95)	0.016
>21 units per week	1,850	1,274	0.76 (0.62–0.93)	0.009	244	0.82 (0.65–1.02)	0.077	341	0.81 (0.66–0.99)	0.039
Women †										
Current non-drinker	1,959	1,534	1	–	343	1	–	548	1	–
Current drinker	10,898	7,634	0.77 (0.69–0.87)	<0.001	1219	0.69 (0.61–0.79)	<0.001	1781	0.65 (0.57–0.73)	<0.001
Women ‡										
Current non-drinker	1,959	1,534	1	–	343	1	–	548	1	–
Current drinker	10,898	7,634	0.84 (0.74–0.95)	0.005	1219	0.77 (0.66–0.88)	<0.001	1781	0.70 (0.62–0.80)	<0.001
Women ‡										
Current non-drinker	1,959	1,534	1	–	343	1	–	548	1	–
(0,7] units per week	7,463	5,326	0.85 (0.75–0.96)	0.010	899	0.79 (0.68–0.91)	0.001	1330	0.74 (0.65–0.84)	<0.001
(7,14] units per week	2,115	1,465	0.88 (0.75–1.02)	0.087	211	0.74 (0.61–0.90)	0.002	288	0.62 (0.52–0.74)	<0.001
(14,21] units per week	843	533	0.69 (0.57–0.83)	<0.001	72	0.63 (0.47–0.83)	0.001	109	0.63 (0.49–0.80)	<0.001
>21 units per week	477	310	0.78 (0.62–0.98)	0.035	37	0.59 (0.41–0.85)	0.005	54	0.56 (0.40–0.77)	<0.001

OR = Odds ratio, CI = Confidence intervals. Comparison group: Lifelong abstainer †Adjusted for age ‡ Adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

Table 6.11 | Sensitivity analysis using multiple imputation using the Random Forest non-parametric algorithm. Age-adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 hospital admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 25,639 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Current non-drinker	1,091	856	1	–	211	1	–	327	1	–
Current drinker	10,516	7,575	0.85 (0.73–0.99)	0.039	1562	0.87 (0.74–1.03)	0.097	2146	0.77 (0.66–0.89)	<0.001
Men ‡										
Current non-drinker	1,091	856	1	–	211	1	–	327	1	–
Current drinker	10,516	7,575	0.91 (0.78–1.06)	0.236	1562	0.93 (0.79–1.10)	0.393	2146	0.83 (0.71–0.96)	0.013
Men ‡										
Current non-drinker	1,091	856	1	–	211	1	–	327	1	–
(0,7] units per week	5,211	3,855	0.95 (0.80–1.11)	0.501	824	0.95 (0.80–1.13)	0.570	1141	0.84 (0.72–0.98)	0.028
(7,14] units per week	2,432	1,747	0.93 (0.78–1.11)	0.400	345	0.91 (0.75–1.11)	0.335	469	0.80 (0.67–0.95)	0.012
(14,21] units per week	1,285	890	0.86 (0.70–1.04)	0.119	181	0.93 (0.74–1.17)	0.553	238	0.81 (0.66–1.00)	0.050
>21 units per week	1,588	1,083	0.81 (0.67–0.97)	0.025	212	0.88 (0.70–1.09)	0.233	298	0.84 (0.69–1.03)	0.087
Women †										
Current non-drinker	2,372	1,843	1	–	402	1	–	649	1	–
Current drinker	11,660	8,134	0.77 (0.69–0.86)	<0.001	1313	0.71 (0.63–0.81)	<0.001	1961	0.68 (0.61–0.75)	<0.001
Women ‡										
Current non-drinker	2,372	1,843	1	–	402	1	–	649	1	–
Current drinker	11,660	8,134	0.85 (0.76–0.94)	0.002	1313	0.79 (0.70–0.90)	<0.001	1961	0.75 (0.67–0.84)	<0.001
Women ‡										
Current non-drinker	2,372	1,843	1	–	402	1	–	649	1	–
(0,7] units per week	8,747	6,184	0.86 (0.77–0.96)	0.006	1045	0.82 (0.72–0.93)	0.003	1558	0.77 (0.69–0.86)	<0.001
(7,14] units per week	2,001	1,347	0.82 (0.72–0.95)	0.007	186	0.70 (0.57–0.84)	<0.001	270	0.64 (0.54–0.76)	<0.001
(14,21] units per week	646	429	0.79 (0.65–0.96)	0.018	60	0.68 (0.51–0.92)	0.011	92	0.67 (0.52–0.86)	0.002
>21 units per week	266	174	0.79 (0.60–1.04)	0.096	22	0.60 (0.38–0.96)	0.031	41	0.81 (0.56–1.17)	0.255

OR = Odds ratio, CI = Confidence intervals. Comparison group: Lifelong abstainer †Adjusted for age ‡ Adjusted for age, smoking status, education level(low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes
Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities
Variables used in the multiple imputation include: age, sex, social class, education level, smoking status, beer, wine, sherry, spirits (at present and at age 20 and 30), physical activity, prevalent disease, hospital admission and hospital days

Table 6.12 | Sensitivity analysis excluding hospital events before April 2004. Age-adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 2004–2009 in 23,740 men and women aged 40–79 years 1993–1997

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	More than 20 hospital days OR (95% CI)	p value
Men †										
Current non-drinker	908	490	1	–	58	1	–	118	1	–
Current drinker	9,975	5,154	1.03 (0.89–1.18)	0.696	550	0.99 (0.75–1.31)	0.948	980	0.95 (0.77–1.17)	0.616
Men ‡										
Current non-drinker	908	490	1	–	58	1	–	118	1	–
Current drinker	9,975	5,154	1.03 (0.90–1.19)	0.648	550	1.01 (0.76–1.35)	0.920	980	0.99 (0.80–1.23)	0.932
Men ‡										
Current non-drinker	908	490	1	–	58	1	–	118	1	–
(0,7] units per week	4,873	2,597	1.07 (0.92–1.24)	0.400	295	1.08 (0.80–1.46)	0.598	512	1.01 (0.81–1.27)	0.918
(7,14] units per week	2,346	1,215	1.05 (0.89–1.23)	0.579	120	0.94 (0.67–1.31)	0.715	227	0.99 (0.77–1.28)	0.969
(14,21] units per week	1,237	621	1.01 (0.85–1.21)	0.895	59	0.91 (0.62–1.33)	0.631	106	0.90 (0.67–1.21)	0.477
>21 units per week	1,519	721	0.92 (0.77–1.09)	0.332	76	0.95 (0.66–1.37)	0.795	135	0.97 (0.73–1.29)	0.840
Women †										
Current non-drinker	1,959	1,128	1	–	94	1	–	280	1	–
Current drinker	10,898	5,361	0.80 (0.73–0.89)	<0.001	429	0.87 (0.69–1.10)	0.250	889	0.69 (0.60–0.80)	<0.001
Women ‡										
Current non-drinker	1,959	1,128	1	–	94	1	–	280	1	–
Current drinker	10,898	5,361	0.86 (0.77–0.95)	0.004	429	0.99 (0.78–1.27)	0.956	889	0.76 (0.65–0.89)	<0.001
Women ‡										
Current non-drinker	1,959	1,128	1	–	94	1	–	280	1	–
(0,7] units per week	8,121	4,034	0.85 (0.77–0.95)	0.003	325	0.99 (0.77–1.27)	0.917	682	0.75 (0.64–0.89)	<0.001
(7,14] units per week	1,911	917	0.87 (0.76–1.00)	0.050	75	1.07 (0.77–1.49)	0.682	132	0.71 (0.56–0.90)	0.004
(14,21] units per week	615	295	0.88 (0.73–1.07)	0.204	22	0.97 (0.59–1.57)	0.891	55	0.93 (0.67–1.28)	0.658
>21 units per week	251	115	0.83 (0.63–1.10)	0.196	7	0.72 (0.33–1.59)	0.418	20	0.82 (0.49–1.38)	0.455

OR = Odds ratio, CI = Confidence intervals. Comparison group: Lifelong abstainer †Adjusted for age ‡ Adjusted for age, smoking status, education level(low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes
Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities
Variables used in the multiple imputation include: age, sex, social class, education level, smoking status, beer, wine, sherry, spirits (at present and at age 20 and 30), physical activity, prevalent disease, hospital admission and hospital days

6.6 Discussion

In this cohort of middle-aged and older men and women, there was no evidence of a higher hospital usage for current alcohol consumers when compared with those who do not currently report drinking alcohol. Participants who consumed alcohol were not observed to have a higher rate of hospital admission or time in hospital over the observation period of 10 years. In fact the results indicate lower hospital usage for current compared with current non-drinkers for both men and women for all levels of alcohol consumption and hospital usage before and after adjustment for age and other factors previously documented to relate to hospital usage in this cohort. There are a number of possible explanations for these findings.

6.6.1 Confounding

The frequency and pattern of alcohol use is strongly related to age, sex, education, social class, obesity, and prevalent ill health, all of which are also related to hospital usage so confounding is a major issue. However, multivariable regression models adjusting for all these variables hardly changed the findings. In addition, I stratified by main confounders (table 6.5) as well as excluding those with known prevalent heart disease, cancer and diabetes, and the results remained consistent in the subgroups. However, measurement of covariates might not be sufficiently accurate to ensure adequate adjustment and I cannot exclude the possibility of residual confounding with known or other unknown factors associated with both alcohol intake and hospital usage, which could either attenuate or strengthen the associations.

6.6.2 Bias

Differential follow-up might have occurred if participants had chosen to use private hospitals instead of NHS hospitals and the alcohol consumption of those participants differed from the study population. Participants in higher social class groups might be higher alcohol consumers and also use private healthcare not recorded in NHS hospital statistics. If this occurred it might attenuate some of the inverse associations observed. However, private healthcare use was minimal in Norfolk over the period being examined while the results presented reflect the use of National Health Service hospitals which is the predominant healthcare system.

Similarly, differential misclassification in hospital usage may be explained by early death rates. Participants who died early from alcohol attributable diseases may have lower hospital usage over the period under examination having not used hospital services for the entire period. This is unlikely as over this time period the risk of death was in fact lower in alcohol drinkers compared with non-alcohol drinkers, odds ratio (OR) 0.67 (95% CI 0.57-0.80) for men and OR 0.66 (95% CI 0.57-0.76) for women. A sensitivity analysis excluding hospital admissions prior to 2004 showed attenuated associations for men which might indicate that prevalent illness could lead to a reduction or cessation in alcohol consumption although this was not apparent in women.

Under-reporting of consumption in this study is likely given the known problems in capturing alcohol intake by questionnaire. Self-reported alcohol consumption in surveys suggest much lower consumption than estimates based on alcohol sales data [177–179]. In the 1998 Australian National Drug Strategy Household Survey, reported intake accounted for only 46.5% of known alcohol sales for the preceding 12-month period. When asked to estimate average consumption, there is a tendency to report a figure closer to median than mean consumption with heavy drinking episodes disregarded. There is also a tendency for past alcohol consumption to be remembered less well than more recent consumption. Questions relating to past consumption are insufficiently sensitive to determine periods of abstaining, binge drinking, patterns of consumption or heavy use. Nevertheless, random measurement errors or systematic underreporting of heavy alcohol consumption would only attenuate the findings observed.

Those who enrol in studies, typically in middle age, represent healthy survivors while those worst affected by alcohol misuse may be less likely to participate. Participants who drink moderately may not be representative of moderate drinkers of similar age in the general population due to differing consumption patterns over the life course [180,181]. It has also been suggested that while high levels of alcohol consumption are associated with harm in all socioeconomic groups, there appears to be a disproportionate level of harm for individuals with low socioeconomic status [182,183]. A meta-analyses that controlled for quality-related study characteristics found that moderate drinking had no net mortality benefit compared with lifetime abstention or occasional drinking [96]. However, in a large study of linked electronic UK health records using recruitment at general practice rather than individual level, moderate drinking was associated with a lower risk of several cardiovascular diseases [95].

6.6.3 Inclusion of former drinkers in the current non-drinkers reference group

The choice of reference group in describing my results may influence interpretation. Non-drinkers comprise heterogeneous subgroups with different characteristics. Former drinkers may have stopped consuming alcohol because of illness, irrespective of whether their illness was caused by drinking. They have been reported to have increased risk for cardiovascular mortality compared with long-term abstainers, a phenomenon described as the "sick-quitter" hypothesis (although some consider this term no longer acceptable) [84]. Lifelong abstainers, ostensibly an ideal reference group having no exposure, may have characteristics that are unusual in the general population [184–186]. Lifelong teetotalism is rare in men (less than 2% of those in the current study) and the reasons for abstaining such as cultural or religious beliefs, may introduce other biases obscuring the results. It has also been noted that there are substantial inconsistencies in self-reports of lifetime abstention. Others have suggested moderate drinkers with no previous history of heavy drinking as a reference group since that is the most commonly observed behaviour and forms the largest group [85,187]. The consumption of alcohol in middle-aged men and women tends to decline with age with the largest decline in heavy drinkers but with a reduction across all intake categories.

I opted to use both current non-drinkers and lifelong abstainers as reference groups in the main analyses presented. In the context of hospital usage my objective was to examine the impact on hospital services of cohort participants in relation to current alcohol use rather than pathological processes that may be involved in alcohol and disease associations. To this extent participants' previous history of alcohol consumption was less relevant than the more pragmatic question of their use of services given their current drinking status. However, I have also presented analyses using the alternative reference group of lifetime abstainers in order to better explore this issue. Estimates are less stable given the very small proportion of men who were lifetime non-drinkers. These analyses suggest that in men, the highest hospital usage was observed in former drinkers but with current alcohol drinkers also having higher hospital usage than lifelong abstainers. However, findings in women were not materially different, irrespective of whether lifelong abstainers or former drinkers were used as a reference group. There was no evidence of the "sick-quitter" effect found in women affecting the risk of hospitalisation observed in current drinkers.

6.6.4 Findings in context

These results are somewhat unexpected in the light of current beliefs about alcohol intake in the general population and hospital usage. The many diseases related to the high consumption of alcohol would lead us to expect a positive association between hospital usage and alcohol intake. Mortality rates for liver disease have increased four-fold since 1970 with liver disease the third most common cause of premature death in the UK [174]. Obesity related diseases also have a profound impact on hospital services and since alcohol's energy density is second only to fat, a positive association might be expected. However, cardiovascular disease is a predominant reason for hospital admissions, and an inverse association between alcohol intake and cardiovascular disease has been reported in many epidemiological studies [82,84,87,188]. While causality has not been established, plausible biological mechanisms such as the reduction of plaque deposit in arteries, the reduction of blood clot formation and the dissolving of blood clots[91], have supported the reported beneficial associations for ischaemic heart disease (IHD) and diabetes at moderate levels of alcohol intake. Hospitalisations might reflect the balance between positive and negative health effects of alcohol consumption in a particular study population. Most studies based on hospital cases without a population denominator are unable to assess the potential impact of moderate alcohol consumption if associated with lower hospital usage.

6.6.5 Strengths of the study

Most studies of hospital usage only have data on patients who are hospitalised, that is cases without denominators, so are unable to assess overall risk associated with alcohol consumption in the general population. I was able to examine hospital usage over a defined time period in a clearly defined community-based population using a prospective cohort design. Use of record linkage with routinely collected hospital admissions data means that ascertainment is virtually complete as use of private healthcare in Norfolk at this time period was minimal. I have previously reported that age, BMI and smoking status predict future hospital usage in this cohort over a 10-year period of follow-up [150]. Loss to follow-up is small (approximately 2%) as few study participants have moved away from the area they were recruited.

Study participants are very well characterised and I was able to take into account many potentially confounding variables documented to relate to hospital usage in this population as well as prevalent ill health. The assessment by study participants of their alcohol intake in their 20s and 30s enabled us to differentiate between current non-drinkers and lifelong abstainers. EPIC-Norfolk is homogeneous with respect to race and ethnicity with 99% describing themselves as white.

Income was not measured in EPIC-Norfolk. However, in the UK national health system, income is not the most important risk factor for hospital admissions in contrast to other health systems where treatment and medicines or health insurance must be purchased. Health insurance schemes vary, with more expensive insurance providing a broader range of treatments[144]. Preexisting conditions may not be covered and certain drugs and medicines can fall outside insurance schemes unlike the NHS where there is a standard prescription charge[189]. While it is recognised that income may influence hospital usage in the UK indirectly through loss of pay or transport costs, education and occupational social class are stronger sociodemographic indicators in this respect than income.

6.6.6 Limitations in generalisability

Potential selection biases may limit the interpretation of the data since participants were recruited in middle-age and represent survivors who may over-represent resilient and less risky drinkers. Since very few cohort participants reported heavy drinking, a limitation of the study is the inability to examine any possibly deleterious effect of very high consumption. While I did not observe a higher risk of admissions even with the highest alcohol intake categories when comparing current non-drinkers to current drinkers, there were very few people in this study population with very high alcohol consumption levels. Hence the generalisability of these findings to other populations where there are substantially more heavy drinkers may be limited. The use of current non-drinker as the reference category must also be considered alongside any interpretation of these results as evidence that the consumption of alcohol may be beneficial, but there were very few men who were lifelong abstainers in this cohort.

By using total hospital usage, I was able to assess hospital admissions not just for conditions for which alcohol might increase risk, but also the possible lower service use if alcohol at moderate intake levels were to have the postulated cardioprotective effects. The results presented here reflect hospital usage in a middle-aged and older age group and thus I am not able to comment on associations in younger people, where binge drinking resulting in acute alcohol poisoning, road traffic and other accidents are a major problem. Nevertheless, older people are by far the greatest users of hospital services and in this older cohort, which was similar to UK national samples in many respects, there was no evidence that current alcohol intake was associated with a higher level of hospital usage.

6.7 Conclusions

Current alcohol consumption was not associated with higher but lower subsequent hospital usage compared with current non-drinkers in this middle-aged and older population. The associations were consistent after multivariable adjustment for age, smoking, BMI, education, social class and prevalent illness in both men and women. In men, this association may in part be due to whether former drinkers are included in the non-drinker reference group but in women, the association was consistent irrespective of the choice of reference group. I should note however, that there were few participants in this cohort with very high current alcohol intake. The measurement of past drinking, the separation of non-drinkers into former drinkers and lifelong abstainers and the choice of reference group are all influential in interpreting the risk of alcohol consumption on future hospitalisation.

6.8 Key points

What is already known on this subject

• A large body of evidence from observational studies has suggested there are non-linear associations for alcohol with all-cause mortality and cardiovascular diseases. However, some recent studies using techniques such as Mendelian Randomisation have not replicated these findings. Concerns about selection bias and the choice of reference group may explain why inverse associations were found in the past.

• There are more than 8000 alcohol related deaths in the UK each year. However, modelling studies have identified a much higher death rate when the 230 diseases wholly or partly attributable to alcohol are considered.

• The direct and indirect costs to the NHS attributable to alcohol misuse are £3.5 billion per year.

What this study adds

• The many diseases related to the high consumption of alcohol lead us to expect a positive association between hospital usage and alcohol intake. However, I found there was no positive association of alcohol in current non-drinkers with hospitalisation — the association was in fact inverse. The association remained inverse in women when never-drinkers were used as the reference group.

• Cardiovascular disease is a predominant reason for hospital admissions in EPIC-Norfolk and these results might reflect the balance between positive and negative health effects in an older cohort of moderate drinkers.

7 Usual physical activity and subsequent hospital usage over 20 years

7.1 Overview

In this chapter, usual physical activity and the likelihood of subsequent hospitalisation is examined. It has been widely reported that pre-admission physical activity interventions lower hospital length of stay and it is also known that usual physical activity is associated with lower rates of mortality from many chronic diseases in the general population but few studies have examined usual physical activity as a predictor of hospital usage. In EPIC-Norfolk, physical activity was assessed by questionnaire with occupational questions to determine the level of physical activity for certain types of jobs and leisure-time questions to quantify time spent jogging, cycling and other physically demanding activities. The questions were validated in an earlier study against heart rate monitoring with individual calibration. Physical activity was measured at two time-points and associations with hospital usage in two subsequent 10-year time periods were examined. Change in physical activity was also assessed and the financial impact on the NHS quantified.

7.2 Abstract

Luben et al., BMC Geriatrics, 2020

While physical activity interventions have been reported to reduce hospital stays, it is not clear if, in the general population, usual physical activity patterns may be associated with subsequent hospital usage independently of other lifestyle factors. I examined the relationship between reported usual physical activity and subsequent admissions to hospital and time spent in hospital for 11,228 men and 13,786 women aged 40–79 years in the general population. Participants from a British prospective population-based study were followed for 20 years (1999–2019) using record linkage to document hospital usage. Total physical activity was estimated by combining workplace and leisure time activity reported in a baseline lifestyle questionnaire and repeated in a subset at a second time point approximately 12 years later.

Compared with those reporting no physical activity, participants who were the most active had a lower likelihood of spending more than 20 days in hospital odds ratio (OR) 0.88 (95% confidence interval (CI) 0.81–0.96) over the next 20 years after multivariable adjustment for age, sex, smoking status, education, social class and body mass index. Participants reporting any activity had a mean of 0.42 fewer hospital days per year between 1999 and 2009 compared with inactive participants, an estimated potential saving to the National Health Service (NHS) of £247 per person per year, or approximately 7% of UK health expenditure. Participants who remained physically active or became active 12 years later had lower risk of subsequent hospital usage than those who remained inactive or became inactive, p-trend < 0.001.

Usual physical activity in this middle-aged and older population predicts lower future hospitalisations — time spent in hospital and number of admissions — independently of behavioural and sociodemographic factors. Small feasible differences in usual physical activity in the general population may potentially have a substantial impact on hospital usage and costs.

7.3 Introduction

Historically UK government spending on health has risen on average by 3.7% per year since 1948, outpacing economic growth over the period [3,4]. As a result, health expenditure as a proportion of UK Gross Domestic Product (GDP) has increased from 3.6% to 7.5% over the same period. Approximately a half of government health expenditure is used for hospitals [190]. There are many factors which may influence hospital usage, not all of which are related to ill health, while increases in expenditure are only partly explained by demographic changes [14]. Changes in modifiable lifestyle factors have the potential to lower hospital length of stay. There is growing evidence of the effectiveness of preoperative exercise programmes and other pre-admission interventions in reducing hospital length of stay and readmission rates [72–75,191] but it is unclear whether in the general population, usual physical activity is related to hospital usage. Long-term randomised controlled trials (RCTs) of physical activity interventions with health endpoints are not generally feasible, so evidence is largely based on observational studies.

Physical activity is associated with lower rates of mortality from all causes and cardiovascular disease [63–65]. It is also associated with a lower risk of many non-fatal diseases [66–69] but few studies have examined the relationship between usual physical activity in middle and later life and subsequent hospital usage in the general population [70]. The measurement of usual physical activity is problematic. Objective measurements, such as accelerometry have only been developed relatively recently and hence studies based on large, free-living, community-based populations with long follow-up have used self-reported activity from questionnaires. Studies with longer follow-up time are less likely to be affected by reverse causality, which is a feature of studies with short duration of follow-up where individuals who report low physical activity at baseline are inactive by virtue of being affected by the outcome of interest. Self-reported physical activity is most often assessed by questions related to leisure-time activities [192,193]. Few studies capture both occupational and leisure-time activity.

Hospital usage can be measured by total admissions and length of stay over a fixed follow-up period. These non-disease specific outcome measures can be used to examine the overall level of health service usage [150]. Ageing populations put ever-increasing pressure on healthcare services and it is therefore important to establish if modest differences in modifiable lifestyle behaviours such as physical activity are related to hospitalisation [40,194–196].

This study examines the relationship between measures of physical activity using a validated physical activity scale, change in physical activity, and subsequent hospital usage, in older men and women living in the general community. Associations are examined over an initial 10-year follow-up period and again in a second 10-year follow-up period with independent measures, taking into account a range of demographic and lifestyle factors. A sensitivity analysis is used to investigate the role of reverse causality.

7.4 Methods

7.4.1 Statistical analysis

For the main analysis, 625 men and women who died before 1999 were excluded. Dichotomous variables were created for the socioeconomic status variables. Professional, managerial and technical and non-manual skilled occupations (codes I, II and IIIa respectively) were classed as non-manual while manual skilled, partly skilled and unskilled (codes IIIb, IV and V respectively) were classed as manual. Educational attainment was categorised into "Higher education level" (which includes those with qualifications at secondary level or above) and "Lower education level" (those with no qualifications). The numbers of individuals with missing values for covariables were: 53 BMI, 218 smoking status, 545 social class, 18 education level. The physical activity score has no missing values since those with missing data were classified being inactive.

Logistic regression was used to model hospitalisation outcomes on physical activity category, adjusting for covariables. Several dichotomous outcome categories were calculated based on total admissions and length of stay spanning two periods: 1999–2009 (10-year follow-up) and 1999–2019 (20-year follow-up). Total admissions from 10-year follow-up were used to define "any hospital admissions" and "7 or more admissions" while length of stay from 10-year follow-up was used to create "greater than 20 hospital days". These thresholds were chosen to represent those with higher levels of hospital usage and were consistent with previous work. Dichotomous outcome categories based on 20-year follow-up and having approximately the same proportion of the population as their 10-year follow-up counterparts include "12 or more admissions" and "greater than 50 hospital days" while "7 or more admissions" and "greater than 20 hospital days" were also calculated for this period to serve as a comparison. Hospital days are defined as the sum of total bed days (overnight stays) and day cases. Linear regression was used to calculate the absolute difference in adjusted mean bed days between inactive participants and participants reporting any activity.

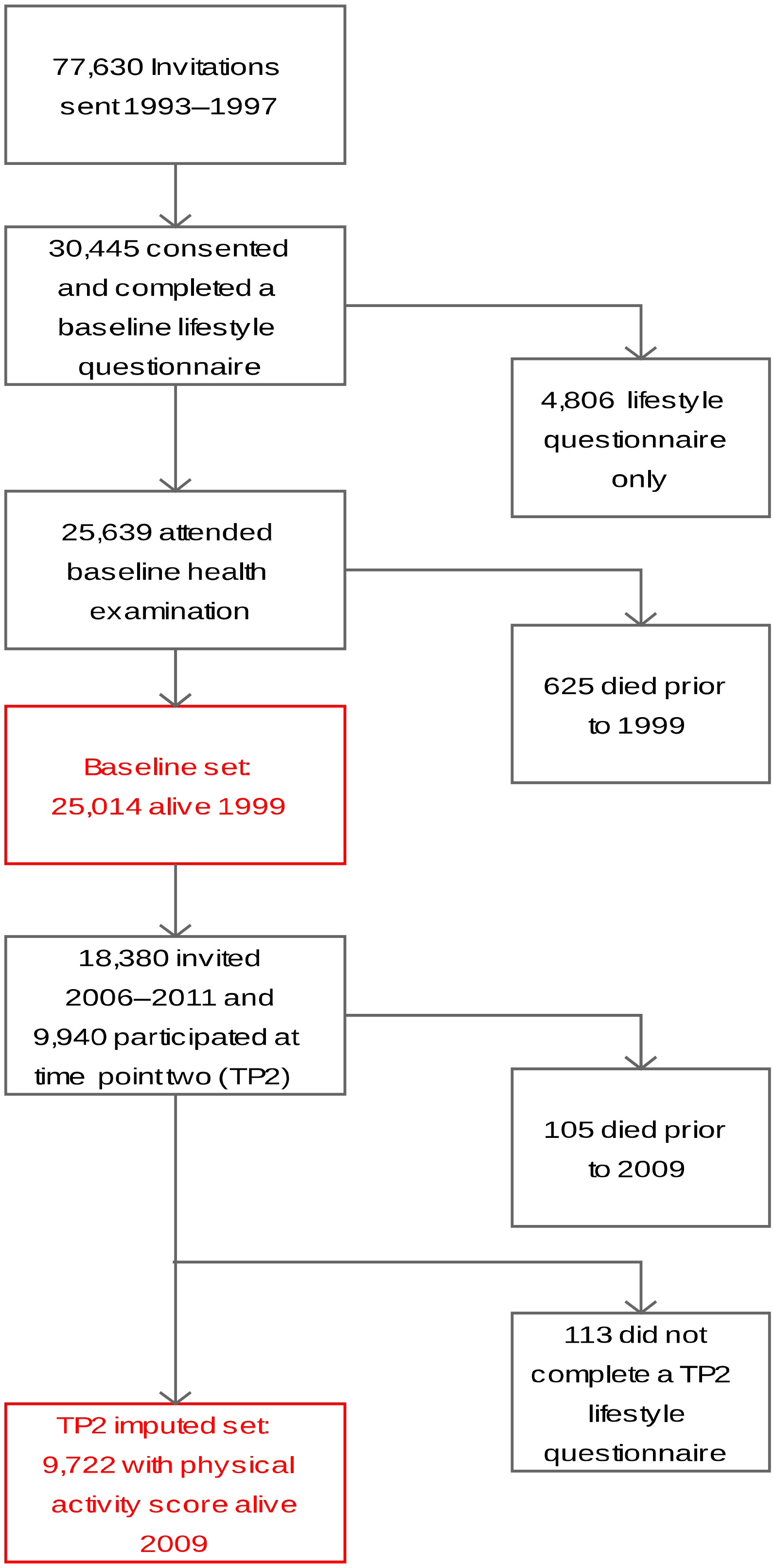
To address change in physical activity, I also used physical activity measured at TP2 approximately 12 years later as a second baseline. I excluded 105 participants who died prior to 2009, leaving 9,722. Since there was some overlap between date of health check and the hospitalisation period, hospital events occurring prior to TP2 heath check were not used. Multiple imputation was used to address missing values, in particular for body mass index at TP2 where data for 1,733 were not available for participants who completed a TP2 questionnaire but did not attend a health examination. Predictive mean matching with 5 multiple imputations and 50 iterations was used with baseline variables BMI, occupational social class and education attainment and TP2 current smoking. Changed-activity categories use combinations of physical activity categories at the baseline and TP2. The category shown as "Inactive/Inactive" is the set of participants who reported being inactive at baseline and remained inactive when asked again at TP2. The group who initially reported any activity but became inactive later is shown as "Any-activity/Inactive" while the other two categories "Inactive/Any-activity" and "Any-activity/Any-activity" were similarly defined.

The cost to the NHS of one bed day is £496, calculated using the Reference Costs for English Hospitals 2017/18 for elective (5.4 £bn) and non-elective (18 £bn) admissions [7] and the total available beds (approximately 129,200) [197]. The cost per hospital day (overnight stays and day cases) is £587 when the cost of day case activity is included (4.4 £bn per year). The reported OECD UK per capita expenditure on health in 2017, was £3,375 (exchange rate at the time of writing) [8]. Per-person costs were calculated by multiplying the cost per hospital day and hospital days per person. Percentage of NHS per-capita health expenditure was calculated as the ratio of per-person cost and OECD UK per-capita expenditure.

Adjusted mean hospital days by physical activity category were determined first by calculating hospital days for each one-year period restricted to participants surviving to the start of the given year. Linear regression of hospital days on physical activity adjusted for age, sex, occupational social class, educational attainment, current smoking and body mass index was then used. Adjusted means by category were obtained using estimated marginal means. The overall mean difference of days was calculated by taking the mean of the annual differences for each of two periods (1999–2009 and 2009–2019).

Sensitivity analyses were conducted in which the physical activity exposure was dichotomised into inactive and any-activity groups, using the outcome more than 20 hospital days over the period 1999–2019. Multivariable-adjusted odds ratios were examined, stratified by sex, age <65 and ≥65 years, manual and non-manual social class, lower (no qualifications) and higher level of education, former or never smoking and current smoking, BMI ≤30, >30 kg/m^2, chromic disease (heart attack, stroke or cancer) and no reported chronic disease, survival to the end of follow-up (March 2019) and died during follow-up period. A further multivariable model was performed using the narrower follow-up period of 2004–2019, a minimum of five years after participants reported their level of physical activity excluding participants who died prior to 2004. Figure 7.1 illustrates the recruitment phase and outcome periods over time.

Figure 7.1 | Timeline for study participants showing baseline and time-point 2 recruitment and attrition due to death, non-completion of questionnaires and non-attendance at health examinations



7.5 Results

Characteristics of the study population according to the four categories of physical activity score are described in table 7.1. Active participants tend to be younger, non-smokers, without chronic disease and have higher educational attainment, however those with manual social class also tend to be more active.

Table 7.1 | Descriptive characteristics by physical activity category measured at baseline 1993-1997

	Total	Inactive (n=7,559 30.2%)	Moderately inactive (n=7,187 28.7%)	Moderately active (n=5,688 22.7%)	Active (n=4,580 18.3%)
Body mass index, kg/m²					
Mean ±SD	26.4 ±3.9	27.0 ±4.2	26.3 ±3.9	26.0 ±3.7	25.9 ±3.5
Age, years					
Mean ±SD	59.0 ±9.3	62.5 ±9.1	58.8 ±9.2	57.1 ±8.7	56.1 ±8.4
Cigarette smoking (n (%))					
Current	2,904 (11.7)	984 (13.2)	770 (10.8)	662 (11.7)	488 (10.7)
Former	10,423 (42.0)	3,326 (44.6)	2,818 (39.5)	2,312 (40.9)	1,967 (43.2)
Never	11,469 (46.3)	3,151 (42.2)	3,540 (49.7)	2,678 (47.4)	2,100 (46.1)
Social class dichotomised (n (%))					
Non-manual	14,717 (60.1)	4,394 (60.2)	4,791 (67.8)	3,261 (58.3)	2,271 (50.4)
Manual	9,752 (39.9)	2,900 (39.8)	2,278 (32.2)	2,337 (41.7)	2,237 (49.6)
Level of education (n (%))					
Higher level	15,866 (63.5)	4,252 (56.4)	4,757 (66.2)	3,823 (67.2)	3,034 (66.2)
Lower level	9,130 (36.5)	3,289 (43.6)	2,430 (33.8)	1,865 (32.8)	1,546 (33.8)
Prevalent disease (n (%))					
No reported chronic disease	22,721 (91.0)	6,606 (87.7)	6,573 (91.5)	5,246 (92.3)	4,296 (93.9)
Self-report chronic disease	2,254 (9.0)	927 (12.3)	608 (8.5)	439 (7.7)	280 (6.1)
Hospital activity 1999–2019					
No admissions	2,483 (9.9)	625 (8.3)	726 (10.1)	613 (10.8)	519 (11.3)
One or more admissions	22,497 (90.1)	6,915 (91.7)	6,453 (89.9)	5,072 (89.2)	4,057 (88.7)
Time in hospital 1999–2019					
Mean ±SD	34.0 ±63.7	42.4 ±68.2	32.9 ±64.1	29.9 ±66.4	26.8 ±48.8
Median (IQR)	14.0 (3.0 - 41.0)	21.0 (6.0 - 56.0)	13.0 (3.0 - 39.0)	11.0 (3.0 - 33.0)	10.0 (2.8 - 30.0)
Number of admissions 1999–2019					
Mean ±SD	7.8 ±26.5	8.4 ±29.0	7.6 ±24.5	7.8 ±32.2	6.9 ±14.8
Median (IQR)	4.0 (2.0 - 9.0)	5.0 (2.0 - 9.0)	4.0 (2.0 - 8.0)	4.0 (2.0 - 8.0)	4.0 (2.0 - 8.0)
Survival to the end of follow-up (n (%))					
Alive after March 2019	15,919 (63.6)	3,732 (49.4)	4,746 (66.0)	4,047 (71.1)	3,394 (74.1)
Died prior to March 2019	9,095 (36.4)	3,827 (50.6)	2,441 (34.0)	1,641 (28.9)	1,186 (25.9)

Prevalent disease is self-reported heart attack, stroke or cancer at baseline. Higher education level represents those with qualifications to at least secondary level.

In table 7.2 odds ratios are shown, first age and sex adjusted and then additionally adjusted for social class, educational attainment, BMI and smoking status. For the 10-year follow-up period 1999–2009, outcomes of any hospital admission, 7 or more hospital admissions and more than 20 days stay in hospital are shown according to the baseline physical activity score. The multivariable-adjusted models indicate that participants with a physical activity score of at least moderately inactive had fewer hospital admissions and fewer days in hospital, than those who were inactive. The associations for inactive vs active were OR 0.73 (95% CI 0.65–0.82) p-trend < 0.001 across activity score for 7 or more hospital admissions and OR 0.75 (95% CI 0.67–0.83) p-trend < 0.001 for more than 20 hospital days.

Table 7.2 | Multivariable logistic regression of risk factors by physical activity category for hospital admissions and length of hospital stay categories over 10 years (1999 to 2009) and 20 years (1999 to 2019) in 25,014 men and women and 10 years (2009-2019) using the TP2 baseline in 9,722 men and women

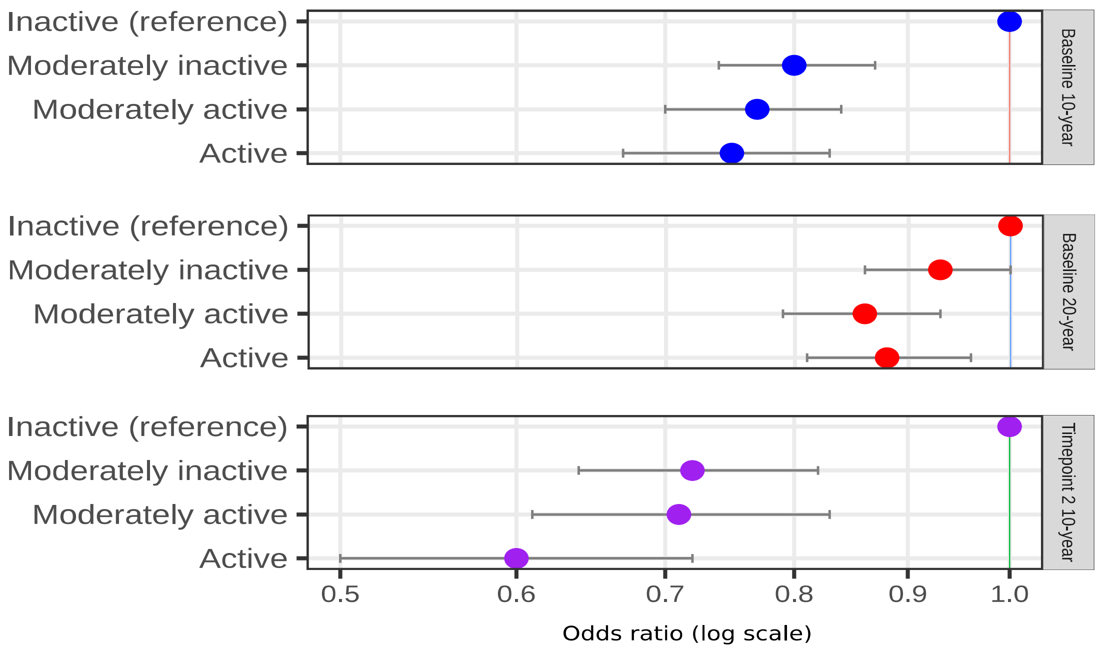
	Inactive n=7,559	Moderately inactive n=7,187	Moderately active n=5,688	Active n=4,580	p (trend)
10-year follow-up					
Outcome of any hospital admissions (18,179/25,014)					
n (%)	5,878 (78%)	5,103 (71%)	3,980 (70%)	3,218 (70%)	
Model 1†	1.00	0.87 (0.80–0.94)	0.90 (0.83–0.97)	0.96 (0.88–1.05)	0.373
Model 2‡	1.00	0.91 (0.84–0.98)	0.91 (0.84–0.99)	0.95 (0.87–1.04)	0.286
Outcome of seven or more hospital admissions (3,462/25,014)					
n (%)	1,392 (18%)	891 (12%)	689 (12%)	490 (11%)	
Model 1†	1.00	0.76 (0.69–0.83)	0.79 (0.71–0.87)	0.71 (0.63–0.79)	< 0.001
Model 2‡	1.00	0.80 (0.72–0.88)	0.82 (0.73–0.91)	0.73 (0.65–0.82)	< 0.001
Outcome of more than 20 hospital days (4,976/25,014)					
n (%)	2,122 (28%)	1,299 (18%)	893 (16%)	662 (14%)	
Model 1†	1.00	0.75 (0.69–0.81)	0.72 (0.66–0.79)	0.71 (0.64–0.79)	< 0.001
Model 2‡	1.00	0.80 (0.74–0.87)	0.77 (0.70–0.84)	0.75 (0.67–0.83)	< 0.001
20-year follow-up					
Outcome of any hospital admissions (22,497/25,014)					
n (%)	6,915 (91%)	6,453 (90%)	5,072 (89%)	4,057 (89%)	
Model 1†	1.00	1.06 (0.94–1.19)	1.07 (0.95–1.21)	1.08 (0.95–1.22)	0.238
Model 2‡	1.00	1.11 (0.98–1.24)	1.10 (0.97–1.25)	1.08 (0.95–1.23)	0.274
Outcome of seven or more hospital admissions (8,849/25,014)					
n (%)	2,969 (39%)	2,490 (35%)	1,879 (33%)	1,511 (33%)	
Model 1†	1.00	0.94 (0.88–1.01)	0.92 (0.85–0.99)	0.94 (0.87–1.02)	0.055
Model 2‡	1.00	0.98 (0.91–1.05)	0.94 (0.87–1.01)	0.96 (0.89–1.05)	0.194
Outcome of 12 or more hospital admissions (3,989/25,014)					
n (%)	1,354 (18%)	1,088 (15%)	894 (16%)	653 (14%)	
Model 1†	1.00	0.90 (0.82–0.98)	0.95 (0.87–1.05)	0.85 (0.76–0.94)	0.010
Model 2‡	1.00	0.95 (0.87–1.04)	0.98 (0.89–1.08)	0.87 (0.78–0.97)	0.040
Outcome of more than 20 hospital days (10,174/25,014)					
n (%)	3,800 (50%)	2,836 (39%)	1,996 (35%)	1,542 (34%)	
Model 1†	1.00	0.87 (0.81–0.93)	0.82 (0.76–0.88)	0.84 (0.77–0.91)	< 0.001
Model 2‡	1.00	0.93 (0.86–1.00)	0.86 (0.79–0.93)	0.88 (0.81–0.96)	< 0.001
Outcome of more than 50 hospital days (5,178/25,014)					
n (%)	2,065 (27%)	1,411 (20%)	994 (17%)	708 (15%)	
Model 1†	1.00	0.85 (0.79–0.93)	0.86 (0.78–0.94)	0.81 (0.73–0.89)	< 0.001
Model 2‡	1.00	0.91 (0.84–0.99)	0.91 (0.83–1.00)	0.84 (0.76–0.94)	0.001
	Inactive n=3,937	**Moderately inactive n=2,686**	**Moderately active n=1,655**	**Active n=1,444**	**p (trend)**
10-year follow-up from TP2 baseline					
Outcome of any hospital admissions (7,855/9,722)					
n (%)	3,332 (85%)	2,127 (79%)	1,267 (77%)	1,129 (78%)	
Model 1†	1.00	0.93 (0.81–1.06)	0.85 (0.73–0.99)	1.00 (0.85–1.17)	0.484
Model 2‡	1.00	0.97 (0.85–1.11)	0.90 (0.77–1.05)	1.04 (0.88–1.22)	0.922
Outcome of seven or more hospital admissions (1,802/9,722)					
n (%)	874 (22%)	466 (17%)	259 (16%)	203 (14%)	
Model 1†	1.00	0.89 (0.78–1.01)	0.81 (0.69–0.94)	0.73 (0.62–0.87)	< 0.001
Model 2‡	1.00	0.93 (0.82–1.06)	0.84 (0.72–0.99)	0.77 (0.64–0.91)	0.001
Outcome of more than 20 hospital days (2,170/9,722)					
n (%)	1,217 (31%)	489 (18%)	273 (16%)	191 (13%)	
Model 1†	1.00	0.69 (0.61–0.78)	0.69 (0.59–0.80)	0.57 (0.48–0.68)	< 0.001
Model 2‡	1.00	0.72 (0.64–0.82)	0.71 (0.61–0.83)	0.60 (0.50–0.72)	< 0.001

† Adjusted for age and sex. ‡ Adjusted for age, sex, manual social class, lower education level, current cigarette smoker, body mass index > 30kg/m².

Attenuated results were observed for longer follow-up. Odds ratios over the 20-year period 1999–2019 are presented for any hospital admission, ≥7 admissions, ≥12 admissions, >20 hospital days and >50 hospital days and associations were OR 0.96 (95% CI 0.89–1.05) p-trend 0.194 for ≥7 admissions, OR 0.87 (95% CI 0.78–0.97) p-trend 0.040 for ≥12 admissions, and OR 0.88 (95% CI 0.81–0.96) p-trend < 0.001 for >20 hospital days, OR 0.84 (95% CI 0.76–0.94) p-trend 0.001 for >50 hospital days. Associations for >20 hospital days and >50 hospital days were similar, while the inverse association using the threshold of ≥12 admissions was higher than that for the ≥7 admissions threshold.

Physical activity category at TP2 baseline was determined in 9,827 men and women. The characteristics of participants at TP2 are described in table 4.8 in chapter 4. The associations for inactive vs active for 20 hospital days over the subsequent 10-year follow-up period (2009 to 2019) were stronger than those for the first 10-year follow-up period OR 0.60 (95% CI 0.50–0.72) p-trend < 0.001 and similar for 7 or more admissions OR 0.77 (95% CI 0.64–0.91) p-trend 0.001. Figure 7.2 illustrates these associations, contrasting the 3 time periods, baseline 10-year, baseline 20-year and TP2 10-year, using the outcome of hospital stay >20 days in fully adjusted multivariable models.

Figure 7.2 | Multivariable odds ratios for baseline physical activity categories over 10-year (1999-2009) and 20-year (1999-2019) time periods in 25,014 men and women and time-point 2 physical activity categories over 10-years (2009-2019) in 9,827 men and women, using the outcome of >20 hospital days



Multivariable logistic regression odds ratios and 95% confidence interval adjusted for age, current cigarette smoking, low education level, manual social class, body mass index > 30 kg/m²

Table 7.3 shows multivariable-adjusted odds ratios for outcome more than 20 hospital days during the 1999–2019 follow-up in participants who were inactive compared with those reporting any activity at baseline, stratified by key variables in subgroups. The directions of the associations did not differ by subgroup. Higher inverse associations were seen in women, in the under 65s, in those with no chronic disease at baseline and those surviving to the end of follow-up although confidence intervals overlapped in each case. Table 7.3 also shows that the association for the period 2004–2019, excluding the first five years of the outcome period was OR 0.93 (95% CI 0.87–1.00).

Table 7.3 | Multivariable logistic regression of simple physical activity index and more than 20 hospital days in subgroups after 20 years follow-up

	Inactive (n=7,559) (ref)	Any-activity (n=17,455) OR (95% CI)†
Men and women		
Men (n=11,228)	1	0.92 (0.84–1.01)
Women (n=13,786)	1	0.87 (0.80–0.95)
By age above and below 65 years		
Younger than 65 years (n=17,372)	1	0.86 (0.80–0.93)
65 years and older (n=7,642)	1	0.91 (0.83–1.01)
Manual and non-manual social class		
Non-manual (n=14,717)	1	0.89 (0.82–0.97)
Manual (n=9,752)	1	0.89 (0.81–0.99)
By level of education		
Higher level (n=15,866)	1	0.91 (0.84–0.98)
Lower level (n=9,130)	1	0.87 (0.78–0.95)
By smoking status		
Former or never smoker (n=21,892)	1	0.88 (0.83–0.95)
Current smoker (n=2,904)	1	0.97 (0.82–1.16)
By level of body mass index		
BMI ≤ 30 kg/m² (n=21,158)	1	0.90 (0.84–0.97)
BMI > 30 kg/m² (n=3,803)	1	0.86 (0.75–1.00)
Prevalent disease		
No reported chronic disease (n=22,721)	1	0.90 (0.84–0.96)
Self-report chronic disease (n=2,254)	1	0.94 (0.78–1.14)
Survival to end of follow-up		
Alive after March 2019 (n=15,919)	1	0.90 (0.82–0.98)
Died prior to March 2019 (n=9,095)	1	0.99 (0.90–1.10)
Excluding first five years		
Admissions between 2004–2019 (n=23,487)	1	0.93 (0.87–1.00)

† Adjusted for age, sex, manual social class, lower education level , current cigarette smoker, body mass index > 30kg/m².

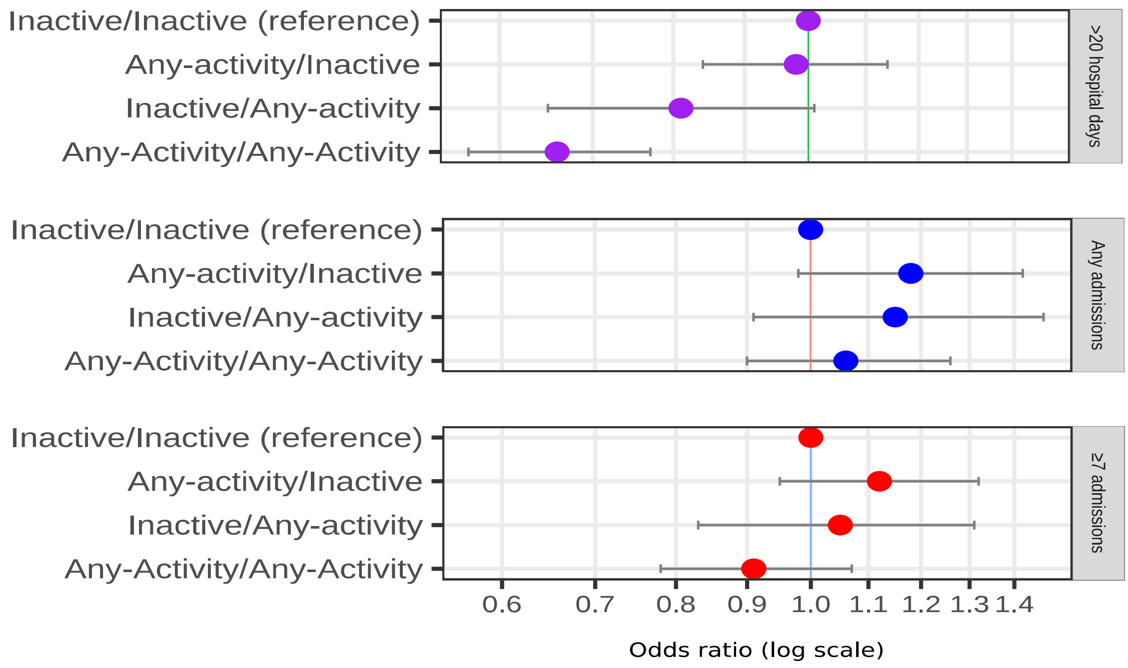
Table 7.4 shows odds ratios by all combinations of change in physical activity category between baseline and TP2 were determined using the TP2 baseline and subsequent 10-year follow-up. The multivariable-adjusted odds ratios comparing "Inactive/Inactive" (the reference) and "Any-activity/Any-activity" were OR 0.66 (95% CI 0.57–0.77) p-trend < 0.001 across changed-activity categories for more than 20 hospital days and OR 0.91 (95% CI 0.78–1.07) p-trend 0.026 for seven or more hospital admissions. Participants who remained physically active or became active had lower risk of subsequent hospital usage than those who remained inactive or became inactive. Figure 7.3 illustrates changed-activity categories associations, using the 3 outcome measures, >20 hospital days, any admissions and ≥7 admissions in fully adjusted multivariable models.

Table 7.4 | Multivariable logistic regression of risk factors by change in physical activity category between baseline and TP2 for hospital admissions and length of hospital stay categories over 10 years (2009 to 2019) in 9,722 men and women

	Inactive/Inactive n=1,441	Any-activity/Inactive n=2,496	Inactive/Any-activity n=790	Any-activity/Any-activity n=4,995	p (trend)
Outcome of any hospital admissions (7,855/25,014)					
n (%)					
Model 1†	1.00	1.16 (0.96–1.39)	1.10 (0.87–1.39)	1.00 (0.85–1.18)	0.246
Model 2‡	1.00	1.18 (0.98–1.42)	1.15 (0.91–1.47)	1.06 (0.90–1.26)	0.751
Outcome of seven or more hospital admissions (1,802/25,014)					
n (%)					
Model 1†	1.00	1.09 (0.93–1.28)	1.00 (0.80–1.25)	0.86 (0.74–1.00)	0.002
Model 2‡	1.00	1.12 (0.95–1.32)	1.05 (0.83–1.31)	0.91 (0.78–1.07)	0.026
Outcome of more than 20 hospital days (2,170/25,014)					
n (%)					
Model 1†	1.00	0.96 (0.83–1.11)	0.78 (0.62–0.96)	0.62 (0.54–0.72)	< 0.001
Model 2‡	1.00	0.98 (0.84–1.14)	0.81 (0.65–1.01)	0.66 (0.57–0.77)	< 0.001

† Adjusted for age at TP2 and sex. ‡ Adjusted for age at TP2, sex, baseline manual social class, baseline lower education level, current cigarette smoker at TP2, body mass index > 30kg/m² at TP2. Multiple imputation was used for 1,733 missing BMI at TP2 calculated using baseline BMI and other covariates for participants who completed questionnaires but did not attend a health examination.

Figure 7.3 | Multivariable odds ratios and 95% confidence intervals for combinations of change in physical activity categories between baseline and time-point 2 in 9,722 men and women for outcomes >20 hospital days, any admissions and ≥7 admissions



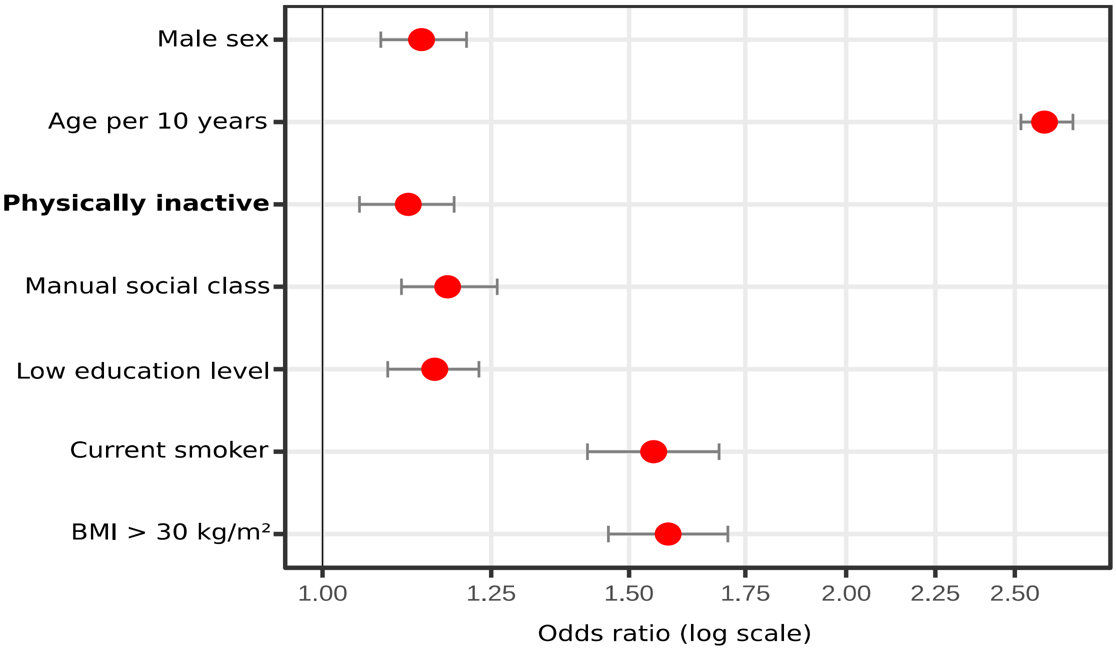
Multivariable logistic regression odds ratio and 95% confidence interval adjusted for age, current cigarette smoking, low education level, manual social class, body mass index > 30 kg/m²

Table 7.5 shows all terms in a series of multivariable logistic regression models for inactive physical activity (vs any-activity) and various dichotomous outcomes over the period 1999–2019 for all, men and women. Covariables age per 10 years, manual social class, lower education level, current smoking and BMI>30 kg/m^2 are modelled; all are independently associated with the number of hospital admissions and length of stay. Associations were similar in men and women. The duration outcomes >20 and >50 hospital days were associated with the binary physical activity classification although associations with numbers of hospital admissions were attenuated. Figure 7.4 illustrates the multivariable adjusted 20 hospital days association for men and women over the 20 year period 1999–2019.

Table 7.5 | Multivariable logistic regression of risk factors for any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999 to 2019 in 25,014 men and women

	All subjects OR (95% CI)	p value	Men OR (95% CI)	p value	Women OR (95% CI)	p value
Outcome of any hospital admissions						
Male sex	1.13 (1.03–1.23)	0.007				
Age per 10 years	2.07 (1.96–2.19)	< 0.001	2.15 (1.98–2.33)	< 0.001	2.01 (1.87–2.17)	< 0.001
Inactive	0.91 (0.82–1.01)	0.073	0.91 (0.78–1.07)	0.243	0.91 (0.80–1.05)	0.187
Manual social class	1.15 (1.05–1.26)	0.003	1.19 (1.03–1.38)	0.016	1.12 (0.99–1.27)	0.077
Lower education level	1.42 (1.27–1.58)	< 0.001	1.23 (1.04–1.47)	0.016	1.54 (1.35–1.77)	< 0.001
Current smoker	1.18 (1.03–1.35)	0.019	1.14 (0.93–1.40)	0.207	1.20 (1.01–1.45)	0.046
BMI>30 kg/m²	1.30 (1.14–1.49)	< 0.001	1.19 (0.97–1.47)	0.108	1.38 (1.16–1.64)	< 0.001
Outcome of seven or more hospital admissions						
Male sex	1.21 (1.15–1.28)	< 0.001				
Age per 10 years	1.45 (1.40–1.49)	< 0.001	1.45 (1.38–1.51)	< 0.001	1.45 (1.39–1.51)	< 0.001
Inactive	1.04 (0.98–1.10)	0.197	1.02 (0.93–1.11)	0.735	1.06 (0.98–1.15)	0.145
Manual social class	1.16 (1.09–1.23)	< 0.001	1.16 (1.06–1.26)	< 0.001	1.16 (1.07–1.25)	< 0.001
Lower education level	1.14 (1.07–1.21)	< 0.001	1.13 (1.03–1.23)	0.011	1.15 (1.06–1.24)	< 0.001
Current smoker	1.33 (1.23–1.45)	< 0.001	1.25 (1.11–1.41)	< 0.001	1.41 (1.26–1.58)	< 0.001
BMI>30 kg/m²	1.38 (1.28–1.48)	< 0.001	1.38 (1.23–1.54)	< 0.001	1.38 (1.25–1.52)	< 0.001
Outcome of more than 20 hospital days						
Male sex	1.14 (1.08–1.21)	< 0.001				
Age per 10 years	2.60 (2.52–2.70)	< 0.001	2.53 (2.41–2.66)	< 0.001	2.67 (2.54–2.80)	< 0.001
Inactive	1.12 (1.05–1.19)	< 0.001	1.08 (0.99–1.19)	0.084	1.14 (1.05–1.25)	0.002
Manual social class	1.18 (1.11–1.26)	< 0.001	1.20 (1.10–1.31)	< 0.001	1.17 (1.07–1.27)	< 0.001
Lower education level	1.16 (1.09–1.23)	< 0.001	1.18 (1.07–1.30)	< 0.001	1.14 (1.05–1.24)	0.002
Current smoker	1.55 (1.42–1.69)	< 0.001	1.53 (1.35–1.74)	< 0.001	1.56 (1.38–1.76)	< 0.001
BMI>30 kg/m²	1.58 (1.46–1.71)	< 0.001	1.54 (1.37–1.74)	< 0.001	1.61 (1.45–1.78)	< 0.001
Outcome of 12 or more hospital admissions						
Male sex	1.31 (1.22–1.41)	< 0.001				
Age per 10 years	1.26 (1.21–1.31)	< 0.001	1.31 (1.24–1.38)	< 0.001	1.22 (1.15–1.29)	< 0.001
Inactive	1.06 (0.98–1.15)	0.124	1.07 (0.96–1.20)	0.193	1.05 (0.94–1.17)	0.352
Manual social class	1.20 (1.12–1.29)	< 0.001	1.19 (1.07–1.32)	0.001	1.22 (1.10–1.35)	< 0.001
Lower education level	1.06 (0.98–1.15)	0.119	1.00 (0.90–1.12)	0.934	1.12 (1.01–1.25)	0.035
Current smoker	1.42 (1.28–1.57)	< 0.001	1.28 (1.10–1.48)	0.001	1.58 (1.37–1.82)	< 0.001
BMI>30 kg/m²	1.33 (1.21–1.45)	< 0.001	1.38 (1.21–1.58)	< 0.001	1.28 (1.13–1.45)	< 0.001
Outcome of more than 50 hospital days						
Male sex	1.02 (0.95–1.09)	0.647				
Age per 10 years	2.41 (2.32–2.51)	< 0.001	2.22 (2.10–2.36)	< 0.001	2.58 (2.44–2.74)	< 0.001
Inactive	1.12 (1.04–1.20)	0.002	1.03 (0.93–1.15)	0.558	1.19 (1.08–1.31)	< 0.001
Manual social class	1.17 (1.09–1.26)	< 0.001	1.21 (1.09–1.34)	< 0.001	1.14 (1.04–1.26)	0.007
Lower education level	1.15 (1.07–1.24)	< 0.001	1.16 (1.04–1.30)	0.006	1.14 (1.03–1.25)	0.011
Current smoker	1.56 (1.41–1.73)	< 0.001	1.51 (1.30–1.74)	< 0.001	1.61 (1.40–1.85)	< 0.001
BMI>30 kg/m²	1.48 (1.35–1.61)	< 0.001	1.46 (1.27–1.66)	< 0.001	1.50 (1.33–1.68)	< 0.001

Figure 7.4 | Multivariable odds ratios of spending >20 days in hospital over a 20-year period



Multivariable logistic regression odds ratios and 95% confidence interval adjusted for sex, age, current cigarette smoking, low education level, manual social class, body mass index > 30 kg/m²

Table 7.6 shows the adjusted mean hospital days for inactive and any-activity participants by year, and the absolute difference in days between the categories. The mean of the differences was calculated for 1999–2009 using baseline physical activity and 2009–2019 using physical activity at TP2 and cumulative costs were determined assuming £587 per hospital day.

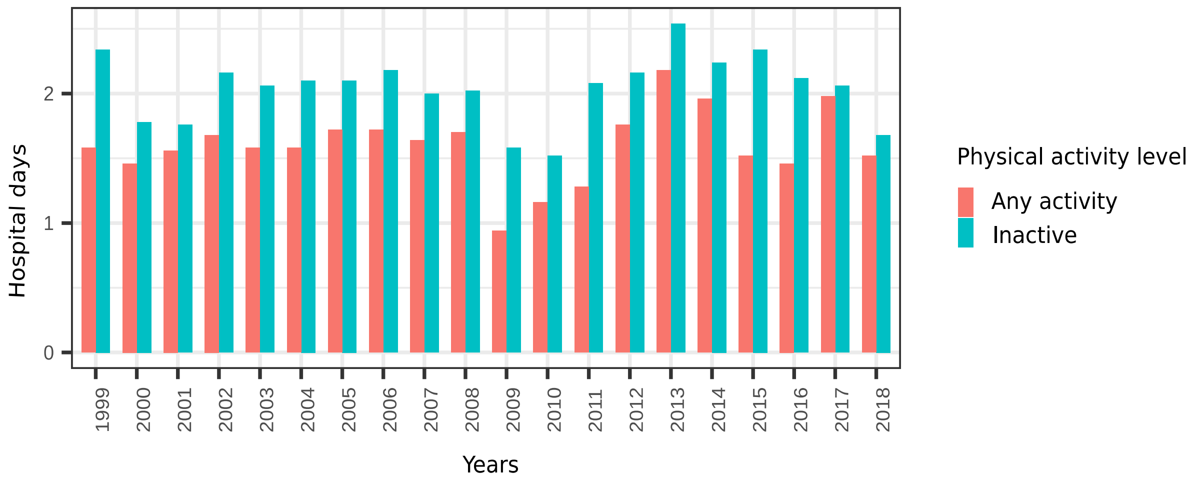
The difference in multivariable-adjusted mean hospital days between inactive participants and participants reporting any activity was 0.42 days per year over the first 10 years of follow-up, an estimated potential saving to the NHS of £247 per person per year or approximately 7% of health expenditure. The difference in hospital days over the subsequent 10 years (2009–2019) was slightly higher, with any-activity participants having 0.46 fewer hospital days, an estimated potential saving of £268 per person per year or approximately 8% of health expenditure. Figure 7.5 shows the multivariable adjusted differences in mean hospital days by year, contrasting inactive participants with participants who do any activity.

Table 7.6 | Adjusted † mean hospital days by physical activity category for two periods, mean difference in days and cumulative cost, 1999–2009 using baseline physical activity and 2009–2019 using physical activity at TP2

	Cohort survivors	Hospital Days inactive	Hospital Days any-activity	Difference in hospital days	Mean difference over period	Cumulative cost £
1999–2009						
1999	24,785	2.34	1.58	0.74	0.42	248
2000	24,528	1.78	1.46	0.34	0.42	495
2001	24,237	1.76	1.56	0.20	0.42	743
2002	23,916	2.16	1.68	0.48	0.42	991
2003	23,575	2.06	1.58	0.46	0.42	1,239
2004	23,221	2.10	1.58	0.52	0.42	1,486
2005	22,864	2.10	1.72	0.36	0.42	1,734
2006	22,456	2.18	1.72	0.46	0.42	1,982
2007	22,003	2.00	1.64	0.34	0.42	2,230
2008	21,557	2.02	1.70	0.32	0.42	2,477
2009–2019						
2009	9,642	1.58	0.94	0.62	0.46	2,746
2010	9,533	1.52	1.16	0.38	0.46	3,015
2011	9,389	2.08	1.28	0.78	0.46	3,283
2012	9,222	2.16	1.76	0.42	0.46	3,552
2013	9,023	2.54	2.18	0.38	0.46	3,821
2014	8,859	2.24	1.96	0.28	0.46	4,089
2015	8,619	2.34	1.52	0.82	0.46	4,358
2016	8,362	2.12	1.46	0.66	0.46	4,627
2017	8,101	2.06	1.98	0.08	0.46	4,895
2018	7,948	1.68	1.52	0.18	0.46	5,164

† Adjusted for age, sex, manual social class, lower education level, current cigarette smoker, body mass index > 30kg/m².

Figure 7.5 | Multivariable adjusted mean hospital days by inactive and any-activity participants, for each year 1999-2008 using baseline physical activity and each year 2009-2019 using physical activity at time-point 2



Multivariable logistic regression mean hospital days adjusted for sex, age, current cigarette smoking, low education level, manual social class, body mass index > 30 kg/m²

7.6 Discussion

Usual physical activity assessed at baseline survey in 1993–1997 was inversely associated with future hospital usage independently of sociodemographic and lifestyle factors in this middle-aged and older cohort of men and women over a 20-year follow-up period. Compared with study participants who were inactive, active participants had a lower likelihood of having more than 20 hospital days or more than 12 admissions. Stronger associations were seen over a 10-year follow-up period with moderate inactivity or greater being associated with lower risk of seven or more hospital admissions or more than 20 hospital days. There was a dose response over physical activity categories over both the 10-year and 20-year follow-up periods for both hospital duration and number of admissions. There are a number of possible explanations for these findings.

7.6.1 Strengths and limitations of the study

Reverse causality may partly explain the associations I observed. Participants may be physically inactive occupationally or less able to take part in leisure time activity because of known or preclinical illness which may also predispose to increased later hospitalisation [198]. However, sensitivity analyses excluding those with a self-reported chronic disease at baseline (heart attack, stroke or cancer), who might have lower physical activity, did not materially differ from the main findings. Also, a sensitivity analysis excluding hospital admissions occurring in the first five years of follow-up (the period 2004–2019), that is, those who were more likely to have preclinical illness and lowered physical activity, again did not show materially different associations.

Confounding is a major issue in examining the relationship between lifestyle factors and health outcomes. Individuals who are more physically active are likely to differ from those who are less active with respect to other factors relating to the likelihood of future hospitalisation including age, sex, smoking, body mass index, social class and education. However, the associations were consistent after multivariable adjustment for these factors and after stratification by these potential confounding variables.

As I examined total hospital usage over long time periods, individuals who died during the follow-up period did not use hospital services for the full period. This may have affected the results if there was differential mortality by physical activity, whereby study participants who were inactive were more likely to have died earlier than the more active participants and hence less likely to use hospital services for the full follow-up period. Sensitivity analysis models, restricted to those surviving to the end of 20-year follow-up, showed stronger associations of physical activity with lower hospital usage than models using the whole population, including those who died during the follow-up period, suggesting there was some attenuation due to selective follow-up.

This study has several strengths. Few studies have examined the physical activity of middle-aged and older men and women and their subsequent healthcare utilisation. The literature falls into two groups, studies based on exercise interventions and observational studies. While most intervention studies provide some evidence that a physically active lifestyle improves health, intervention protocols vary and differences in dropout rates between groups in RCTs limit generalisability [77]. Intervention studies typically have smaller study size and shorter follow-up time and while observational studies are generally larger, there a few studies comparable in size to the present study. My study being well characterised allowed adjustment for a broad range of relevant factors. I also used linked hospital data and did not depend on self-reported outcome data. Many studies are based on particular population groups or particular disease outcomes and some rely on self-selection to exercise programs. Few studies examine free living community-based populations [71,199]. My study used a prospective cohort design and was able to examine hospital usage over a long follow-up period with a reliable population-based denominator.

My study was based on a free-living population of older men and women living in the general community in the United Kingdom where the NHS provides healthcare free at the point of delivery. Potential major confounders such as income and ability to pay, that might therefore affect and limit access and use of health services, are less likely to apply in this study. Income was not measured in

EPIC-Norfolk. However, the UK national health system differs from other health systems where healthcare relies on the purchase of health insurance. Insurance schemes vary in the care they provide, with their cost affecting the range of treatments, exclusion of certain drugs, preexisting conditions, maternity care and ambulance call-out charges [144,189]. Hence, people of low income or low socioeconomic status are much less likely to have access to health services. While it is recognised that income may influence hospital usage in the UK indirectly through loss of pay or transport costs, education and occupational social class are stronger sociodemographic indicators in this respect than income. However, if differential access makes some with lower social class less likely to access health services, the results presented are likely to be attenuated. The NHS also enables record linkage for virtually complete follow-up of the population. Though admissions to private hospitals in Norfolk were not included in my data which only counts NHS hospitals, the use of private hospitals in Norfolk was minimal in comparison with the use of NHS facilities.

Measurement of usual occupational and leisure time physical activity was assessed using a self-reported questionnaire. Objective measures such as accelerometry and similar techniques were not available when the EPIC-Norfolk cohort was recruited. However, the score was previously validated using heart rate monitoring with individual calibration and based on both occupational and leisure-based components of physical activity.

It is also clear that a single measurement of physical activity is insufficient to determine accurately usual levels of activity over the life course. Events such as retirement or illness or progressive ageing related conditions such as frailty may result in a change to the amount of physical activity undertaken [200]. While I was unable to establish the length of time over which consistent physical activity was maintained, I was able to examine longitudinal measurements of physical activity at two time-points in a subset of participants. The associations observed at the later time-point were comparable with (in fact stronger than) those observed at the first time-point, despite the cohort mean age being approximately 10 years older and having a much higher proportion of retirees. Change in behaviour over the 20-year follow-up period is a more likely explanation for the attenuated associations observed, rather than age or employment status. Participants who remained inactive or became inactive had the highest risk of subsequent hospitalisation. However, random measurement error is likely only to attenuate associations, and therefore unlikely to explain any of the associations observed between physical activity and hospitalisation.

7.6.2 Comparison with other studies

Physical activity has been associated with many health benefits including protection against cardiovascular disease [63,65,201] which remains the leading cause of hospitalisation. Nocon et al report findings of 33 studies in a systematic review. The majority of studies reported significant reductions in the risk of cardiovascular and all-cause mortality for physically active participants in both men and women. However, studies that used questionnaires to assess physical activity reported lower risk reductions than studies that used objective measures. The findings of a systematic review from Ahad Wahid et al., which examined 36 studies, had similar findings but using a continuous index of physically active and examined both CVD and type 2 diabetes. Bennett et al. was able to differentiate between occupational and nonoccupational physical activity using a questionnaire in a large study using the China Kadoorie Biobank. They found that, among Chinese adults, higher occupational or nonoccupational physical activity was associated with lower risk of fatal and non-fatal cardiovascular disease. Many other chronic diseases have been reported to be inversely associated with physical activity. [202] reports on the economic burden of physical inactivity by measuring direct health-care costs, productivity losses, and disability-adjusted life-years using data from 142 countries. They considered cardiovascular disease, type 2 diabetes, breast and colon cancer attributable to physical inactivity and estimate that physical inactivity costs health-care systems 53·8 billion worldwide of which 31.2 billion was borne by the public sector. Few studies have reported on physical activity and hospitalisation. Sari et al. [203] examined various chronic diseases including high blood pressure, diabetes, heart disease, cancer, and stroke using the Canadian National Population Health Survey and subsequent hospital length of stay. They reported that moderately active and active individuals have lower hospital length of stay for the entire population but the association was substantially larger in the subgroup with chronic conditions. The large body of literature reported relationships between physical activity and individual conditions also suggest there might be an association with lower hospitalisations. However, in this study, I was able to examine total hospital usage in a general population irrespective of cause of admission.

Small increases in physical activity have been reported to obtain cost savings for health services by reducing hospital admissions [70,195,204–206] with many studies reporting reductions of length of stay after preoperative physical activity interventions. My study, which measured usual physical activity rather than preoperative physical activity interventions, nevertheless observed a 12%–13% lower risk of long stay and high numbers of admissions by physical activity category. The mean difference in hospital days between inactive and any-activity participants in my study was 0.42 days per year over the first 10 years of follow-up. Assuming a cost of £587 per hospital day (inpatient bed days and day cases), the potential saving to the NHS is approximately £247 per person per year for every inactive person who starts to undertake at least some exercise, or about 7% of UK per capita health expenditure. Similar results were observed 10 years later when participants were aged 50–90 years. Calculations such as these are unavoidably crude but serve to illustrate the significant financial contribution, when scaled nationally, that modest changes in lifestyle can achieve quite apart from the obvious personal gain from the reduction in risk of being hospitalised.

While there is evidence suggesting that pre-admission physical activity programmes may lower duration of hospital stay [72–76], these are short term, requiring resources and targeted at only a limited number of individuals. My data indicate that usual physical activity patterns in the general population predict hospital usage over the subsequent 2 decades.

7.7 Conclusions and policy implications

Usual physical activity in this middle-aged and older population predicts lower future hospitalisations — time spent in hospital and number of admissions independently of behavioural and sociodemographic factors. The results presented based on observational data are in line with data from randomised trials. Taken in the context of the totality of the evidence for physical activity and health, the findings suggest that small, feasible differences in usual physical activity in the general population may potentially have a substantial impact on hospital usage and costs.

7.8 Key points

What is already known on this subject

• Pre-admission physical activity interventions have been shown to lower hospital length of stay.
• Usual physical activity is associated with lower rates of mortality from all causes, cardiovascular disease and many non-fatal diseases in the general population, but few studies have examined usual physical activity as a predictor of hospital usage.

What this study adds

• Usual physical activity, assessed using both occupational and leisure-time components validated against heart rate monitoring with individual calibration, predicted lower hospital usage in a British population of men and women followed up over 20 years.
• Modest differences in usual physical activity in the general population may have a potentially substantial impact on future hospital usage and health service costs.

8 Sociodemographic and lifestyle predictors of incident hospital admissions with multimorbidity

8.1 Overview

This chapter examines an outcome which represents a subset of total hospital admissions: hospital admissions with multimorbidity. The majority of patients who require treatment in an acute hospital setting are older people and many have multiple chronic conditions. Multimorbidity is known to predict an increased rate of mortality[207–211]. Many studies of multimorbidity examine participants in a healthcare setting such as primary care and report either cross-sectional or subsequent disease associations in those already identified as multimorbid. However, there are few prospective population-based studies that have considered the predictors of future hospital admissions, where participants, free of serious diseases at baseline, are later admitted to hospital with multiple chronic conditions. This chapter explores the likelihood of such incident hospital admissions with multimorbidity (HAWM) by age and sex and the associations with exposures including potentially modifiable lifestyle factors such as smoking, obesity, physical inactivity and low plant food intake. The difference in age between HAWM participants with and without baseline disease is estimated.

8.2 Abstract

Luben et al., BMJ Open, 2020

The ageing population and prevalence of long-term disorders with multimorbidity are a major health challenge worldwide. The associations between comorbid conditions and mortality risk are well established; however, few prospective community-based studies have reported on prior risk factors for subsequent hospital admissions with multimorbidity (HAWM). The objective of this analysis was to explore the independent associations for a range of demographic, lifestyle and physiological risk factors and the likelihood of subsequent HAWM.

Hospital admissions with multimorbidity in 25,014 men and women aged 40–79 were investigated. The risk factors for incident HAWM, defined as Charlson Comorbidity Index ≥3 and excluding those with serious diseases at baseline, were examined using multivariable logistic regression models for the 10-year period 1999–2009 and repeated with independent measurements in a second 10-year period 2009–2019.

Between 1999 and 2009, 18,179 participants (73% of the population) had a hospital admission. Baseline 5-year and 10-year HAWM were observed in 6% and 12% of participants, respectively. Age per 10-year increase OR 2.19 (95% CI 2.06–2.33) and male sex OR 1.32 (95% CI 1.19–1.47) predicted HAWM over 10 years. In the subset free of the most serious diseases at baseline, current smoking OR 1.86 (95% CI 1.60–2.15), BMI >30 kg/m^2 OR 1.48 (95% CI 1.30–1.70) and physical inactivity OR 1.16 (95% CI 1.04–1.29) were positively associated and plasma vitamin C (a biomarker of plant food intake) per SD increase OR 0.86 (95% CI 0.81–0.91) inversely associated with incident 10-year HAWM after multivariable adjustment for age, sex, social class, education, alcohol consumption, systolic blood pressure and cholesterol. Results were similar when re-examined for a further time period in 2009–2019.

Age, male sex and potentially modifiable lifestyle behaviours including smoking, body mass index, physical inactivity and low fruit and vegetable intake were associated with increased risk of future incident hospital admissions with multimorbidity.

8.3 Introduction

The Academy of Medical Sciences 2018 report highlighted multimorbidity as a global priority for research. Patients with multimorbidity experience reduced wellbeing and quality of life and account for a disproportionately high share of healthcare workload and costs. Management of the rising prevalence of long-term disorders is the main challenge facing healthcare systems worldwide [212–214].

Multimorbidity is commonly defined as the presence of multiple diseases or conditions with a cut-off of two or more conditions [215], however there is no agreed definition or classification system, which makes the existing evidence base difficult to interpret [212]. The term comorbidity predates multimorbidity and was used to predict the effect of additional diseases for those with an index disease of interest [216–218]. The Charlson Comorbidity Index (CCI) [219] was originally created to predict mortality in hospital patients after 1 year and is defined using a set of 17 chronic diseases, weighted according to the risk of death. The index has been widely used, with several authors suggesting extensions or modifications to the original definition [220–225], and it remains a common standard with which other systems are often compared [226].

The associations between comorbid conditions and mortality are well established [207–211]. However, few studies have examined the predictors of incident multimorbidity rather than its consequences [227–232] since most lack detailed demographic, socioeconomic and physiological measurements in population-based men and women prior to the onset of multimorbid disease with subsequent follow-up. Retrospective hospital-based studies examining multimorbidity lack community-based denominators while general practice-based studies are often cross-sectional or examine mortality in already multimorbid patients. Few studies examine factors that predict the likelihood of multimorbidity rather than factors that predict risk of individual component conditions. The large majority of studies conducted to date are cross-sectional, with few prospective community-based studies able to examine incident multimorbidity using subsequent hospitalisation [212,230,231]. In this chapter, I examine the independent associations for a range of demographic, lifestyle and physiological risk factors and the likelihood of subsequent HAWM. A high CCI score over 5-year and 10-year time periods is used to categorise participants as having HAWM, baseline associations are examined and also re-examined in a subset 12 years after baseline since healthcare policy and the criteria used for admission may have changed over time. Previous chapters have examined outcomes that quantify the number and duration of hospital admissions, but in this chapter, the outcome under examination represents a subset of total hospital admissions limited to those participants with multiple serious conditions.

8.4 Methods

The Charlson Comorbidity Index (CCI) is defined using a set of chronic diseases, each having an associated weight (1, 2, 3 or 6) related to the risk of death. The conditions are myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatoid disease, peptic ulcer disease, liver disease, diabetes, hemiplegia or paraplegia, renal disease, cancer and AIDS/HIV. Two levels of severity are defined for liver disease, diabetes and cancer (details are shown in supplementary table S1). All comorbidities are assigned a weight of 1, except hemiplegia/paraplegia, renal disease and malignancies (weight=2); moderate/severe liver disease (weight=3); and metastatic solid tumour and AIDS/HIV (weight=6). For diseases with two levels of severity (liver disease, diabetes and cancer), the less severe version is assigned a weight of 0 if the more severe version is also present in a patient. The CCI diseases were assigned diagnosis codes using the International Classification of Diseases (ICD-10), which was used to link the CCI to Hospital Episode Statistics (HES) records and to cohort participants. The weighted individual disease scores were totalled to create an overall score with a maximum value of 29 [219,223]. CCI was measured for various outcome periods restricted to all hospital events within the given time period: at baseline, 5-year (1999–2004) and 10-year (1999–2009) CCI; and at TP2, 5-year (2009–2014) and 10-year (2009–2019) CCI. Multiple admissions including the same CCI category were only counted once.

8.4.1 Statistical methods

Associations were examined both including and excluding chronic disease at baseline and repeated with independent measurements at TP2 in a subset of participants using a second baseline 12 years approximately after the first. The baseline analysis excludes 625 men and women who died before 1999 while at TP2 a further 126 participants who died prior to 2009 were excluded. Dichotomous variables were created for social class (manual and non-manual), educational attainment (high and low) at baseline and BMI (>30 kg/m^2 and ≤30 kg/m^2) and usual physical activity (active and inactive) at both baseline and TP2. For social class, professional, managerial and technical and non-manual skilled occupations were classed as non-manual while manual skilled, partly skilled and unskilled were classed as manual. For educational attainment, those with qualifications at secondary level or above were classed as high and those with no qualifications as low. Hospital outcomes were categorised into five groups: "No hospital admissions", CCI=0, CCI=1, CCI=2 and hospital admissions with multimorbidity (HAWM) defined as CCI ≥3. Incident HAWM refers to a subset which excludes serious diseases at baseline. Multivariable logistic regression was used for all models and compared HAWM participants (CCI ≥3) with those having CCI ≤2 or no hospital admissions. A sensitivity analysis, using identical models to those in the main analyses for the period 1999–2009, but excluding 80 participants defined as HAWM but having only one condition with a CCI weighting ≥3, gave virtually identical results (results not shown).

The numbers of individuals with missing values for covariables at baseline were 53 for BMI, 218 for smoking status, 545 for social class and 18 for education level. The physical activity score has no missing values since those with missing data were classified as being inactive. Multiple imputation was used to estimate missing values at TP2 most apparent when participants completed questionnaires but did not attend a health examination n=1,891. Predictive mean matching with 5 multiple imputations and 50 iterations was used with baseline and TP2 variables. All analyses were performed using the R statistical language (V3.5.3, R Foundation for Statistical Computing, Vienna, Austria, with packages knitr, Gmisc, ggplot2, tidyverse, intubate, mice.) CCIs were calculated using the R package "comorbidity" [233].

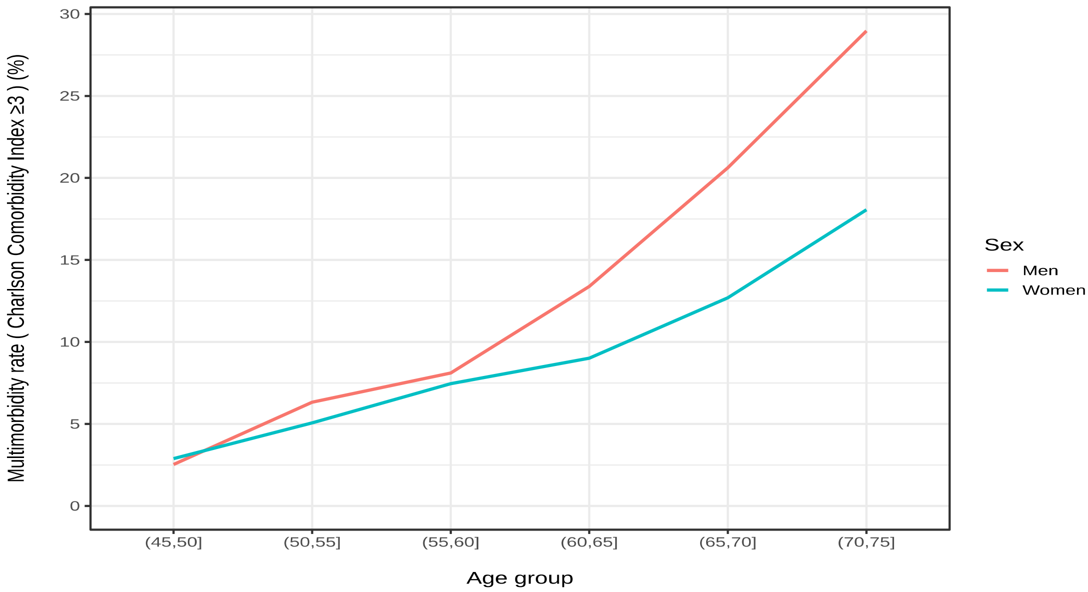
8.5 Results

Table 8.1 shows future 5-year and 10-year CCI hospital admission rates from baseline for n=25,014 and from TP2 for n=9,814, according to demographic characteristics in the study population. Between 1999 and 2009, 18,179 participants (73% of the population) had a hospital admission. Baseline 5-year and 10-year HAWM (CCI ≥3) were observed in 6% and 12% of participants, respectively. Figure 8.1 shows the HAWM rate between 1999–2009 by age group and sex excluding those with cardiovascular disease, cancer or diabetes at baseline. More men had CCI ≥3 than women and those aged >75 years had the highest proportion of admissions with multimorbid conditions, with 14.5% at 5 years and 28.8% at 10 years. HAWM rates at TP2 were slightly higher than baseline, with 5-year and 10-year HAWM observed in 10% and 20% of participants, respectively, and the highest proportion in those >75 years.

Table 8.1 | Charlson Comorbidity Index hospital admission rates by age-group and sex in men and women aged 40–79, 1999–2019

	Total	No admissions	CCI=0	CCI=1	CCI=2	CCI≥3
Baseline 5-year follow-up period, 1999–2004 (n(%))						
Men	11228	5,457 (48.6)	3,340 (29.7)	988 (8.8)	662 (5.9)	781 (7.0)
Women	13786	7,153 (51.9)	4,398 (31.9)	953 (6.9)	643 (4.7)	639 (4.6)
≤55 years	9,567	6,009 (62.8)	2,720 (28.4)	411 (4.3)	236 (2.5)	191 (2.0)
(55–65] years	7,805	3,940 (50.5)	2,479 (31.8)	583 (7.5)	408 (5.2)	395 (5.1)
(65–75] years	6,933	2,489 (35.9)	2,322 (33.5)	830 (12.0)	561 (8.1)	731 (10.5)
>75 years	709	172 (24.3)	217 (30.6)	117 (16.5)	100 (14.1)	103 (14.5)
Baseline 10-year follow-up period, 1999–2009 (n(%))						
Men	11228	2,928 (26.1)	4,151 (37.0)	1,434 (12.8)	1,056 (9.4)	1,659 (14.8)
Women	13786	3,907 (28.3)	5,767 (41.8)	1,601 (11.6)	1,137 (8.2)	1,374 (10.0)
≤55 years	9,567	3,720 (38.9)	4,201 (43.9)	746 (7.8)	476 (5.0)	424 (4.4)
(55–65] years	7,805	1,973 (25.3)	3,259 (41.8)	994 (12.7)	711 (9.1)	868 (11.1)
(65–75] years	6,933	1,059 (15.3)	2,294 (33.1)	1,168 (16.8)	875 (12.6)	1,537 (22.2)
>75 years	709	83 (11.7)	164 (23.1)	127 (17.9)	131 (18.5)	204 (28.8)
Time-point two 5-year follow-up period, 2009–2014 (n(%))						
Men	4252	1,428 (33.6)	1,355 (31.9)	522 (12.3)	389 (9.1)	558 (13.1)
Women	5562	2,234 (40.2)	1,793 (32.2)	686 (12.3)	403 (7.2)	446 (8.0)
≤55 years	342	215 (62.9)	92 (26.9)	19 (5.6)	10 (2.9)	6 (1.8)
(55–65] years	3,090	1,540 (49.8)	1,006 (32.6)	277 (9.0)	143 (4.6)	124 (4.0)
(65–75] years	3,695	1,303 (35.3)	1,301 (35.2)	464 (12.6)	286 (7.7)	341 (9.2)
>75 years	2,687	604 (22.5)	749 (27.9)	448 (16.7)	353 (13.1)	533 (19.8)
Time-point two 10-year follow-up period, 2009–2019 (n(%))						
Men	4252	695 (16.3)	1,294 (30.4)	631 (14.8)	558 (13.1)	1,074 (25.3)
Women	5562	1,166 (21.0)	1,956 (35.2)	914 (16.4)	618 (11.1)	908 (16.3)
≤55 years	342	154 (45.0)	122 (35.7)	37 (10.8)	14 (4.1)	15 (4.4)
(55–65] years	3,090	905 (29.3)	1,241 (40.2)	407 (13.2)	267 (8.6)	270 (8.7)
(65–75] years	3,695	589 (15.9)	1,309 (35.4)	611 (16.5)	473 (12.8)	713 (19.3)
>75 years	2,687	213 (7.9)	578 (21.5)	490 (18.2)	422 (15.7)	984 (36.6)

Figure 8.1 | Multivariable adjusted rate of hospital admissions with multimorbidity, by age group and sex over the 10-year follow-up period 1999–2019 in 22,278 men and women, excluding baseline prevalent diseases



Multivariable logistic regression and 95% confidence intervals adjusted for male sex, age per 10 years, manual social class, low educational level, current smoking, BMI > 30 kg/m^2, alcohol intake, physical inactivity, plasma vitamin C per SD, systolic blood pressure per SD, total cholesterol per SD. Hospital admissions with multimorbidity, defined as Charlson Comorbidity Index ≥3 compared with Charlson ≤2 or no hospital admission, excluding participants with baseline prevalent cardiovascular disease, cancer or diabetes

Descriptive characteristics of the cohort according to 10-year CCI are shown in table 8.2. Participants with higher number of total admissions and longer duration of hospital stay had higher CCI, with mean duration of 57.8 days and 13.4 admissions for participants with CCI ≥3 during the 10-year period. Participants with multimorbidity admissions were more likely at baseline examination to be current smokers, less physically active, have higher BMI and have lower plasma vitamin C (a proxy for a diet rich in fruit and vegetables) and report various prevalent conditions.

Table 8.2 | Descriptive characteristics at baseline in 25,014 men and women aged 40–79 by 10-year Charlson Comorbidity Index, 1999–2009

	Total	No admissions	CCI=0	CCI=1	CCI=2	CCI≥3
Hospital duration 1999–2009, days						
Mean ±SD	16.3 ±46.5	0.0 ±0.0	9.1 ±28.3	24.9 ±71.5	30.4 ±43.0	57.8 ±77.5
Total hospital admissions 1999–2009						
Mean ±SD	3.8 ±16.2	0.0 ±0.0	2.8 ±3.1	4.5 ±6.0	6.4 ±8.3	13.4 ±43.9
Age, years						
Mean ±SD	59.0 ±9.3	55.4 ±8.6	57.9 ±8.8	62.0 ±8.8	62.9 ±8.8	65.0 ±8.0
Body mass index, kg/m²						
Mean ±SD	26.4 ±3.9	25.9 ±3.7	26.2 ±3.8	26.8 ±4.1	26.8 ±4.3	27.3 ±4.2
Cigarette smoking (n (%))						
Current	2,904	751 (25.9)	1,008 (34.7)	410 (14.1)	291 (10.0)	444 (15.3)
Former	10,423	2,558 (24.5)	4,007 (38.4)	1,352 (13.0)	979 (9.4)	1,527 (14.7)
Never	11,469	3,476 (30.3)	4,821 (42.0)	1,245 (10.9)	903 (7.9)	1,024 (8.9)
Social class dichotomised (n (%))						
Non-manual	14717	4,400 (29.9)	5,707 (38.8)	1,733 (11.8)	1,256 (8.5)	1,621 (11.0)
Manual	9752	2,304 (23.6)	4,029 (41.3)	1,214 (12.4)	886 (9.1)	1,319 (13.5)
Level of education (n (%))						
Higher level	15866	4,922 (31.0)	6,333 (39.9)	1,724 (10.9)	1,277 (8.0)	1,610 (10.1)
Lower level	9130	1,910 (20.9)	3,576 (39.2)	1,310 (14.3)	916 (10.0)	1,418 (15.5)
Simple physical activity index (n (%))						
Inactive	7,559	1,681 (22.2)	2,666 (35.3)	1,116 (14.8)	788 (10.4)	1,308 (17.3)
Moderately inactive	7,187	2,084 (29.0)	2,904 (40.4)	819 (11.4)	610 (8.5)	770 (10.7)
Moderately active	5,688	1,708 (30.0)	2,353 (41.4)	608 (10.7)	470 (8.3)	549 (9.7)
Active	4,580	1,362 (29.7)	1,995 (43.6)	492 (10.7)	325 (7.1)	406 (8.9)
Alcohol intake, units per week						
Mean ±SD	7.1 ±9.5	7.7 ±9.6	6.9 ±9.1	6.9 ±9.5	6.7 ±9.8	6.8 ±10.3
Plasma vitamin C, μmol/L						
Mean ±SD	53.5 ±20.3	55.3 ±19.8	55.4 ±19.9	50.5 ±20.3	51.3 ±20.9	47.6 ±20.6
Systolic blood pressure, mmHg						
Mean ±SD	135.3 ±18.3	132.4 ±17.4	133.5 ±17.5	138.7 ±18.7	138.6 ±19.2	142.2 ±19.3
Total cholesterol, mmol/L						
Mean ±SD	6.2 ±1.2	6.1 ±1.1	6.1 ±1.1	6.3 ±1.2	6.2 ±1.2	6.3 ±1.2
Prevalent heart attack (n (%))						
No reported heart attack	24253	6,745 (27.8)	9,764 (40.3)	2,886 (11.9)	2,097 (8.6)	2,761 (11.4)
Self-reported heart attack	728	85 (11.7)	143 (19.6)	146 (20.1)	94 (12.9)	260 (35.7)
Prevalent stroke (n (%))						
No reported stroke	24660	6,786 (27.5)	9,821 (39.8)	2,975 (12.1)	2,151 (8.7)	2,927 (11.9)
Self-reported stroke	329	45 (13.7)	87 (26.4)	57 (17.3)	41 (12.5)	99 (30.1)
Prevalent cancer (n (%))						
No reported cancer	23688	6,595 (27.8)	9,449 (39.9)	2,878 (12.1)	2,031 (8.6)	2,735 (11.5)
Self-reported cancer	1301	237 (18.2)	459 (35.3)	155 (11.9)	162 (12.5)	288 (22.1)
Prevalent diabetes (n (%))						
No reported diabetes	24442	6,760 (27.7)	9,844 (40.3)	2,941 (12.0)	2,111 (8.6)	2,786 (11.4)
Self-reported diabetes	541	71 (13.1)	61 (11.3)	90 (16.6)	81 (15.0)	238 (44.0)

In table 8.3, odds ratios are shown for 5-year and 10-year HAWM, defined as those with CCI ≥3, compared with CCI ≤2 or no hospital admission, adjusted for age, sex, occupational social class and educational attainment in model 1. Model 2 additionally adjusted for prevalent diseases, cardiovascular disease (CVD), cancer and diabetes; model 3 added lifestyle factors, current smoking, alcohol units per week, usual physical activity as well as BMI >30 kg/m^2 and plasma vitamin C; and model 4 added systolic blood pressure and cholesterol. Age, sex and prevalent diseases were strongly associated with multimorbidity admissions in all models. The fully adjusted association of 10-year HAWM with age per 10-years increase had OR of 2.19 (95% CI 2.06–2.33), OR of 1.32 (95% CI 1.19–1.47) for sex, OR of 2.22 (95% CI 1.87–2.62) for prevalent CVD, OR of 2.05 (95% CI 1.73–2.42) for cancer, and OR of 3.41 (95% CI 2.74–4.24) for diabetes. The risk of HAWM in participants with CVD at baseline was equivalent to the risk in those without CVD 10 years older. Similarly, in participants with baseline diabetes and baseline cancer, the risk was equivalent to those without disease aged 17 and 11 years older, respectively.

The models in table 8.4 are similar to those used in table 8.3, but rather than adjusting for prevalent disease, participants who reported heart attack, stroke, cancer or diabetes at baseline were excluded. In this subgroup of participants without known common major diseases, in addition to age and sex, current cigarette smoking OR 1.86 (95% CI 1.60–2.15), BMI >30 kg/m^2 OR 1.48 (95% CI 1.30–1.70) and physical inactivity OR 1.16 (95% CI 1.04–1.29) were positively associated and plasma vitamin C OR 0.86 (95% CI 0.81–0.91) inversely associated with incident 10-year HAWM after multivariable adjustment for age, sex, social class, education, alcohol consumption, systolic blood pressure and cholesterol (model 3). Manual social class and educational attainment were associated with incident HAWM in model 1, but were attenuated in models 2 and 3. An inverse association was observed for total cholesterol, while systolic blood pressure appeared to be associated but the direction of association was not consistent with the repeated analyses from TP2. There was no association for alcohol in these models. The risk of multimorbidity in current cigarette smokers is equivalent to the risk in non-smokers 7 years older, while each 20 μmol/L rise in plasma vitamin C (approximately two servings of fruit and vegetables per day [234]) corresponds to a reduction in risk equivalent to the risk of those 3 years younger. Figure 8.2 illustrates the multivariable odds ratios for age, sex, sociodemographic, lifestyle and other factors with HAWM excluding the most serious baseline diseases.

Table 8.3 | Multivariable logistic regression of risk factors for 5-year and 10-year hospital admissions with multimorbidity in 25,014 men and women

	5-year multimorbidity †, 1999–2004 OR (95% CI)	p value	10-year multimorbidity †, 1999–2009 OR (95% CI)	p value
Model 1				
Male sex	1.49 (1.34–1.67)	< 0.001	1.56 (1.44–1.69)	< 0.001
Age per 10 years	2.27 (2.13–2.44)	< 0.001	2.34 (2.23–2.46)	< 0.001
Manual social class	1.20 (1.07–1.35)	0.002	1.22 (1.12–1.33)	< 0.001
Lower education level	1.15 (1.02–1.30)	0.023	1.19 (1.09–1.30)	< 0.001
Model 2				
Male sex	1.39 (1.24–1.56)	< 0.001	1.47 (1.35–1.60)	< 0.001
Age per 10 years	2.11 (1.97–2.26)	< 0.001	2.21 (2.10–2.32)	< 0.001
Manual social class	1.22 (1.08–1.37)	0.001	1.23 (1.13–1.34)	< 0.001
Lower education level	1.13 (1.00–1.28)	0.053	1.17 (1.07–1.28)	< 0.001
Prevalent CVD	2.23 (1.85–2.68)	< 0.001	2.25 (1.93–2.60)	< 0.001
Prevalent cancer	2.11 (1.75–2.54)	< 0.001	1.92 (1.65–2.22)	< 0.001
Prevalent diabetes	4.41 (3.55–5.45)	< 0.001	4.32 (3.57–5.21)	< 0.001
Model 3				
Male sex	1.24 (1.07–1.42)	0.003	1.33 (1.20–1.47)	< 0.001
Age per 10 years	2.16 (1.99–2.34)	< 0.001	2.29 (2.16–2.43)	< 0.001
Manual social class	1.09 (0.95–1.25)	0.214	1.17 (1.06–1.29)	0.002
Lower education level	1.06 (0.92–1.21)	0.447	1.08 (0.98–1.20)	0.112
Current smoker	1.71 (1.42–2.05)	< 0.001	1.73 (1.51–1.98)	< 0.001
BMI>30 kg/m^2	1.32 (1.12–1.56)	< 0.001	1.45 (1.28–1.63)	< 0.001
Alcohol intake, units per week	1.00 (0.99–1.01)	0.872	1.00 (1.00–1.01)	0.666
Physically inactive	1.26 (1.10–1.44)	< 0.001	1.15 (1.04–1.26)	0.006
Plasma vitamin C per SD	0.81 (0.75–0.86)	< 0.001	0.84 (0.80–0.88)	< 0.001
Prevalent CVD	2.02 (1.63–2.49)	< 0.001	2.17 (1.84–2.57)	< 0.001
Prevalent cancer	2.22 (1.79–2.72)	< 0.001	2.06 (1.74–2.43)	< 0.001
Prevalent diabetes	3.53 (2.73–4.52)	< 0.001	3.54 (2.85–4.39)	< 0.001
Model 4				
Male sex	1.23 (1.07–1.43)	0.005	1.32 (1.19–1.47)	< 0.001
Age per 10 years	2.08 (1.91–2.27)	< 0.001	2.19 (2.06–2.33)	< 0.001
Manual social class	1.09 (0.95–1.25)	0.235	1.16 (1.05–1.28)	0.004
Lower education level	1.06 (0.92–1.22)	0.420	1.09 (0.99–1.21)	0.091
Current smoker	1.72 (1.43–2.07)	< 0.001	1.74 (1.52–2.00)	< 0.001
BMI>30 kg/m^2	1.31 (1.11–1.54)	0.001	1.40 (1.24–1.58)	< 0.001
Alcohol intake, units per week	1.00 (0.99–1.01)	0.878	1.00 (1.00–1.01)	0.800
Physically inactive	1.25 (1.09–1.43)	0.001	1.14 (1.04–1.26)	0.008
Plasma vitamin C per SD	0.81 (0.76–0.87)	< 0.001	0.85 (0.81–0.89)	< 0.001
Systolic blood pressure per SD	1.10 (1.03–1.17)	0.005	1.12 (1.07–1.18)	< 0.001
Total cholesterol per SD	0.99 (0.92–1.05)	0.690	0.99 (0.94–1.04)	0.614
Prevalent CVD	2.06 (1.66–2.54)	< 0.001	2.22 (1.87–2.62)	< 0.001
Prevalent cancer	2.23 (1.80–2.75)	< 0.001	2.05 (1.73–2.42)	< 0.001
Prevalent diabetes	3.42 (2.64–4.39)	< 0.001	3.41 (2.74–4.24)	< 0.001

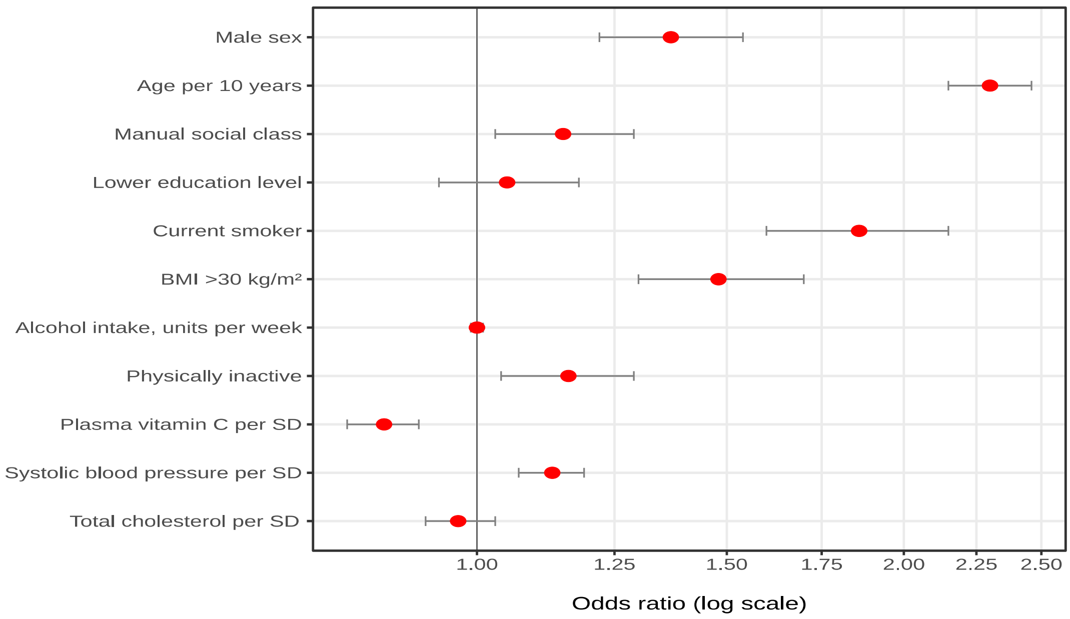
† Charlson Comorbidity Index ≥3 vs Charlson Comorbidity Index ≤2 or no hospital admission.

Table 8.4 | Multivariable logistic regression of risk factors excluding participants with prevalent CVD, cancer or diabetes for 5-year and 10-year hospital admissions with multimorbidity in 22,278 men and women

	5-year multimorbidity †, 1999–2004 OR (95% CI)	p value	10-year multimorbidity †, 1999–2009 OR (95% CI)	p value
Model 1				
Male sex	1.47 (1.29–1.68)	< 0.001	1.52 (1.38–1.67)	< 0.001
Age per 10 years	2.19 (2.02–2.37)	< 0.001	2.31 (2.19–2.45)	< 0.001
Manual social class	1.23 (1.07–1.42)	0.003	1.22 (1.11–1.34)	< 0.001
Lower education level	1.20 (1.04–1.39)	0.011	1.16 (1.05–1.28)	0.003
Model 2				
Male sex	1.32 (1.13–1.55)	< 0.001	1.39 (1.24–1.55)	< 0.001
Age per 10 years	2.24 (2.05–2.46)	< 0.001	2.40 (2.25–2.56)	< 0.001
Manual social class	1.13 (0.96–1.32)	0.131	1.17 (1.05–1.30)	0.006
Lower education level	1.07 (0.91–1.25)	0.416	1.05 (0.93–1.17)	0.428
Current smoker	1.85 (1.50–2.26)	< 0.001	1.84 (1.58–2.13)	< 0.001
BMI>30 kg/m²	1.31 (1.07–1.58)	0.006	1.53 (1.34–1.75)	< 0.001
Alcohol intake, units per week	1.00 (0.99–1.01)	0.789	1.00 (1.00–1.01)	0.805
Physically inactive	1.25 (1.07–1.46)	0.004	1.17 (1.05–1.31)	0.005
Plasma vitamin C per SD	0.82 (0.76–0.89)	< 0.001	0.85 (0.80–0.90)	< 0.001
Model 3				
Male sex	1.32 (1.12–1.56)	0.001	1.37 (1.22–1.54)	< 0.001
Age per 10 years	2.15 (1.95–2.37)	< 0.001	2.30 (2.15–2.46)	< 0.001
Manual social class	1.11 (0.95–1.31)	0.178	1.15 (1.03–1.29)	0.012
Lower education level	1.07 (0.91–1.26)	0.383	1.05 (0.94–1.18)	0.393
Current smoker	1.88 (1.52–2.30)	< 0.001	1.86 (1.60–2.15)	< 0.001
BMI>30 kg/m²	1.30 (1.07–1.58)	0.007	1.48 (1.30–1.70)	< 0.001
Alcohol intake, units per week	1.00 (0.99–1.01)	0.828	1.00 (0.99–1.01)	0.941
Physically inactive	1.24 (1.06–1.45)	0.007	1.16 (1.04–1.29)	0.009
Plasma vitamin C per SD	0.83 (0.77–0.90)	< 0.001	0.86 (0.81–0.91)	< 0.001
Systolic blood pressure per SD	1.12 (1.03–1.21)	0.005	1.13 (1.07–1.19)	< 0.001
Total cholesterol per SD	0.98 (0.91–1.06)	0.607	0.97 (0.92–1.03)	0.328

† Charlson Comorbidity Index ≥3 vs Charlson Comorbidity Index ≤2 or no hospital admission.

Figure 8.2 | Multivariable odds ratios for sociodemographic, lifestyle and physiological risk factors and subsequent 10-year hospital admissions with multimorbidity excluding prevalent baseline diseases over 20-year follow-up 1999–2019 in 22,278 men and women



Multivariable logistic regression and 95% confidence intervals adjusted for male sex, age per 10 years, manual social class, low educational level, current smoking, BMI > 30 kg/m², alcohol intake, physical inactivity, plasma vitamin C per SD, systolic blood pressure per SD, total cholesterol per SD. Hospital admissions with multimorbidity, defined as Charlson Comorbidity Index ≥3 compared with Charlson ≤2 or no hospital admission, excluding participants with baseline prevalent cardiovascular disease, cancer or diabetes

Table 8.5 shows the ICD-10 codes corresponding to CCI disease groups. Table 8.6 shows the descriptive characteristics of participants at TP2 for 10-year CCI. The mean age in this subset, measured approximately 12 years after baseline, was 69.4. The number of hospital admissions and total length of stay were similar to those at baseline, with HAWM participants having much longer duration than non-multimorbid participants or those who had no hospital admissions. HAWM participants were inactive, had lower plasma vitamin C (reflecting a lower intake of fruit and vegetables), were current or former smokers, and had prevalent disease. In table 8.7, multivariable models of 10-year HAWM show that prevalent diabetes, CVD and cancer were all strongly associated. Table 8.8 shows multivariable associations in a group free from the most serious diseases at TP2. Both age and male sex were associated with incident HAWM, with educational attainment, current cigarette smoking, plasma vitamin C, BMI >30 kg/m² and physical inactivity all predicting future multimorbidity. Systolic blood pressure was attenuated while other factors including cholesterol were more strongly associated than at baseline.

Table 8.5 | Charlson Comorbidity Index, ICD-10 codes and weighting

	ICD-10 codes
Myocardial infarction	I21.x, I22.x, I25.2
Congestive heart failure	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43.x, I50.x, P29.0
Peripheral vascular disease	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular disease	G45.x, G46.x, H34.0, I60.x–I69.x
Dementia	F00.x–F03.x, F05.1, G30.x, G31.1
Chronic pulmonary disease	I27.8, I27.9, J40.x–J47.x, J60.x–J67.x, J68.4, J70.1, J70.3
Rheumatic disease	M05.x, M06.x, M31.5, M32.x–M34.x, M35.1, M35.3, M36.0
Peptic ulcer disease	K25.x–K28.x
Mild liver disease	B18.x, K70.0–K70.3, K70.9, K71.3–K71.5, K71.7, K73.x, K74.x, K76.0, K76.2–K76.4, K76.8, K76.9, Z94.4
Diabetes without chronic complication	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9
Diabetes with chronic complication	E10.2–E10.5, E10.7, E11.2–E11.5, E11.7, E12.2–E12.5, E12.7, E13.2–E13.5, E13.7, E14.2–E14.5, E14.7
Hemiplegia or paraplegia	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0–G83.4, G83.9
Renal disease	I12.0, I13.1, N03.2–N03.7, N05.2–N05.7, N18.x, N19.x, N25.0, Z49.0–Z49.2, Z94.0, Z99.2
Any malignancy, including lymphoma and leukaemia, except malignant neoplasm of skin	C00.x–C26.x, C30.x–C34.x, C37.x–C41.x, C43.x, C45.x–C58.x, C60.x–C76.x, C81.x–C85.x, C88.x, C90.x–C97.x
Moderate or severe liver disease	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
Metastatic solid tumour	C77.x–C80.x
AIDS/HIV	B20.x–B22.x, B24.x

All comorbidities are assigned a weight of 1 except hemiplegia/paraplegia, renal disease, and malignancies (weight=2); moderate/severe liver disease (weight=3); metastatic solid tumour and AIDS/HIV (weight=6). For diseases with two levels of severity (liver disease, diabetes and cancer), the less severe version is assigned weight=0 if the more severe version is also present in a patient. Reproduced from documentation for the 'comorbidity' R package (Gasparini, 2019)

Table 8.6 | Descriptive characteristics at TP2 in 9,814 men and women aged 48–92 by 10-year Charlson Comorbidity Index, 2009–2019

	Total	No admissions	CCI=0	CCI=1	CCI=2	CCI≥3
Hospital duration 2009–2019, days						
Mean ±SD	17.7 ±36.2	0.0 ±0.0	6.5 ±14.0	19.3 ±42.8	26.1 ±42.2	46.3 ±48.1
Total hospital admissions 2009–2019						
Mean ±SD	4.4 ±7.9	0.0 ±0.0	2.8 ±3.0	4.5 ±6.0	6.0 ±6.7	10.1 ±13.5
Age at TP2, years						
Mean ±SD	69.4 ±8.4	65.1 ±7.7	67.6 ±7.7	70.5 ±8.1	71.7 ±8.1	74.1 ±7.8
Sex (n (%))						
Men	4252	695 (16.3)	1,294 (30.4)	631 (14.8)	558 (13.1)	1,074 (25.3)
Women	5562	1,166 (21.0)	1,956 (35.2)	914 (16.4)	618 (11.1)	908 (16.3)
Body mass index at TP2, kg/m²						
Mean ±SD	26.9 ±4.3	26.2 ±4.3	26.5 ±4.0	27.3 ±4.4	27.3 ±4.5	27.7 ±4.5
Cigarette smoking at TP2 (n (%))						
Current	442	88 (19.9)	116 (26.2)	65 (14.7)	79 (17.9)	94 (21.3)
Former	4,508	755 (16.7)	1,375 (30.5)	741 (16.4)	565 (12.5)	1,072 (23.8)
Never	4,864	1,018 (20.9)	1,759 (36.2)	739 (15.2)	532 (10.9)	816 (16.8)
Social class dichotomised (n (%))						
Non-manual	6294	1,205 (19.1)	2,127 (33.8)	993 (15.8)	749 (11.9)	1,220 (19.4)
Manual	3411	636 (18.6)	1,087 (31.9)	528 (15.5)	424 (12.4)	736 (21.6)
Level of education (n (%))						
Higher level	7025	1,460 (20.8)	2,419 (34.4)	1,074 (15.3)	791 (11.3)	1,281 (18.2)
Lower level	2787	401 (14.4)	830 (29.8)	471 (16.9)	385 (13.8)	700 (25.1)
Simple physical activity index at TP2 (n (%))						
Inactive	3,924	592 (15.1)	1,072 (27.3)	687 (17.5)	545 (13.9)	1,028 (26.2)
Moderately inactive	2,682	555 (20.7)	940 (35.0)	404 (15.1)	311 (11.6)	472 (17.6)
Moderately active	1,654	387 (23.4)	604 (36.5)	231 (14.0)	167 (10.1)	265 (16.0)
Active	1,442	313 (21.7)	601 (41.7)	195 (13.5)	139 (9.6)	194 (13.5)
Alcohol intake at TP2, units per week						
Mean ±SD	5.7 ±8.2	6.3 ±8.0	5.8 ±7.9	5.5 ±8.3	5.3 ±7.8	5.5 ±9.1
Plasma vitamin C at TP2, µmol/L						
Mean ±SD	63.0 ±22.2	66.0 ±21.5	65.7 ±21.6	63.2 ±22.8	59.9 ±22.4	57.7 ±21.9
Systolic blood pressure at TP2, mmHg						
Mean ±SD	136.5 ±17.1	134.7 ±15.9	135.8 ±16.3	138.5 ±18.4	136.6 ±16.8	138.0 ±18.1
Total cholesterol at TP2, mmol/L						
Mean ±SD	5.4 ±1.1	5.6 ±1.1	5.5 ±1.1	5.3 ±1.1	5.2 ±1.2	5.0 ±1.2
Prevalent heart attack at TP2 (n (%))						
No reported heart attack at TP2	9455	1,833 (19.4)	3,211 (34.0)	1,499 (15.9)	1,116 (11.8)	1,796 (19.0)
Self-reported heart attack at TP2	359	28 (7.8)	39 (10.9)	46 (12.8)	60 (16.7)	186 (51.8)
Prevalent stroke at TP2 (n (%))						
No reported stroke at TP2	9577	1,843 (19.2)	3,215 (33.6)	1,510 (15.8)	1,141 (11.9)	1,868 (19.5)
Self-reported stroke at TP2	237	18 (7.6)	35 (14.8)	35 (14.8)	35 (14.8)	114 (48.1)
Prevalent cancer at TP2 (n (%))						
No reported cancer at TP2	8888	1,744 (19.6)	2,987 (33.6)	1,398 (15.7)	1,052 (11.8)	1,707 (19.2)
Self-reported cancer at TP2	926	117 (12.6)	263 (28.4)	147 (15.9)	124 (13.4)	275 (29.7)
Prevalent diabetes at TP2 (n (%))						
No reported diabetes at TP2	9477	1,834 (19.4)	3,238 (34.2)	1,477 (15.6)	1,124 (11.9)	1,804 (19.0)
Self-reported diabetes at TP2	337	27 (8.0)	12 (3.6)	68 (20.2)	52 (15.4)	178 (52.8)

Table 8.7 | Multivariable logistic regression of risk factors for Charlson 5-year and 10-year hospital admissions with multimorbidity at TP2 in 9,814 men and women

	Charlson 5-year multimorbidity †, 2009–2014 OR (95% CI)	p value	Charlson 10-year multimorbidity †, 2009–2019 OR (95% CI)	p value
Model 1				
Male sex	1.67 (1.46–1.91)	< 0.001	1.72 (1.55–1.91)	< 0.001
Age per 10 years	2.35 (2.16–2.56)	< 0.001	2.36 (2.21–2.53)	< 0.001
Manual social class at baseline	1.02 (0.88–1.18)	0.774	1.11 (0.99–1.24)	0.072
Lower education level at baseline	1.12 (0.96–1.30)	0.154	1.26 (1.12–1.42)	< 0.001
Model 2				
Male sex	1.60 (1.39–1.84)	< 0.001	1.65 (1.48–1.84)	< 0.001
Age per 10 years	2.19 (2.00–2.39)	< 0.001	2.22 (2.07–2.38)	< 0.001
Manual social class at baseline	1.01 (0.87–1.18)	0.850	1.11 (0.99–1.24)	0.082
Lower education level at baseline	1.10 (0.94–1.29)	0.215	1.25 (1.11–1.41)	< 0.001
Prevalent CVD	2.25 (1.78–2.81)	< 0.001	2.60 (2.13–3.18)	< 0.001
Prevalent cancer	1.83 (1.50–2.22)	< 0.001	1.61 (1.37–1.90)	< 0.001
Prevalent diabetes	3.96 (3.08–5.08)	< 0.001	3.91 (3.09–4.96)	< 0.001
Model 3				
Male sex	1.44 (1.24–1.67)	< 0.001	1.52 (1.35–1.71)	< 0.001
Age per 10 years	2.14 (1.95–2.35)	< 0.001	2.23 (2.07–2.39)	< 0.001
Manual social class at baseline	0.97 (0.83–1.13)	0.692	1.07 (0.95–1.20)	0.287
Lower education level at baseline	1.04 (0.89–1.22)	0.598	1.20 (1.06–1.35)	0.004
Current smoker	1.44 (1.02–1.99)	0.032	1.45 (1.11–1.86)	0.005
BMI>30 kg/m^2	1.38 (1.17–1.63)	< 0.001	1.54 (1.35–1.75)	< 0.001
Alcohol intake, units per week	1.00 (0.99–1.01)	0.611	1.00 (0.99–1.01)	0.664
Physically inactive	1.30 (1.12–1.50)	< 0.001	1.13 (1.01–1.26)	0.034
Plasma vitamin C per SD	0.80 (0.74–0.87)	< 0.001	0.83 (0.79–0.88)	< 0.001
Prevalent CVD	2.11 (1.67–2.64)	< 0.001	2.46 (2.01–3.02)	< 0.001
Prevalent cancer	1.81 (1.48–2.20)	< 0.001	1.61 (1.36–1.89)	< 0.001
Prevalent diabetes	3.55 (2.75–4.56)	< 0.001	3.47 (2.74–4.41)	< 0.001
Model 4				
Male sex	1.35 (1.15–1.58)	< 0.001	1.41 (1.25–1.60)	< 0.001
Age per 10 years	2.11 (1.92–2.32)	< 0.001	2.20 (2.04–2.37)	< 0.001
Manual social class at baseline	0.97 (0.83–1.13)	0.692	1.07 (0.95–1.20)	0.287
Lower education level at baseline	1.04 (0.89–1.22)	0.609	1.20 (1.06–1.35)	0.004
Current smoker	1.43 (1.02–1.98)	0.034	1.44 (1.10–1.85)	0.006
BMI>30 kg/m^2	1.37 (1.16–1.62)	< 0.001	1.53 (1.34–1.74)	< 0.001
Alcohol intake, units per week	1.00 (0.99–1.01)	0.449	1.00 (1.00–1.01)	0.416
Physically inactive	1.29 (1.12–1.50)	< 0.001	1.13 (1.01–1.26)	0.038
Plasma vitamin C per SD	0.81 (0.75–0.87)	< 0.001	0.84 (0.79–0.89)	< 0.001
Systolic blood pressure per SD	0.99 (0.92–1.07)	0.854	0.99 (0.94–1.05)	0.769
Total cholesterol per SD	0.91 (0.84–0.98)	0.014	0.89 (0.84–0.95)	< 0.001
Prevalent CVD	2.02 (1.60–2.54)	< 0.001	2.34 (1.91–2.87)	< 0.001
Prevalent cancer	1.81 (1.48–2.20)	< 0.001	1.60 (1.36–1.89)	< 0.001
Prevalent diabetes	3.28 (2.52–4.24)	< 0.001	3.16 (2.48–4.03)	< 0.001

† Charlson Comorbidity Index ≥3 vs Charlson Comorbidity Index ≤2 or no hospital admission.

Table 8.8 | Multivariable logistic regression of risk factors excluding participants with prevalent CVD, cancer or diabetes at TP2 for 5-year and 10-year hospital admissions with multimorbidity at TP2 in 8,185 men and women

	5-year follow-up period †, 2009–2014 OR (95% CI)	p value	10-year follow-up period †, 2009–2019 OR (95% CI)	p value
Model 1				
Male sex	1.44 (1.22–1.70)	< 0.001	1.55 (1.37–1.75)	< 0.001
Age per 10 years	2.36 (2.13–2.62)	< 0.001	2.39 (2.21–2.58)	< 0.001
Manual social class at baseline	0.99 (0.82–1.18)	0.888	1.11 (0.97–1.27)	0.122
Lower education level at baseline	1.12 (0.93–1.36)	0.220	1.26 (1.09–1.44)	0.001
Model 2				
Male sex	1.25 (1.05–1.50)	0.015	1.39 (1.22–1.59)	< 0.001
Age per 10 years	2.36 (2.12–2.63)	< 0.001	2.43 (2.24–2.64)	< 0.001
Manual social class at baseline	0.93 (0.78–1.12)	0.471	1.06 (0.93–1.22)	0.373
Lower education level at baseline	1.06 (0.88–1.29)	0.518	1.21 (1.05–1.39)	0.008
Current smoker	1.81 (1.23–2.59)	0.002	1.66 (1.24–2.20)	< 0.001
BMI>30 kg/m^2	1.42 (1.16–1.73)	< 0.001	1.60 (1.38–1.86)	< 0.001
Alcohol intake, units per week	1.01 (1.00–1.02)	0.238	1.01 (1.00–1.01)	0.109
Physically inactive	1.18 (0.99–1.41)	0.061	1.10 (0.97–1.26)	0.138
Plasma vitamin C per SD	0.79 (0.72–0.86)	< 0.001	0.83 (0.77–0.88)	< 0.001
Model 3				
Male sex	1.16 (0.96–1.40)	0.135	1.29 (1.12–1.49)	< 0.001
Age per 10 years	2.29 (2.05–2.57)	< 0.001	2.39 (2.20–2.60)	< 0.001
Manual social class at baseline	0.93 (0.77–1.12)	0.446	1.06 (0.93–1.21)	0.385
Lower education level at baseline	1.06 (0.88–1.28)	0.534	1.21 (1.05–1.39)	0.009
Current smoker	1.81 (1.23–2.59)	0.002	1.64 (1.23–2.18)	< 0.001
BMI>30 kg/m^2	1.39 (1.14–1.70)	0.001	1.59 (1.36–1.84)	< 0.001
Alcohol intake, units per week	1.01 (1.00–1.02)	0.163	1.01 (1.00–1.02)	0.054
Physically inactive	1.18 (0.99–1.40)	0.071	1.10 (0.96–1.25)	0.161
Plasma vitamin C per SD	0.79 (0.72–0.87)	< 0.001	0.83 (0.77–0.89)	< 0.001
Systolic blood pressure per SD	1.03 (0.95–1.12)	0.466	0.99 (0.93–1.06)	0.866
Total cholesterol per SD	0.88 (0.80–0.96)	0.005	0.89 (0.83–0.95)	< 0.001

† Charlson Comorbidity Index ≥3 vs Charlson Comorbidity Index ≤2 or no hospital admission.

8.6 Discussion

In this community-based population followed prospectively, I observed hospital admission with multimorbidity rates over 5-year and 10-year periods, which as expected were strongly related to increasing age. I also observed that those with HAWM had substantially more days in hospital over the outcome periods. In multivariable analyses, excluding the most serious diseases at baseline, the risk of such admissions is predicted by age, male sex and several potentially modifiable factors. Participants at baseline who smoked cigarettes, had BMI >30, were physically inactive or had a diet low in fruit and vegetables all had higher likelihood of having subsequent hospital admissions with multimorbidity. Measurements made on a subset of the cohort 12 years after baseline who were followed up subsequently confirmed the baseline findings while also demonstrating an association for low education level in an older cohort with HAWM.

8.6.1 Strengths and limitations of the study

Most studies of multimorbidity focus on its consequences and those examining risk factors for multimorbidity are largely cross-sectional. While many prospective studies have examined the relationship between baseline characteristics and specific incident diseases or mortality, establishing multimorbidity as an endpoint is more challenging. By using the CCI to define multimorbidity, I was able to show that the chronic diseases defined by the index had considerably higher average length of stay than other conditions requiring hospitalisation and that length of stay increased with higher CCI score.

The current population-based study in a defined community was able to assess future hospital admissions with multimorbidity to enable estimates of 5-year and 10-year rates by age and sex. I was also able to document the relationship between demographic, lifestyle and physiological factors and subsequent hospital admissions with multimorbidity. The EPIC-Norfolk cohort has been followed for 20 years, enabling us to examine the risk factors for HAWM at two time-points: in mainly middle-aged participants (40–79 years) and mainly old-aged participants (48–92 years) in a sub-cohort 12 years later after major organisational changes had been made to the National Health Service (NHS). I was also able to investigate associations with and without excluding participants with known prevalent conditions at baseline.

While not attempting to examine clusters or pathways of chronic disease, I have identified risk factors that predict any hospital admissions with multimorbidity. It is possible that some factors I observed will be more strongly associated with certain combinations of diseases and others less so. However, the impact of resources experienced by hospitals can best be mitigated by early public health advice, prior to the onset of disease if possible, which can only be general in nature. My findings are in line with current public health advice such as smoking cessation, a diet containing fruit and vegetables and regular exercise and, given the huge additional impact placed on the NHS by multimorbidity [214], should further emphasise the need for public health advice and intervention. While interventions may not always be effective, there is evidence that change in behaviour can be achieved [235–237] and effective frameworks have been reported [238].

Multimorbidity can be defined in a number of ways, such as disease counts or using various indexes [239]. By restricting the definition to a relatively small subset of chronic conditions such as in the CCI, inevitably some conditions will not be counted. It is notable that the CCI does not include depression or mental health, asthma or respiratory diseases, epilepsy, hypothyroidism, musculoskeletal problems or atrial fibrillation, all common in a primary care setting [240]. In addition to the CCI and other commonly used systems [241], authors have used many other definitions with variable numbers of underlying conditions and hence the prevalence of multimorbidity varies widely. However, CCI is a widely used measure of multimorbidity.

Since the CCI is weighted to predict mortality, it may be better able to assess health service impact than a simple disease count, since procedures required for higher weighted conditions will generally be more costly. However, it may be less effective as an indicator of multiple long-term conditions. Some chronic conditions such as musculoskeletal and mental health diseases not included in the CCI are nevertheless likely to require long-stay inpatient care. However, increasing CCI had longer hospital length of stay in the present study and this has also been reported in several other studies [242,243]. Medical conditions such as obesity have well-established links to many diseases but, as non-diseases, are not included in the CCI. The use of CCI ≥3 to define multimorbidity classifies a small number of participants with one serious disease with a high CCI weight as multimorbid. However, a sensitivity analysis excluding these people gave virtually identical results. Studies examining the longitudinal predictors of future multimorbidity generally rely on self-reported disease, but my study used the CCI from linked hospital medical coding.

When examining the relationship between lifestyle factors and health outcomes, confounding will always be a limitation. Individuals who smoke, are less physically active and eat a poor diet for example are likely to differ from those with a contrasting lifestyle with respect to other factors relating to the likelihood of future multimorbidity, including their age, sex, lifestyle factors examined in this study and others unknown. However, the associations I report were consistent after multivariable adjustment for other factors. Differential mortality is another possible limitation and would occur, for any of the factors examined, if participants with an apparently unhealthy characteristic were more likely to have died earlier than those with the contrary healthy characteristic and hence were less likely to use hospital services for the full follow-up period. However, the results for the 5-year follow-up period where very few deaths occurred were consistent with the longer 10-year follow-up period. While it is possible that some participants were multimorbid at baseline, I examined those with and without baseline self-reported major chronic disease and estimated the difference in mean age for HAWM participants with and without baseline disease.

8.6.2 Comparison with other studies

Estimates of the prevalence of multimorbidity vary widely, partly due to the variety of definitions, number of diseases, weighting and so on used in studies, but range from 55% to 98% in the elderly [217]. Most studies report multimorbidity associated with age and present in more than half of those aged 65 and older [214,244]. Age was strongly associated with future HAWM in my study and has been reported to increase hospitalised multimorbidity in elderly patients [19]. Many studies have found that women have a higher rate of multimorbidity than men [217,244–247], but I observed the converse, with male sex strongly predicting future multimorbidity. The use of CCI in the context of prospective hospital admissions rather than cross-sectional multimorbidity in a primary care setting, may explain the higher proportion of multimorbid men. Physical-mental comorbidity is reported higher among women in primary care [248] and mental health, which is not included in the CCI, may be more likely to be treated in a primary care than in an acute hospital setting.

Despite the considerable literature relating to multimorbidity, very few studies have examined the modifiable risk factors of subsequent HAWM. Incident cancer and cardiometabolic multimorbidity were examined in a recent multicentre study which included data from the present study [227]; prediagnostic healthy lifestyle behaviours were reported to be inversely associated with the risk. BMI was also reported to be associated with incident cardiometabolic multimorbidity in a pooled analysis of 16 cohort studies [228]. A Finnish study examined incident multimorbidity in both disease-free and those with baseline diabetes and CVD [230]. They reported some similar findings to the present study such as associations with cigarette smoking, physical inactivity and BMI, but associations for low education level and systolic blood pressure were only found in men. Multimorbidity was defined using five common diseases, and time-to-event 10-year follow-up was used rather than a follow-up period approach in this study. Participants in the Finnish cohort were younger than those in EPIC-Norfolk, with the oldest participant 74 years at the end of follow-up against 90 years in the EPIC-Norfolk baseline and 100 years at TP2. Studies using data from an English longitudinal cohort and using self-reported disease counts to define multimorbidity reported associations in physical activity, obesity and low level of wealth and an increased risk of multimorbidity when combined with other lifestyle factors such as smoking, obesity and inadequate fruit and vegetable consumption [231,232]. However, they found no association with educational attainment or excess alcohol consumption. Education, which was associated in older participants at TP2 in my study, has been linked to multimorbidity in cross-sectional studies [249] and prospectively [230]. Socioeconomic status was reported to predict the development of multimorbidity throughout the life course in a Scottish longitudinal study [250]. Both educational attainment and occupational social class were attenuated in my study possibly due to the models including plasma vitamin C, also a marker of socioeconomic status. While smoking was a strong predictor, I did not find an association with alcohol drinking. However, other studies in the literature are inconsistent, with some finding no association with cigarette smoking and alcohol consumption in cross-sectional analyses [212].

8.6.3 Generalisability

While hospital admissions with multimorbidity provide an objective indicator of both health service and individual impact of the condition, studies of hospital admissions in many countries are limited by factors relating to differential accessibility to healthcare such as health insurance, income and healthcare policy. Although not entirely free of differential accessibility, the NHS in the UK, with service free at the point of delivery for all residents, provides an opportunity to examine hospitalised multimorbidity with fewer of these constraints. Health care policy and criteria for admission change over time, not least in the UK over the 20-year period of this study, so I examined admissions and risk factors for multimorbidity over two independent time periods using new repeated measures and found consistent results.

8.7 Conclusions and policy implications

I observed in a long-term population-based study that age, male sex and potentially modifiable factors including smoking, BMI, physical inactivity and a diet low in fruit and vegetables predict future incident hospital admission with multimorbidity. Multimorbidity is increasingly common among older hospital inpatients due in part to improved efficacy of treatments and drugs. While considerable effort is being focused on the progression, disease clustering and treatment of patients with multimorbidity, there has been less attention on the long-term predictors of future incident multimorbidity. It would therefore be informative if more studies were to examine this outcome and were able to replicate the results presented here. However, taken in the context of the totality of available evidence and notwithstanding the limitations of observational data, this study suggests that modest difference in lifestyles may have the potential to mitigate the future impact of multimorbidity in the population.

8.8 Key points

What is already known on this subject

• The majority of patients in secondary care are elderly and have multiple chronic conditions.
• Multimorbidity predicts future increased mortality but most studies are conducted in individuals who access healthcare.
• Cross-sectional studies have reported associations with lifestyle factors but there are few prospective population-based studies of predictors of future multimorbidity.

What this study adds

• In this population-based prospective study, followed over 20 years, I examined the likelihood of hospitalisation with multimorbidity by demographic characteristics including age and sex.
• I examined the demographic, lifestyle and physiological risk factors that predict incident multimorbidity over a 10-year period and identified potentially modifiable lifestyle factors such as smoking, obesity, physical inactivity and low plant food intake.
• Consistent associations were observed with repeat measures in a subsequent 10-year time period.

9 Discussion

9.1 Summary of key findings

In a population of middle-aged and older men and women aged 40–79 and followed over 25 years, who were resident in Norfolk UK, and participants in a longitudinal cohort study, the European Prospective Investigation of Cancer in Norfolk (EPIC-Norfolk), I explored the epidemiology of hospital usage using record linkage with routine hospital admission data. These included hospital usage according to sociodemographic characteristics and factors, including potentially modifiable behavioural factors, predicting future hospital usage. Though the purpose of these analyses was to describe hospital usage from any cause rather than specific conditions, I also explored characteristics of those with hospital admissions associated with multimorbidity.

9.1.1 Simple and easily measurable demographic and behavioural factors predict the risk of future hospitalisation in a general population cohort

Over the first 10 years of follow-up, 73% of study participants had at least one admission to hospital, 14% with ≥7 admissions and 20% with >20 hospital days. Over 20 years, 90% of participants had a hospital admission, 65% had ≥7 admissions and 59% had >20 hospital days. Absolute rates of hospital usage by age and sex in NHS hospitals were estimated for cohort participants. 21% of men and 19% of women had >20 hospital days over a 10-year follow-up period. 47% of participants aged ≤45 and 12% of those aged 75–80 did not attend hospital over the 10 years. Only 4% of participants aged ≤45 had >20 hospital days compared with 51% of those aged 75–80. 87% of men and women over 75 years would expect to be admitted to hospital on one or more occasions over the subsequent 10 years.

Age was the strongest predictor of hospital usage but strong independent associations were also observed for male sex, educational status, occupational social class, smoking and high body mass index. Those with body mass index >30 kg/m^2 had a similar likelihood of >20 hospital days to current smokers. A simple five-point risk score, constructed using male sex, manual social class, no educational qualifications, current smoking and BMI >30 kg/m^2, was used to estimate the percentage of the cohort in categories of number of admissions and total hospital days stratified by age bands. Twofold and threefold differences in future hospital usage between those with high and low risk scores were observed. Up to the age of 75 years the number of hospital admissions one might expect increases with the risk score. For those aged 55–65 years only 13% might expect to spend 20 days in hospital over the next 10 years but this increased to 30% for those with a risk score of four or five.

9.1.2 Residential area deprivation index predicts subsequent admissions to hospital and time spent in hospital independently of individual social class and lifestyle factors

Compared with those having residential Townsend Area Deprivation Index lower than the average for England and Wales, those with a higher than average deprivation index had a higher likelihood of spending >20 days in hospital.

Residential area deprivation was associated with future hospital usage independently of individual sociodemographic factors, in particular age, sex, social class and education as well as lifestyle factors including smoking and BMI. Study participants living in the most deprived areas at or below the national average, were more likely to spend >20 days in hospital or be admitted to hospital on ≥7 occasions. There were also significant interactions between residential area deprivation and individual social class and education level, such that residential area deprivation has greater impact on those with low education level or manual social class; those with manual social class and lower education level were at greater risk of hospitalisation when living in an area with higher deprivation index. Participants were approximately divided between those living in urban and those in rural areas with the least deprived and most deprived predominantly urban dwellers. Study participants in Townsend quintiles 1 and 5 were closer by road from their home to the Norfolk and Norwich hospital but the time taken for the journey did not vary greatly. Neither distance from hospital nor urban or rural location explain the associations of residential area deprivation with hospital usage.

9.1.3 No evidence found of higher hospital usage for current alcohol consumers when compared with those who do not currently report drinking alcohol

Compared with current non-drinkers, men and women who reported any alcohol drinking had a lower risk of spending >20 days in hospital in multivariable-adjusted models. Women who were current drinkers were less likely to have any hospital admissions, ≥7 admissions or >20 hospital days. In men, the association may in part be due to whether former drinkers are included in the non-drinker reference group but in women, the association was consistent irrespective of the choice of reference group. Hospitalisations might reflect the balance between positive and negative health effects of alcohol consumption in a particular study population. Cardiovascular disease is a predominant reason for hospital admissions in middle-aged and older men and women and an inverse association between alcohol intake and cardiovascular disease has been reported in many epidemiological studies at lower levels of consumption. However, the measurement of past drinking, the separation of non-drinkers into former drinkers and life-long abstainers and the choice of reference group are all influential in interpreting the risk of alcohol consumption on future hospitalisation.

9.1.4 Usual physical activity in a middle-aged and older population predicts time spent in hospital and number of admissions independently of behavioural and sociodemographic factors

Active participants tend to be younger, non-smokers, without chronic disease and have higher educational attainment, however those with manual social class also tend to be more active. Usual physical activity, assessed at the baseline survey in 1993–1997, was inversely associated with future hospital usage independently of sociodemographic and lifestyle factors. Participants with a baseline physical activity score of at least moderately inactive had fewer hospital admissions and fewer days in hospital over 10 years, than those who were inactive. Similar associations were observed over 10 years from TP2 and similar but attenuated results were observed for 20-year follow-up. Participants who remained physically active or became active between baseline and TP2 had lower risk of subsequent hospital usage than those who remained inactive or became inactive. Those reporting any activity had a mean of 0.42 fewer hospital days per year between 1999 and 2009 compared with inactive participants, an estimated potential saving to the NHS of £247 per person per year, or approximately 7% of UK health expenditure.

9.1.5 Age, male sex and potentially modifiable factors including smoking, physical inactivity and a diet low in fruit and vegetables predict future incident hospitalised multimorbidity

Baseline 5-year and 10-year incident multimorbidity was observed in 11% and 21% of participants respectively and strongly related to increasing age. Participants admitted to hospital with multimorbidity had substantially longer duration of stay over the outcome periods. More men had Charlson Comorbidity Index (CCI) ≥2 than women and those aged >75 years had the highest proportion of multimorbid conditions with 29% at 5 years and 47% at 10 years. Participants at baseline who smoked cigarettes, had BMI >30, were physically inactive or had a diet low in fruit and vegetables all had higher likelihood of having subsequent hospital admissions with multimorbidity. Measurements of the cohort at TP2 confirmed the baseline findings while also demonstrating a multimorbidity association for low education level in the older cohort. The risk of multimorbidity in participants with CVD, diabetes and cancer at baseline is equivalent to the risk in those without the disease 9, 16 and 9 years older respectively. The risk of multimorbidity in current cigarette smokers is equivalent to the risk in non-smokers 7 years older, while each 20 µmol/L rise in plasma vitamin C, corresponding to approximately two servings of fruit and vegetables per day, lowers risk by a level equivalent to the risk in a person 2 years younger.

9.2 Strengths

9.2.1 The National Health Service

The study population is community-based and free-living and comprises older men and women living in the UK where the NHS is free at the point of use. Confounders, such as the ability to pay that might affect and limit access and use of health services, are less likely to apply in this study. The UK NHS differs from other health systems where healthcare relies on the purchase of health insurance. These schemes can vary in the care they provide according to the cost of insurance with elements that fall outside the schemes [144,189]. Hence, people of low income or low socioeconomic status are much less likely to have access to these health services. Studies of hospital admissions in many countries are limited by factors relating to differential accessibility to healthcare such as health insurance, income and healthcare policy. Though not entirely free of differential accessibility, the NHS, with service free at the point of delivery for all residents, provides an opportunity to examine hospital usage with fewer of these constraints. Income was not measured in EPIC-Norfolk. While it is recognised that income may influence hospital usage in the UK indirectly through loss of pay or transport costs, education and occupational social class are stronger sociodemographic indicators in this respect than income. However, if differential access makes some with lower social class less likely to access health services, the results presented are likely to be attenuated. Data on hospital usage, including number of admissions and total length of stay, estimate both the Health Service and the individual impact of these outcomes. The main period being examined (1999–2009) approximately coincides with administrative control by Primary Care Trusts (PCT, 2002–2013), a period of relative stability for the NHS. However, a second follow-up period, 2009–2019 in which many changes to health policy and administration were introduced, was available to confirm and contrast with the results from the main period.

9.2.2 The EPIC-Norfolk cohort

EPIC-Norfolk is a large cohort of middle-aged and older men and women resident in Norfolk, United Kingdom, that is very well characterised making it possible to take into account many variables potentially related to hospital usage and disease. There are few prospective studies comparable in size and duration to EPIC-Norfolk that have such detailed and varied measures. The cohort has both area-based measures from census data and individual measures from questionnaires available. It has repeated measures in a subset of participants and local and national record linkage was used to individually link participants to health databases. EPIC-Norfolk participants were recruited from general practices in Norfolk with a response rate of approximately 40%. A profile of the baseline cohort [113] examined the characteristics of the cohort which were highly comparable to those reported from the national “Health Survey for England” except for a lower rate of smokers indicating likely generalisability to the British population.

The National Health Service collects usage data including hospital records on all UK residents and cohort record linkage is possible using the unique NHS number to local or national databases. EPIC-Norfolk participants have been followed for 20 years using record linkage and flagging with NHS Digital. Capture of death certificates and hospital admissions are therefore almost complete and there is virtually no loss to follow-up. Few study participants (<2%) have moved away from the Norfolk area over the period of follow-up. The long follow-up period enabled sensitivity analyses to be performed to explore associations that might be attributed to reverse causality by eliminating events close in time to exposure measurements. It also allowed the examination of two consecutive 10-year follow-up periods and the confirmation of associations using repeated, independent exposure measurements.

9.2.3 Repeated independent measurements

Cohort participants were asked to attend health checks and complete questionnaires on several occasions with a baseline examination and lifestyle questionnaire prior to the initial 10-year follow-up period and a subsequent examination and questionnaire at TP2 corresponding to the start of the second 10-year follow-up period. It was therefore possible to examine associations using two independent measurements in participants approximately 10 years apart, for two organisational periods within the NHS. This enabled exploration of consistency and replicability of the findings using independent measures over different time periods, when both exposures and criteria for hospital usage might have changed. While there have been important changes to health service organisation and processes over the period under examination, analyses using two different 10-year follow-up periods enables exploration of consistency and replicability of the findings over different time periods using independent measures.

9.2.4 Population denominators

This thesis examines hospital activity using a prospective cohort design in a population of community-dwelling participants with clearly defined population denominators. The EPIC-Norfolk cohort was recruited from a free-living population resident in Norfolk and unlike general practice or hospital-based studies is able to compare characteristics of hospital attenders and those who did not need to use those services. Most studies of hospital usage only have data on patients who are hospitalised, that is, cases without denominators, so are unable to assess overall risk associated with lifestyle factors in the general population. Use of record linkage with routinely collected hospital admissions data ensured that ascertainment was virtually complete as use of private healthcare in Norfolk over the time period was minimal. The use of linked hospital data meant that it was not necessary to depend on self-reported outcomes that may be incomplete due to non-response and may be subject to recall and other biases.

9.3 Limitations

9.3.1 Selection bias

Potential selection biases may limit the interpretation of the findings presented here since participants were recruited in middle-age from participating GP practices and those participating were more likely to be more health conscious or in better general health than non-participants. For example, there was a lower proportion of current cigarette smokers in participants compared with the national Health Survey for England. I was also unable to explore relationships with very high alcohol intake levels as very few participants reported very high intake. Recruitment of the cohort was restricted to men and women registered at participating GP practices, although almost everyone in the UK is registered with a GP and invitations were sent to everyone registered aged 40–79 years. The findings presented here reflect hospital usage in a middle-aged and older age cohort and thus I was not able to comment on associations in younger people. The catchment for EPIC-Norfolk GP practices varies, with some urban and some rural-based practices, some in more deprived and some in less deprived areas. It is likely that the demographic and socioeconomic characteristics of people registered with a given GP practice also varies, with differences both within and between EPIC-Norfolk and non-EPIC-Norfolk practices.

9.3.2 Measurement errors in exposures

Measurement error is likely when participants complete self-reported questionnaires and this may result in informational biases. Measurement error may not always be present at random but may be more likely in particular subgroups. For example, the under-reporting of alcohol consumption (generally perceived as an undesirable health behaviour) may be more common in heavy drinkers while the over-reporting of physical activity (generally perceived as a desirable health behaviour) may be more common in the less active. Questions requesting information from the past may be remembered less well than more recent events and the phrasing of questions may be insufficiently sensitive to reflect accurately all lifestyle behaviours. Objective measures, such as physical activity measured by accelerometry, eliminate certain types of bias, but were not available at baseline. Accelerometry has only been developed relatively recently and is generally not feasible in large, free-living, community-based populations. Nevertheless, large random measurement errors in exposure are likely to attenuate associations rather than produce spurious associations.

9.3.3 Measurement errors in outcomes

Information on treatment in private hospitals and clinics, unlike NHS hospitals, is not routinely collated or made available to researchers. This would include records of common orthopaedic procedures such as hip or knee replacement, cosmetic procedures such as the removal of varicose veins and other procedures offered as a private service that may be restricted or not available on the NHS. It is possible that some of the associations observed, for example between those in higher social class groups and lower hospital usage, could be explained by private treatment. However, most serious long-term conditions are treated in NHS hospitals and generally the use of private hospitals in the Norfolk area over the time period being examined was minimal. Hence, record linkage of routinely collected hospital episode data gave virtually complete ascertainment. It also should be noted that participants undergoing procedures paid for by the NHS but carried out in private hospitals are recorded in HES data.

The main outcomes used in this thesis do not depend on diagnosis or procedure coding but simply on the number of admissions and dates of admission and discharge, although some exploration of hospitalisation by diagnosis categories is presented in chapter 3. The associations found with these broad hospitalisation outcomes, representing the totality of hospital activity, may differ from associations with the individual component conditions. However, associations may be driven by specific very common conditions, such as the relationship between alcohol and cardiovascular disease. It is also possible that the patterns of illness and treatment seen in cohort participants differed from the general population. However, comparison of cohort hospital usage with routinely published national reports (presented in chapter 2) suggests the cohort is broadly similar. Hospital medical coding is typically performed by experienced nosologists who interpret hand-written medical notes by hospital doctors using coding systems such as ICD-10 or OPCS-4. Direct electronic capture of patient notes has only recently been introduced by some UK hospitals and was rarely used over the period being examined. Some inaccuracy in paper-based medical coding would be expected given the time pressures experienced by clinical staff in UK hospitals and transcription error is possible when hand-written information is passed from doctors to coders.

9.3.4 Confounding and interaction

Confounding is a major issue when examining the relationship between lifestyle factors and health outcomes. Individuals with more poor health behaviours are likely to differ from those with fewer poor health behaviours with respect to other factors relating to the likelihood of future hospitalisation. These include age and sex and several other factors both known and unknown. In order to reduce possible confounding, multivariable modelling of suspected confounding factors was used and to further explore confounding, associations were examined stratified by the main potential confounders to determine whether the results remained consistent in the subgroups. While associations were generally consistent after adjustment for the main risk factors measured in EPIC-Norfolk and when stratified by individual factors, this will not have entirely eliminated confounding. The accuracy of the measurement might not be sufficient to ensure adequate adjustment, so the possibility of residual confounding with known or unknown factors associated with lifestyle and hospital usage cannot be excluded. It is also not possible to tell whether these unknown factors attenuate or strengthen the associations observed. Some interactions were observed such as between area deprivation and individual sociodemographic factors which highlighted stronger associations among more deprived groups.

9.3.5 Participant relocation

Participants may have moved house during the follow-up periods under examination and differential relocation may have caused loss to follow-up, for example if participants in higher socioeconomic groups were more likely to move. However, while 22% of the cohort moved house between the years 2000 and 2014, the large majority of participants relocated locally in Norfolk, with others moving elsewhere in England. Initially, linkage of the cohort to HES records was performed locally and HES records were not available for participants who moved outside the Norfolk area. However, the results presented here use linkage to national databases and HES records were available for participants who relocated within England. Hence there was virtually no loss to follow-up. HES data was not available for participants who moved to Wales, Scotland, Northern Ireland or outside the UK but they were very few in number. The organisation and collection of mortality data from death certificates differs from the data warehousing of HES data and is routinely available for England and Wales with a slightly different mechanism for the collation of Scottish death certificates.

Participants who moved house during follow-up may have altered their area deprivation category. Study participants who moved house may have been misclassified for some of the period over which hospitalisation was assessed. Area deprivation was determined by a snapshot of postcodes of residence in the year 2000 using data collected at the 1991 UK national census. Hence it is possible that the deprivation index assigned did not precisely reflect the level of deprivation for a participant at the time questionnaires were completed, either because of area improvements or worsening or participant relocation. Since the Townsend Area Deprivation Index was not measured at enumeration district level in the UK census beyond 1991, no directly comparable measure was available at later time points to examine change. However, a sensitivity analysis of non-movers found very similar results to the main analyses. Any misclassification due to moves or changes over time in residential area deprivation scoring were minimal and resultant measurement error would only be likely to attenuate associations with the residential area score.

9.3.6 Changes in health service policy

Changes were made in health policy over the period under examination and although I was able to report associations over two 10-year follow-up periods, this was limited to participants of a given age range within a certain time period. The first 10-year follow-up period was a relatively stable period for the NHS under Primary Care Trusts while the subsequent 10-year period involved a reorganisation of health service administration. It was not possible to give a detailed comparison of the two periods given the 10-year difference in mean age of the cohort participants and characteristics that differed in some respects between those attending a baseline health check and those attending a health check at TP2; essentially participants at the TP2 health examination represented not just survivors but were healthier than those still alive who did not attend this repeat examination.

9.3.7 Differential survival

Hospital usage was examined over long time periods of 10 and 20 years and individuals who died during the follow-up period did not use hospital services for the full period. This may have affected results if there was differential mortality by exposure whereby study participants with poor health behaviours were more likely to have died earlier than participants without those behaviours and hence less likely to use hospital services for the full follow-up period. For example, study participants living in more deprived areas may have died earlier and not used hospital services for the full period and participants who died early from alcohol attributable diseases may have lower hospital usage over the period under examination having not used hospital services for the entire period. For alcohol, it is unlikely that misclassification of the outcome measures would alter the results as over the time period the risk of death was in fact lower in alcohol drinkers than non-alcohol drinkers. For area deprivation analyses, the death rate was higher among those living in the most deprived areas. Sensitivity analyses restricted to participants surviving to the end of follow-up were more strongly associated with outcome measures than those in the main analysis, and similarly associations in the second follow-up period were stronger than those in the first.

9.3.8 Reverse causality

Reverse causality is also a possible limitation for these analyses. Individuals who have prevalent illness or poor health status that might predispose them to greater future hospital usage may have changed their health behaviours or report them differently. For example, participants with low physical activity at baseline may be inactive because they have conditions requiring hospitalisation. Similarly, those in poor health at recruitment may have lower occupational social class increasing the chance of them living in a more deprived area. EPIC-Norfolk has long follow-up and hence is less likely to be affected by reverse causality, which is typically a feature of studies with short duration of follow-up. In order to assess whether reverse causality had altered the associations for physical activity, area deprivation and others, additional sensitivity analyses were used. These sensitivity analyses use the same statistical models as the main analyses, but make certain exclusions to enable exploration of associations that might be attributed to reverse causality. One approach was to explore relationships that exclude outcomes occurring in the first few years of follow-up. Events occurring soon after baseline could have been present at baseline when exposures were measured but either not yet diagnosed or not sufficiently serious to require an inpatient hospital admission. If sensitivity analyses excluding events occurring soon after baseline show similar results to the main analyses, it is less likely that the associations were due to reverse causality. Since the total number of events in the sensitivity analysis is lower than in the main analysis, it has lower statistical power, however there are sufficient events for the analysis due to the long follow-up period in EPIC-Norfolk. Another approach used sensitivity analyses to explore relationships using the same statistical models as in the main analysis but after excluding participants with the most serious baseline self-reported disease. Participants with cancer or cardiovascular disease at baseline were more likely to have chosen or been advised by their GP to change their behaviour, for example drinking less alcohol or stopping smoking.

9.4 Comparison with other studies

Most studies examining hospital usage in the UK are based on hospital data but are limited in their capacity to estimate accurately denominator populations or to assess characteristics prior to hospitalisation and how they may relate to relative or absolute risk of hospital usage prospectively [41,42,46,133,134]. The EPIC-Norfolk cohort was recruited from the general population resident in Norfolk and unlike hospital-based studies is able to compare characteristics of hospital attenders and those who did not need to use those services. The initial 10-year period under examination approximately coincides with administrative control by Primary Care Trusts (PCT, 2002–2013) with hospital usage free at the point of delivery under the UK NHS. Inequality in healthcare favouring the better off has been observed in many countries that use healthcare insurance and where eligibility for government healthcare is based on income thresholds. Associations observed in studies based on hospital data within these healthcare systems may be influenced by these factors [144–146]. The NHS is not constrained by ability to pay and hence I was able to examine the independent associations of socioeconomic factors with subsequent hospitalisation.

Most studies examining deprivation in the context of health, disease and mortality either rely on area-based measures collected, for example, from census data or from individual level data from questionnaires. I had access to both forms of information, having derived individual social class and education level from self-reported questionnaires and area level measures from residential postcode linkage. Socioeconomic risk-factors of hospitalisation have been examined using individual level exposures such as occupational social class, income and education and at area level using various deprivation indices, but few studies have reported on both individual and area-based measures. Individual occupational social class, income and level of education have all been reported to be associated with chronic disease risk. Area-based deprivation measures, available routinely in the UK using postal code linkage, have also been reported to be associated with hospital usage. However, the participants in such studies are often limited to those attending hospital and so a suitable population denominator is lacking. Studies reporting health associations for both individual and area measures are less common, with few examining the independent association of residential area deprivation on subsequent hospital usage. Hospital-based studies using patients as study participants do not have a reliable population-based denominator and cannot estimate overall risk in the population. Studies often attempt to define a denominator using separate population estimates while not individually linking. I was able to examine hospital usage over 20 years in a clearly defined community-based population using a prospective cohort design.

Sociodemographic and health-related characteristics and the effects of deprivation were examined in the UK Biobank cohort in men and women aged 40–69 recruited 2006–2010 [107]. Participation in both EPIC-Norfolk and Biobank was higher in less socioeconomically deprived areas. Foster et al [251] reported that deprivation in UK Biobank modified the associations observed between lifestyle category and health outcomes. They report that disproportionate lifestyle-associated risk in more deprived groups was seen with both area-level and individual-level measures of socioeconomic status (household income and educational attainment) confirming the findings presented here. However, individual-level occupational social class was not presented. Dixon et al [43] examined adiposity and inpatient hospital costs in the UK Biobank Cohort. They report an association between BMI and inpatient hospital costs which is consistent with the findings presented here albeit for a different type of hospitalisation outcome.

Norfolk is an area of generally low deprivation with >80% of the study population living in areas with deprivation levels below the national average. However, recruitment did not extend to all areas of the county and while several EPIC-Norfolk GP practices were based in Norwich, there were no collaborating GP practices in other cities with high deprivation levels. Few participants live in areas of high deprivation such as those found in some larger cities in other parts of the country. Studies of those living in deprived cities or regions in the UK have reported a socioeconomic gradient in hospital usage more extreme than the findings presented here. However, while EPIC-Norfolk does not provide any information on the most extreme forms of deprivation, there was sufficient heterogeneity to observe large differences in hospital usage. The ten-year follow-up to the Marmot report [54] provides evidence that social inequality in health remains. Many of the conclusions regarding healthy life expectancy in the report concur with the findings presented here regarding long hospitalisation. It stated that people in more deprived areas spend more of their lives in ill-health than those in less deprived areas, demonstrated by the positive relationship between the Index of Multiple Deprivation score and healthy life expectancy. The report supports my findings of an association between area-level deprivation and subsequent hospital stay of more than 20 days.

The relationship between alcohol consumption and future hospital usage at lower levels of consumption is contentious. The nature of the cardioprotective effect of alcohol on mortality has been the subject of considerable debate over many years. A large body of epidemiological evidence, some reporting evidence for plausible biological mechanisms, have reported beneficial associations for ischaemic heart disease and diabetes at moderate levels of alcohol intake [82–84,87–95,188]. My findings concur with this literature, albeit in the context of hospitalisation outcomes, reflecting the balance between positive and negative health effects. More recent literature [172] using different modelling techniques disputes the earlier findings and suggests alcohol has no safe limit. Holmes et al [252] used Mendelian randomisation and reported that those with a genetic variant associated with non-drinking and lower alcohol consumption had a more favourable cardiovascular profile and a reduced risk of coronary heart disease than those without the genetic variant. They suggest their finding challenges the concept of a cardioprotective effect associated with light to moderate alcohol consumption in observational studies. Millwood et al [253] also used Mendelian randomisation in a study of 500,000 men and women in China to contrast conventional epidemiology with genotype-predicted mean alcohol intake. Their findings suggest that effects of moderate alcohol intake on risk of IHD are largely non-causal. However, stroke is the predominant form of IHD in China while IHD is much more common in EPIC-Norfolk participants. Very few women drank alcohol in the China Kadoorie Biobank cohort while it was much more common in women in Norfolk. The inverse association in EPIC-Norfolk women was stronger than in men and was apparent when comparing lifelong abstainers to current drinkers. Costanzo et al [254] examined the association between alcohol consumption and hospitalisation burden in 24,325 men and women in an Italian population (the Moli-sani Study). They found associations similar to those in EPIC-Norfolk for moderate consumption but were also able to examine heavy drinking which was not possible in EPIC-Norfolk.

Many studies have reported that physical activity is associated with lower rates of mortality from all causes and cardiovascular disease and a lower risk of many non-fatal diseases [63–69]. However, few studies have examined the relationship between usual physical activity in middle and later life and subsequent hospital usage in the general population . Studies with longer follow-up time are less likely to be affected by reverse causality which is a feature of studies with short duration of follow-up where individuals who report low physical activity at baseline are inactive by virtue of being affected by the outcome of interest. Self-reported physical activity is most often assessed by questions related to leisure-time activities and few studies capture both occupational and leisure-time activity. Small increases in physical activity have been reported to obtain cost savings for health services by reducing hospital admissions, with many studies reporting reductions of length of stay after preoperative physical activity interventions [70,195,204–206]. My study has observed a 12%–13% lower risk of long stay and high numbers of admissions by physical activity category. While there is evidence suggesting that pre-admission physical activity programmes may lower duration of hospital stay these are short term, require resources and are targeted at only a limited number of individuals. The data presented here indicate that usual physical activity patterns in the general population predict hospital usage over the subsequent 2 decades. Recent evidence from the UK Biobank cohort supports the findings presented here. Pearce et al. [255] found positive associations in CVD and respiratory disease incidence using hospital episode data and validated physical activity energy expenditure predicted from self-report.

The associations between comorbid conditions and mortality are well established [207–211]. However, studies reporting the predictors of incident multimorbidity rather than its consequences are rare since most lack detailed measurements in population-based participants prior to the onset of multimorbid disease. My findings agree with most studies, reporting multimorbidity associated with age and present in more than half of those 65 years and older. Age was strongly associated with future hospitalisation and incident multimorbidity in this study and has been reported to increase hospitalised multimorbidity in elderly patients. Many studies have found that women have a higher rate of multimorbidity than men, but I observed the converse with male sex strongly predicting future multimorbidity. One possible reason for this observation is men are reported to be less likely to have a mental health disorder than were women, but the CCI does not include mental illnesses [214]. Wikström et al reported some similar findings to the present study with associations for cigarette smoking, physical inactivity and BMI in all participants but low education level and systolic blood pressure only associated in men. Dhalwani et al and Mounce et al also reported associations from the English Longitudinal Cohort Study that supported the findings presented here such as positive associations with physical activity, obesity and low level of wealth and an increased risk of multimorbidity when combined with other lifestyle factors such as smoking, obesity and inadequate fruit and vegetable consumption [231,232]. Similarly, Katikireddi et al [250] reported that socioeconomic status predicted the development of multimorbidity throughout the life course.

9.5 Findings in context / generalisability

While it is not possible to infer causal links between the lifestyle factors and hospital admissions, differences in social class and education may reflect real differences in health status need or demand. I investigated hospital usage irrespective of the reasons for admission or type of procedures carried out to encompass a broad range of attendance patterns by using number of occasions and length of time that hospital services were used. The hospitalisation outcomes are able to estimate both the Health

Service and the individual impact of hospitalisation. The main hospital discharge diagnoses and procedures observed in EPIC-Norfolk participants over the outcome period are summarised and illustrated in chapter 3. However, the outcomes used for the main analyses in the thesis, the number and duration of admissions and HAWM, do not consider the reason for admission. In this respect the approach differed from the more usual exposure-outcome analyses reported in cohort studies, since it assesses the impact of sociodemographic and lifestyle factors on hospital resources.

Reports into health inequalities, by authors such as Black, Acheson and Marmot, attribute social inequalities influencing health to many factors including income, education, housing, diet, employment and conditions of work. The Working Group on Inequalities in Health, published in 1980 and also known as the Black Report, found that ill-health and death are unequally distributed among the population of Britain, and that inequalities had been widening since the establishment of the NHS in 1948. The report concluded that these inequalities were not mainly attributable to failings in the NHS, but rather to many other social inequalities influencing health. The Independent Inquiry into Inequalities in Health Report by Donald Acheson, published in 1998, reiterated the findings of earlier reports concluding that inequalities in health has been steadily increasing and that differences in material deprivation are a major cause of the increase. The 2010 Marmot Review, "Fair Society, Healthy Lives" [53] highlighted the disparity between the poorest and wealthiest areas of England. People living in the poorest area die on average 7 years earlier that those in the richest areas and spend much longer living with disability. The report stated that health inequalities result from social inequalities and reducing health inequalities is a matter of fairness and social justice. He also stated that health inequalities are largely preventable with suitable investment which would be offset by reduction in losses due to illness. The report "Health Equity in England: The Marmot Review 10 years on" [54] noted that increases in life expectancy have slowed since 2010 with the slowdown greatest in more deprived areas of the country. It reported that the difference in life expectancy at birth in 2016–2018 was 7.7 years for women and 9.5 years for men between the highest and lowest area deprivation deciles.

I was not able to examine physical features of the environment in this study. Ecological measurements such as the quality of housing, access to recreational facilities, local services provided, community support and levels of crime may affect health and hospital usage. However, I was able to examine both individual and area level deprivation in the same study participants, and the interaction observed suggests that there is a higher risk of hospitalisation in more deprived areas of residence disproportionately for those with lower individual social class and education. My results are based on observational data which is subject to confounding and limited to one geographical area with deprivation levels below the national average. However, the findings are consistent with a large body of evidence, including the aforementioned reports, which describe inequalities in health in the UK.

The associations presented here of usual alcohol intake and future hospital usage are somewhat unexpected in the light of current beliefs about the risks of alcohol consumption in the general population. The many diseases related to the high consumption of alcohol would lead us to expect a positive association between hospital usage and alcohol intake. Alcohol-related liver disease, for example, is now the third most common cause of premature death in the UK having increased four-fold since the 1970s [174]. However, cardiovascular disease is a predominant reason for hospital admissions in middle-aged and older men and women, and although not recognised as causal, an inverse association between alcohol intake and cardiovascular disease has been widely reported. Hospitalisations might reflect the balance between positive and negative health effects of lower levels of alcohol consumption in particular study populations, but are only apparent when using a population denominator.

Small increases in physical activity have been reported to obtain cost savings for health services by reducing hospital admissions and reductions of length of stay after preoperative physical activity interventions [70,195,204–206]. The findings presented here show a 12%–13% lower risk of long stay admissions by physical activity category. The mean difference in hospital days between inactive and any-activity participants in my study was 0.42 days per year. Assuming a cost of £587 per hospital day, a potential saving to the NHS of approximately £247 per person per year or about 7% of UK per capita health expenditure can be achieved by modest changes in lifestyle. When seen in the context of National Health Service spending, calculations such as these, although crude, illustrate the significant financial contribution that modest changes in lifestyle can achieve in addition to the obvious benefit for individuals. While pre-admission physical activity programmes may lower duration of hospital stay, these are short term, requiring resources and targeted at only a limited number of individuals. My data indicates that usual physical activity patterns in the general population predict hospital usage over the subsequent 2 decades.

The EPIC-Norfolk cohort was recruited using general practice registration databases and achieved a response rate of approximately 40% which is much higher than some other UK population-based studies such as the UK Biobank study [256,257] which had a response rate of 5.5%. Consequently, in Biobank, generalisability may be an issue since the characteristics of Biobank participants may differ from those seen nationally. Fry et al compared the characteristics of UK Biobank with the national Health Survey for England [107]. They concluded that while there was evidence of a "healthy volunteer" selection bias, exposure-disease relationships may be widely generalisable and does not require participants to be representative of the population at large. However, in the context of hospitalisation, the EPIC-Norfolk cohort may be more suitable to assess risk, such as the absolute rates of future long hospital stay presented in chapter 4.

9.6 Implications for practice and policy.

Historically, UK government spending on health has risen on average by 3.7% per year since 1948, outpacing economic growth over the period. As a result, health expenditure as a proportion of UK Gross Domestic Product has increased from 3.6% to 7.5% over the same period. Approximately a half of government health expenditure is used for hospitals. There are many factors which may influence hospital usage, not all of which are related to ill health, while increases in expenditure are only partly explained by demographic changes. Changes in modifiable lifestyle factors have the potential to lower hospital length of stay.

Simple demographic and behavioural indicators are related to the future probability of cumulative hospital admissions and hospital days. While the strongest of these are increasing age and male sex, the modifiable factors examined, including cigarette smoking, BMI, physical activity, manual social class and low education were all strongly associated with hospital usage. These simple indicators are easy to collect and may assist healthcare providers and those planning services to predict future hospital usage. My findings suggest that small feasible changes in behaviour may have a considerable benefit for the individual and the health services but it does not follow that making these changes is straightforward or even possible. While potentially modifiable factors such as smoking and body mass index may predict future hospital usage, this should not be interpreted as implying that these modifiable factors are entirely under the control of individuals and it is important to recognised the broader structuring effects that cause disadvantage and inhibit health at multiple levels. While numerous interventions for the modifiable factors examined have been proposed and used, they have not always be effective. This may be due to structural influences that inhibit these apparently simple lifestyle changes. Michie et al. discuss characterising and designing behaviour change interventions and report effective frameworks [238]. However, there is evidence that change in behaviour can be achieved, most notably in cigarette smoking but also in other areas [235–237].

Despite an overall increase in life expectancy, inequality remains in society with lower life and health expectancy observed more often in disadvantaged groups. While lifestyle factors may account for some part of this, the reported differences in death rates cannot be explained by individual behaviour alone. My findings suggest that material living conditions, poor quality housing and poor infrastructure are associated with subsequent hospitalisation and that there is a socioeconomic gradient in hospital usage for factors measured both individually and at area level. Residential area deprivation has greater impact in those with a low education level or manual social class. However, geographical variation in the quality and availability of health services remains problematic, with people in some parts of the UK, generally the more deprived areas, finding it harder to obtain the services they need than people who live elsewhere, generally the more affluent areas [128,163,258]. Effective NHS and government policy should therefore involve addressing deprivation both at the individual and infrastructural levels to identify and target those most at risk within the community. NHS policies focused on reducing health inequalities in older people need to work alongside wider government initiatives to improve the quality of housing, transport and infrastructure and access to recreation and green space.

Current alcohol intake was associated with lower hospital usage compared with current non-drinkers in middle-aged and older men and women. While the associations found may be partly explained by information or selection biases, I found no evidence to suggest that reducing the UK alcohol drinking limits to below their current levels would reduce hospital usage. However, methodological considerations such as the measurement of past drinking, the separation of non-drinkers into former drinkers and life-long abstainers and the choice of reference group are all influential in interpreting the risk of alcohol consumption on future hospitalisation.

There is growing evidence of the effectiveness of preoperative exercise programmes and other pre-admission interventions in reducing hospital length of stay and readmission rates but my analyses suggest that in the general population, usual physical activity is related to hospital usage. The evidence I have presented suggests small feasible differences in usual physical activity in the general population may potentially have a substantial impact on hospital usage and costs. Change in behaviour is achievable since it would only involve increasing usual physical activity from inactivity to at least some activity.

Multimorbidity is now commonplace among increasing elderly hospital inpatients. While considerable effort is being focused on the progression, disease clustering and treatment of patients with multimorbidity, there has been less attention on the long-term predictors of future incident multimorbidity. The evidence presented here suggests that modest difference in lifestyles may have the potential to mitigate the future impact of multimorbidity in the population. Interventions must therefore start earlier, prior to any indication of multimorbidity, in order to be effective.

9.7 Future research

There are many areas of research that relate to the work presented in this thesis, some of which I began to work on, but I could not include them all and hence they are classified under future research. I will briefly explain why these are subject areas that warrant further examination.

Respiratory disease is the third leading cause of death for EPIC-Norfolk participants after cancer and heart disease. It would therefore seem likely that this group of diseases would also have an impact on hospitals. EPIC-Norfolk participants were asked at baseline and later health checks to use a spirometer in order that their lung function could be tested. These data can be used to examine baseline and change in lung function and test for associations with hospital usage in participants with or without obstructive lung diseases such as asthma, bronchitis and chronic obstructive pulmonary disease (COPD). Special account would need to be taken of current and past smoking habit.

The demographic, socioeconomic and lifestyle predictors of illness requiring hospitalised critical care are limited. There are few prospective studies examining the risk factors for critical care in community-based populations, short-term and long-term survival after a period of critical care and whether factors prior to illness alter the risk of survival [259–262]. Hospital usage in the last year of life is typically considerably higher than the preceding years. However, hospital usage generally increases with age in the healthy elderly. While the increasing cost of healthcare is often attributed to older people, longevity may delay rather than eliminates the treatment costs associated with the treatment of those who become ill at the end of life [263]. Just as with general hospital usage, most research on critical care is based on those already in hospital with short term follow up. This cohort provides a unique opportunity to explore potential factors measured before critical care episodes that might predict future critical care on a population basis. Unlike studies based on hospitalised case series, it is also possible to examine long term follow-up in EPIC-Norfolk participants after episodes critical care. The pattern of hospital usage in older people in the years prior to death can also be explored, both for those who die in hospital and those who die elsewhere. Using critical care data from ICNARC, which I linked to EPIC-Norfolk in 2019, I hope to explore these questions. I also hope to examine end-of-life associations in the EPIC-Norfolk cohort.

Hospital Episode Statistics are collated nationally in a data warehouse containing records of all patients admitted to NHS hospitals. The systematic capture of detailed hospital records makes research in this field feasible. There are, however, many conditions that do not require treatment as a hospital inpatient and are instead treated by GPs in a primary care setting. While hospital records capture the most serious illness, they underestimate the prevalence and incidence of many conditions. Some conditions only result in hospital treatment late in the progression of the disease while others may never require treatment in hospital. GP practices act as gatekeepers to various forms of secondary care including mental health services which are not captured as HES records. Capturing data from GP practice systems is currently much harder to achieve than capturing hospital records. There is no equivalent warehousing capability for primary care and there are several general practice computer systems that differ in the structure of their underlying databases. Different coding systems are used with non-standardised coding rules that often vary by practice while familiarity with the practice computer reporting systems also varies. The computer systems are primarily designed to assist GP consultations for a single individual and have limited capability to collate information at overall practice level. The makers of the GP practice systems have made some attempt to centralise their records, and some regional GP record linkage systems exist, but national GP records are not currently available for researchers throughout the UK. If these issues can be overcome and linkage between population cohorts such as EPIC-Norfolk can be achieved, many new areas of research will be possible.

HES records can be used in many different ways to examine hospitalisation. The findings presented here used outcomes based primarily on admission counts and duration of stay, whereas exposure-outcome survival analysis has generally used groups of related ICD-10 diagnoses. However, other elements of the HES record are used less frequently. OPCS-4 procedure codes provide a different perspective to diagnosis coding but are a rich and detailed resource which would allow, for example, the examination of operations. I have previously used OPCS-4 codes to ascertain cataract surgery, since this identifies people whose cataracts require treatment as opposed to a simple diagnosis. Detailed economic costings can be derived from ICD-10 diagnosis and OPCS-4 procedural codes. Health Resource Groups (HRGs), which are used routinely for case-mix analysis in NHS hospitals, can be derived from diagnosis and procedure codes and linked to NHS Reference unit costs. This process allows a cost to be assigned to an individual hospital episode. Other related hospital data such as outpatient attendances and accident and emergency data which previously only contained basic medical coding, have recently included more detailed information. The mental health minimum dataset also provides a rich source of information for a different type of hospital and for diseases such as those related to mental illness and dementia which may not be so easily studied using acute hospital data. Hospitals routinely collect large volumes of digital data including results from biochemistry, histology and medical imaging such as retinal images, mammography and MRI. The information contained within these data is valuable in a research setting but extracting useful data requires big-data techniques due to the number and size of digital files involved.

9.8 Conclusions

Simple demographic and behavioural indicators are related to the future probability of cumulative hospital admissions, length of stay and multimorbidity. Increasing age, male sex and modifiable factors such as smoking, body mass index and usual physical activity are all strongly associated with subsequent hospital usage. There is also a socioeconomic gradient in hospital usage for individually measured social class and education and for area level deprivation, apparently independently of measured behavioural factors and known prevalent illnesses, which should be further explored. Modest feasible differences in lifestyles in the general population may potentially mitigate the future impact of long hospital stay and multimorbidity and have a substantial impact on hospital usage and costs.

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11 Appendices

Journal papers

- Predicting admissions and time spent in hospital over a decade in a population-based record linkage study, Luben et al, BMJ Open, 2016
- Alcohol consumption and future hospital usage: The EPIC-Norfolk prospective population study, Luben et al, PLOS One, 2018
- Residential area deprivation and risk of subsequent hospital admission in a British population, Luben et al, BMJ Open, 2019
- Usual physical activity and subsequent hospital usage over 20 years in a general population: the EPIC-Norfolk cohort, Luben et al, BMC Geriatrics, 2020
- Sociodemographic and lifestyle predictors of incident hospital admissions with multimorbidity in a general population, 1999-2019, Luben et al, BMJ Open, 2020

Questionnaires

- EPIC-Norfolk Baseline Health and Lifestyle Questionnaire
- EPIC-Norfolk Follow-up 4 Lifestyle Questionnaire

BMJ Open

Predicting admissions and time spent in hospital over a decade in a population-based record linkage study: the EPIC-Norfolk cohort

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ABSTRACT

Objective: To quantify hospital use in a general population over 10 years follow-up and to examine related factors in a general population-based cohort.

Design: A prospective population-based study of men and women.

Setting: Norfolk, UK.

Participants: 11 228 men and 13 786 women aged 40–79 years in 1993–1997 followed between 1999 and 2009.

Main outcomes measures: Number of hospital admissions and total bed days for individuals over a 10-year follow-up period identified using record linkage; five categories for admissions (from zero to highest ≥7) and hospital bed days (from zero to highest ≥20 nights).

Results: Over a period of 10 years, 18 179 (72.7%) study participants had at least one admission to hospital, 13.8% with 7 or more admissions and 19.9% with 20 or more nights in hospital. In logistic regression models with outcome ≥7 admissions, low education level OR 1.14 (1.05 to 1.24), age OR per 10-year increase 1.75 (1.67 to 1.82), male sex OR 1.32 (1.22 to 1.42), manual social class 1.22 (1.13 to 1.32), current cigarette smoker OR 1.53 (1.37 to 1.71) and body mass index >30 kg/m² OR 1.41 (1.28 to 1.56) all independently predicted the outcome with p<0.0001. Results were similar for those with ≥20 hospital bed days. A risk score constructed using male sex, manual social class, no educational qualifications; current smoker and body mass index >30 kg/m², estimated percentages of the cohort in the categories of admission numbers and hospital bed days in stratified age bands with twofold to threefold differences in future hospital use between those with high-risk and low-risk scores.

Conclusions: The future probability of cumulative hospital admissions and bed days appears independently related to a range of simple demographic and behavioural indicators. The strongest of these is increasing age with high body mass index and smoking having similar magnitudes for predicting risk of future hospital usage.

Strengths and limitations of this study

- Prospective cohort design, with a population of community-dwelling participants enabling us to examine hospital activity with clearly defined population denominators.
- Large study size of middle aged and older men and women with a long follow-up time and detailed measurements of demographic and behavioural indicators.
- It was not possible for us to infer causal links between the lifestyle factors and hospital admissions.
- We were not able to examine non-National Health Service hospitals and clinics where study participants paid for treatment.

INTRODUCTION

In the UK, the number of men and women over 65 years of age was 10.8 million in 2012 and is projected to increase to 17.8 million by 2037 with those over-85s doubling in number to 3.6 million.[1] Two-thirds of people admitted to hospital are over 65 years old with those over 85 years accounting for 25% of bed days.[2] Though increasing age is associated with increased health service usage, other factors may help identify those at greatest risk of admission. Most studies examining hospital activity start from those hospitalised but are limited with respect to population denominators;[3–7] even those that use general practice record linkage studies only include people who attended general practices while population-based studies that have measured factors prospectively prior to admission are limited.[8–13]

In this study we examined the relationship between simple and easily measurable demographic and behavioural factors to predict in a general population cohort resident in Norfolk, the future risk of use of National Health Service (NHS) hospitals over a 10-year period from 1999 to 2009, a period of relative stability for the NHS under Primary Care Trusts.

METHODS

The European Prospective Investigation into Cancer, Norfolk (EPIC-Norfolk), is a cohort of men and women aged 40–79 years living in Norfolk recruited from participating general practitioner practices between 1993 and 1998.[14 15]

Study design

A total of 25 639 participants completed a lifestyle questionnaire on recruitment and attended a clinic where weight and height and other measurements were made by trained nurses using standard protocols. Body mass index (BMI) was calculated as weight in kilograms divided by height^2 in square metres. The lifestyle questionnaire included questions relating to current and former employment.

Occupational social class was defined according to the Registrar General's classification. Non-manual occupations were represented by codes I (professional), II (managerial and technical), IIIa (non-manual skilled) occupations, while manual occupations were represented by codes IIIb (manual skilled), IV (partly skilled) and V (unskilled) occupations.

Educational attainment was established using the question 'Do you have any of the following qualifications' followed by a list of common UK qualifications. Participants were categorised according to the highest qualification attained in three groups: those with no formal qualifications; those with formal qualifications usually associated with a school age between 16 and 18 years; and those with degree level qualifications.

Smoking status was derived from two questions each of which could be answered as yes or no: 'Have you ever smoked as much as one cigarette a day for as long as a year?' and for those who answered yes to the first question 'Do you smoke cigarettes now?'

Record linkage

Between 1999 and 2009, cohort participants were linked to hospital records using their unique NHS numbers.[16] We used databases maintained by the East Norfolk Primary Health Care trust (PCT) an approach with the advantage that all hospital activity for Norfolk residents was captured wherever they were treated in England and Wales. The majority (95%) of admissions were to the Norfolk and Norwich University Hospitals NHS Foundation Trust (formerly Norfolk and Norwich Hospital), the remainder being admissions to other hospitals in Norfolk and neighbouring counties, community and mental healthcare trusts admissions, surgery performed in general practices and a small number of emergency admission elsewhere in the country. The PCT changed their computer systems several times over the period of study and although the data were collected from the same sources, different database systems such as Health Interlock, East Norfolk Core minimum data set (ENCORE) and others were used for linkage at different times.

Participants were also followed for mortality through linkage with the Office for National Statistics. Data from hospital records were available for inpatient episodes and outpatient visits. Records of inpatient data were organised with one row corresponding to one hospital episode. Typically patients would have several episodes for each admission. Dates of the start and end of each episode and the admission and discharge dates were included.

Each episode also had associated with it one of more International Classification of Disease V.10 (ICD10) diagnosis code and one or more OPCS Classification of Interventions and Procedures V.4 (OPCS4) procedure code. Using these data it was possible to build a fairly detailed picture of a person's hospital stay. Outpatient data were more limited in scope, restricted to dates of a clinic visit and the specialty concerned.

Time in hospital was calculated using admission and discharge dates by summing the time between admission and discharge for each person. We used the formula one plus (discharge date minus admission date) to ensure that time in hospital for those admitted and discharged on the same day (day cases) was considered. Hospital admissions were also calculated using admission, discharge, episode start and end dates. To avoid counting immediate readmissions, where one hospital stay followed on rapidly from another, contiguous admissions were merged and counted as a single admission.

Over the 10 years of follow-up, the numbers of admissions were categorised as 0, 1, 2–3, 4–6 and ≥7. Bed days were also classified into five categories, none, day case, 1–4 nights, 5–19 nights and ≥20 nights. Three main outcomes were used: hospital admissions ≥7; Bed days ≥20 nights; and no admissions; and compared respectively with those not in those categories.

Statistical analyses

We examined the distribution of hospital admissions by baseline descriptive data. ORs for each of the main outcomes: ≥7 hospital admissions; bed days ≥20 and no hospital admissions were calculated using unmatched logistic regression with independent variables age, smoking, BMI >30, manual social class and no educational qualifications. We then created a summary risk score, defined as the sum of five baseline risk factors dichotomised as binary categories each coded one or zero. The categories, each contributing one point were male sex, manual social class, low education level (those with no qualifications), current smoker and BMI >30 kg/m^2. Those with scores four and five were combined into a single category as the number with score equal to five was very low.

We used logistic regression rather than survival analysis to prevent the censoring of participants who had died, since we wished to make no distinction between non-attendance of hospital due to good health and non-attendance because of death. The number of missing values were: 53 BMI, 218 smoking status, 545 social class, 18 level of education. We examined mortality rates in the cohort by risk score stratified by age over three periods of follow-up time: 1993–1998, 1999–2004; and 1999–2009 to explore the possibility of differential mortality and therefore attrition of the population in the different risk groups which might explain some of the patterns observed. In addition, to explore the possibility of the effect of participant migration during the period under examination a sensitivity analysis was conducted on the subset of the cohort whose postcode area was Norfolk ('NR') at both the start and end of the period. All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria V.3.1.2 with packages knitr, Gmisc and IRanges) and Stata statistical software V.12 (Stata Corporation, College Station, Texas, USA).

RESULTS

For the current analyses, we excluded the 625 men and women from the baseline cohort who died before 1999 leaving 11 228 men and 13 786 women. Over a period of 10 years, between 1999 and 2009, 8300 (72.7%) male and 9879 (72.7%) female study participants were admitted to hospital. In total 92% of these admissions were to the Norfolk and Norwich Hospital. Descriptive characteristics of the cohort are shown in table 1. Table 2 shows the distribution of characteristics by hospital admission category. The proportion of study participants with no hospital admissions decreased monotonically across categories of age band, smoking status (never, former, current), six levels of social class, level of education (high, medium, low) and four categories of BMI while the proportion shows a monotonic increase for the same variables in the highest categories of admission. Table 3 shows similar analyses and results for increasing categories of and bed day numbers.

Table 4 shows the independent relationships using logistic modelling between demographic and behavioural factors in relation to hospital admissions. High numbers of admissions and bed days were positively associated with male sex, age, manual social class, smoking and high BMI while no hospital admissions were inversely associated with these factors. The strongest risk factors for more than 7 admissions were age OR 1.75 (1.67 to 1.82) per 10-year increase, being a current cigarette smoker OR 1.53 (1.37 to 1.71) and BMI ≥30 kg/m² OR 1.41 (1.28 to 1.56). Age was the strongest risk factor for high bed day usage >20 days OR 2.54 (2.44 to 2.65) per 10 years increase in age. Current smoking OR 1.59 (1.44 to 1.77) and BMI ≥30 kg/m² OR 1.54 (1.41 to 1.68) were also important risk factors.

The demographic and lifestyle factors were used to construct a risk score. Table 5 shows that an increase in the absolute rate of admissions and bed days across score categories was observed in all but the oldest age category. Conversely, the percentage not admitted to hospital over 10 years decreased over increasing risk score categories. In the participants <75 years similar increases in the absolute rates of admissions and bed days were also observed with increasing risk score apart from the highest score categories, though the gradient attenuated with increasing age.

Table 6 shows mortality rates over different time periods by age group and risk score. There was a mortality gradient by increasing risk score and the gradient was

Table 1 Descriptive characteristics of men and women in the EPIC-Norfolk cohort 1993–1997 and hospital admission 1999–2009

	Men (n=11 228 44%)	Women (n=13 786 55%)
Hospital activity, 1999–2009 (n (%))		
One or more admissions	8300 (74)	9879 (72)
No admissions	2928 (26)	3907 (28)
Total hospital days, 1999–2009		
Mean±SD, full cohort	17.1±43.4	15.6±48.8
Mean±SD, excluding non-attenders	23.2±49.1	21.8±56.5
Median(IQR), full cohort	4.0 (0.0–17.0)	3.0 (0.0–13.0)
Median(IQR), excluding non-attenders	9.0 (3.0–25.0)	7.0 (2.0–21.0)
Number of admissions, 1999–2009		
Mean±SD, full cohort	4.2±16.2	3.6±16.3
Mean±SD, excluding non-attenders	5.7±18.6	5.0±19.0
Median(IQR), full cohort	2.0 (0.0–5.0)	2.0 (0.0–4.0)
Median(IQR), excluding non-attenders	3.0 (2.0–6.0)	3.0 (1.0–5.0)
Body mass index, kg/m²		
Mean±SD	26.5±3.3	26.2±4.3
Age, years		
Mean±SD	59.3±9.2	58.8±9.3
Smoking status (n (%))		
Current	1356 (12)	1548 (11)
Former	6044 (54)	4379 (32)
Never	3748 (34)	7721 (57)
Social class (n (%))		
Professional (1)	854 (8)	870 (6)
Technical (2)	4229 (38)	4720 (35)
Clerical NM (3.1)	1381 (13)	2663 (20)
Clerical M (3.2)	2781 (25)	2845 (21)
Semiskilled (4)	1466 (13)	1800 (13)
Unskilled (5)	321 (3)	539 (4)
Level of education (n (%))		
Low	3348 (30)	5782 (42)
Medium	6895 (61)	6396 (46)
High	976 (9)	1599 (12)
Body mass index (n (%))		
<24 kg/m²	2369 (21)	4616 (34)
24–27 kg/m²	4392 (39)	4216 (31)
27–30 kg/m²	2957 (26)	2608 (19)
>30 kg/m²	1486 (13)	2317 (17)

Table 2 Distribution of characteristics of 25 014 men and women in 1993–1997 by category of number of hospital admissions 1999–2009

	Number of hospital admissions,* 1999–2009					
	0 (n=6835 27%)	1 (n=4582 18%)	2–3 (n=6034 24%)	4–6 (n=4101 16%)	≥7 (n=3462 14%)	p Value
Total hospital days, 1999–2009						
Mean±SD	0.0±0.0	5.4±42.1	11.2±28.9	24.3±39.3	62.2±84.0	<0.0001
Median(IQR)	0.0 (0.0–0.0)	1.0 (1.0–3.0)	5.0 (3.0–11.0)	13.0 (7.0–27.0)	40.0 (22.0–73.8)	
Number of admissions, 1999–2009						
Mean±SD	0.0±0.0	1.0±0.0	2.4±0.5	4.8±0.8	16.5±41.3	<0.0001
Median(IQR)	0.0 (0.0–0.0)	1.0 (1.0–1.0)	2.0 (2.0–3.0)	5.0 (4.0–5.0)	10.0 (8.0–14.0)	
Body mass index, kg/m²						
Mean±SD	25.9±3.7	26.1±3.8	26.4±3.9	26.8±4.0	27.1±4.2	<0.0001
Sex (n (%))						
Men	2928 (26)	2012 (18)	2586 (23)	1938 (17)	1764 (16)	<0.0001
Women	3907 (28)	2570 (19)	3448 (25)	2163 (16)	1698 (12)	
Age, years						
Mean±SD	55.4±8.6	57.3±8.9	59.9±9.1	62.4±8.9	63.0±8.6	<0.0001
Age band (n (%))						
<45	481 (47)	246 (24)	186 (18)	64 (6)	55 (5)	<0.0001
45–50	1789 (41)	989 (23)	898 (21)	415 (10)	275 (6)	
50–55	1450 (35)	828 (20)	988 (24)	507 (12)	396 (9)	
55–60	1096 (28)	764 (20)	958 (25)	599 (15)	492 (13)	
60–65	877 (23)	713 (18)	980 (25)	690 (18)	636 (16)	
65–70	659 (17)	593 (15)	1018 (27)	836 (22)	732 (19)	
70–75	400 (13)	371 (12)	824 (27)	778 (25)	722 (23)	
75–80	83 (12)	78 (11)	182 (26)	212 (30)	154 (22)	
Smoking status (n (%))						
Current	751 (26)	514 (18)	665 (23)	485 (17)	489 (17)	<0.0001
Former	2558 (25)	1833 (18)	2549 (24)	1818 (17)	1665 (16)	
Never	3476 (30)	2199 (19)	2772 (24)	1754 (15)	1268 (11)	
Social class (n (%))						
Professional (1)	599 (35)	335 (19)	380 (22)	234 (14)	176 (10)	<0.0001
Technical (2)	2754 (31)	1697 (19)	2068 (23)	1348 (15)	1082 (12)	
Clerical NM (3.1)	1047 (26)	732 (18)	981 (24)	690 (17)	594 (15)	
Clerical M (3.2)	1397 (25)	1039 (18)	1375 (24)	961 (17)	854 (15)	
Semiskilled (4)	744 (23)	555 (17)	868 (27)	603 (18)	496 (15)	
Unskilled (5)	163 (19)	139 (16)	222 (26)	160 (19)	176 (20)	
Level of education (n (%))						
Low	1910 (21)	1545 (17)	2321 (25)	1815 (20)	1539 (17)	<0.0001
Medium	4122 (31)	2563 (19)	3059 (23)	1918 (14)	1629 (12)	
High	800 (31)	471 (18)	652 (25)	362 (14)	290 (11)	
Body mass index (n (%))						
<24 kg/m²	2225 (32)	1365 (20)	1660 (24)	969 (14)	766 (11)	<0.0001
24–27 kg/m²	2410 (28)	1599 (19)	2105 (24)	1349 (16)	1145 (13)	
27–30 kg/m²	1320 (24)	1008 (18)	1327 (24)	1048 (19)	862 (15)	
>30 kg/m²	873 (23)	600 (16)	930 (24)	725 (19)	675 (18)	

*Includes day cases where admission and discharge are on the same day.

steeper for the shorter follow-up time. Sensitivity analyses (see online supplementary table) based only on individuals who were at the same postcode throughout the whole duration of this study showed similar results.

DISCUSSION

Our data report hospital usage patterns measured either by the number of hospital admissions or by total bed days, over a 10-year follow-up period in a population of middle aged and older men and women in the UK. We observed that age, male sex, manual social class low education level, current smoking and BMI >30 kg/m² independently predicted multiple admissions and extended time in hospital. A simple five-point risk score constructed using male sex, manual social class, no educational qualifications, current smoking and BMI >30 kg/m², estimated percentages of the cohort in the categories of admission numbers and hospital bed days in stratified age bands with twofold to threefold

Table 3 Distribution of characteristics of 25 014 men and women in 1993–1997 by category of total hospital days 1999–2009

	Categories of total hospital days 1999–2009					
	None (n=6835 27%)	Day case (n=2777 11%)	1–4 nights (n=4950 20%)	5–19 nights (n=5476 22%)	≥20 nights (n=4976 20%)	p Value
Total hospital days, 1999–2009						
Mean±SD	0.0±0.0	1.0±0.0	3.1±1.1	11.4±4.2	65.7±87.7	<0.0001
Median(IQR)	0.0 (0.0–0.0)	1.0 (1.0–1.0)	3.0 (2.0–4.0)	11.0 (8.0–14.0)	44.0 (29.0–73.0)	
Number of admissions, 1999–2009						
Mean±SD	0.0±0.0	1.0±0.0	2.3±1.0	4.1±2.5	11.9±35.0	<0.0001
Median(IQR)	0.0 (0.0–0.0)	1.0 (1.0–1.0)	2.0 (2.0–3.0)	4.0 (2.0–5.0)	7.0 (4.0–12.0)	
Body mass index, kg/m²						
Mean±SD	25.9±3.7	25.9±3.6	26.1±3.8	26.8±4.0	27.1±4.3	<0.0001
Sex (n (%))						
Men	2928 (26)	1230 (11)	2084 (19)	2572 (23)	2414 (21)	<0.0001
Women	3907 (28)	1547 (11)	2866 (21)	2904 (21)	2562 (19)	
Age, years						
Mean±SD	55.4±8.6	56.0±8.5	58.1±8.8	60.6±8.8	64.9±8.2	<0.0001
Age band (n (%))						
<45	481 (47)	179 (17)	197 (19)	133 (13)	42 (4)	<0.0001
45–50	1789 (41)	672 (15)	929 (21)	699 (16)	277 (6)	
50–55	1450 (35)	568 (14)	918 (22)	800 (19)	433 (10)	
55–60	1096 (28)	457 (12)	854 (22)	907 (23)	595 (15)	
60–65	877 (23)	422 (11)	771 (20)	999 (26)	827 (21)	
65–70	659 (17)	289 (8)	741 (19)	987 (26)	1162 (30)	
70–75	400 (13)	160 (5)	456 (15)	799 (26)	1280 (41)	
75–80	83 (12)	30 (4)	84 (12)	152 (21)	360 (51)	
Smoking status (n (%))						
Current	751 (26)	295 (10)	521 (18)	684 (24)	653 (22)	<0.0001
Former	2558 (25)	1118 (11)	1992 (19)	2388 (23)	2367 (23)	
Never	3476 (30)	1351 (12)	2396 (21)	2354 (21)	1892 (16)	
Social class (n (%))						
Professional (1)	599 (35)	210 (12)	320 (19)	343 (20)	252 (15)	<0.0001
Technical (2)	2754 (31)	1045 (12)	1753 (20)	1818 (20)	1579 (18)	
Clerical NM (3.1)	1047 (26)	467 (12)	797 (20)	880 (22)	853 (21)	
Clerical M (3.2)	1397 (25)	603 (11)	1130 (20)	1347 (24)	1149 (20)	
Semiskilled (4)	744 (23)	336 (10)	695 (21)	760 (23)	731 (22)	
Unskilled (5)	163 (19)	76 (9)	167 (19)	204 (24)	250 (29)	
Level of education (n (%))						
Low	1910 (21)	860 (9)	1773 (19)	2237 (25)	2350 (26)	<0.0001
Medium	4122 (31)	1629 (12)	2591 (19)	2734 (21)	2215 (17)	
High	800 (31)	287 (11)	582 (23)	501 (19)	405 (16)	
Body mass index (n (%))						
<24 kg/m²	2225 (32)	885 (13)	1460 (21)	1312 (19)	1103 (16)	<0.0001
24–27 kg/m²	2410 (28)	978 (11)	1761 (20)	1827 (21)	1632 (19)	
27–30 kg/m²	1320 (24)	603 (11)	1058 (19)	1366 (25)	1218 (22)	
>30 kg/m²	873 (23)	310 (8)	658 (17)	958 (25)	1004 (26)	

differences in future hospital use between those with high and low risk scores.

More than half of women under 55 years of age with risk score of zero will expect one or more hospital admission over the next decade but only 5% would have more than 7 admissions or more than 20 nights in hospital. Up to the age of 75 years the number of hospital admissions one might expect increases with the risk score. For those aged 55–65 years only 13% might expect to spend 20 nights in hospital over the next 10 years but this increased to 30% for those with a risk score of four or five. Eighty-seven per cent of men and women over 75 years would expect to be admitted to hospital on one or more occasions over 10 years irrespective of their risk score.

While the trend for increasing hospital use with risk score was not consistent in the oldest age group >75 with the highest risk score, numbers in this group were not large. Possible explanations include substantial differential mortality early on in follow-up resulting in attrition as observed in table 6 so that fewer individuals were at risk of hospital admissions and bed day use over the full 10-year follow-up period.

Table 4 Multivariable logistic regression of risk factors for no hospital admissions, ≥7 hospital admissions and ≥20 days of hospital stay from 1999 to 2009 in 25 014 men and women aged 40–79 years 1993–1997

	Logistic regression					
	All participants		Men		Women	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Outcome of no hospital admissions†						
Female sex	1.11 (1.05 to 1.18)	<0.001	–	–	–	–
Age per 10 years	0.56 (0.54 to 0.57)	<0.001	0.49 (0.47 to 0.52)	<0.001	0.61 (0.58 to 0.64)	<0.001
Non-manual social class	1.29 (1.21 to 1.38)	<0.001	1.35 (1.22 to 1.48)	<0.001	1.24 (1.14 to 1.35)	<0.001
High education level	1.26 (1.18 to 1.35)	<0.001	1.18 (1.06 to 1.32)	0.003	1.32 (1.21 to 1.45)	<0.001
Former or never smoker	1.23 (1.12 to 1.34)	<0.001	1.22 (1.07 to 1.41)	0.004	1.22 (1.08 to 1.39)	0.001
BMI<30 kg/m²	1.25 (1.15 to 1.36)	<0.001	1.22 (1.06 to 1.40)	0.005	1.28 (1.14 to 1.43)	<0.001
Outcome of seven or more hospital admissions†						
Male sex	1.32 (1.22 to 1.42)	<0.001	–	–	–	–
Age per 10 years	1.75 (1.67 to 1.82)	<0.001	1.94 (1.82 to 2.06)	<0.001	1.58 (1.49 to 1.68)	<0.001
Manual social class	1.22 (1.13 to 1.32)	<0.001	1.21 (1.09 to 1.36)	<0.001	1.23 (1.10 to 1.37)	<0.001
Low education level	1.14 (1.05 to 1.24)	0.002	1.05 (0.93 to 1.18)	0.407	1.24 (1.11 to 1.39)	<0.001
Current smoker	1.53 (1.37 to 1.71)	<0.001	1.42 (1.21 to 1.66)	<0.001	1.65 (1.41 to 1.92)	<0.001
BMI >30 kg/m²	1.41 (1.28 to 1.56)	<0.001	1.43 (1.24 to 1.66)	<0.001	1.39 (1.22 to 1.59)	<0.001
Outcome of 20 or more hospital nights†						
Male sex	1.20 (1.12 to 1.28)	<0.001	–	–	–	–
Age per 10 years	2.54 (2.44 to 2.65)	<0.001	2.70 (2.54 to 2.88)	<0.001	2.41 (2.28 to 2.55)	<0.001
Manual social class	1.20 (1.12 to 1.29)	<0.001	1.23 (1.11 to 1.37)	<0.001	1.17 (1.06 to 1.29)	0.003
Low education level	1.17 (1.09 to 1.26)	<0.001	1.07 (0.96 to 1.19)	0.220	1.27 (1.15 to 1.40)	<0.001
Current smoker	1.59 (1.44 to 1.77)	<0.001	1.64 (1.41 to 1.90)	<0.001	1.56 (1.35 to 1.80)	<0.001
BMI >30 kg/m²	1.54 (1.41 to 1.68)	<0.001	1.52 (1.33 to 1.74)	<0.001	1.56 (1.39 to 1.75)	<0.001

†Each variable adjusted for all others listed.
BMI, body mass index.

Comparison with other studies

Most studies examining hospital usage in the UK are based on hospital data but are limited in their capacity to estimate accurately denominator populations or to assess characteristics prior to hospitalisation and how they may relate to relative or absolute risk of hospital usage prospectively.

The EPIC-Norfolk cohort was recruited from the general population resident in Norfolk and unlike hospital-based studies is able to compare characteristics

Table 5 Absolute percent with no hospital admissions, ≥7 hospital admissions or >20 hospital nights during follow-up 1999–2009 in men and women 40–79 years in 1993–1997

	Outcome rate by score* and age band % outcome rate (outcome frequency/total participants)				
	0	1	2	3	4–5†
Outcome of no hospital admissions (years)					
<55	43 (913/2112)	42 (1445/3425)	34 (862/2537)	33 (365/1107)	28 (62/222)
55–65	32 (425/1314)	28 (749/2681)	22 (487/2176)	19 (223/1170)	16 (40/253)
65–75	23 (229/994)	17 (377/2241)	12 (244/2008)	12 (130/1099)	11 (25/235)
>75	13 (12/95)	11 (28/254)	13 (25/199)	11 (11/96)	0 (0/14)
Outcome of 7 or more hospital admissions (years)					
<55	5 (114/2112)	6 (203/3425)	9 (238/2537)	11 (124/1107)	15 (33/222)
55–65	10 (133/1314)	13 (350/2681)	15 (328/2176)	19 (225/1170)	21 (54/253)
65–75	14 (141/994)	19 (427/2241)	23 (452/2008)	27 (294/1099)	31 (73/235)
>75	21 (20/95)	21 (54/254)	23 (46/199)	22 (21/96)	14 (2/14)
Outcome of 20 or more hospital nights (years)					
<55	5 (105/2112)	7 (230/3425)	10 (244/2537)	11 (127/1107)	14 (32/222)
55–65	13 (173/1314)	16 (439/2681)	18 (397/2176)	25 (289/1170)	30 (76/253)
65–75	26 (262/994)	32 (721/2241)	37 (738/2008)	42 (465/1099)	48 (113/235)
>75	45 (43/95)	50 (127/254)	51 (102/199)	55 (53/96)	43 (6/14)

*Score is defined as the sum of the following binary categories, each contributing one point: male sex, manual social class, low education level, current smoker, body mass index >30 kg/m².
†Scores 4 and 5 combined into a single category due to low numbers having score=5.

Table 6 Mortality rates by risk score and age group during before 1993–1998, 1999–2003 and 1999–2009

	Mortality rate* by score† and age band				
	0	1	2	3	4–5‡
Mortality rates before 1993–1998, 1999–2004 and 1999–2009					
<55 years	1993–1999: 0.3	1993–1999: 0.6	1993–1999: 0.5	1993–1999: 0.7	1993–1999: 2.2
	1999–2004: 1.2	1999–2004: 1.4	1999–2004: 2.0	1999–2004: 2.9	1999–2004: 4.4
	1999–2009: 2.2	1999–2009: 3.0	1999–2009: 4.8	1999–2009: 6.4	1999–2009: 7.5
55–65 years	1993–1999: 1.0	1993–1999: 1.3	1993–1999: 1.2	1993–1999: 1.8	1993–1999: 4.2
	1999–2004: 2.9	1999–2004: 4.7	1999–2004: 5.2	1999–2004: 6.8	1999–2004: 12.5
	1999–2009: 7.6	1999–2009: 10.4	1999–2009: 11.5	1999–2009: 15.0	1999–2009: 22.3
65–75 years	1993–1999: 3.8	1993–1999: 5.1	1993–1999: 5.1	1993–1999: 8.0	1993–1999: 7.8
	1999–2004: 8.2	1999–2004: 11.6	1999–2004: 13.4	1999–2004: 17.6	1999–2004: 25.1
	1999–2009: 19.7	1999–2009: 27.7	1999–2009: 30.4	1999–2009: 37.0	1999–2009: 45.1
>75 years	1993–1999: 3.1	1993–1999: 3.8	1993–1999: 5.2	1993–1999: 20.0	1993–1999: 22.2
	1999–2004: 19.4	1999–2004: 24.2	1999–2004: 30.5	1999–2004: 29.2	1999–2004: 33.3
	1999–2009: 48.0	1999–2009: 51.5	1999–2009: 60.0	1999–2009: 46.7	1999–2009: 44.4

*The denominator does not exclude deaths prior to 1999.
†Score is defined as the sum of the following binary categories, each contributing one point: male sex, manual social class, low education level, current smoker, body mass index >30 kg/m².
‡Scores 4 and 5 combined into a single category due to low numbers having score=5.

of hospital attenders and those who did not need to use those services. The period under examination approximately coincides with administrative control by Primary Health Trusts (PCT, 2002–2013) with hospital usage free at the point of delivery under the UK NHS.

Health service usage for study participants resident in the Norfolk area is the responsibility of the East Norfolk PCT irrespective of where in the country the usage occurred. Linkage to the PCT has the advantage of capturing episodes at any UK hospital, not just those in the area. Our study included data from several UK hospitals although the large majority were from Norfolk hospitals. We were able to estimate the probability of hospital admissions and total bed days over a 10-year period according and how they varied according to a range of simple and easily measured demographic and behavioural characteristics generally available in general practice.

A limitation in our study is the lack of information about non-NHS hospital and clinics where study participants paid for treatment. This would include common cosmetic procedures such as the removal of varicose veins and other procedures offered as a private service that may be restricted or not available on the NHS. Data on treatment in private hospitals or clinics were not available to us. It is possible that some of the associations we observed between those in higher social class groups and lower hospital usage are explained by private treatment. However, most serious long-term conditions are treated in NHS hospitals. The differences by sex and BMI we observed were independent of social class and education. It is also possible that individuals may have differentially moved away during follow-up. However, the sensitivity analyses (see online supplementary table) based only on those individuals living in the same post code observed essentially similar results. We have not attempted to examine the reason for admission and simply examined and restricted ourselves to the number of occasions when hospital services were used. The most common reasons for admission were related to diseases of the circulatory system (essential hypertension and chronic ischaemic heart disease being the most common) and diseases of the digestive system (the most common being gastritis, diaphragmatic hernia and diverticular disease). We have also not looked at the survival of those who did or did not use hospital services. Future exploration of these areas will help give us a clearer and more detailed understanding.

While it is not possible to infer causal links between the lifestyle factors and hospital admissions, differences in social class and education may reflect real differences in health status need or demand. Alternatively, thresholds for admission may vary.

In this study, we have identified a range of simple demographic and behavioural indicators that are related to the future probability of cumulative hospital admissions and bed days. The strongest of these are increasing age and male sex. However, the modifiable factors we examined are all strongly associated with hospital usage. Current cigarette smokers were 59% more likely to have 20 of more nights in hospital while those with BMI >30 kg/m² are 54% more likely, indicating an important role of potentially modifiable factors for hospital usage. These and the other simple indicators we have examined are easy to collect and may assist healthcare providers and those planning services to predict future hospital use.

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Contributors RL managed the data collection, linked cohort data to HES records, cleaned and analysed the data, and drafted and revised the paper. He is guarantor. KTK conceived the research, analysed the data and drafted, and revised the paper. SH coordinated the research and revised the draft paper. NW conceived the research and revised the draft paper.

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Competing interests None declared.

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RESEARCH ARTICLE

Alcohol consumption and future hospital usage: The EPIC-Norfolk prospective population study

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Data Availability Statement: The authors will make the dataset available under a Data Transfer Agreement to any bona fide researcher who wishes to obtain the dataset in order to undertake a replication analysis. The EPIC-Norfolk study depends on data from NHS digital or its previous equivalent bodies. NHS Digital do not allow the sharing of data at individual record level without having a data sharing agreement in place. Researchers wishing to request data can contact the EPIC-Norfolk Management Committee at Department of Public Health and Primary Care, Strangeways Research Laboratory, Worts

Abstract

Background

Heavy drinkers of alcohol are reported to use hospitals more than non-drinkers, but it is unclear whether light-to-moderate drinkers use hospitals more than non-drinkers.

Objective

We examined the relationship between alcohol consumption in 10,883 men and 12,857 women aged 40–79 years in the general population and subsequent admissions to hospital and time spent in hospital.

Methods

Participants from the EPIC-Norfolk prospective population-based study were followed for ten years (1999–2009) using record linkage.

Results

Compared to current non-drinkers, men who reported any alcohol drinking had a lower risk of spending more than twenty days in hospital multivariable adjusted OR 0.80 (95%CI 0.68–0.94) after adjusting for age, smoking status, education, social class, body mass index and prevalent diseases. Women who were current drinkers were less likely to have any hospital admissions multivariable adjusted OR 0.84 (95%CI 0.74–0.95), seven or more admissions OR 0.77 (95% CI 0.66–0.88) or more than twenty hospital days OR 0.70 (95%CI 0.62–0.80). However, compared to lifelong abstainers, men who were former drinkers had higher risk of any hospital admissions multivariable adjusted OR 2.22 (95%CI 1.51–3.28) and women former drinkers had higher risk of seven or more admissions OR 1.30 (95%CI 1.01–1.67).

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Conclusion

Current alcohol consumption was associated with lower risk of future hospital usage compared with non-drinkers in this middle aged and older population. In men, this association may in part be due to whether former drinkers are included in the non-drinker reference group but in women, the association was consistent irrespective of the choice of reference group. In addition, there were few participants in this cohort with very high current alcohol intake. The measurement of past drinking, the separation of non-drinkers into former drinkers and lifelong abstainers and the choice of reference group are all influential in interpreting the risk of alcohol consumption on future hospitalisation.

Introduction

Alcohol misuse and its consequences continue to have a profound effect on society in general and on health services in particular. In 2015 there were 8,758 alcohol-related deaths in the UK [1] but a much higher estimate of 21,162 deaths and 914,929 hospital admissions wholly or partly attributable to harm from alcohol in England in 2010/11 has been calculated [2]. The direct and indirect costs to the NHS attributable to alcohol misuse have been estimated at approximately 3.5 billion pounds every year with estimates placing the overall economic burden to be between 1.3% and 2.7% of UK annual GDP [3,4]. Alcohol has been linked to 230 disease and injury categories in systematic reviews and for the majority of these, higher consumption is associated with a greater likelihood of disease. However, the level and pattern of alcohol drinking that constitutes misuse or excess varies by condition. National drinking guidelines also vary widely [5–7], suggesting lack of agreement of the levels of consumption considered acceptable. Alcohol-attributable fractions (AAF), the proportion of a disease or outcome that is attributed to excess alcohol consumption, vary greatly by condition [8]. Liver disease for example, constitutes the third commonest cause of premature death in the UK and three-quarters of deaths from liver disease are the result of excess alcohol consumption [9]. Alcoholic beverages were classified as carcinogenic by the International Agency for Research on Cancer (IARC) and many cancers are partly attributable to alcohol with monotonic increasing risk albeit with AAF at much lower levels.

The relationship between alcohol consumption and future hospital usage at lower levels of consumption are less clear. Whether alcohol has a cardioprotective effect has been the subject of considerable debate over many years [8,10–14]. A large body of epidemiological evidence together with evidence for plausible biological mechanisms, have reported beneficial associations for ischaemic heart disease (IHD) and diabetes at moderate levels of alcohol intake. Associations with other diseases such as Alzheimer's disease and gall bladder disease have also been reported to be mainly beneficial in systematic reviews [8,15–21].

The UK Health Education Council's guidance on alcohol drinking limits, first introduced in 1984, suggested limits considerably higher than those now recommended [5]. Recent public health guidelines in the UK examining lifetime risk associated with alcohol intake recommended a maximum weekly consumption of 14 units or 112 grams (1 UK unit = 8 grams of alcohol) for both men and women. This is based on modelling of the chronic and acute effects of alcohol using published systematic reviews and meta-analysis as the evidence base [6]. However, drinking guidelines vary widely by country, and while this may reflect cultural norms it also suggests a lack of agreement of the level at which consumption becomes harmful [7].

We have previously reported that age, body mass index (BMI) and smoking status predict future hospital use in a community based population of middle aged and older men and women over a ten year period of follow-up [22]. In the analyses presented here, we examined the relationship between current alcohol consumption in this cohort and their subsequent hospital usage over a period of ten years. This paper examines whether current drinking behaviour predicts the frequency or total days of future hospital admission from any cause over a fixed ten year period. Though we did not aim to describe the numerous pathological mechanisms that might be involved, we explored how conditions commonly found in older people might influence the overall relationship between alcohol consumption and future hospital usage. Our study is not designed to derive a prognostic model for predicting hospital use but rather to examine the relationship between usual alcohol consumption patterns at the more moderate levels generally observed in middle aged and older men and women living in the community and subsequent hospital usage.

Materials and methods

The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) is a general population cohort of men and women aged 40–79 years living in Norfolk recruited from general practices between 1993–1997. The National Health Service means that general practice registers approximate population registers. The study has ethics committee approval from Norfolk Research Ethics Committee (Rec Ref: 98CN01) and all participants gave informed signed consent for study participation including access to medical records. The methods used were carried out in accordance with the relevant guidelines and regulations.

The design and recruitment of the study has been described in detail elsewhere [23,24]. Briefly, 77,630 were invited to participate of whom 30,445 consented to take part and completed a lifestyle questionnaire and 25,639 men and women subsequently attended a health examination.

Alcohol exposure definitions

In the baseline questionnaire, participants were asked "Are you a non-drinker/teetotaller now?" and "At present, about how many alcoholic drinks do you have each week" for four types of alcohol: Beer, cider or lager (pints); wine (glasses), sherry or fortified wines (glasses) and spirits (singles). Current non-drinkers were defined as those who answered "yes" to being a non-drinker now and did not report consuming beer, wine or spirits at present. Similarly, current drinkers were defined as answering "no" to the question or report drinking at present.

Participants were also asked "Have you ever drunk alcohol in the past?" and two similar questions relating to consumption of the four alcohol types when aged 20 and aged 30. Former drinkers were defined as current non-drinkers who answered "yes" to ever drinking alcohol or reported consuming alcohol aged 20 or 30. Lifelong abstainers were defined as participants who are neither current drinkers nor former drinkers.

Current units and past units were calculated from the questionnaire responses with one unit equal to a half pint of beer, one glass of wine or fortified wine or a single measure of spirits. The capacity of a glass was not specified, but assumed to be 125ml for wine and 50ml for fortified wines. An additional category "occasional", representing consumption of less than one drink per week, contributed half a unit when ticked for an alcohol type. Heavy current drinkers are defined as participants with >35 current units per week while heavy former drinkers are defined as participants with >35 past units per week. Those with current units greater than zero were divided into four categories: (0,7], (7,14], (14,21] and >21 units per week. Past alcohol consumption is defined as the higher of units reported consumed aged 20 and aged 30.

Other covariates

Participants were also asked details of their current job and their partner's current job. Occupational social class was defined according to the Registrar General's classification [25]. Non-manual occupations were represented by codes 1 (professional), 2 (managerial and technical), 3.1 (non-manual skilled) occupations, while manual occupations were represented by codes 3.2 (manual skilled), 4 (partly skilled), and 5 (unskilled) occupations. Partner's social class was used where available for women and former occupation used where no current occupation was reported [26].

Educational attainment was established using the question "Do you have any of the following qualifications?" followed by a list of common UK qualifications. Participants were categorised according to the highest qualification attained in four groups: those with no formal qualifications; those with formal qualifications usually associated with a school age between 16 ('O' level or equivalent) or 18 years ('A' level or equivalent); and those with degree level qualifications.

Smoking status was derived from two questions each of which could be answered as yes or no: "Have you ever smoked as much as one cigarette a day for as long as a year?" and for those who answered "yes" to the first question "Do you smoke cigarettes now?"

Participants were asked: "Has a doctor ever told you that you have any of the following?" followed by a list of conditions including diabetes, heart attack, stroke and cancer. Personal history of disease was defined by "yes" responses to these four conditions. Trained nurses measured height and weight according to standard protocols at the health examination. Body Mass Index (BMI) was calculated as weight in kilogrammes divided by height squared in square metres.

Ascertainment of hospital usage and mortality through record linkage

Between 1999 and 2009, cohort participants were also linked to hospital records held by the East Norfolk Primary Health Care Trust using their unique National Health Service number. The database contained hospital episode statistics (HES) coded using the International Classification of Disease (ICD), revision 10, for all Norfolk residents wherever they were treated, including hospitals in other areas in the UK. Linking the EPIC-Norfolk cohort to HES records enables a well defined population denominator to explore future hospital usage patterns. Details of the linkage and outcome variables have been previously reported [22].

Time in hospital over the ten year period was calculated using admission and discharge dates from HES. The sum (in days) of one plus (discharge date minus admission date) was used in order that day cases (admission and discharge on the same day) were considered as well as bed days (overnight stays). The number of hospital admissions was also determined from the HES data with contiguous admissions counted as a single admission. Three dichotomous outcome categories were then calculated: 'Any hospital admissions' and '7 or more admissions' using total admissions and '>20 hospital days' using total bed days and day cases. In addition to total hospital usage for any reason, we also explored usage related to conditions that have been associated with alcohol in systematic literature reviews [8,27].

All participants were followed up for mortality by cause by flagging for death at the UK Office for National Statistics (ONS), and trained nosologists coded death certificates using the ICD, revisions 9 and 10.

Statistical analysis

For the analyses presented here, we excluded 625 men and women from the baseline cohort who died before 1999 and excluded 1274 for whom alcohol intake was not known or inconsistent leaving 23,740 individuals. Men and women were examined separately recognising the different alcohol consumption patterns and conditions between the sexes. Logistic regression models were used to examine associations between alcohol intake and hospital usage outcome categories for total admissions, and in exploratory analyses for various diagnostic codes. The terms "beneficial" and "detrimental" used in S3 and S4 Tables were defined by Rehm and colleagues in their systematic reviews of disease burden [8,20] and approximated by the lists of ICD version 10 codes shown. Logistic regression was used rather than survival analysis since the outcomes under examination are the total number of admissions and total bed days and day cases occurring over a fixed period of ten years. The numbers of individuals with missing values for covariates were: 51 BMI, 180 smoking status, 466 social class. Logistic regression was also used to examine the risk of death in alcohol drinkers compared to non-alcohol drinkers over the period under examination. Three sensitivity analyses were conducted: using the random forest non-parametric algorithm for multiple imputation; using the value of 1.8 units per glass of wine instead of 1 unit per glass; admissions limited to those after March 2004. All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria version 3.4.0 with packages knitr, Gmisc, missForest) and Stata statistical software version 14 (Stata Corporation, College Station, Texas, USA).

Results

Descriptive characteristics of the 10,883 men and 12,857 women by categories of alcohol intake are shown in Table 1 (for men) and Table 2 (for women). Those reporting no current alcohol intake are divided into lifelong abstainers and former drinkers, while those with intake greater than zero are divided into four categories (0,7], (7,14], (14,21] and >21 units per week. Hospital activity is shown in three categories: any hospital admissions; 7 or more admissions and >20 hospital days. Mean and median admissions and bed days/day cases are shown separately for all cohort participants and only those who had attended hospital during the period under examination to enable estimates based only on those attending hospital as well as estimates using a total population denominator. Means and medians calculated using the cohort denominator are lower since they include non-attenders. Men and women currently drinking more than 21 units per week tended to be younger, more likely to be current smokers and more likely to have drunk >21 units per week in their 20s and 30s. Current heavy drinkers (those consuming more than 35 units per week) comprised 448 (4.1%) men and 24 (0.2%) women while 89 men and 1 woman drank heavily in the past but were current non-drinkers.

S1 and S2 Tables show age and mean current intake by categories of hospital admissions and bed days/day cases respectively for men and women separately. Admissions are grouped as: zero, 1, 2–3, 4–6 and ≥7 while bed days/day cases are grouped as zero, day case, 1–4, 5–19 and 20+.

Table 3 shows the relationships between dichotomous and grouped alcohol categories and hospital usage for men and women separately. In Table 3, model 1 (age adjusted) and model 2 (multivariable adjusted) compare non-drinkers with current drinkers while model 3 (multivariable adjusted) compares non-drinkers with intake in four bands. Compared to non-drinkers, men who currently drink had a lower risk of spending more than twenty days in hospital with multivariable adjusted OR 0.80 (95% CI 0.68–0.94). Women who currently drink were also less likely to have any hospital admissions multivariable adjusted OR 0.84 (95% CI 0.74–0.95), seven or more admissions OR 0.77 (95% CI 0.66–0.88) or more than twenty hospital

Table 1. Descriptive characteristics by alcohol category for men in the EPIC-Norfolk cohort 1993–1997 and hospital admission 1999–2009.

	All (n = 10,883)	Lifelong abstainer (n = 207 1.9%)	Former drinker (n = 701 6.4%)	(0,7] units per week (n = 4,873 44.8%)	(7,14] units per week (n = 2,346 21.6%)	(14,21] units per week (n = 1,237 11.4%)	>21 units per week (n = 1,519 14.0%)
Hospital activity, 1999–2009 (n(%))							
Any hospital admissions	8,025 (73.7)	149 (72.0)	584 (83.3)	3,671 (75.3)	1,700 (72.5)	867 (70.1)	1,054 (69.4)
7 or more admissions	1,688 (15.5)	30 (14.5)	156 (22.3)	783 (16.1)	336 (14.3)	175 (14.1)	208 (13.7)
20 or more hospital nights	2,316 (21.3)	53 (25.6)	229 (32.7)	1,072 (22.0)	452 (19.3)	224 (18.1)	286 (18.8)
Total hospital days, 1999–2009							
Mean ±SD, cohort	16.9 ±43.3	17.8 ±38.4	24.9 ±44.3	17.2 ±43.4	15.6 ±40.1	15.0 ±39.2	16.0 ±50.2
Mean ±SD, hospital attenders†	23.0 ±49.0	24.8 ±43.3	29.9 ±46.9	22.8 ±48.7	21.5 ±45.7	21.4 ±45.4	23.1 ±58.9
Median(IQR), cohort	4.0 (0.0–16.0)	6.0 (0.0–21.0)	9.0 (2.0–30.0)	4.0 (1.0–17.0)	3.0 (0.0–15.0)	3.0 (0.0–14.0)	3.0 (0.0–13.0)
Median(IQR), hospital attenders†	9.0 (3.0–25.0)	12.0 (4.0–28.0)	14.0 (4.0–39.0)	9.0 (3.0–25.0)	8.0 (2.0–22.0)	7.0 (2.0–21.0)	8.0 (2.0–23.0)
Number of admissions, 1999–2009							
Mean ±SD, cohort	4.2 ±16.2	3.7 ±5.0	5.5 ±17.5	4.1 ±11.7	4.0 ±19.5	4.0 ±19.8	4.0 ±19.9
Mean ±SD, hospital attenders†	5.6 ±18.7	5.1 ±5.3	6.6 ±19.0	5.5 ±13.2	5.5 ±22.7	5.7 ±23.4	5.8 ±23.7
Median(IQR), cohort	2.0 (0.0–5.0)	2.0 (0.0–5.0)	3.0 (1.0–6.0)	2.0 (1.0–5.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)
Median(IQR), hospital attenders†	3.0 (2.0–6.0)	3.0 (2.0–6.0)	4.0 (2.0–7.0)	3.0 (2.0–6.0)	3.0 (1.0–6.0)	3.0 (1.0–5.0)	3.0 (1.0–5.8)
Alcohol intake, units per week							
Mean ±SD	10.2 ±11.9	0.0 ±0.0	0.0 ±0.0	3.0 ±2.0	10.5 ±2.0	17.7 ±2.1	33.4 ±13.1
Age, years							
Mean ±SD	59.2 ±9.2	63.6 ±8.2	62.1 ±9.3	59.7 ±9.1	58.8 ±9.3	57.9 ±9.2	57.4 ±9.0
Prevalent disease (n(%))							
Prevalent heart disease or stroke	691 (6)	11 (5)	65 (9)	347 (7)	146 (6)	53 (4)	69 (5)
Prevalent cancer	398 (4)	10 (5)	32 (5)	168 (3)	85 (4)	49 (4)	54 (4)
Prevalent diabetes	323 (3)	10 (5)	47 (7)	151 (3)	57 (2)	30 (2)	28 (2)
Smoking status (n(%))							
Current	1,308 (12)	11 (5)	107 (15)	552 (11)	236 (10)	144 (12)	258 (17)
Former	5,881 (54)	41 (20)	401 (58)	2,449 (51)	1,287 (55)	725 (59)	978 (65)
Never	3,628 (34)	152 (75)	189 (27)	1,836 (38)	812 (35)	363 (29)	276 (18)
Body mass index, kg/m^2							
Mean ±SD	26.5 ±3.3	26.5 ±3.2	26.7 ±3.8	26.4 ±3.3	26.3 ±3.1	26.7 ±3.2	27.0 ±3.4
Level of education (n(%))							
Low	3,190 (29)	92 (44)	302 (43)	1,632 (33)	555 (24)	284 (23)	325 (21)
'O' level or equivalent	948 (9)	17 (8)	48 (7)	394 (8)	216 (9)	118 (10)	155 (10)
'A' level or equivalent	5,037 (46)	69 (33)	294 (42)	2,223 (46)	1,123 (48)	577 (47)	751 (49)
Degree	1,708 (16)	29 (14)	57 (8)	624 (13)	452 (19)	258 (21)	288 (19)
Social class (n(%))							
Professional (1)	828 (8)	23 (11)	33 (5)	311 (6)	209 (9)	126 (10)	126 (8)
Technical (2)	4,126 (39)	56 (28)	190 (28)	1,641 (34)	964 (42)	566 (46)	709 (48)
Clerical NM (3.1)	1,345 (13)	32 (16)	78 (11)	612 (13)	319 (14)	136 (11)	168 (11)
Clerical M (3.2)	2,697 (25)	35 (17)	220 (32)	1,361 (28)	549 (24)	247 (20)	285 (19)
Semi-skilled (4)	1,404 (13)	45 (22)	129 (19)	715 (15)	226 (10)	117 (10)	172 (12)
Unskilled (5)	305 (3)	11 (5)	35 (5)	153 (3)	47 (2)	30 (2)	29 (2)
Past alcohol consumption‡ (n(%))							

(*Continued*)

Table 1. (Continued)

	All (n = 10,883)	Lifelong abstainer (n = 207 1.9%)	Former drinker (n = 701 6.4%)	(0,7] units per week (n = 4,873 44.8%)	(7,14] units per week (n = 2,346 21.6%)	(14,21] units per week (n = 1,237 11.4%)	>21 units per week (n = 1,519 14.0%)
(0,7] units per week	3,824 (36)	0 (0)	356 (51)	2,487 (51)	644 (27)	195 (16)	142 (9)
(7,14] units per week	2,299 (22)	0 (0)	128 (18)	1,039 (21)	647 (28)	280 (23)	205 (14)
(14,21] units per week	1,547 (15)	0 (0)	68 (10)	535 (11)	433 (18)	273 (22)	238 (16)
>21 units per week	2,981 (28)	0 (0)	149 (21)	792 (16)	619 (26)	488 (39)	933 (61)

† Denominator restricted to cohort participants who attended hospital during the period under examination

‡Past alcohol consumption is defined as the higher of units reported consumed aged 20 and aged 30

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

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days OR 0.70 (95% CI 0.62–0.80). We did not observe a higher risk of hospitalisation at any level of intake including those consuming 21 units or more per week. Table 4 differs from Table 3 by the use of lifelong abstainers as reference category. Compared to lifelong abstainers, men who currently drink had a higher risk of any hospital admissions OR 1.53 (95% CI 1.10–2.13) while in women the association was inverse OR 0.84 (95% CI 0.70–1.01). Men who were former drinkers had a higher risk than lifelong abstainers OR 2.22 (95% CI 1.51–3.28) while former drinking women showed no difference OR 1.01 (95% CI 0.80–1.27). The associations were similar in all categories of intake.

Table 5 displays logistic regression models for the outcome of any hospital admissions comparing non-drinkers with current drinkers in various subgroups. Separate models for men and women are stratified by a dichotomised subgroup: age above or below 65 years; smoking status; BMI above and below 30kg/m2; manual and non-manual social class; low or other education level and prevalent disease (heart disease, cancer or diabetes). Odds ratios (OR) within all strata were in consistent directions with no interaction by age, smoking status or BMI.

S3 Table shows relationships between dichotomous and grouped alcohol categories and hospital usage but uses modified admission and bed day/day case counts containing only admissions that include discharge codes entirely attributable to alcohol intake or partly attributable and considered "detrimental" (alcohol intake positively associated with disease) according to previous systematic reviews of the literature. S4 Table shows similar relationships for discharge codes considered "beneficial" (alcohol intake inversely associated with disease) [8]. In both sub-classifications, men and women who currently drink have a lower risk of admission compared to non-drinkers.

Sensitivity analyses using 1.8 units per glass of wine instead of 1 unit (S5 Table) [28] and using multiple imputation (S6 Table) gave similar results to those presented in the main tables. A sensitivity analysis (S7 Table) with admissions limited to those after March 2004 gave similar results for women but attenuated results for men. Participants excluded due to missing alcohol intake (n = 1274) were older and predominantly women (73%) with a lower proportion having non-manual social classes and education to age 16 or above.

Discussion

In this cohort of middle-aged and older men and women, there was no evidence of a higher hospital usage for current alcohol consumers when compared with those who do not currently report drinking alcohol. Participants who consumed alcohol were not observed to have a higher rate of hospital admission or time in hospital over the observation period of ten years. In fact the results indicate lower hospital usage for current compared to current non-drinkers

Table 2. Descriptive characteristics by alcohol category for women in the EPIC-Norfolk cohort 1993–1997 and hospital admission 1999–2009.

	All (n = 12,857)	Lifelong abstainer (n = 873 6.8%)	Former drinker (n = 1,086 8.4%)	(0,7] units per week (n = 8,121 63.2%)	(7,14] units per week (n = 1,911 14.9%)	(14,21] units per week (n = 615 4.8%)	>21 units per week (n = 251 2.0%)
Hospital activity, 1999–2009 (n(%))							
Any hospital admissions	9,168 (71.3)	691 (79.2)	843 (77.6)	5,769 (71.0)	1,295 (67.8)	405 (65.9)	165 (65.7)
7 or more admissions	1,562 (12.1)	140 (16.0)	203 (18.7)	963 (11.9)	178 (9.3)	57 (9.3)	21 (8.4)
20 or more hospital nights	2,329 (18.1)	257 (29.4)	291 (26.8)	1,412 (17.4)	251 (13.1)	83 (13.5)	35 (13.9)
Total hospital days, 1999–2009							
Mean ±SD, cohort	15.2 ±48.9	22.5 ±43.0	23.8 ±64.7	14.3 ±46.3	11.7 ±53.4	12.8 ±46.6	10.9 ±25.9
Mean ±SD, hospital attenders †	21.3 ±56.7	28.5 ±46.5	30.7 ±72.0	20.2 ±53.9	17.2 ±64.2	19.4 ±56.3	16.6 ±30.5
Median(IQR), cohort	3.0 (0.0–13.0)	6.0 (1.0–25.0)	6.0 (1.0–23.0)	3.0 (0.0–12.0)	2.0 (0.0–9.0)	2.0 (0.0–9.0)	2.0 (0.0–10.0)
Median(IQR), hospital attenders†	7.0 (2.0–21.0)	11.0 (3.0–32.0)	11.0 (3.0–33.0)	6.0 (2.0–20.0)	5.0 (2.0–15.0)	6.0 (2.0–16.0)	5.0 (2.0–16.0)
Number of admissions, 1999–2009							
Mean ±SD, cohort	3.5 ±16.3	4.1 ±7.6	5.3 ±34.0	3.3 ±8.4	3.3 ±23.5	3.8 ±27.8	2.3 ±3.6
Mean ±SD, hospital attenders†	4.9 ±19.1	5.1 ±8.2	6.9 ±38.5	4.6 ±9.7	4.9 ±28.4	5.8 ±34.2	3.6 ±4.0
Median(IQR), cohort	2.0 (0.0–4.0)	2.0 (1.0–5.0)	2.0 (1.0–5.0)	2.0 (0.0–4.0)	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–3.0)
Median(IQR), hospital attenders†	3.0 (1.0–5.0)	3.0 (2.0–6.0)	3.0 (2.0–6.0)	3.0 (1.0–5.0)	2.0 (1.0–4.0)	2.0 (1.0–5.0)	2.0 (1.0–5.0)
Alcohol intake, units per week							
Mean ±SD	4.4 ±5.7	0.0 ±0.0	0.0 ±0.0	2.5 ±1.9	10.1 ±2.0	17.0 ±2.2	27.8 ±7.1
Age, years							
Mean ±SD	58.5 ±9.2	63.0 ±8.6	60.5 ±9.1	58.2 ±9.1	57.1 ±9.1	57.4 ±9.4	55.4 ±9.2
Prevalent disease (n(%))							
Prevalent heart disease or stroke	272 (2)	35 (4)	48 (4)	152 (2)	28 (1)	8 (1)	1 (0)
Prevalent cancer	838 (7)	58 (7)	71 (7)	527 (6)	117 (6)	44 (7)	21 (8)
Prevalent diabetes	186 (1)	26 (3)	33 (3)	107 (1)	15 (1)	2 (0)	3 (1)
Smoking status (n(%))							
Current	1,449 (11)	52 (6)	156 (15)	831 (10)	242 (13)	106 (17)	62 (25)
Former	4,152 (33)	110 (13)	375 (35)	2,472 (31)	790 (42)	291 (47)	114 (46)
Never	7,142 (56)	692 (81)	541 (50)	4,753 (59)	865 (46)	217 (35)	74 (30)
Body mass index, kg/m^2							
Mean ±SD	26.2 ±4.3	26.8 ±4.7	26.7 ±4.9	26.2 ±4.4	25.6 ±3.8	25.4 ±3.9	25.7 ±3.7
Level of education (n(%))							
Low	5,253 (41)	531 (61)	610 (56)	3,371 (42)	534 (28)	149 (24)	58 (23)
'O' level or equivalent	1,518 (12)	69 (8)	111 (10)	1,008 (12)	228 (12)	69 (11)	33 (13)
'A' level or equivalent	4,658 (36)	219 (25)	303 (28)	2,943 (36)	821 (43)	268 (44)	104 (41)
Degree	1,428 (11)	54 (6)	62 (6)	799 (10)	328 (17)	129 (21)	56 (22)
Social class (n(%))							
Professional (1)	830 (7)	35 (4)	37 (4)	486 (6)	171 (9)	65 (11)	36 (15)
Technical (2)	4,475 (36)	237 (28)	268 (25)	2,670 (34)	864 (46)	314 (51)	122 (50)
Clerical NM (3.1)	2,490 (20)	129 (15)	232 (22)	1,626 (20)	361 (19)	105 (17)	37 (15)
Clerical M (3.2)	2,655 (21)	213 (25)	267 (25)	1,772 (22)	301 (16)	71 (12)	31 (13)
Semi-skilled (4)	1,637 (13)	159 (19)	181 (17)	1,079 (14)	152 (8)	52 (9)	14 (6)
Unskilled (5)	482 (4)	63 (8)	71 (7)	310 (4)	29 (2)	4 (1)	5 (2)

(*Continued*)

Table 2. (Continued)

	All (n = 12,857)	Lifelong abstainer (n = 873 6.8%)	Former drinker (n = 1,086 8.4%)	(0,7] units per week (n = 8,121 63.2%)	(7,14] units per week (n = 1,911 14.9%)	(14,21] units per week (n = 615 4.8%)	>21 units per week (n = 251 2.0%)
Past alcohol consumption‡ (n(%))							
(0,7] units per week	9,875 (83)	0 (0)	976 (90)	7,185 (90)	1,304 (68)	322 (52)	88 (35)
(7,14] units per week	1,351 (11)	0 (0)	77 (7)	612 (8)	435 (23)	160 (26)	67 (27)
(14,21] units per week	384 (3)	0 (0)	18 (2)	135 (2)	103 (5)	83 (14)	45 (18)
>21 units per week	248 (2)	0 (0)	15 (1)	68 (1)	65 (3)	49 (8)	51 (20)

† Denominator restricted to cohort participants who attended hospital during the period under examination

‡Past alcohol consumption is defined as the higher of units reported consumed aged 20 and aged 30

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

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Table 3. Age adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 hospital admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997.

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	20 or more hospital nights OR (95% CI)	p value
Men †										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
Current drinker	9975	7292	0.81 (0.68–0.97)	0.021	1502	0.84 (0.71–1.00)	0.052	2034	0.74 (0.63–0.87)	<0.001
Men ‡										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
Current drinker	9975	7292	0.85 (0.71–1.02)	0.083	1502	0.88 (0.73–1.05)	0.162	2034	0.80 (0.68–0.94)	0.008
Men ‡										
Current non-drinker	908	733	1	–	186	1	–	282	1	–
(0,7] units per week	4873	3671	0.89 (0.74–1.08)	0.231	783	0.90 (0.74–1.09)	0.266	1072	0.82 (0.69–0.97)	0.024
(7,14] units per week	2346	1700	0.85 (0.69–1.04)	0.106	336	0.85 (0.68–1.04)	0.120	452	0.76 (0.62–0.92)	0.005
(14,21] units per week	1237	867	0.79 (0.64–0.99)	0.037	175	0.88 (0.69–1.12)	0.284	224	0.75 (0.60–0.94)	0.012
>21 units per week	1519	1054	0.78 (0.63–0.96)	0.020	208	0.85 (0.68–1.08)	0.187	286	0.83 (0.67–1.03)	0.095
Women †										
Current non-drinker	1959	1534	1	–	343	1	–	548	1	–
Current drinker	10898	7634	0.77 (0.69–0.87)	<0.001	1219	0.69 (0.61–0.79)	<0.001	1781	0.65 (0.57–0.73)	<0.001
Women ‡										
Current non-drinker	1959	1534	1	–	343	1	–	548	1	–
Current drinker	10898	7634	0.84 (0.74–0.95)	0.005	1219	0.77 (0.66–0.88)	<0.001	1781	0.70 (0.62–0.80)	<0.001
Women ‡										
Current non-drinker	1959	1534	1	–	343	1	–	548	1	–
(0,7] units per week	8121	5769	0.85 (0.75–0.96)	0.010	963	0.79 (0.68–0.91)	0.001	1412	0.73 (0.64–0.83)	<0.001
(7,14] units per week	1911	1295	0.82 (0.70–0.96)	0.012	178	0.69 (0.56–0.85)	<0.001	251	0.61 (0.51–0.73)	<0.001
(14,21] units per week	615	405	0.75 (0.61–0.93)	0.008	57	0.67 (0.49–0.91)	0.011	83	0.61 (0.46–0.80)	<0.001
>21 units per week	251	165	0.79 (0.59–1.07)	0.124	21	0.63 (0.39–1.01)	0.054	35	0.69 (0.46–1.04)	0.078

OR = Odds ratio, CI = Confidence intervals. Comparison group: Current non-drinker

†Adjusted for age

‡ Adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

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Table 4. Age adjusted and multivariable logistic regression of risk factors for any hospital admissions (compared to none), ≥7 hospital admissions (compared to <7 admissions) and >20 days of hospital stay (compared to ≤20 days) from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997.

	All	n	Any hospital admissions OR (95% CI)	p value	n	Seven or more admissions OR (95% CI)	p value	n	20 or more hospital nights OR (95% CI)	p value
Men †										
Lifelong abstainer	207	149	1	–	30	1	–	53	1	–
Former drinker	701	584	2.33 (1.60–3.40)	<0.001	156	1.84 (1.20–2.84)	0.006	229	1.63 (1.13–2.36)	0.009
Current drinker	9975	7292	1.52 (1.11–2.10)	0.010	1502	1.37 (0.92–2.03)	0.123	2034	1.08 (0.78–1.51)	0.632
Men ‡										
Lifelong abstainer	207	149	1	–	30	1	–	53	1	–
Former drinker	701	584	2.22 (1.51–3.28)	<0.001	156	1.70 (1.08–2.65)	0.021	229	1.47 (1.00–2.16)	0.051
Current drinker	9975	7292	1.53 (1.10–2.13)	0.011	1502	1.34 (0.89–2.02)	0.163	2034	1.08 (0.76–1.52)	0.676
Men ‡										
Lifelong abstainer	207	149	1	–	30	1	–	53	1	–
Former drinker	701	584	2.22 (1.51–3.27)	<0.001	156	1.70 (1.08–2.65)	0.021	229	1.47 (1.00–2.16)	0.051
(0,7] units per week	4873	3671	1.61 (1.15–2.24)	0.005	783	1.37 (0.90–2.07)	0.137	1072	1.10 (0.78–1.57)	0.578
(7,14] units per week	2346	1700	1.53 (1.09–2.14)	0.015	336	1.29 (0.84–1.97)	0.241	452	1.02 (0.71–1.46)	0.917
(14,21] units per week	1237	867	1.43 (1.00–2.02)	0.047	175	1.34 (0.86–2.08)	0.197	224	1.01 (0.69–1.48)	0.952
>21 units per week	1519	1054	1.40 (0.99–1.98)	0.056	208	1.30 (0.84–2.02)	0.233	286	1.13 (0.78–1.63)	0.533
Women †										
Lifelong abstainer	873	691	1	–	140	1	–	257	1	–
Former drinker	1086	843	1.04 (0.83–1.30)	0.733	203	1.34 (1.06–1.71)	0.016	291	1.06 (0.86–1.31)	0.569
Current drinker	10898	7634	0.79 (0.66–0.94)	0.007	1219	0.82 (0.67–0.99)	0.042	1781	0.67 (0.57–0.79)	<0.001
Women ‡										
Lifelong abstainer	873	691	1	–	140	1	–	257	1	–
Former drinker	1086	843	1.01 (0.80–1.27)	0.924	203	1.30 (1.01–1.67)	0.042	291	1.02 (0.82–1.27)	0.884
Current drinker	10898	7634	0.84 (0.70–1.01)	0.063	1219	0.89 (0.72–1.09)	0.263	1781	0.71 (0.60–0.84)	<0.001
Women ‡										
Lifelong abstainer	873	691	1	–	140	1	–	257	1	–
Former drinker	1086	843	1.01 (0.80–1.27)	0.932	203	1.30 (1.01–1.67)	0.043	291	1.02 (0.82–1.26)	0.891
(0,7] units per week	8121	5769	0.85 (0.71–1.02)	0.088	963	0.91 (0.74–1.13)	0.397	1412	0.73 (0.62–0.87)	<0.001
(7,14] units per week	1911	1295	0.82 (0.67–1.01)	0.063	178	0.80 (0.62–1.03)	0.089	251	0.62 (0.50–0.77)	<0.001
(14,21] units per week	615	405	0.76 (0.59–0.97)	0.028	57	0.78 (0.55–1.10)	0.156	83	0.61 (0.46–0.83)	0.001
>21 units per week	251	165	0.80 (0.58–1.10)	0.171	21	0.73 (0.44–1.20)	0.215	35	0.70 (0.46–1.07)	0.099

OR = Odds ratio, CI = Confidence intervals. Comparison group: Lifelong abstainer

† Adjusted for age

‡ Adjusted for age, smoking status, education level (low/others), social class (manual/non-manual), body mass index (continuous), prevalent heart disease or stroke, prevalent cancer and prevalent diabetes

Round brackets in intervals denote strict inequalities; square brackets denote non-strict inequalities

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for both men and women for all levels of alcohol consumption and hospital usage before and after adjustment for age and other factors previously documented to relate to hospital usage in this cohort. There are a number of possible explanations for these findings.

Confounding

The frequency and pattern of alcohol use is strongly related to age, sex, education, social class, obesity, and prevalent ill health, all of which are also related to hospital use so confounding is a

Table 5. Logistic regression models for any hospital admissions comparing non-drinkers with current drinkers in subgroups in 23,740 men and women aged 40–79 years 1993–1997.

	Men non-drinker (ref)	Men current drinker OR (95% CI)	Women non-drinker (ref)	Women current drinker OR (95% CI)
By age above and below 65 years				
Less than 65 years	1	0.89 (0.72–1.11)	1	0.79 (0.68–0.92)
65 years and above	1	0.79 (0.56–1.12)	1	0.94 (0.75–1.19)
By smoking status				
Current smoker	1	0.85 (0.70–1.03)	1	0.85 (0.74–0.96)
Non-smoker	1	0.87 (0.52–1.45)	1	0.64 (0.43–0.96)
By BMI				
BMI>30	1	0.92 (0.76–1.11)	1	0.81 (0.70–0.92)
BMI≤30	1	0.50 (0.28–0.90)	1	0.91 (0.68–1.22)
By social class				
Manual social class	1	0.90 (0.70–1.16)	1	0.78 (0.66–0.92)
Non-manual social class	1	0.81 (0.62–1.05)	1	0.89 (0.74–1.06)
By education				
Low education level	1	0.88 (0.71–1.11)	1	0.77 (0.65–0.91)
Other education level	1	0.80 (0.59–1.10)	1	0.89 (0.75–1.07)
By prevalent disease				
No reported disease	1	0.82 (0.68–0.99)	1	0.81 (0.72–0.92)
Pre-existing heart disease, cancer or diabetes	1	1.22 (0.55–2.72)	1	0.70 (0.28–1.72)

OR = Odds ratio, CI = Confidence intervals. Comparison group: Current non-drinker. All models adjusted for age, smoking status, education level (low/others), social class (manual/non-manual) and body mass index (continuous) except where a dichotomous adjustment variable was the subgroup being examined

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major issue. However, multivariable regression models adjusting for all these variables hardly changed the findings. In addition, we stratified by main confounders (Table 5) as well as excluding those with known prevalent heart disease, cancer and diabetes, and the results remained consistent in the subgroups. However, measurement of covariates might not be sufficiently accurate to ensure adequate adjustment and we cannot exclude the possibility of residual confounding with known or other unknown factors associated with both alcohol intake and hospital usage, which could either attenuate or strengthen the associations.

Bias

Differential follow-up might have occurred if participants had chosen to use private hospitals instead of NHS hospitals and the alcohol consumption of those participants differed from the study population. Participants in higher social class groups might be higher alcohol consumers and also use private healthcare not recorded in NHS hospital statistics. If this occurred it might attenuate some of the inverse associations observed. However, private health care use is minimal in Norfolk and these results do reflect the use of National Health Service hospitals which is the predominant health care system.

Similarly, differential misclassification in hospital use may be explained by early death rates. Participants who died early from alcohol attributable diseases may have lower hospital usage over the period under examination having not used hospital services for the entire period. This is unlikely as over this time period the risk of death was in fact lower in alcohol drinkers compared to non-alcohol drinkers hazard ratio (OR) 0.67 (95% CI 0.57–0.80) for men and OR 0.66 (95% CI 0.57–0.76) for women. A sensitivity analysis excluding hospital admissions prior to 2004 showed attenuated associations for men which might indicate that prevalent illness could lead to a reduction or cessation in alcohol consumption although this was not apparent in women.

Under-reporting of consumption in this study is likely given the known problems in capturing alcohol intake by questionnaire. Self-reported alcohol consumption in surveys suggest much lower consumption than estimates based on alcohol sales data [29–31]. In the 1998 Australian National Drug Strategy Household Survey, reported intake accounted for only 46.5% of known alcohol sales for the preceding 12-month period. When asked to estimate average consumption, there is a tendency to report a figure closer to median than mean consumption with heavy drinking episodes disregarded. There is also a tendency for past alcohol consumption to be remembered less well than more recent consumption. Questions relating to past consumption are insufficiently sensitive to determine periods of abstaining, binge drinking, patterns of consumption or heavy use. Nevertheless, random measurement errors or systematic underreporting of heavy alcohol consumption would only attenuate the findings observed.

Those who enrol in studies, typically in middle age, represent healthy survivors while those worst affected by alcohol misuse may be less likely to participate. Participants who drink moderately may not be representative of moderate drinkers of similar age in the general population due to differing consumption patterns over the life course [32,33]. It has also been suggested that while high levels of alcohol consumption are associated with harm in all socioeconomic groups, there appears to be a disproportionate level of harm for individuals with low socioeconomic status [34,35]. A meta-analyses that controlled for quality-related study characteristics found that moderate drinking had no net mortality benefit compared with lifetime abstention or occasional drinking [36]. However, in a large study of linked electronic UK health records using recruitment at general practice rather than individual level, moderate drinking was associated with a lower risk of several cardiovascular diseases [37].

Inclusion of former drinkers in the current non-drinkers reference group

The choice of reference group in describing our results may influence interpretation. Non-drinkers comprise heterogeneous subgroups with different characteristics. Former drinkers may have stopped consuming alcohol because of illness, irrespective of whether their illness was caused by drinking. They have been reported to have increased risk for cardiovascular mortality compared to long-term abstainers, a phenomenon described as the "sick-quitter" hypothesis [11]. Lifelong abstainers, ostensibly an ideal reference group having no exposure, may have characteristics that are unusual in the general population [38–40]. Lifelong teetotalism is rare in men (less than 2% of those in the current study) and the reasons for abstaining such as cultural or religious beliefs, may introduce other biases obscuring the results. It has also been noted that there are substantial inconsistencies in self-reports of lifetime abstention. Others have suggested moderate drinkers with no previous history of heavy drinking as a reference group since that is the most commonly observed behaviour and forms the largest group [12,41]. The consumption of alcohol in middle aged men and women tends to decline with age with the largest decline in heavy drinkers but with a reduction across all intake categories.

We opted to use both current non-drinkers and lifelong abstainers as reference groups in the main analyses presented. In the context of hospital usage our objective was to examine the burden on hospital services of cohort participants in relation to current alcohol use rather than pathological processes that may be involved in alcohol and disease associations. To this extent participants' previous history of alcohol consumption was less relevant than the more pragmatic question of their use of services given their current drinking status. However, we have also presented analyses using the alternative reference group of lifetime abstainer in order to explore better this issue. Estimates are less stable given the very small proportion of men who were lifetime non-drinkers. These analyses suggest that in men, the highest hospital usage was observed in former drinkers but with current alcohol drinkers also having higher hospital usage than lifelong abstainers. However, findings in women were not materially different, irrespective of whether lifelong abstainers or former drinkers were used as a reference group. There was no evidence of the "sick quitter" effect found in women affecting the risk of hospitalisation observed in current drinkers.

Findings in context

These results are somewhat unexpected in the light of current beliefs about alcohol intake in the general population and hospital usage. The many diseases related to the high consumption of alcohol would lead us to expect a positive association between hospital usage and alcohol intake. Mortality rates for liver disease have increased four-fold since 1970 with liver disease the third most common cause of premature death in the UK [9]. Obesity related diseases also have a profound impact on hospital services and since alcohol's energy density is second only to fat, a positive association might be expected. However, cardiovascular disease is a predominant reason for hospital admissions, and an inverse association between alcohol intake and cardiovascular disease has been reported in many epidemiological studies [10,11,14,42]. While causality has not been established, plausible biological mechanisms such as the reduction of plaque deposit in arteries, the reduction of blood clot formation and the dissolving of blood clots[18], have supported the reported beneficial associations for ischaemic heart disease (IHD) and diabetes at moderate levels of alcohol intake. Hospitalisations might reflect the balance between positive and negative health effects of alcohol consumption in a particular study population. Most studies based on hospital cases without a population denominator are unable to assess the potential impact of moderate alcohol consumption if associated with lower hospital use.

Strengths of the study

Most studies of hospital use only have data on patients who are hospitalised, that is, cases without denominators so are unable to assess overall risk associated with alcohol consumption in the general population. We were able to examine hospital usage over a defined time period in a clearly defined community based population using a prospective cohort design. Use of record linkage with routinely collected hospital admissions data means that ascertainment is virtually complete as use of private healthcare in Norfolk at this time period was minimal. We have previously reported that age, BMI and smoking status predict future hospital use in this cohort over a ten year period of follow-up [22]. Loss to follow-up is small (approximately 2%) as few study participants have moved away from the area they were recruited.

Study participants are very well characterised and we were able to take into account many potentially confounding variables documented to relate to hospital usage in this population as well as prevalent ill health. Income was not measured in EPIC-Norfolk. However, in the UK national health system, income is not a major determinant of hospital admissions, and education and occupational social class are stronger sociodemographic indicators in this respect than income. EPIC-Norfolk is homogeneous with respect to race and ethnicity with 99% describing themselves as white. The assessment by study participants of their alcohol intake in their 20s and 30s enabled us to differentiate between current non-drinkers and lifelong abstainers.

The measurement of past alcohol consumption allows the separation of non-drinkers into former drinkers and lifelong abstainers.

Limitations in generalisability

Potential selection biases may limit the interpretation of the data since participants were recruited in middle-age and represent survivors who may over-represent resilient and less risky drinkers. Since very few cohort participants reported heavy drinking, a limitation of the study is the inability to examine any possibly deleterious effect of very high consumption. While we did not observe a higher risk of admissions even with the highest alcohol intake categories when comparing current non-drinkers to current drinkers, there were very few people in this study population with very high alcohol consumption levels. Hence the generalisability of these findings to other populations where there are substantially more heavy drinkers may be limited. The use of current non-drinker as reference category must also be considered alongside any interpretation of these results as evidence that the consumption of alcohol may be beneficial but we had very few men who were lifelong abstainers in this cohort.

By using total hospital usage, we were able to assess hospital admissions not just for conditions for which alcohol might increase risk, but also the possible lower service use if alcohol at moderate intake levels were to have the postulated cardioprotective effects. The results presented here reflect hospital usage in a middle aged and older age group and thus we are not able to comment on associations in younger people where binge drinking resulting in acute alcohol poisoning, road traffic and other accidents are a major problem. Nevertheless, older people are by far the greatest users of hospital services and in this older cohort, which was similar to UK national samples in many respects, there was no evidence that current alcohol intake was associated with a higher level of hospital use.

Conclusions

Current alcohol consumption was not associated with higher but lower hospital usage compared with current non-drinkers in this middle aged and older population. The associations were consistent after multivariable adjustment for age, smoking, BMI, education, social class and prevalent illness in both men and women. In men, this association may in part be due to whether former drinkers are included in the non-drinker reference group but in women, the association was consistent irrespective of the choice of reference group. We should note however, that there were few participants in this cohort with very high current alcohol intake. The measurement of past drinking, the separation of non-drinkers into former drinkers and lifelong abstainers and the choice of reference group are all influential in interpreting the risk of alcohol consumption on future hospitalisation.

Supporting information

S1 Table. Distribution of characteristics of 23,740 men and women in 1993–1997 by category of number of hospital admissions 1999–2009.
(PDF)

S2 Table. Distribution of characteristics of 23,740 men and women in 1993–1997 by category of total hospital days 1999–2009.
(PDF)

S3 Table. Age adjusted and multivariable logistic regression of risk factors restricted to "detrimental" hospital admissions for any hospital admissions, $\geq$7 admissions and $>$20 days of hospital stay from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997.
(PDF)

S4 Table. Age adjusted and multivariable logistic regression of risk factors restricted to "beneficial" hospital admissions for any hospital admissions, ≥7 admissions and >20 days of hospital stay from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997.
(PDF)

S5 Table. Sensitivity analysis for wine strength 1.8 units per glass Age adjusted and multivariable logistic regression of risk factors for any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999–2009 in 23,740 men and women aged 40–79 years 1993–1997.
(PDF)

S6 Table. Sensitivity analysis using multiple imputation using the random forest non-parametric algorithm Age adjusted and multivariable logistic regression of risk factors for any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999–2009 in 25,639 men and women aged 40–79 years 1993–1997.
(PDF)

S7 Table. Sensitivity analysis excluding hospital events before April 2004 Age adjusted and multivariable logistic regression of risk factors for any hospital admissions, ≥7 admissions and >20 days of hospital stay from 2004–2009 in 23,740 men and women aged 40–79 years 1993–1997.
(PDF)

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BMJ Open

Residential area deprivation and risk of subsequent hospital admission in a British population: the EPIC-Norfolk cohort

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ABSTRACT

Objectives To investigate whether residential area deprivation index predicts subsequent admissions to hospital and time spent in hospital independently of individual social class and lifestyle factors.

Design Prospective population-based study.

Setting The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) study.

Participants 11 214 men and 13 763 women in the general population, aged 40–79 years at recruitment (1993–1997), alive in 1999.

Main outcome measure Total admissions to hospital and time spent in hospital during a 19-year time period (1999–2018).

Results Compared to those with residential Townsend Area Deprivation Index lower than the average for England and Wales, those with a higher than average deprivation index had a higher likelihood of spending >20 days in hospital multivariable adjusted OR 1.18 (95% CI 1.07 to 1.29) and having 7 or more admissions OR 1.11 (95% CI 1.02 to 1.22) after adjustment for age, sex, smoking status, education, social class and body mass index. Occupational social class and educational attainment modified the association between area deprivation and hospitalisation; those with manual social class and lower education level were at greater risk of hospitalisation when living in an area with higher deprivation index (p-interaction=0.025 and 0.020, respectively), while the risk for non-manual and more highly educated participants did not vary greatly by area of residence.

Conclusion Residential area deprivation predicts future hospitalisations, time spent in hospital and number of admissions, independently of individual social class and education level and other behavioural factors. There are significant interactions such that residential area deprivation has greater impact in those with low education level or manual social class. Conversely, higher education level and social class mitigated the association of area deprivation with hospital usage.

Strengths and limitations of this study

- ► This study is able to examine hospital activity using a prospective cohort design in a population of community-dwelling participants with clearly defined population denominators.
- ► It uses a large cohort of middle-aged and older men and women with 19 years of follow-up time and detailed measurements of demographic and behavioural indicators.
- ► Both area-based census measures and individual social class and education level from questionnaires are used.
- ► Differential misclassification in hospital use may be explained by early death rates.
- ► Socioeconomic determinants of hospitalisation were examined in the context of UK National Health Service hospitals, which are free at the point of use and so not directly influenced by income.

INTRODUCTION

The considerable differences in mortality by social class are well documented[1–4] with those in higher social classes having a typical life expectancy several years longer than those with the lowest. Similarly, life expectancy and health expectancy varies between UK cities and regions with large variations in expected years of life in good health.[5 6] Despite increasing overall life expectancy, inequality remains with lower life and health expectancy observed more often in disadvantaged groups. While lifestyle factors may account for some part of this, the reported differences in death rates cannot be explained by individual behaviour alone.[7 8] Material deprivation was defined by Townsend as 'a state of observable and demonstrable disadvantage relative to the local community or wider society … to which an individual, family or group belongs'. Deprivation indices use factors such as unemployment, the standard of housing, overcrowding and rates of car ownership which together can assess the level of deprivation within a neighbourhood.[9]

Hospitalisation can be measured using the frequency of admission or the length of stay. When measured over a period of time, the outcome represents burden of resources that might be attributable to a population. Inequality in healthcare utilisation favouring patients who are better off is apparent in half of the Organisation for Economic Co-operation and Development countries.[10–12] The UK National Health Service is free at the point of use and consequently should provide equitable healthcare not constrained by ability to pay.

Socioeconomic determinants of hospitalisation have been examined using individual level exposures such as occupational social class, income and education and at area level using various deprivation indices but few studies have both individual and area-based measures. Individual occupational social class, income and level of education have all been reported to be associated with chronic disease risk.[13 14] We previously reported that a range of simple demographic and behavioural indicators are related to the future probability of cumulative hospital admissions and bed days.[15] Increasing age and male sex and the modifiable factors current cigarette smoking, body mass index (BMI) >30 kg/m^2, manual social class and low education level were all associated with higher future hospital usage over a 10-year period. Area-based deprivation measures, available routinely in the UK using postal code linkage, have also reported associations with hospital usage.[16–20] However, the participants in such studies are often limited to those attending hospital and so a suitable population denominator is lacking. Studies reporting health associations for both individual and area measures are less common[21–23] and we are unaware of any studies examining the independent association of residential area deprivation on subsequent hospital usage.

In this paper, we examine residential area deprivation using the Townsend Area Deprivation Index with subsequent hospital usage over a 19-year period. We explore the independent contribution of residential area deprivation in men and women participants of the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) study and its association with future hospitalisation after allowing for the individual level factors previously shown to be associated. We also examine possible interactions between area and individual deprivation measures. Our aim is to determine whether factors such as material living conditions, poor quality housing and poor infrastructure are associated with subsequent hospitalisation in a setting where access to healthcare is unconstrained by ability to pay.

METHODS

We used data collected as part of EPIC-Norfolk, a general population cohort.

Study design

EPIC-Norfolk is a cohort of men and women living in Norfolk. Recruitment took place between 1993 and 1997 at 35 general practices with invitations sent to all those registered with the practices aged 40–79 years. The design and recruitment of the study has been previously described in detail.[24 25] Briefly, a total of 77 630 invitations were sent to adults registered at participating GP practices; 30 445 (40%) consented to participate in the study of whom 25 639 men and women completed a lifestyle questionnaire and attended a health examination. Residential postcode, recorded at the end of recruitment, was used to link to the UK 1991 national census data.[26] Between 1999 and 2018, the cohort was linked to databases maintained by the East Norfolk Primary Care Trust (PCT) and later to national databases held by NHS Digital.[27] Hospital Episode Statistics (HES) records which included admission and discharge dates were used to calculate time in hospital and number of admissions. Contiguous admissions were merged and counted as a single admission. Details of linkage of the EPIC-Norfolk cohort participants to hospital records have been previously reported.[15]

Residential area deprivation score for participants

The Townsend Area Deprivation Index is an area deprivation measurement calculated using four components: the percentage unemployed of economically active residents aged over 16 years, the percentage of households with no car, the percentage of households not owner occupied and the percentage of households with more than one person per room. These are respectively: a measure of lack of material resources and insecurity, a proxy for current income, a proxy for current wealth and a measure of material living conditions. The index used in this study was constructed using data collected at the 1991 UK census, which takes place every 10 years. Each Townsend component was calculated at Enumeration District (ED), a small area containing an average 175 households used by the census administrators both as output areas and for data collection. Townsend components were then standardised as z-scores at ED level for England and Wales. Study participants were linked to an ED using their home postcode at the end of recruitment in the year 2000. The link was then used to establish a residential Townsend Area Deprivation Index for each individual.

Covariables

Participants' height and weight were measured in light clothing without shoes by trained nurses in a clinic setting as part of a health examination between 1993 and 1997. Height was measured to the nearest 0.1 cm using a stadiometer (Chasemores, UK) and weight to the nearest 0.1 kg BMI was calculated using measured weight in kilograms divided by measured height^2 in square metres.

Participants completed a lifestyle questionnaire which included questions about their and their partner's current and past employment. Occupational social class was defined according to the Registrar General's classification[28] and dichotomised into non-manual and manual social classes. Professional, managerial and technical and non-manual skilled occupations (codes I, II and IIIa, respectively) were classed as non-manual while manual skilled, partly skilled and unskilled (codes IIIb, IV and V, respectively) were classed as manual. Social class for men used (in order of priority) their own current employment, own past employment, partner's current employment or partner's past employment according to whether a social class classification could be defined for a given occupation type. Similarly, social class for women used (in order of priority) their partner's current employment, partner's past employment, own current employment, own past employment. The use of partner's social class for women in the EPIC-Norfolk cohort born between 1918 and 1948 has been previously discussed.[29]

The question "Do you have any of the following qualifications" together with a list of common UK qualifications was used to establish educational attainment. Participants were categorised according to the highest qualification they attained: those with no formal qualifications, those with formal qualifications usually associated with completing school aged between 16 and 18 years and those with degree level qualifications.

Smoking status was derived from two questions: "Have you ever smoked as much as one cigarette a day for as long as a year" and "Do you smoke cigarettes now". The responses to both questions were 'yes' or 'no' and participants were asked to leave the second question blank if they answered 'no' to the first.

Travel time and travel distance between participants home postcode and the Norfolk and Norwich University Hospitals NHS Foundation Trust was calculated using the Open Source Routing Machine,[30] which calculates the shortest path between two points over the road network. Postcode of home residence was used to establish if a participant had moved house over the follow-up period. It was available at two points in time: in the year 2000 and the year 2014. Participants whose postcode or house location changed during the period were classified as having moving house but were not excluded from the analyses. Urban and rural categories were established using the 1991 census.

Ascertainment of hospital usage and mortality through record linkage

Details of linkage of the EPIC-Norfolk cohort participants to hospital records have been previously reported.[15] Briefly, linkage using unique NHS numbers was performed between 1999 and 2018 to databases maintained by the East Norfolk Primary Healthcare Trust and to national databases held by NHS Digital.[27] All hospital activity for EPIC-Norfolk participants was captured wherever they were treated in England and Wales. HES records which included admission and discharge dates were used to calculate time in hospital and number of admissions. Contiguous admissions were merged and counted as a single admission.

Statistical analysis

For the current analyses, we excluded the 625 men and women from the baseline cohort who died before 1999. A further 37 who did not have a valid UK postcode were excluded leaving 24 977 participants. Dichotomous variables were created for the three socioeconomic status variables. Occupational social class was categorised into non-manual and manual: social classes I, II and III non-manual were classified as 'non-manual', while social classes III manual, IV and V were classified as 'manual'. Educational level was categorised into 'higher level' (which includes those with qualifications at secondary level or above) and 'lower level' (those with no qualification). Townsend Area Deprivation Index was divided into quintiles. Lower Townsend scores correspond to lower levels of deprivation. Quintiles 1–4 are all below zero and hence below (less deprived than) the national average for England and Wales. Quintile 5 (−0.64, 6.99] corresponds to Townsend scores close to or above the national average (more deprived). Overall Townsend score and components were also dichotomised with scores below zero defined as 'less deprived' and scores above 0 as 'more deprived'. Hospital admissions were categorised into five groups: 0, 1, 2–3, 4–6 and ≥7 while time in hospital was divided into categories: none, day case, 2–5 days, 6–20 days and >20 days. The cut-points were chosen to be consistent with earlier work.[15] Since time in hospital was skewed with some people remaining in hospital for extended periods, length of stay longer than 365 days was truncated for graphical presentation. A dichotomous urban/rural variable was defined with 'urban' and 'urban sparse' as urban and 'town', 'village' or 'hamlet' as rural. Three dichotomous outcome categories were calculated: any hospital admissions (vs no admissions), 7 or more admissions (vs fewer than 7) using total admissions and >20 hospital days (vs 20 or fewer) using total bed days (overnight stays) and day cases. Multivariable logistic regression was used for all models. All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria, V.3.5.3 with packages knitr, Gmisc, ggplot2, tidyverse, intubate).

RESULTS

Table 1 shows descriptive characteristics by quintiles of residential Townsend Area Deprivation Index for 11 214 men and 13 763 women. The majority (n=20 996) of study participants had deprivation index below zero while n=3 981, approximately corresponding to those in quintile 5, had levels above the national average. Participants in quintile 5 were much more likely to live in an urban setting (70.2%) while those in quintiles 2, 3 and 4 were more likely to live in a rural location. Travel distance was lowest for participants in quintile 1 and 5, perhaps due to a higher proportion living in cities and travel times followed a similar pattern. Participants in quintile 5 were the most likely to move house (26.1% between 2000 and 2014). Hospital admissions and time in hospital are shown for both the full cohort and restricted to those who attended hospital; 10.5% of study participants had no admissions over the 19 years from 1999 to 2018.

Table 1 Descriptive characteristics by quintiles of Townsend Area Deprivation Index

	Total	Quintile 1 (−6.74, −3.81)	Quintile 2 (−3.81, −2.94]	Quintile 3 (−2.94, −2.09]	Quintile 4 (−2.09, −0.64]	Quintile 5 (−0.64, 6.99]	P value
Sex (n (%))							
Men	11 214 (44.9)	2271 (45.2)	2262 (45.4)	2280 (45.2)	2226 (45.0)	2175 (43.7)	0.41
Women	13 763 (55.1)	2752 (54.8)	2723 (54.6)	2760 (54.8)	2722 (55.0)	2806 (56.3)	
Age, years							
Mean±SD	59.0±9.3	58.8±9.0	59.0±9.2	58.8±9.2	59.2±9.4	59.4±9.5	0.002
Body mass index, kg/m²							
Mean±SD	26.4±3.9	26.1±3.8	26.3±3.8	26.4±3.9	26.5±4.0	26.5±4.1	<0.001
Cigarette smoking (n (%))							
Current	2895 (11.7)	457 (9.2)	501 (10.1)	569 (11.4)	575 (11.7)	793 (16.1)	<0.001
Former	10 411 (42.0)	2033 (40.7)	2083 (42.1)	2044 (41.0)	2132 (43.4)	2119 (43.1)	
Never	11 453 (46.3)	2502 (50.1)	2361 (47.7)	2378 (47.6)	2203 (44.9)	2009 (40.8)	
Social class dichotomised (n (%))							
Non-manual	14 691 (60.1)	3336 (67.4)	3170 (64.8)	2950 (59.8)	2840 (58.9)	2395 (49.5)	<0.001
Manual	9741 (39.9)	1610 (32.6)	1722 (35.2)	1985 (40.2)	1982 (41.1)	2442 (50.5)	
Level of education (n (%))							
Higher level	15 841 (63.5)	3439 (68.5)	3373 (67.7)	3218 (63.9)	3084 (62.4)	2727 (54.8)	<0.001
Lower level	9118 (36.5)	1584 (31.5)	1611 (32.3)	1819 (36.1)	1858 (37.6)	2246 (45.2)	
Travel distance to hospital, km							
Mean±SD	20.4±13.1	16.5±11.3	20.6±12.1	22.0±12.2	25.2±13.2	17.5±14.5	<0.001
Travel time to hospital, min							
Mean±SD	20.8±10.3	18.0±8.9	20.8±9.5	21.9±9.4	24.4±10.6	19.0±11.6	<0.001
Urban or rural location (n (%))							
Urban	11 214 (44.9)	2500 (49.8)	1832 (36.8)	1810 (35.9)	1575 (31.8)	3497 (70.2)	<0.001
Rural	13 763 (55.1)	2523 (50.2)	3153 (63.2)	3230 (64.1)	3373 (68.2)	1484 (29.8)	
Moved house between 2000 and 2014 (n (%))							
Moved house	5355 (22.2)	963 (19.8)	972 (20.4)	1091 (22.4)	1060 (22.4)	1269 (26.1)	<0.001
Did not move house	18 728 (77.8)	3903 (80.2)	3799 (79.6)	3774 (77.6)	3662 (77.6)	3590 (73.9)	
Deaths prior to March 2018 (n (%))							
Dead	8727 (35.0)	1630 (32.5)	1704 (34.3)	1703 (33.9)	1781 (36.1)	1909 (38.4)	<0.001
Alive	16 198 (65.0)	3386 (67.5)	3270 (65.7)	3327 (66.1)	3155 (63.9)	3060 (61.6)	
Hospital activity 1999–2018							
No admissions	2628 (10.5)	543 (10.8)	528 (10.6)	539 (10.7)	559 (11.3)	459 (9.2)	0.011
One or more admissions	22 316 (89.5)	4476 (89.2)	4449 (89.4)	4494 (89.3)	4383 (88.7)	4514 (90.8)	
7 or more admissions	16 497 (66.1)	3417 (68.1)	3295 (66.2)	3332 (66.2)	3291 (66.6)	3162 (63.6)	<0.001
>20 hospital days	15 144 (60.7)	3185 (63.5)	3054 (61.4)	3097 (61.5)	2959 (59.9)	2849 (57.3)	<0.001
Time spent in hospital 1999–2018, days							
Full cohort 1999–2018, mean±SD	32.8±63.0	30.5±54.9	33.0±69.0	31.2±57.2	32.5±62.9	37.0±69.6	<0.001
Hospital attenders 1999–2018, mean±SD	36.7±65.6	34.2±57.0	36.9±72.0	34.9±59.5	36.6±65.7	40.8±72.0	<0.001
Number of inpatient admissions 1999–2018							
Full cohort 1999–2018, mean±SD	7.5±26.0	7.3±22.8	8.2±36.1	7.6±30.8	6.7±11.7	7.6±21.4	0.073
Hospital attenders 1999–2018, mean±SD	8.4±27.3	8.2±24.0	9.2±38.1	8.6±32.5	7.6±12.1	8.4±22.3	0.095

Round brackets in intervals denote strict inequalities (< or >); square brackets denote non-strict inequalities (≤ or ≥).

Table 2 Multivariable logistic regression of risk factors by quintiles of Townsend Area Deprivation Index for any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay from 1999 to 2018 in 24 977 men and women and in a subset of 16 198 men and women alive in March 2018

	Quintile 1 (−6.74, −3.81)	Quintile 2 (−3.81, −2.94]	Quintile 3 (−2.94, −2.09]	Quintile 4 (−2.09, −0.64]	Quintile 5 (−0.64, 6.99]	P (trend)
Outcome of any hospital admissions						
Model 1	1.00	1.02 (0.89–1.16)	1.01 (0.89–1.15)	0.93 (0.82–1.05)	1.17 (1.02–1.34)	0.175
Model 1*	1.00	1.05 (0.91–1.21)	1.03 (0.89–1.18)	0.95 (0.83–1.09)	1.25 (1.08–1.45)	0.056
Model 2	1.00	1.00 (0.88–1.14)	1.00 (0.87–1.14)	0.90 (0.79–1.03)	1.09 (0.95–1.26)	0.731
Model 2*	1.00	1.04 (0.90–1.20)	1.01 (0.88–1.16)	0.91 (0.79–1.05)	1.18 (1.01–1.37)	0.341
Outcome of 7 or more hospital admissions						
Model 1	1.00	1.08 (0.99–1.18)	1.09 (1.00–1.18)	1.05 (0.97–1.15)	1.20 (1.10–1.31)	<0.001
Model 1*	1.00	1.06 (0.95–1.19)	1.15 (1.03–1.29)	1.15 (1.03–1.29)	1.39 (1.25–1.56)	<0.001
Model 2	1.00	1.07 (0.98–1.16)	1.05 (0.96–1.15)	1.01 (0.92–1.10)	1.11 (1.02–1.22)	0.107
Model 2*	1.00	1.05 (0.93–1.17)	1.11 (0.99–1.24)	1.09 (0.97–1.22)	1.28 (1.14–1.43)	<0.001
Outcome of >20 hospital days						
Model 1	1.00	1.09 (1.00–1.19)	1.10 (1.00–1.20)	1.14 (1.04–1.24)	1.27 (1.17–1.39)	<0.001
Model 1*	1.00	1.08 (0.96–1.22)	1.15 (1.02–1.30)	1.23 (1.09–1.40)	1.45 (1.28–1.64)	<0.001
Model 2	1.00	1.08 (0.99–1.18)	1.05 (0.96–1.15)	1.09 (1.00–1.19)	1.18 (1.07–1.29)	0.001
Model 2*	1.00	1.06 (0.94–1.21)	1.09 (0.96–1.23)	1.16 (1.03–1.32)	1.34 (1.18–1.51)	<0.001

Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, manual social class, low education, current cigarette smoker, body mass index >30 kg/m^2.
*Excluding participants who died prior to April 2018.

Table 2 shows the multivariable logistic regression for quintiles of Townsend Area Deprivation Index and three outcomes: any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay between 1999 and 2018. Model 1 is adjusted for age and sex while model 2 is additionally adjusted for manual social class, lower education level, current cigarette smoking and BMI >30 kg/m^2. Additionally, each model is repeated in the subset of participants who survived to the end of the follow-up period. Compared to those with Townsend Area Deprivation Index quintiles 1–4 (lower than the average for England and Wales), those with a deprivation index in quintile 5 had a higher risk of spending >20 days in hospital multivariable adjusted OR 1.18 (95% CI 1.07 to 1.29) and for 7 or more hospital admissions OR 1.11 (95% CI 1.02 to 1.22), but there was no association for any hospital admission. The multivariable adjusted p value for trend across quintiles of Townsend Area Deprivation Index was 0.001 for >20 hospital days and 0.107 for 7 or more admissions. Associations in the subset of participants surviving to March 2018 (n=16 198) were higher than those for the full cohort.

Figure 1 shows graphs of length of hospital stay by quintiles of Townsend Area Deprivation Index and demonstrates the disparity between individual socioeconomic factors and hospital stay when area deprivation index is also considered. In the first plot, results are stratified by higher and lower educational attainment. The difference in days between the least deprived (quintile 1) and the most deprived (quintile 5) is 6 days for those with lower educational attainment and 3 days for those with higher educational attainment. The second plot shows results stratified by manual and non-manual social class. The difference in days between the least deprived and the most deprived is 8 days for those with a manual social class and 3 days for those with a non-manual social class. Significant interactions were observed between social class, level of education and Townsend Area Deprivation Index (p-interaction=0.025 and 0.020, respectively).

Online supplementary table 1 shows the multivariable logistic regression for risk factors for outcomes of any hospital admissions, ≥7 hospital admissions and >20 days of hospital stay between 1999 and 2018. Models are presented for all participants, men and women and each risk factor is adjusted for all others for the nine models. Male sex is only included in the models for all participants. Age, social class, education BMI and the four individual components of Townsend Area Deprivation Index are modelled. As previously reported, age, male sex, lower education level, manual social class, current cigarette smoking and a BMI >30 kg/m^2 were all associated with increased hospitalisation. No single component of the Townsend Area Deprivation Index was more strongly associated for all outcomes for both men and women. However, the unemployment component was associated with seven or more hospital admissions. Areas with low car ownership appeared to have a greater association in women than men.

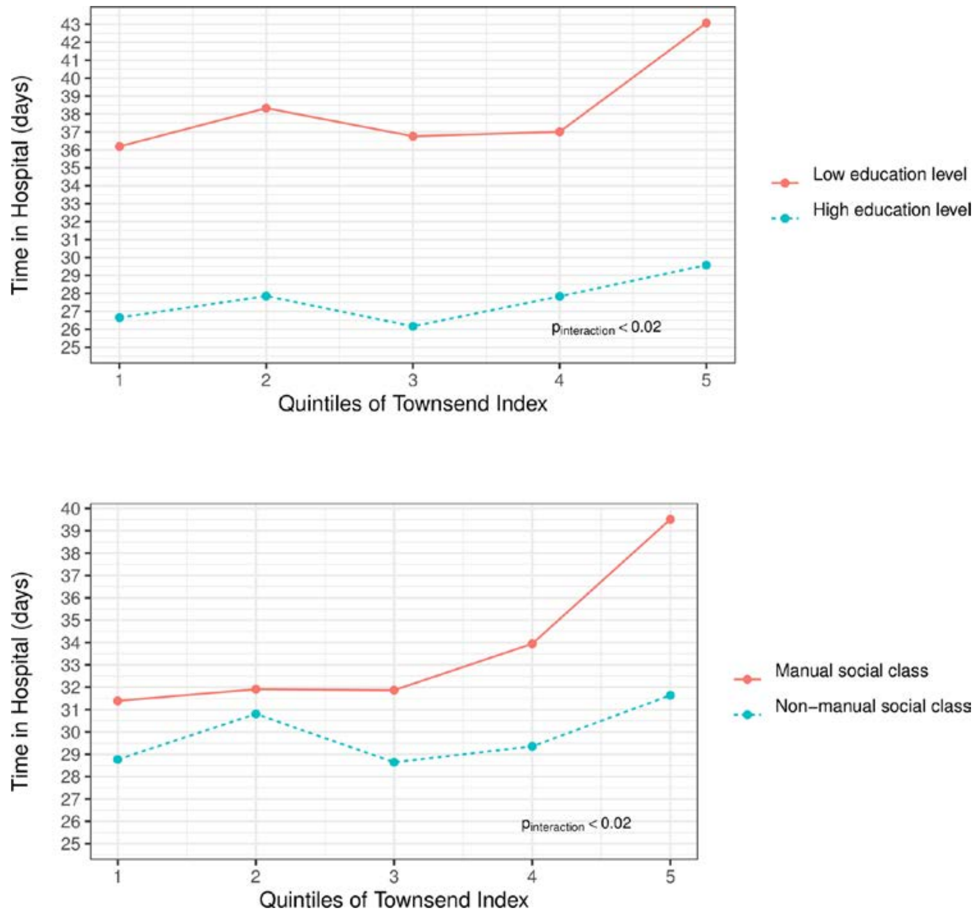

Figure 1 Hospitalisation by deprivation index. Length of hospital stay over 19 years of follow-up by quintiles of Townsend Area Deprivation Index grouped by categories of education level and categories of social class. Low education level is defined as those having no qualifications and high education as those with at least some qualifications at secondary level or above. Length of stay is truncated to 365 days for those staying longer than 365 days. Interaction tested using multivariable adjusted linear regression with covariables age, sex, education level (higher/lower), body mass index (≤30/>30 kg/m^2), smoking status (current/non-current).

Online supplementary table 2 displays logistic regression models for the outcome of >20 hospital days for Townsend Area Deprivation Index in various subgroups. Models are stratified by a dichotomised subgroup: men and women, age above or below 65 years, manual and non-manual social class, lower or higher education level, smoking status, BMI above and below 30 kg/m^2, urban or rural home postcode and moved house between the year 2000 and 2014. ORs within all strata were in consistent directions with no interaction by age, smoking status or BMI.

The numbers of individuals with missing values for covariables were: 53 BMI, 218 smoking status, 545 social class, 18 education level.

DISCUSSION

Residential area deprivation was associated with future hospital usage independently of individual sociodemographic factors, in particular age, sex, social class and education as well as lifestyle factors including smoking and BMI in this cohort of middle-aged and older men and women. Study participants in the highest fifth of the Townsend Area Deprivation Index—those living in the most deprived areas, at or below the national average, were more likely to spend >20 days in hospital or be admitted to hospital on >7 occasions. There were also significant interactions between residential area deprivation and individual social class and education level. Participants with a manual social class living in an area with higher deprivation index spent longer in hospital than those with manual occupations living in less deprived areas. Similarly, those with lower education level living in more deprived areas had the greatest risk of hospitalisation. This suggests that hospitalisation is greatest when those with poorer individual socioeconomic factors are combined with residential deprivation. We considered a number of possible explanations for these findings.

Strengths and limitations of this study

The EPIC-Norfolk cohort is very well characterised. This enabled us to take into account many potentially confounding variables understood to be related to hospital usage and disease. The UK National Health Service is free at the point of use and consequently income is not a major determinant of hospital admissions. Despite this, social class, education and residential deprivation were all independently related to hospital use. Our study examines hospital activity using a prospective cohort design in a population of community-dwelling participants with clearly defined population denominators. It uses a large cohort of middle-aged and older men and women with 19 years of follow-up time having both area-based census measures and individual social class and education level from questionnaires available.

Townsend Area Deprivation Index is associated with individual sociodemographic factors such as occupational social class and education and other factors including age, sex and BMI. Since all these factors are also related to hospital use, some level of confounding will be present. However, multivariable regression models adjusting for all these variables only modestly attenuated the area deprivation associations. In online supplementary table S2, we stratified by the main confounders and the results remained consistent in the subgroups. The accuracy of the measurement might not be sufficient to ensure adequate adjustment, so we cannot exclude the possibility of residual confounding with known or other unknown factors associated with both Townsend Area Deprivation Index and hospital usage. These unknown factors may either attenuate or strengthen the associations. Interactions between area deprivation and individual sociodemographic factors highlighted stronger associations among more deprived groups.

The use of area-based measurements has some limitations. The factors used in the Townsend score may vary in their ability to assess deprivation according to setting. In urban areas, lower car ownership rates may reflect the availability of other transport options and closer proximity of work places and facilities such as shops. In rural areas, overcrowding may be less common while car ownership may be more of a necessity while simultaneously a drain on resources. The deprivation index is based on data from the UK census that only takes place every 10 years and over the period under examination, areas may change becoming more or less deprived.

Area deprivation was determined by postcode of residence in the year 2000. Study participants who moved house may have been misclassified for some of the period over which hospitalisation was assessed. However, while 22% of the cohort moved house between the years 2000 and 2014, the large majority of participants relocated locally in Norfolk, with others moving elsewhere in England and Wales. Since the Townsend Area Deprivation Index was not measured at enumeration district level in the UK census beyond 1991, no directly comparable measure was available at later time points to examine change. However, a sensitivity analysis of non-movers found very similar results to the main analyses and any misclassification due to moves or changes over time in residential area deprivation scoring and resultant measurement error would only be likely to attenuate associations with the residential area score. HES record were available for participants who relocated within England and Wales and hence there was virtually no loss to follow-up.

Differential misclassification in hospital use may be explained by early death rates. Study participants living in more deprived areas may have died earlier and not used hospital services for the full period. However, while the death rate was higher among those living in the most deprived areas, 65% of the cohort survived beyond 2018 and models restricted to survivors were more strongly associated with outcome measures than those in the main analysis. Sociodemographic factors may be less relevant for the very seriously ill who require hospital treatment at the end of life.

It may also be possible that individuals did not use NHS facilities but private hospitals differently by socioeconomic status which might explain lower use in the higher sociodemographic groups. However, the use of private hospitals in the Norfolk area over this time period was minimal[27] and hence record linkage of routinely collected hospital episode data gave virtually complete ascertainment. Reverse causation is also possible whereby those in poor health at recruitment may have lower occupational social class increasing the chance of them living in a more deprived area. However, hospitalisation rates were low in the period directly after recruitment.

Comparison with other studies

Inequality in healthcare favouring the better off has been observed in many countries[10–12] and healthcare insurance and eligibility for government healthcare based on income thresholds may influence the associations observed. NHS healthcare is not constrained by ability to pay and hence we were able to examine the independent association of residential area deprivation—material living conditions, poor quality housing and poor infrastructure—and its association with subsequent hospitalisation.

There is some evidence to suggest that travel time is associated with hospital use,[31 32] but there was no strong association in this study. Study participants were approximately evenly divided into those living in urban and those in rural areas. The moderately deprived (those with Townsend quintile 2–4) were more likely to live in rural areas while the most deprived (Townsend quintile 5) were predominantly urban dwellers. Study participants in Townsend quintiles 1 and 5 were closer by road from their home to the Norfolk and Norwich hospital but the time taken for the journey did not vary greatly. Neither distance from hospital nor urban or rural location explained our findings, since those in the lowest deprivation areas are mainly urban with the shortest travel time to hospital. Studies examining urban/rural populations and car ownership have noted differences in deprivation characteristics.[33 34] However, irrespective of travel distance or time, owning or having access to a car would make a considerable difference in being able to access local facilities. Although there may be more regular public transport services in cities, this will vary and cost and limited travel options may restrict access to hospital and to friends and relatives, to better quality supermarkets and to parks and recreational facilities.

Most studies examining deprivation in the context of health, disease and mortality either rely on area-based measures collected, for example, from census data[16–20] or from individual level data from questionnaires.[13 14] We had access to both forms of information, having derived individual social class and education level from self-reported questionnaires and area level measures from residential postcode linkage. Hospital-based studies using patients as study participants do not have a reliable population-based denominator and cannot estimate overall risk in the population. Studies often attempt to define a denominator using separate population estimates while not individually linking.[16 35 36] We were able to examine hospital usage over 19 years in a clearly defined community-based population using a prospective cohort design.

Norfolk is an area of generally low deprivation with >80% of the study population living in areas with deprivation levels below the national average. Few participants live in areas of high deprivation such as those found in some larger cities in other parts of the country. Those living in more deprived cities or regions have a socioeconomic gradient in hospital usage more extreme than we were able to observe[37] but while our study does not provide any information on the most extreme forms of deprivation, there was sufficient heterogeneity to observe large differences in hospital use.

Our results provide further evidence adding to the substantial literature linking deprivation to health. Unlike many studies, we used overall measures of hospital activity, including both elective and emergency admissions and found evidence of an independent association of residential area deprivation not accounted for by known individual factors such as social class and education. Our results also demonstrate that the combination of residential area deprivation with lower levels of education or manual social class result in the highest levels of hospitalisation.

The Black report[2 3] concluded that health inequalities were not mainly attributable to failings in the NHS, but rather to many other social inequalities influencing health: income, education, housing, diet, employment and conditions of work. It suggested two mechanisms for how social determinants influence health: cultural/behavioural and materialist/structuralist. Some authors have pointed out that research on the determinants of health are generally focused on the individual but patterns of population health are unclear without examining structural determinants at the societal level.[38] Townsend's residential deprivation index uses aggregate measures of particular characteristics for people living in an area. It has been used mainly as a surrogate for individual measures of deprivation in many studies.[21] We were not able to examine physical features of the environment in this study. Ecological measurements such as the quality of housing, access to recreational facilities, local services provided, community support and levels of crime may affect health and hospital usage. However, we were able to examine both individual and area level deprivation in the same study participants, and the interaction we observed suggests that there is a higher risk of hospitalisation in more deprived areas of residence disproportionately for those with lower individual social class and education. Conversely, individuals with non-manual social class and higher levels of education appear more resilient to hospitalisation irrespective of the level of deprivation of their residence.

CONCLUSIONS AND POLICY IMPLICATIONS

There is a socioeconomic gradient in hospital usage for factors measured both individually and at area level. Residential area deprivation predicts future hospitalisations, time spent in hospital and number of admissions, independently of individual social class and education level and other behavioural factors. There are significant interactions such that residential area deprivation has greater impact in those with low education level or manual social class. Conversely, higher education level and social class mitigated the association of area deprivation with hospital usage. Effective NHS and government policy should therefore involve addressing deprivation both at the individual and infrastructural levels to identify and target those most at risk within the community. NHS policies focused on reducing health inequalities in the elderly need to work alongside wider government initiatives to improve the quality of housing, transport and infrastructure and access to recreation and green space.

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Competing interests RL, SH, K-TK and NW report grants from MRC and CRUK during the conduct of the study.

Patient and public involvement statement The EPIC-Norfolk study have an active Participants Advisory Panel, which meets quarterly to advise on research protocols, suggest ideas and provide feedback on the research including proposed new studies and collaborations. All participants of the EPIC-Norfolk study are informed about the study through regular newsletters as well as public meetings. Information is also disseminated through local community talks in the Norfolk area and science festivals.

Patient consent for publication Not required.

Ethics approval The work was approval by the Norfolk Research Ethics Committee (98CN01). All participants gave informed signed consent for study participation including access to medical records

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data from the EPIC Norfolk cohort are available upon request to the study steering group at https://www.epic-norfolk.org.uk/.

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RESEARCH ARTICLE
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Usual physical activity and subsequent hospital usage over 20 years in a general population: the EPIC-Norfolk cohort

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Abstract

Background: While physical activity interventions have been reported to reduce hospital stays, it is not clear if, in the general population, usual physical activity patterns may be associated with subsequent hospital use independently of other lifestyle factors.

Objective: We examined the relationship between reported usual physical activity and subsequent admissions to hospital and time spent in hospital for 11,228 men and 13,786 women aged 40–79 years in the general population.

Methods: Participants from a British prospective population-based cohort study were followed for 20 years (1999–2019) using record linkage to document hospital usage. Total physical activity was estimated by combining workplace and leisure time activity reported in a baseline lifestyle questionnaire and repeated in a subset at a second time point approximately 12 years later.

Results: Compared to those reporting no physical activity, participants who were the most active had a lower likelihood of spending more than 20 days in hospital odds ratio (OR) 0.88 (95% confidence interval (CI) 0.81–0.96) over the next 20 years after multivariable adjustment for age, sex, smoking status, education, social class and body mass index. Participants reporting any activity had a mean of 0.42 fewer hospital days per year between 1999 and 2009 compared to inactive participants, an estimated potential saving to the National Health Service (NHS) of £247 per person per year, or approximately 7% of UK health expenditure. Participants who remained physically active or became active 12 years later had lower risk of subsequent hospital usage than those who remained inactive or became inactive, p-trend < 0.001.

Conclusion: Usual physical activity in this middle-aged and older population predicts lower future hospitalisations - time spent in hospital and number of admissions independently of behavioural and sociodemographic factors. Small feasible differences in usual physical activity in the general population may potentially have a substantial impact on hospital usage and costs.

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What is already known on this subject

- Pre-admission physical activity interventions have been shown to lower hospital length of stay.
- Usual physical activity is associated with lower rates of mortality from all causes, cardiovascular disease and many non-fatal diseases in the general population, but few studies have examined usual physical activity as a predictor of hospital usage.

What this study adds

- Usual physical activity, assessed using both occupational and leisure-time components validated against heart rate monitoring with individual calibration, predicted lower hospital usage in a British population of men and women followed up over 20 years.
- Modest differences in usual physical activity in the general population may have a potentially substantial impact on future hospital usage and health service costs.

Introduction

Historically UK government spending on health has risen on average by 3.7% per year since 1948, outpacing economic growth over the period [1, 2]. As a result, health expenditure as a proportion of UK Gross Domestic Product (GDP) has increased from 3.6 to 7.5% over the same period. Approximately a half of government health expenditure is used for hospitals [3]. There are many factors which may influence hospital usage, not all of which are related to ill health while increases in expenditure are only partly explained by demographic changes [4]. Changes in modifiable lifestyle factors have the potential to lower hospital length of stay. There is growing evidence of the effectiveness of preoperative exercise programmes and other pre-admission interventions in reducing hospital length of stay and readmission rates [5–9] but it is unclear whether in the general population, usual physical activity is related to hospital use. Long-term randomised controlled trials (RCTs) of physical activity interventions with health endpoints are not generally feasible, so evidence is largely based on observational studies.

Physical activity is associated with lower rates of mortality from all causes and cardiovascular disease [10–12]. It is also associated with a lower risk of many non-fatal diseases [13–16] but few studies have examined the relationship between usual physical activity in middle and later life and subsequent hospital usage the general population [17]. The measurement of usual physical activity is problematic. Objective measurements, such as accelerometry have only been developed relatively recently and hence studies based on large, free-living, community-based populations with long follow-up have used self-reported activity from questionnaires. Studies with longer follow-up time are less likely to be affected by reverse causality, which is a feature of studies with short duration of follow-up where individuals who report low physical activity at baseline are inactive by virtue of being affected by the outcome of interest. Self-reported physical activity is most often assessed by questions related to leisure-time activities [18, 19]. Few studies capture both occupational and leisure-time activity.

Hospital usage can be measured by total admissions and length of stay over a fixed follow-up period. These non-disease specific outcome measures can be used to examine the overall level of health service usage [20]. Ageing populations put ever-increasing pressure on health care services and it is therefore important to establish if modest differences in modifiable lifestyle behaviours such as physical activity are related to hospitalisation [21–24].

This study examines the relationship between measures of physical activity using a validated physical activity scale, change in physical activity, and subsequent hospital usage, in older men and women living in the general community over a 10-year period, and a subsequent 10-year follow-up period, taking into account a range of demographic and lifestyle factors.

Materials and methods

The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) is a general population cohort study of men and women aged 40–79 years living in Norfolk recruited from general practices between 1993 and 1997. The response rate for recruitment was approximately 40%. The cohort has similar characteristics to national population surveys except for a lower prevalence of current smokers [25]. The study has ethics committee approval and all participants gave informed, signed consent for study participation including access to medical records. The cohort is flagged for mortality and hospital admissions from linkage to national databases held by NHS Digital and hence there is virtually no loss to follow-up.

At recruitment, participants completed a lifestyle questionnaire where they were asked about their occupational and leisure physical activity. Occupational activity was assessed using a four category question ("sedentary", "standing", "moderate physical work" and "heavy manual work") with examples such as office worker, shop assistant, plumber and construction worker respectively. Leisure activity in both summer and winter was assessed from the number of hours per week spent cycling, attending keep fit classes or aerobics and swimming or jogging. Estimated average hours of leisure activity was calculated as the mean of summer and winter activities and categorised using 0, (0,3.5], (3.5,7] and > 7. A combined score, divided into four ordered categories with individuals labelled as “inactive”, “moderately inactive”, “moderately active” and “active” was created combining leisure and occupational elements. Those who did not complete the activity question were placed in the inactive category. The score was validated against energy expenditure measured by free-living heart rate monitoring with individual calibration [26]. It has been reported to predict all-cause mortality and cardiovascular disease incidence [27].

Participants attending the baseline health examination had their height to the nearest 0.1 kg measured using a stadiometer (Chasemores, UK) and their weight to the nearest 100 g measured in light clothing without shoes (Salter, West Bromwich, UK). Body mass index (BMI) was calculated using measured weight in kilograms divided by the square of measured height in square metres. Two yes/no questions were used to derive smoking status: “Have you ever smoked as much as one cigarette a day for as long as a year?” and, where a positive response was given, “Do you smoke cigarettes now?” Participants also completed questions about their employment and that of their partner with details of both current and past employment recorded. Occupational social class was defined according to the Registrar General’s classification [28, 29]. A list of common UK qualifications was used to establish educational attainment and participants were asked to mark all relevant qualifications. These were then categorised using the highest qualification attained. Participants were asked at baseline “Has the doctor ever told you that you have any of the following?” followed by a list of common conditions including “Heart attack (myocardial infarction)”, “Stroke” and “Cancer”.

Surviving participants were invited to complete a lifestyle questionnaire and attend a health examination (second time-point, “TP2”) between 2006 and 2011 [30] . Questions on physical activity and cigarette smoking, similar to those at baseline, were included in a postal questionnaire, completed by a subset of 9827 of the original cohort. Weight and height were measured on 8094 by clinic staff and body mass index calculated in the same way as at baseline described previously.

Ascertainment of hospital usage through record linkage

The National Health Service (NHS) in Britain treats residents without charge at the point of service so covers virtually all major health service usage. The EPIC-Norfolk cohort was regularly linked to hospital records from 1999 onwards as previously reported [20]. Briefly, NHS numbers were used to perform linkage to hospital databases between 1999 and 2019. Initially, up to 2009, linkage was made via the East Norfolk Primary Health Care Trust while later, national databases held by NHS Digital were used [31]. All hospital activity for EPIC-Norfolk participants was captured wherever they were treated in England and Wales. Hospital episode statistics (HES) records which included admission and discharge dates were used to calculate time in hospital and numbers of admissions. Contiguous admissions were merged and counted as a single admission.

Statistical analysis

For the main analysis, 625 men and women who died before 1999 were excluded. Dichotomous variables were created for the socioeconomic status variables. Professional, managerial and technical and non-manual skilled occupations (codes I, II and IIIa respectively) were classed as non-manual while manual skilled, partly skilled and unskilled (codes IIIb, IV and V respectively) were classed as manual. Educational attainment was categorised into “Higher education level” (which includes those with qualifications at secondary level or above) and “Lower education level” (those with no qualifications). The numbers of individuals with missing values for covariables were: 53 BMI, 218 smoking status, 545 social class, 18 education level. Validation of the physical activity measures [26] suggested that participants with missing data be classified inactive.

Logistic regression was used to model hospitalisation outcomes on physical activity category, adjusting for covariables. Several dichotomous outcome categories were calculated based on total admissions and length of stay spanning two periods: 1999–2009 (10-year follow-up) and 1999–2019 (20-year follow-up). Total admissions from 10-year follow-up were used to define “any hospital admissions” and “7 or more admissions” while length of stay from 10-year follow-up was used to create “greater than 20 hospital days”. These thresholds were chosen to represent those with higher levels of hospital usage and were consistent with previous work [20]. Dichotomous outcome categories based on 20-year follow-up and having approximately the same proportion of the population as their 10-year follow-up counterparts include “12 or more admissions” and “greater than 50 hospital days” while “7 or more admissions” and “greater than 20 hospital days” were also calculated for this period to serve as a comparison. Hospital days are defined as the sum of total bed days (overnight stays) and day-cases. Linear regression was used to calculate the absolute difference in adjusted mean bed days between inactive participants and participants reporting any activity.

To address change in physical activity, we also used physical activity measured at TP2 approximately 12 years later as a second baseline. We excluded 105 participants who died prior to 2009, leaving 9722. Multiple imputation was used to address missing values, in particular for body mass index at TP2 where data for 1733 were not available for participants who completed a TP2 questionnaire but did not attend a health examination. Predictive mean matching with 5 multiple imputations and 50 iterations was used with baseline variables BMI, occupational social class and education attainment and TP2 current smoking. Changed-activity categories use combinations of physical activity categories at the baseline and TP2. The category shown as "Inactive/Inactive" is the set of participants who reported being inactive at baseline and remained inactive when asked again at TP2. The group who initially reported any activity but became inactive later is shown as "Any-activity/Inactive" while the other two categories "Inactive/Any-activity" and "Any-activity/Any-activity" were similarly defined.

The cost to the NHS of one bed-day is £496, calculated using the Reference Costs for English Hospitals 2017/18 for elective (5.4 £bn) and non-elective (18 £bn) admissions [32] and the total available beds (approximately 129,200) [33]. The cost per hospital day (overnight stays and day-cases) is £587 when the cost of day-case activity is included (4.4 £bn per year). The reported OECD UK per capita expenditure on health in 2017, was £3375 (exchange rate at the time of writing) [34]. Per-person costs were calculated by multiplying the cost per hospital day and hospital days per person. Percentage of NHS per-capita health expenditure was calculated as the ratio of per-person cost and OECD UK per-capita expenditure.

Adjusted mean hospital days by physical activity category were determined first by calculating hospital days for each one year period restricted to participants surviving to the start of the given year. Linear regression of hospital days on physical activity adjusted for age, sex, occupational social class, educational attainment, current smoking and body mass index was then used. Adjusted means by category were obtained using estimated marginal means. The overall mean difference of days was calculated by taking the mean of the annual differences for each of two periods (1999–2009 and 2009–2019).

Sensitivity analyses were conducted in which the physical activity exposure was dichotomised into inactive and any-activity groups, using the outcome more than 20 hospital days over the period 1999–2019. Multivariable adjusted odds ratios were examined, stratified by sex, age < 65 and ≥ 65 years, manual and non-manual social class, lower (no qualifications) and higher level of education, former or never smoking and current smoking, BMI ≤30, > 30 kg/m^2, chromic disease (heart attack, stroke or cancer) and no reported chronic disease, survival to the end of follow-up (March 2019) and died during follow-up period. A further multivariable model was performed using the narrower follow-up period of 2004–2019, a minimum of five years after participants reported their level of physical activity excluding participants who died prior to 2004.

All analyses were performed using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria version 3.6.0 with packages ggeffects, knitr, Gmisc, tidyverse, intubate, mice).

Results

Characteristics of the study population according to the four categories of physical activity score are described in Table 1. Active participants tend to be younger, non-smokers, without chronic disease and have higher educational attainment, however those with manual social class also tend to be more active.

Prevalent disease is self-reported heart attack, stroke or cancer at baseline. Higher education level represents those with qualifications to at least secondary level.

In Table 2 odds ratios are shown first age and sex adjusted and then additionally adjusted for social class, educational attainment, BMI and smoking status. For the 10-year follow-up period 1999–2009, outcomes of any hospital admission, 7 or more hospital admissions and more than 20 days stay in hospital are shown according to the baseline physical activity score. The multivariable-adjusted models indicate that participants with a physical activity score of at least moderately inactive had fewer hospital admissions and fewer days in hospital, than those who were inactive. The associations for inactive vs active were OR 0.73 (95% CI 0.65–0.82) p-trend < 0.001 across activity score for seven or more hospital admissions and OR 0.75 (95% CI 0.67–0.83) p-trend < 0.001 for more than 20 hospital days.

Attenuated results were observed for longer follow-up. Odds ratios over the 20-year period 1999–2019 are presented for any hospital admission, ≥7 admissions, ≥12 admissions, > 20 hospital days and > 50 hospital days and associations were OR 0.96 (95% CI 0.89–1.05) p-trend 0.194 for ≥7 admissions, OR 0.87 (95% CI 0.78–0.97) p-trend 0.040 for ≥12 admissions, and OR 0.88 (95% CI 0.81–0.96) p-trend < 0.001 for > 20 hospital days, OR 0.84 (95% CI 0.76–0.94) p-trend 0.001 for > 50 hospital days. Associations for > 20 hospital days and > 50 hospital days were similar, while the inverse association using the threshold of ≥12 admissions was higher than that for the ≥7 admissions threshold.

Physical activity category at TP2 baseline was determined in 9827 men and women. The associations for inactive vs active for 20 hospital days over the subsequent 10-year follow-up period (2009 to 2019) were stronger than those for the first 10-year follow-up period OR 0.60 (95% CI 0.50–0.72) p-trend < 0.001 and similar for 7 or more admissions OR 0.77 (95% CI 0.64–0.91) p-trend 0.001.

Table 1 | Descriptive characteristics by physical activity category measured at baseline 1993–1997

	Total	Inactive (*n* = 7559 30.2%)	Moderately inactive (*n* = 7187 28.7%)	Moderately active (*n* = 5688 22.7%)	Active (*n* = 4580 18.3%)
Body mass index, kg/m^2					
Mean ± SD	26.4 ± 3.9	27.0 ± 4.2	26.3 ± 3.9	26.0 ± 3.7	25.9 ± 3.5
Age, years					
Mean ± SD	59.0 ± 9.3	62.5 ± 9.1	58.8 ± 9.2	57.1 ± 8.7	56.1 ± 8.4
Cigarette smoking (n (%))					
Current	2904 (11.7)	984 (13.2)	770 (10.8)	662 (11.7)	488 (10.7)
Former	10,423 (42.0)	3326 (44.6)	2818 (39.5)	2312 (40.9)	1967 (43.2)
Never	11,469 (46.3)	3151 (42.2)	3540 (49.7)	2678 (47.4)	2100 (46.1)
Social class dichotomised (n (%))					
Non-manual	14,717 (60.1)	4394 (60.2)	4791 (67.8)	3261 (58.3)	2271 (50.4)
Manual	9752 (39.9)	2900 (39.8)	2278 (32.2)	2337 (41.7)	2237 (49.6)
Level of education (n (%))					
Higher level	15,866 (63.5)	4252 (56.4)	4757 (66.2)	3823 (67.2)	3034 (66.2)
Lower level	9130 (36.5)	3289 (43.6)	2430 (33.8)	1865 (32.8)	1546 (33.8)
Prevalent disease (n (%))					
No reported chronic disease	22,721 (91.0)	6606 (87.7)	6573 (91.5)	5246 (92.3)	4296 (93.9)
Self-report chronic disease	2254 (9.0)	927 (12.3)	608 (8.5)	439 (7.7)	280 (6.1)
Hospital activity 1999–2019					
No admissions	2483 (9.9)	625 (8.3)	726 (10.1)	613 (10.8)	519 (11.3)
One or more admissions	22,497 (90.1)	6915 (91.7)	6453 (89.9)	5072 (89.2)	4057 (88.7)
Time in hospital 1999–2019					
Mean ± SD	34.0 ± 63.7	42.4 ± 68.2	32.9 ± 64.1	29.9 ± 66.4	26.8 ± 48.8
Median (IQR)	14.0 (3.0–41.0)	21.0 (6.0–56.0)	13.0 (3.0–39.0)	11.0 (3.0–33.0)	10.0 (2.8–30.0)
Number of admissions 1999–2019					
Mean ± SD	7.8 ± 26.5	8.4 ± 29.0	7.6 ± 24.5	7.8 ± 32.2	6.9 ± 14.8
Median (IQR)	4.0 (2.0–9.0)	5.0 (2.0–9.0)	4.0 (2.0–8.0)	4.0 (2.0–8.0)	4.0 (2.0–8.0)
Survival to the end of follow-up (n (%))					
Alive after March 2019	15,919 (63.6)	3732 (49.4)	4746 (66.0)	4047 (71.1)	3394 (74.1)
Died prior to March 2019	9095 (36.4)	3827 (50.6)	2441 (34.0)	1641 (28.9)	1186 (25.9)

Table 3 shows multivariable-adjusted odds ratios for outcome more than 20 hospital days during the 1999–2019 follow-up in participants who were inactive compared to those reporting any activity at baseline, stratified by key variables in subgroups. The directions of the associations did not differ by subgroup. Higher inverse associations were seen in women, in the under 65 s, in those with no chronic disease at baseline and those surviving to the end of follow-up although confidence intervals overlapped in each case. Table 3 also shows that the association for the period 2004–2019, excluding the first 5 years of the outcome period was OR 0.93 (95% CI 0.87–1.00).

Table 4 shows odds ratios by all combinations of change in physical activity category between baseline and TP2 were determined using the TP2 baseline and subsequent 10-year follow-up. The multivariable-adjusted odds ratios comparing “Inactive/Inactive” (the reference) and “Any-activity/Any-activity” were OR 0.66 (95% CI 0.57–0.77) p-trend < 0.001 across changed-activity categories for more than 20 hospital days and OR 0.91 (95% CI 0.78–1.07) p-trend 0.026 for seven or more hospital admissions. Participants who remained physically active or became active had lower risk of subsequent hospital usage than those who remained inactive or became inactive.

Supplementary Table S1 shows all terms in a series of multivariable logistic regression models for inactive physical activity (vs any-activity) and various dichotomous outcomes over the period 1999–2019 for all, men and women. Covariables age per 10 years, manual social class, lower education level, current smoking and BMI >

Table 2 | Multivariable logistic regression of risk factors by physical activity category for hospital admissions and length of hospital stay categories over 10 years (1999 to 2009) and 20 years (1999 to 2019) in 25,014 men and women and 10 years (2009–2019) using the TP2 baseline in 9722 men and women

	Inactive *n* = 7559	Moderately inactive *n* = 7187	Moderately active *n* = 5688	Active n = 4580	p (trend)
10-year follow-up					
Outcome of any hospital admissions (18,179/25014)					
n (%)	5878 (78%)	5103 (71%)	3980 (70%)	3218 (70%)	
Model 1[a]	1.00	0.87 (0.80–0.94)	0.90 (0.83–0.97)	0.96 (0.88–1.05)	0.373
Model 2[b]	1.00	0.91 (0.84–0.98)	0.91 (0.84–0.99)	0.95 (0.87–1.04)	0.286
Outcome of seven or more hospital admissions (3462/25014)					
n (%)	1392 (18%)	891 (12%)	689 (12%)	490 (11%)	
Model 1[a]	1.00	0.76 (0.69–0.83)	0.79 (0.71–0.87)	0.71 (0.63–0.79)	< 0.001
Model 2[b]	1.00	0.80 (0.72–0.88)	0.82 (0.73–0.91)	0.73 (0.65–0.82)	< 0.001
Outcome of more than 20 hospital days (4976/25014)					
n (%)	2122 (28%)	1299 (18%)	893 (16%)	662 (14%)	
Model 1[a]	1.00	0.75 (0.69–0.81)	0.72 (0.66–0.79)	0.71 (0.64–0.79)	< 0.001
Model 2[b]	1.00	0.80 (0.74–0.87)	0.77 (0.70–0.84)	0.75 (0.67–0.83)	< 0.001
20-year follow-up					
Outcome of any hospital admissions (22,497/25014)					
n (%)	6915 (91%)	6453 (90%)	5072 (89%)	4057 (89%)	
Model 1[a]	1.00	1.06 (0.94–1.19)	1.07 (0.95–1.21)	1.08 (0.95–1.22)	0.238
Model 2[b]	1.00	1.11 (0.98–1.24)	1.10 (0.97–1.25)	1.08 (0.95–1.23)	0.274
Outcome of seven or more hospital admissions (8849/25014)					
n (%)	2969 (39%)	2490 (35%)	1879 (33%)	1511 (33%)	
Model 1[a]	1.00	0.94 (0.88–1.01)	0.92 (0.85–0.99)	0.94 (0.87–1.02)	0.055
Model 2[b]	1.00	0.98 (0.91–1.05)	0.94 (0.87–1.01)	0.96 (0.89–1.05)	0.194
Outcome of 12 or more hospital admissions (3989/25014)					
n (%)	1354 (18%)	1088 (15%)	894 (16%)	653 (14%)	
Model 1[a]	1.00	0.90 (0.82–0.98)	0.95 (0.87–1.05)	0.85 (0.76–0.94)	0.010
Model 2[b]	1.00	0.95 (0.87–1.04)	0.98 (0.89–1.08)	0.87 (0.78–0.97)	0.040
Outcome of more than 20 hospital days (10,174/25014)					
n (%)	3800 (50%)	2836 (39%)	1996 (35%)	1542 (34%)	
Model 1[a]	1.00	0.87 (0.81–0.93)	0.82 (0.76–0.88)	0.84 (0.77–0.91)	< 0.001
Model 2[b]	1.00	0.93 (0.86–1.00)	0.86 (0.79–0.93)	0.88 (0.81–0.96)	< 0.001
Outcome of more than 50 hospital days (5178/25014)					
n (%)	2065 (27%)	1411 (20%)	994 (17%)	708 (15%)	
Model 1[a]	1.00	0.85 (0.79–0.93)	0.86 (0.78–0.94)	0.81 (0.73–0.89)	< 0.001
Model 2[b]	1.00	0.91 (0.84–0.99)	0.91 (0.83–1.00)	0.84 (0.76–0.94)	0.001
10-year follow-up from TP2 baseline					
	Inactive *n* = 3937	Moderately inactive *n* = 2686	Moderately active *n* = 1655	Active *n* = 1444	p (trend)
Outcome of any hospital admissions (7855/9722)					
n (%)	3332 (85%)	2127 (79%)	1267 (77%)	1129 (78%)	
Model 1†	1.00	0.93 (0.81–1.06)	0.85 (0.73–0.99)	1.00 (0.85–1.17)	0.484
Model 2‡	1.00	0.97 (0.85–1.11)	0.90 (0.77–1.05)	1.04 (0.88–1.22)	0.922

Table 2 | Multivariable logistic regression of risk factors by physical activity category for hospital admissions and length of hospital stay categories over 10 years (1999 to 2009) and 20 years (1999 to 2019) in 25,014 men and women and 10 years (2009–2019) using the TP2 baseline in 9722 men and women *(Continued)*

	Inactive *n* = 7559	Moderately inactive *n* = 7187	Moderately active *n* = 5688	Active n = 4580	p (trend)
Outcome of seven or more hospital admissions (1802/9722)					
n (%)	874 (22%)	466 (17%)	259 (16%)	203 (14%)	
Model 1[a]	1.00	0.89 (0.78–1.01)	0.81 (0.69–0.94)	0.73 (0.62–0.87)	< 0.001
Model 2[b]	1.00	0.93 (0.82–1.06)	0.84 (0.72–0.99)	0.77 (0.64–0.91)	0.001
Outcome of more than 20 hospital days (2170/9722)					
n (%)	1217 (31%)	489 (18%)	273 (16%)	191 (13%)	
Model 1[a]	1.00	0.69 (0.61–0.78)	0.69 (0.59–0.80)	0.57 (0.48–0.68)	< 0.001
Model 2[b]	1.00	0.72 (0.64–0.82)	0.71 (0.61–0.83)	0.60 (0.50–0.72)	< 0.001

[a] Adjusted for age, sex, manual social class, lower education level, current cigarette smoker, body mass index > 30 kg/m^2.

Table 3 | Multivariable logistic regression of simple physical activity index and more than 20 hospital days in subgroups after 20 years follow-up

	Inactive (n = 7559) (ref)	Any-activity (*n* = 17,455) OR (95% CI)[a]
Men and women		
Men (*n* = 11,228)	1	0.92 (0.84–1.01)
Women (*n* = 13,786)	1	0.87 (0.80–0.95)
By age above and below 65 years		
Younger than 65 years (*n* = 17,372)	1	0.86 (0.80–0.93)
65 years and older (*n* = 7642)	1	0.91 (0.83–1.01)
Manual and non-manual social class		
Non-manual (*n* = 14,717)	1	0.89 (0.82–0.97)
Manual (*n* = 9752)	1	0.89 (0.81–0.99)
By level of education		
Higher level (*n* = 15,866)	1	0.91 (0.84–0.98)
Lower level (*n* = 9130)	1	0.87 (0.78–0.95)
By smoking status		
Former or never smoker (*n* = 21,892)	1	0.88 (0.83–0.95)
Current smoker (*n* = 2904)	1	0.97 (0.82–1.16)
By level of body mass index		
BMI ≤ 30 kg/m^2 (*n* = 21,158)	1	0.90 (0.84–0.97)
BMI > 30 kg/m^2 (*n* = 3803)	1	0.86 (0.75–1.00)
Prevalent disease		
No reported chronic disease (*n* = 22,721)	1	0.90 (0.84–0.96)
Self-report chronic disease (*n* = 2254)	1	0.94 (0.78–1.14)
Survival to end of follow-up		
Alive after March 2019 (*n* = 15,919)	1	0.90 (0.82–0.98)
Died prior to March 2019 (*n* = 9095)	1	0.99 (0.90–1.10)
Excluding first five years		
Admissions 2004–2019 (*n* = 23,487)	1	0.93 (0.87–1.00)

[a] Adjusted for age, sex, manual social class, lower education level, current cigarette smoker, body mass index > 30 kg/m^2.

Table 4 | Multivariable logistic regression of risk factors by change in physical activity category between baseline and TP2 for hospital admissions and length of hospital stay categories over 10 years (2009 to 2019) in 9722 men and women

	Inactive/Inactive *n* = 1441	Any-activity/Inactive *n* = 2496	Inactive/Any-activity *n* = 790	Any-activity/Any-activity *n* = 4995	p (trend)
Outcome of any hospital admissions (7855/25014)					
n (%)					
Model 1[a]	1.00	1.16 (0.96–1.39)	1.10 (0.87–1.39)	1.00 (0.85–1.18)	0.246
Model 2[b]	1.00	1.18 (0.98–1.42)	1.15 (0.91–1.47)	1.06 (0.90–1.26)	0.751
Outcome of seven or more hospital admissions (1802/25014)					
n (%)					
Model 1[a]	1.00	1.09 (0.93–1.28)	1.00 (0.80–1.25)	0.86 (0.74–1.00)	0.002
Model 2[b]	1.00	1.12 (0.95–1.32)	1.05 (0.83–1.31)	0.91 (0.78–1.07)	0.026
Outcome of more than 20 hospital days (2170/25014)					
n (%)					
Model 1[a]	1.00	0.96 (0.83–1.11)	0.78 (0.62–0.96)	0.62 (0.54–0.72)	< 0.001
Model 2[b]	1.00	0.98 (0.84–1.14)	0.81 (0.65–1.01)	0.66 (0.57–0.77)	< 0.001

[a] Adjusted for age at TP2 and sex. [b] Adjusted for age at TP2, sex, baseline manual social class, baseline lower education level, current cigarette smoker at TP2, body mass index > 30 kg/m^2 at TP2. Multiple imputation was used for 1733 missing BMI at TP2 calculated using baseline BMI and other covariates for participants who completed questionnaires but did not attend a health examination

30 kg/m^2 are modelled; all are independently associated with number of hospital admissions and length of stay. Associations were similar in men and women. The duration outcomes 20 or 50 hospital days were associated with the binary physical activity classification although associations with numbers of hospital admissions were attenuated.

Supplementary Table S2 shows the adjusted mean hospital days for inactive and any-activity participants by year, and the absolute difference in days between the categories. The mean of the differences was calculated for 1999–2009 using baseline physical activity and 2009–2019 using physical activity at TP2 and cumulative costs were determined assuming £587 per hospital day.

The difference in multivariable adjusted mean hospital days between inactive participants and participants reporting any activity was 0.42 days per year over the first 10 years of follow-up, an estimated potential saving to the NHS of £247 per person per year or approximately 7% of health expenditure. The difference in hospital days over the subsequent 10 years (2009–2019) was slightly higher, with any-activity participants having 0.46 fewer hospital days, an estimated potential saving of £268 or approximately 8% of health expenditure.

Discussion

Usual physical activity assessed at baseline survey in 1993–1997 was inversely associated with future hospital usage independently of sociodemographic and lifestyle factors in this middle-aged and older cohort of men and women over a 20-year follow-up period. Compared to study participants who were inactive, active participants had a lower likelihood of having more than 20 hospital days or more than 12 admissions. Stronger associations were seen over a 10-year follow-up period with moderate inactivity or greater being associated with lower risk of seven or more hospital admissions or more than 20 hospital days. There was a dose response over physical activity categories over both the 10-year and 20-year follow-up periods for both hospital duration and number of admissions. There are a number of possible explanations for these findings.

Strengths and limitations of study

Reverse causality may partly explain the associations we observed. Participants may be physically inactive occupationally or less able to take part in leisure time activity because of known or preclinical illness which may also predispose to increased later hospitalisation [35]. However, sensitivity analyses excluding those with a self-reported chronic disease at baseline (heart attack, stroke or cancer), who might have lower physical activity, did not differ materially from the main findings. Also, a sensitivity analysis excluding hospital admissions occurring in the first 5 years of follow-up (the period 2004–2019), that is, those who were more likely to have preclinical illness and lowered physical activity, again did not show materially different associations.

Confounding is a major issue in examining the relationship between lifestyle factors and health outcomes. Individuals who are more physically active are likely to differ from those who are less active with respect to other factors relating to the likelihood of future hospitalisation including age, sex, smoking, body mass index, social class and education. However, the associations were consistent after multivariable-adjustment for these factors and after stratification by these potential confounding variables.

As we examined total hospital usage over long time periods, individuals who died during the follow-up period did not use hospital services for the full period. This may have affected the results if there was differential mortality by physical activity, whereby study participants who were inactive were more likely to have died earlier than the more active participants and hence less likely to use hospital services for the full follow-up period. Sensitivity analysis models restricted to those surviving to the end of 20-year follow-up showed stronger associations of physical activity with lower hospital use than models using the whole population, including those who died during the follow-up period, suggesting there was some attenuation due to selective follow-up.

This study has several strengths. Few studies have examined the physical activity of middle-aged and older men and women and their subsequent healthcare utilisation. The literature falls into two groups, studies based on exercise interventions and observational studies. While most intervention studies provide some evidence that a physically active lifestyle improves health, intervention protocols vary and differences in dropout rates between groups in RCTs limit generalisability [36]. Intervention studies may also typically have smaller study size and shorter follow-up time and while observational studies are generally larger, there are few studies comparable in size to the present study. Our study, being well characterised, allowed adjustment for a broad range of relevant factors. We also used linked hospital data and did not depend on self-reported outcome data. Many studies are based on particular population groups or particular disease outcomes and some rely on self-selection to exercise programs. Few studies examine free living community-based populations [37, 38], however we used a prospective cohort design and were able to examine hospital usage over a long follow-up period with a reliable population-based denominator.

Our study was based on a free-living population of older men and women living in the general community in the United Kingdom where the NHS provides health care free at the point of delivery. Potential major confounders such as income, and ability to pay that might therefore affect and limit access and use of health services, are less likely to apply in this study. The NHS also enables record linkage for virtually complete follow-up of the population. Though admissions to private hospitals in Norfolk were not included in our data which only counts NHS hospitals, the use of private hospitals in Norfolk was minimal in comparison with the use of NHS facilities.

Measurement of usual occupational and leisure time physical activity was assessed using a self-reported questionnaire. Objective measures such as accelerometry and similar techniques were not available when the EPIC-Norfolk cohort was recruited. However, the physical activity score used was previously validated using heart rate monitoring with individual calibration and based on both occupational and leisure-based components of physical activity.

It is also clear that a single measurement of physical activity is insufficient to determine accurately usual levels of activity over the life course. Events such as retirement or illness or progressive ageing related conditions such as frailty may result in a change to the amount of physical activity undertaken [39]. While we are unable to establish the length of time over which consistent physical activity was maintained, we were able to examine longitudinal measurements of physical activity at two time-points in a subset of participants. The associations observed at the later time-point were comparable with (in fact stronger than) those observed at the first time-point, despite the cohort mean age being approximately 10 years older and having a much higher proportion of retirees. Change in behaviour over the 20-year follow-up period is a more likely explanation for the attenuated associations observed, rather than age or employment status. Participants who remained inactive or became inactive had the highest risk of subsequent hospitalisation. Additionally, random measurement error is likely only to attenuate associations, and therefore unlikely to explain any of the associations observed between physical activity and hospitalisation.

Comparison with other studies

Physical activity has been associated with many health benefits including protection against cardiovascular [10, 12, 40] and many other chronic diseases [41, 42] so there are many plausible reasons why it might also be associated with lower hospitalisations from individual conditions. Chronic conditions such as cardiovascular disease remain leading causes of hospitalisation. However, in this study, we were able to examine total hospital usage in a general population irrespective of cause of admission.

Small increases in physical activity have been reported to obtain cost savings for health services by reducing hospital admissions [17, 22, 43–45] with many studies reporting reductions of length of stay after preoperative physical activity interventions. Our study has observed a 12–13% lower risk of long stay and high numbers of admissions by physical activity category. The mean difference in bed days between inactive and any-activity participants in our study was 0.42 days per year over the first 10 years of follow-up. Assuming a cost of £587 per hospital day (inpatient bed-days and day-cases), the potential saving to the NHS is approximately £247 per person per year for every inactive person who starts to undertake at least some exercise, or about 7% of UK per capita health expenditure. Similar results were observed 10 years later when participants were aged 50–90 years. Calculations such as these are unavoidably crude but serve to illustrate the significant financial contribution, when scaled nationally, that modest changes in lifestyle can achieve quite apart from the obvious personal gain from the reduction in risk of being hospitalised.

While there is evidence suggesting that pre-admission physical activity programmes may lower duration of hospital stay [5–8, 46], these are short term, requiring resources and targeted at only a limited number of individuals. Our data indicate that usual physical activity patterns in the general population predict hospital usage over the subsequent 2 decades.

Conclusions and policy implications

Usual physical activity in this middle-aged and older population predicts lower future hospitalisations - time spent in hospital and number of admissions independently of behavioural and sociodemographic factors. Small, feasible differences in usual physical activity in the general population may potentially have a substantial impact on hospital usage and costs.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12877-020-01573-0.

Additional file 1: Table S1. Multivariable logistic regression of risk factors for any hospital admissions, ≥7 hospital admissions and > 20 days of hospital stay from 1999 to 2019 in 25,014 men and women. **Table S2.** Adjusted mean hospital days by physical activity category for two periods, mean difference in days and cumulative cost, 1999–2009 using baseline physical activity and 2009–2019 using physical activity at TP2. **Figure S1.** Flow diagram showing numbers of participants at various stages in the EPIC-Norfolk study including invitations, consents, attendance at health examinations and questionnaire completion.

Abbreviations

BMI: Body mass index; CI: Confidence interval; EPIC-Norfolk: European Prospective Investigation into Cancer in Norfolk; GDP: Gross Domestic Product; HES: Hospital episode statistics; OECD: Organisation for Economic Co-operation and Development; OR: Odds ratio; TP2: Time-point two

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Transparency

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Patient and public involvement

The EPIC-Norfolk Study have an active Participants Advisory Panel which meets quarterly to advise on research protocols, suggest ideas and provide feedback on the research including proposed new studies and collaborations. All participants of the EPIC-Norfolk study are informed about the study through regular newsletters as well as public meetings. Information is also disseminated through local community talks in the Norfolk area and science festivals.

Authors' contributions

KTK,NW SH and RL were involved in the conception and design of the study. RL drafted the manuscript, with support from KTK and PP. SH contributed to data interpretation. RL was responsible for external data linkage. SH and RL contributed to data collection and acquisition. All authors read and critically revised the manuscript and approved the final manuscript. RL is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Availability of data and materials

The authors will make the dataset available under a Data Transfer Agreement to any bona fide researcher who wishes to obtain the dataset in order to undertake a replication analysis. Although the dataset is anonymised, the breadth of the data included and the multiplicity of variables that are included in this analysis file as primary variables or confounding factors, means that provision of the dataset to other researchers without a Data Transfer Agreement would constitute a risk. Requests for data sharing/access should be submitted to the EPIC Management Committee (epic-norfolk@mrc-epid.cam.ac.uk).

Ethics approval and consent to participate

The work has ethics committee approval from Norfolk Research Ethics Committee (Rec Ref: 98CN01) for EPIC-Norfolk baseline and later collections. The work was also approved by the East Norfolk and Waveney NHS research governance committee (2005EC07L) and the Norfolk research ethics committee (05/Q0101/191) for the EPIC-Norfolk Third Health Check collection. All participants gave informed signed consent for study participation including access to medical records.

Consent for publication

Not applicable.

Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and report: RL,SH,KTK and NW report grants from MRC and CRUK during the conduct of the study; The sponsors had no role in any of the following: study design, data collection, data analysis, interpretation of data, writing of the article, decision to submit it for publication. All authors are independent of funders and sponsors and had access to all the data. No conflicts of interest were declared by any author (apart from the two grants) and they have no other relationships or activities that could appear to have influenced the submitted work.

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Sociodemographic and lifestyle predictors of incident hospital admissions with multimorbidity in a general population, 1999–2019: the EPIC-Norfolk cohort

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ABSTRACT

Background The ageing population and prevalence of long-term disorders with multimorbidity are a major health challenge worldwide. The associations between comorbid conditions and mortality risk are well established; however, few prospective community-based studies have reported on prior risk factors for incident hospital admissions with multimorbidity. We aimed to explore the independent associations for a range of demographic, lifestyle and physiological determinants and the likelihood of subsequent hospital incident multimorbidity.

Methods We examined incident hospital admissions with multimorbidity in 25 014 men and women aged 40–79 in a British prospective population-based study recruited in 1993–1997 and followed up until 2019. The determinants of incident multimorbidity, defined as Charlson Comorbidity Index ≥3, were investigated using multivariable logistic regression models for the 10-year period 1999–2009 and repeated with independent measurements in a second 10-year period 2009–2019.

Results Between 1999 and 2009, 18 179 participants (73% of the population) had a hospital admission. Baseline 5-year and 10-year incident multimorbidities were observed in 6% and 12% of participants, respectively. Age per 10-year increase (OR 2.19, 95% CI 2.06 to 2.33) and male sex (OR 1.32, 95% CI 1.19 to 1.47) predicted incident multimorbidity over 10 years. In the subset free of the most serious diseases at baseline, current smoking (OR 1.86, 95% CI 1.60 to 2.15), body mass index >30 kg/m² (OR 1.48, 95% CI 1.30 to 1.70) and physical inactivity (OR 1.16, 95% CI 1.04 to 1.29) were positively associated and plasma vitamin C (a biomarker of plant food intake) per SD increase (OR 0.86, 95% CI 0.81 to 0.91) inversely associated with incident 10-year multimorbidity after multivariable adjustment for age, sex, social class, education, alcohol consumption, systolic blood pressure and cholesterol. Results were similar when re-examined for a further time period in 2009–2019.

Conclusion Age, male sex and potentially modifiable lifestyle behaviours including smoking, body mass index, physical inactivity and low fruit and vegetable intake were associated with increased risk of future incident hospital admissions with multimorbidity.

Strengths and limitations of this study

- We examined future hospital admission with multimorbidity using a prospective design and a community-based population.
- The relationship between demographic, lifestyle and physiological factors and subsequent multimorbidity was documented.
- Measurements were made at two time-points: in mainly middle-aged participants (40–79 years) and mainly old-aged participants (48–92 years).
- Participants were followed over 20 years, allowing several time periods to be examined.
- Restricting the definition of multimorbidity to a subset of chronic conditions means some conditions will not be counted.

INTRODUCTION

The Academy of Medical Sciences 2018 report highlighted multimorbidity as a global priority for research. Patients with multimorbidity experience reduced well-being and quality of life and account for a disproportionately high share of healthcare workload and costs. Management of the rising prevalence of long-term disorders is the main challenge facing healthcare systems worldwide.[1–3]

Multimorbidity is commonly defined as the presence of multiple diseases or conditions with a cut-off of two or more conditions[4]; however, there is no agreed definition or classification system, which makes the existing evidence base difficult to interpret.[1] The term comorbidity predates multimorbidity and was used to predict the effect of additional diseases for those with an index disease of interest.[5–7] The Charlson Comorbidity Index (CCI)[8] was originally created to predict mortality in hospital patients after 1 year and is defined using a set of 17 chronic diseases, weighted according to the risk of death. The index has been widely used, with several authors suggesting extensions or modifications to the original definition,[9–14] and it remains a common standard with which other systems are often compared.[15]

The associations between comorbid conditions and mortality are well established.[16–20] However, few studies have examined the determinants of incident multimorbidity rather than its consequences,[21–26] since most lack detailed demographic, socioeconomic and physiological measurements in population-based men and women prior to the onset of multimorbid disease with subsequent follow-up. Retrospective hospital-based studies examining multimorbidity lack community-based denominators, while general practice-based studies are often cross-sectional or examine mortality in already multimorbid patients. Few studies examine factors that predict the likelihood of multimorbidity rather than factors that predict risk of individual component conditions. The large majority of studies conducted to date are cross-sectional, with few prospective community-based studies able to examine incident multimorbidity from subsequent hospitalisation.[1 24 25] In this study, we examine the independent associations for a range of demographic, lifestyle and physiological determinants and the likelihood of subsequent hospital incident multimorbidity. We use the CCI over 5-year and 10-year time periods and re-examine these associations independently in a subset 12 years after baseline since healthcare policy and the criteria used for admission may have changed over time. We have previously reported on risk factors for hospitalisation,[27–29] but here we explore in more detail hospital admissions with multimorbidity, a measure of both health service and individual burden.

METHODS

We used data from the European Prospective Investigation into Cancer in Norfolk cohort (EPIC-Norfolk).[30 31] From this cohort, 25 639 men and women aged 40–79 were recruited from general practices in Norfolk, completed a lifestyle questionnaire and attended a baseline health check from 1993 to 1997. Participants were reapproached approximately 12 years later, aged 48–92, with 9814 completing a second questionnaire and 8049 attending a health check at time-point 2 (TP2). Figure 1 shows a flow diagram of the number of participants at various stages. The cohort was followed until 2019 with annual record linkage to hospital episode data. Since linkage was to national databases and migration of cohort participants was rare, there was almost no loss to follow-up.

The CCI is defined using a set of chronic diseases, each having an associated weight (1, 2, 3 or 6) related to the risk of death. The conditions are myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatoid disease, peptic ulcer disease, liver disease, diabetes, hemiplegia or paraplegia, renal disease,

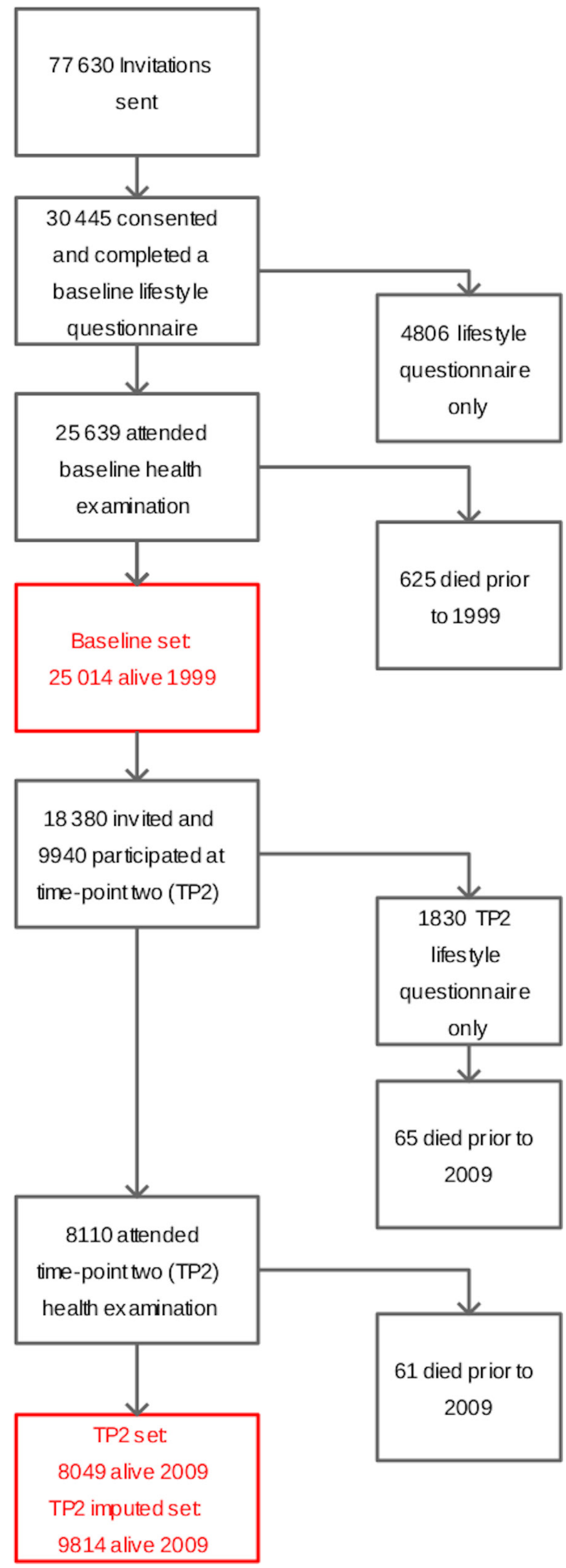

Figure 1 Flow diagram of cohort recruitment and approaches.

cancer and AIDS/HIV. Two levels of severity are defined for liver disease, diabetes and cancer (details are shown in online supplemental table S1). All comorbidities are assigned a weight of 1, except hemiplegia/paraplegia, renal disease and malignancies (weight=2); moderate/severe liver disease (weight=3); and metastatic solid tumour and AIDS/HIV (weight=6). For diseases with two levels of severity (liver disease, diabetes and cancer), the less severe version is assigned a weight of 0 if the more severe version is also present in a patient. The CCI diseases were assigned diagnosis codes using the International Classification of Diseases (ICD-10), which was used to link the CCI to Hospital Episode Statistics records and to cohort participants. The weighted individual disease scores were totalled to create an overall score with a maximum value of 29.[8 12] CCI was measured for various outcome periods restricted to all hospital events within the given time period: at baseline, 5-year (1999–2004) and 10-year (1999–2009) CCI; and at TP2, 5-year (2009–2014) and 10-year (2009–2019) CCI. Multiple admissions including the same CCI category were only counted once.

Participants attending the baseline and TP2 health examinations had their height to the nearest 0.1 cm measured using a stadiometer (Chasemores, UK) and their weight to the nearest 100 g measured in light clothing without shoes (Salter, West Bromwich, UK). Body mass index (BMI) was calculated using measured weight in kilograms divided by the square of measured height in square metres. Trained nurses obtained non-fasting blood samples by venepuncture into plain and citrate bottles. Bloods were assayed at the Department of Clinical Biochemistry, University of Cambridge, UK. Serum concentrations of total cholesterol were measured with the RA-1000 Technicon analyser (Bayer Diagnostics, Basingstoke). Plasma was stabilised in a standardised volume of metaphosphoric acid stored at −70°C and vitamin C concentrations measured using a fluorometric assay within 1 week.[32] Systolic blood pressure was measured using an Accutorr sphygmomanometer (Datascope Medical, Huntington, UK). Participants sat for 3 min before two measurements were taken with the arm horizontal and held at mid-sternum level. Systolic blood pressure was defined as the average of the two measurements.

At baseline and again at TP2, participants completed a lifestyle questionnaire. Two yes/no questions were used to derive smoking status: 'Have you ever smoked as much as one cigarette a day for as long as a year?' and, where a positive response was given, 'Do you smoke cigarettes now?' Participants also completed questions about their employment and that of their partner, with details of both current and past employment recorded. Occupational social class was defined according to the Registrar General's classification.[33 34] A list of common UK qualifications was used to establish educational attainment and participants were asked to mark all relevant qualifications. These were then categorised using the highest qualification attained. Participants were asked about their occupational and leisure physical activity. A combined score was created combining leisure and occupational elements and divided into four ordered categories, with those who did not complete the question placed in the inactive category. The score was validated against energy expenditure measured by free-living heart rate monitoring with individual calibration.[35 36] Participants were asked 'Are you a non-drinker/teetotaller now?' and 'At present, about how many alcoholic drinks do you have each week' for various types of alcohol. Current units were calculated from the questionnaire responses, with one unit equal to a half pint of beer, one glass of wine or fortified wine or a single measure of spirits. Prevalent disease was established from the question 'Has the doctor ever told you that you have any of the following?' followed by a list of common conditions including 'Heart attack (myocardial infarction)', 'Stroke', 'Cancer' and 'Diabetes'.

Statistical methods

Associations were examined both including and excluding chronic disease at baseline and repeated with independent measurements at TP2 in a subset of participants using a second baseline 12 years approximately after the first. The baseline analysis excludes 625 men and women who died before 1999, while at TP2 a further 126 participants who died prior to 2009 were excluded. Dichotomous variables were created for social class (manual and non-manual), educational attainment (high and low) at baseline, and BMI (>30 kg/m^2 and ≤30 kg/m^2) and usual physical activity (active and inactive) at both baseline and TP2. For social class, professional, managerial and technical and non-manual skilled occupations were classed as non-manual, while manual skilled, partly skilled and unskilled were classed as manual. For educational attainment, those with qualifications at secondary level or above were classed as high and those with no qualification as low. Hospital outcomes were categorised into five groups: 'No hospital admissions', CCI=0, CCI=1, CCI=2 and hospital admissions with multimorbidity (incident multimorbidity) defined as CCI ≥3. Multivariable logistic regression was used for all models and compared multimorbid participants (CCI ≥3) with those having CCI ≤2 or no hospital admissions. A sensitivity analysis, using identical models to those in the primary analyses for the period 1999–2009, but excluding 80 participants defined as multimorbid having only one condition with a CCI weighting ≥3, gave virtually identical results (results not shown).

The numbers of individuals with missing values for covariables at baseline were 53 for BMI, 218 for smoking status, 545 for social class and 18 for education level. The physical activity score has no missing values since those with missing data were classified as being inactive. Multiple imputation was used to estimate missing values at TP2 most apparent when participants completed questionnaires but did not attend a health examination (n=1891). Predictive mean matching with 5 multiple imputations and 50 iterations was used with baseline and TP2 variables. All analyses were performed using the R statistical language (V3.5.3, R Foundation for Statistical Computing, Vienna, Austria, with packages knitr, Gmisc, ggplot2, tidyverse, intubate, mice). CCIs were calculated using the R package 'comorbidity'.[37]

Table 1 Charlson Comorbidity Index (CCI) hospital admission rates by age group and sex in men and women aged 40–79, 1999–2019

	Total	No admissions	CCI=0	CCI=1	CCI=2	CCI ≥3
Baseline 5-year follow-up period, 1999–2004, n (%)						
Men	11 228	5457 (48.6)	3340 (29.7)	988 (8.8)	662 (5.9)	781 (7.0)
Women	13 786	7153 (51.9)	4398 (31.9)	953 (6.9)	643 (4.7)	639 (4.6)
≤55 years	9567	6009 (62.8)	2720 (28.4)	411 (4.3)	236 (2.5)	191 (2.0)
55–65 years	7805	3940 (50.5)	2479 (31.8)	583 (7.5)	408 (5.2)	395 (5.1)
65–75 years	6933	2489 (35.9)	2322 (33.5)	830 (12.0)	561 (8.1)	731 (10.5)
>75 years	709	172 (24.3)	217 (30.6)	117 (16.5)	100 (14.1)	103 (14.5)
Baseline 10-year follow-up period, 1999–2009, n (%)						
Men	11 228	2928 (26.1)	4151 (37.0)	1434 (12.8)	1056 (9.4)	1659 (14.8)
Women	13 786	3907 (28.3)	5767 (41.8)	1601 (11.6)	1137 (8.2)	1374 (10.0)
≤55 years	9567	3720 (38.9)	4201 (43.9)	746 (7.8)	476 (5.0)	424 (4.4)
55–65 years	7805	1973 (25.3)	3259 (41.8)	994 (12.7)	711 (9.1)	868 (11.1)
65–75 years	6933	1059 (15.3)	2294 (33.1)	1168 (16.8)	875 (12.6)	1537 (22.2)
>75 years	709	83 (11.7)	164 (23.1)	127 (17.9)	131 (18.5)	204 (28.8)
Time-point 2, 5-year follow-up period, 2009–2014, n (%)						
Men	4252	1428 (33.6)	1355 (31.9)	522 (12.3)	389 (9.1)	558 (13.1)
Women	5562	2234 (40.2)	1793 (32.2)	686 (12.3)	403 (7.2)	446 (8.0)
≤55 years	342	215 (62.9)	92 (26.9)	19 (5.6)	10 (2.9)	6 (1.8)
55–65 years	3090	1540 (49.8)	1006 (32.6)	277 (9.0)	143 (4.6)	124 (4.0)
65–75 years	3695	1303 (35.3)	1301 (35.2)	464 (12.6)	286 (7.7)	341 (9.2)
>75 years	2687	604 (22.5)	749 (27.9)	448 (16.7)	353 (13.1)	533 (19.8)
Time-point 2, 10-year follow-up period, 2009–2019, n (%)						
Men	4252	695 (16.3)	1294 (30.4)	631 (14.8)	558 (13.1)	1074 (25.3)
Women	5562	1166 (21.0)	1956 (35.2)	914 (16.4)	618 (11.1)	908 (16.3)
≤55 years	342	154 (45.0)	122 (35.7)	37 (10.8)	14 (4.1)	15 (4.4)
55–65 years	3090	905 (29.3)	1241 (40.2)	407 (13.2)	267 (8.6)	270 (8.7)
65–75 years	3695	589 (15.9)	1309 (35.4)	611 (16.5)	473 (12.8)	713 (19.3)
>75 years	2687	213 (7.9)	578 (21.5)	490 (18.2)	422 (15.7)	984 (36.6)

RESULTS

Table 1 shows future 5-year and 10-year CCI hospital admission rates from baseline for 25 014 and from TP2 for 9814, according to demographic characteristics in the study population. Between 1999 and 2009, 18 179 participants (73% of the population) had a hospital admission. Baseline 5-year and 10-year incident multimorbidities (CCI ≥3) were observed in 6% and 12% of participants, respectively. Figure 2 shows the 10-year multimorbidity rates by age group and sex excluding those with cardiovascular disease, cancer or diabetes at baseline. More men had CCI ≥3 than women and those aged >75 years had the highest proportion of admissions with multimorbid conditions, with 14.5% at 5 years and 28.8% at 10 years. Multimorbidity rates at TP2 were slightly higher than baseline, with 5-year and 10-year incident CCI ≥3 observed in 10% and 20% of participants, respectively, and the highest proportion in those >75 years.

Descriptive characteristics of the cohort according to 10-year CCI are shown in table 2. Participants with higher number of total admissions and longer duration of hospital stay had higher CCI, with mean duration of 58 days and 13 admissions for participants with CCI ≥3 during the 10-year period. Participants with multimorbidity admissions were more likely at baseline examination to be current smokers, less physically active, have higher BMI and have lower plasma vitamin C (a proxy for a diet rich in fruit and vegetables) and report various prevalent conditions.

In table 3, ORs are shown for 5-year and 10-year incident multimorbidity, defined as those with CCI ≥3, compared with CCI ≤2 or no hospital admission, adjusted for age, sex, occupational social class and educational attainment in model 1. Model 2 additionally adjusted for prevalent diseases, cardiovascular disease (CVD), cancer and diabetes; model 3 added lifestyle factors, current

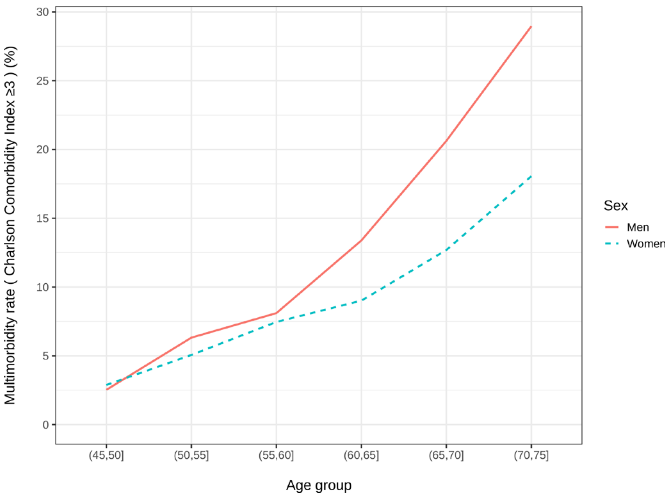

Figure 2 Rate of hospital admissions with multimorbidity, defined as Charlson Comorbidity Index ≥3, by age group and sex, over the 10-year follow-up period 1999–2009, excluding those with cardiovascular disease, cancer or diabetes at baseline.

smoking, alcohol units per week, usual physical activity as well as BMI >30 kg/m² and plasma vitamin C; and model 4 added systolic blood pressure and cholesterol. Age, sex and prevalent diseases were strongly associated with multimorbidity admissions in all models. The fully adjusted association of 10-year incident multimorbidity with age per 10-year increase had OR of 2.19 (95% CI 2.06 to 2.33), OR of 1.32 (95% CI 1.19 to 1.47) for sex, OR of 2.22 (95% CI 1.87 to 2.62) for prevalent CVD, OR of 2.05 (95% CI 1.73 to 2.42) for cancer, and OR of 3.41 (95% CI 2.74 to 4.24) for diabetes. The risk of multimorbidity in participants with CVD at baseline was equivalent to the risk in those without CVD 10 years older. Similarly, in participants with baseline diabetes and baseline cancer, the risk was equivalent to those without disease aged 17 and 11 years older, respectively.

The models in table 4 are similar to those used in table 3, but rather than adjusting for prevalent disease, participants who reported heart attack, stroke, cancer or diabetes at baseline were excluded. In this subgroup of participants without known common major diseases, in addition to age and sex, current cigarette smoking (OR 1.86, 95% CI 1.60 to 2.15), BMI >30 kg/m² (OR 1.48, 95% CI 1.30 to 1.70) and physical inactivity (OR 1.16, 95% CI 1.04 to 1.29) were positively associated and plasma vitamin C (OR 0.86, 95% CI 0.81 to 0.91) inversely associated with incident 10-year hospital admissions with multimorbidity after multivariable adjustment for age, sex, social class, education, alcohol consumption, systolic blood pressure and cholesterol (model 3). Manual social class and educational attainment were associated with incident multimorbidity in model 1, but were attenuated in models 2 and 3. An inverse association was observed for total cholesterol, while systolic blood pressure appeared to be associated but the direction of association was not consistent with the repeated analyses from TP2. There was no association for alcohol in these models. The risk of multimorbidity in current cigarette smokers is equivalent to the risk in non-smokers 7 years older, while each 20 µmol/L rise in plasma vitamin C (approximately two servings of fruit and vegetables per day[38]) corresponds to a reduction in risk equivalent to the risk of those 3 years younger.

Online supplemental table S1 shows the ICD-10 codes corresponding to CCI disease groups. Online supplemental table S2 shows the descriptive characteristics of participants at TP2 for 10-year CCI. The mean age in this subset, measured approximately 12 years after baseline, was 69.4. The number of hospital admissions and total length of stay were similar to those at baseline, with multimorbid participants (CCI ≥3) having much longer duration than non-multimorbid participants or those who had no hospital admissions. Multimorbid participants were inactive, had lower plasma vitamin C (reflecting a lower intake of fruit and vegetables), were current or former smokers, and had prevalent disease. In online supplemental table S3, multivariable models of 10-year incident multimorbidity show that prevalent diabetes, CVD and cancer were all strongly associated. online supplemental table S4 shows multivariable associations in a group free from the most serious diseases at TP2. Both age and male sex were associated with subsequent multimorbidity, with educational attainment, current cigarette smoking, plasma vitamin C, BMI >30 kg/m² and physical inactivity all predicting future multimorbidity. Systolic blood pressure was attenuated while other factors including cholesterol were more strongly associated than at baseline.

DISCUSSION

In this community-based population followed prospectively, we observed incident hospital multimorbidity admission rates over 5-year and 10-year periods, which as expected were strongly related to increasing age. We also observed that those with multimorbid hospital admissions had substantially more days in the hospital over the outcome periods. In multivariable analyses, the risk of such admissions is predicted by age, male sex and several potentially modifiable factors. Participants at baseline who smoked cigarettes, had BMI >30, were physically inactive or had a diet low in fruit and vegetables all had higher likelihood of having subsequent hospital admissions with multimorbidity. Measurements made on a subset of the cohort 12 years after baseline who were followed up subsequently confirmed the baseline findings while also demonstrating an association for low education level in an older cohort with incident multimorbidity.

Strengths and limitations of the study

Most studies of multimorbidity focus on its consequences and those examining risk factors for multimorbidity are largely cross-sectional. While many prospective studies have examined the relationship between baseline characteristics and specific incident diseases or mortality, establishing multimorbidity as an endpoint is more

Table 2 Descriptive characteristics at baseline in 25 014 men and women aged 40–79 by 10-year Charlson Comorbidity Index (CCI), 1999–2009

	Total	No admissions	CCI=0	CCI=1	CCI=2	CCI ≥3
Hospital duration 1999–2009, days						
Mean±SD	16.3±46.5	0.0±0.0	9.1±28.3	24.9±71.5	30.4±43.0	57.8±77.5
Total hospital admissions 1999–2009						
Mean±SD	3.8±16.2	0.0±0.0	2.8±3.1	4.5±6.0	6.4±8.3	13.4±43.9
Age, years						
Mean±SD	59.0±9.3	55.4±8.6	57.9±8.8	62.0±8.8	62.9±8.8	65.0±8.0
Body mass index, kg/m²						
Mean±SD	26.4±3.9	25.9±3.7	26.2±3.8	26.8±4.1	26.8±4.3	27.3±4.2
Cigarette smoking, n (%)						
Current	2904	751 (25.9)	1008 (34.7)	410 (14.1)	291 (10.0)	444 (15.3)
Former	10 423	2558 (24.5)	4007 (38.4)	1352 (13.0)	979 (9.4)	1527 (14.7)
Never	11 469	3476 (30.3)	4821 (42.0)	1245 (10.9)	903 (7.9)	1024 (8.9)
Social class dichotomised, n (%)						
Non-manual	14 717	4400 (29.9)	5707 (38.8)	1733 (11.8)	1256 (8.5)	1621 (11.0)
Manual	9752	2304 (23.6)	4029 (41.3)	1214 (12.4)	886 (9.1)	1319 (13.5)
Level of education, n (%)						
Higher level	15 866	4922 (31.0)	6333 (39.9)	1724 (10.9)	1277 (8.0)	1610 (10.1)
Lower level	9130	1910 (20.9)	3576 (39.2)	1310 (14.3)	916 (10.0)	1418 (15.5)
Simple physical activity index, n (%)						
Inactive	7559	1681 (22.2)	2666 (35.3)	1116 (14.8)	788 (10.4)	1308 (17.3)
Moderately inactive	7187	2084 (29.0)	2904 (40.4)	819 (11.4)	610 (8.5)	770 (10.7)
Moderately active	5688	1708 (30.0)	2353 (41.4)	608 (10.7)	470 (8.3)	549 (9.7)
Active	4580	1362 (29.7)	1995 (43.6)	492 (10.7)	325 (7.1)	406 (8.9)
Alcohol intake, units per week						
Mean±SD	7.1±9.5	7.7±9.6	6.9±9.1	6.9±9.5	6.7±9.8	6.8±10.3
Plasma vitamin C, µmol/L						
Mean±SD	53.5±20.3	55.3±19.8	55.4±19.9	50.5±20.3	51.3±20.9	47.6±20.6
Systolic blood pressure, mm Hg						
Mean±SD	135.3±18.3	132.4±17.4	133.5±17.5	138.7±18.7	138.6±19.2	142.2±19.3
Total cholesterol, mmol/L						
Mean±SD	6.2±1.2	6.1±1.1	6.1±1.1	6.3±1.2	6.2±1.2	6.3±1.2
Prevalent heart attack, n (%)						
No reported heart attack	24 253	6745 (27.8)	9764 (40.3)	2886 (11.9)	2097 (8.6)	2761 (11.4)
Self-reported heart attack	728	85 (11.7)	143 (19.6)	146 (20.1)	94 (12.9)	260 (35.7)
Prevalent stroke, n (%)						
No reported stroke	24 660	6786 (27.5)	9821 (39.8)	2975 (12.1)	2151 (8.7)	2927 (11.9)
Self-reported stroke	329	45 (13.7)	87 (26.4)	57 (17.3)	41 (12.5)	99 (30.1)
Prevalent cancer, n (%)						
No reported cancer	23 688	6595 (27.8)	9449 (39.9)	2878 (12.1)	2031 (8.6)	2735 (11.5)
Self-reported cancer	1301	237 (18.2)	459 (35.3)	155 (11.9)	162 (12.5)	288 (22.1)
Prevalent diabetes, n (%)						
No reported diabetes	24 442	6760 (27.7)	9844 (40.3)	2941 (12.0)	2111 (8.6)	2786 (11.4)
Self-reported diabetes	541	71 (13.1)	61 (11.3)	90 (16.6)	81 (15.0)	238 (44.0)

Table 3 Multivariable logistic regression of risk factors for 5-year and 10-year hospital admissions with multimorbidity in 25 014 men and women

	5-year multimorbidity*, 1999–2004 OR (95% CI)	P value	10-year multimorbidity*, 1999–2009 OR (95% CI)	P value
Model 1				
Male sex	1.49 (1.34 to 1.67)	<0.001	1.56 (1.44 to 1.69)	<0.001
Age per 10 years	2.27 (2.13 to 2.44)	<0.001	2.34 (2.23 to 2.46)	<0.001
Manual social class	1.20 (1.07 to 1.35)	0.002	1.22 (1.12 to 1.33)	<0.001
Lower education level	1.15 (1.02 to 1.30)	0.023	1.19 (1.09 to 1.30)	<0.001
Model 2				
Male sex	1.39 (1.24 to 1.56)	<0.001	1.47 (1.35 to 1.60)	<0.001
Age per 10 years	2.11 (1.97 to 2.26)	<0.001	2.21 (2.10 to 2.32)	<0.001
Manual social class	1.22 (1.08 to 1.37)	0.001	1.23 (1.13 to 1.34)	<0.001
Lower education level	1.13 (1.00 to 1.28)	0.053	1.17 (1.07 to 1.28)	<0.001
Prevalent CVD	2.23 (1.85 to 2.68)	<0.001	2.25 (1.93 to 2.60)	<0.001
Prevalent cancer	2.11 (1.75 to 2.54)	<0.001	1.92 (1.65 to 2.22)	<0.001
Prevalent diabetes	4.41 (3.55 to 5.45)	<0.001	4.32 (3.57 to 5.21)	<0.001
Model 3				
Male sex	1.24 (1.07 to 1.42)	0.003	1.33 (1.20 to 1.47)	<0.001
Age per 10 years	2.16 (1.99 to 2.34)	<0.001	2.29 (2.16 to 2.43)	<0.001
Manual social class	1.09 (0.95 to 1.25)	0.214	1.17 (1.06 to 1.29)	0.002
Lower education level	1.06 (0.92 to 1.21)	0.447	1.08 (0.98 to 1.20)	0.112
Current smoker	1.71 (1.42 to 2.05)	<0.001	1.73 (1.51 to 1.98)	<0.001
BMI >30 kg/m^2	1.32 (1.12 to 1.56)	<0.001	1.45 (1.28 to 1.63)	<0.001
Alcohol intake, units per week	1.00 (0.99 to 1.01)	0.872	1.00 (1.00 to 1.01)	0.666
Physically inactive	1.26 (1.10 to 1.44)	<0.001	1.15 (1.04 to 1.26)	0.006
Plasma vitamin C per SD	0.81 (0.75 to 0.86)	<0.001	0.84 (0.80 to 0.88)	<0.001
Prevalent CVD	2.02 (1.63 to 2.49)	<0.001	2.17 (1.84 to 2.57)	<0.001
Prevalent cancer	2.22 (1.79 to 2.72)	<0.001	2.06 (1.74 to 2.43)	<0.001
Prevalent diabetes	3.53 (2.73 to 4.52)	<0.001	3.54 (2.85 to 4.39)	<0.001
Model 4				
Male sex	1.23 (1.07 to 1.43)	0.005	1.32 (1.19 to 1.47)	<0.001
Age per 10 years	2.08 (1.91 to 2.27)	<0.001	2.19 (2.06 to 2.33)	<0.001
Manual social class	1.09 (0.95 to 1.25)	0.235	1.16 (1.05 to 1.28)	0.004
Lower education level	1.06 (0.92 to 1.22)	0.420	1.09 (0.99 to 1.21)	0.091
Current smoker	1.72 (1.43 to 2.07)	<0.001	1.74 (1.52 to 2.00)	<0.001
BMI >30 kg/m^2	1.31 (1.11 to 1.54)	0.001	1.40 (1.24 to 1.58)	<0.001
Alcohol intake, units per week	1.00 (0.99 to 1.01)	0.878	1.00 (1.00 to 1.01)	0.800
Physically inactive	1.25 (1.09 to 1.43)	0.001	1.14 (1.04 to 1.26)	0.008
Plasma vitamin C per SD	0.81 (0.76 to 0.87)	<0.001	0.85 (0.81 to 0.89)	<0.001
Systolic blood pressure per SD	1.10 (1.03 to 1.17)	0.005	1.12 (1.07 to 1.18)	<0.001
Total cholesterol per SD	0.99 (0.92 to 1.05)	0.690	0.99 (0.94 to 1.04)	0.614
Prevalent CVD	2.06 (1.66 to 2.54)	<0.001	2.22 (1.87 to 2.62)	<0.001
Prevalent cancer	2.23 (1.80 to 2.75)	<0.001	2.05 (1.73 to 2.42)	<0.001
Prevalent diabetes	3.42 (2.64 to 4.39)	<0.001	3.41 (2.74 to 4.24)	<0.001

*Charlson Comorbidity Index ≥3 vs Charlson Comorbidity Index ≤2 or no hospital admission.
BMI, body mass index; CVD, cardiovascular disease.

Table 4 Multivariable logistic regression of risk factors excluding participants with prevalent CVD, cancer or diabetes for 5-year and 10-year hospital admissions with multimorbidity in 22 278 men and women

	5-year multimorbidity*, 1999–2004 OR (95% CI)	P value	10-year multimorbidity*, 1999–2009 OR (95% CI)	P value
Model 1				
Male sex	1.47 (1.29 to 1.68)	<0.001	1.52 (1.38 to 1.67)	<0.001
Age per 10 years	2.19 (2.02 to 2.37)	<0.001	2.31 (2.19 to 2.45)	<0.001
Manual social class	1.23 (1.07 to 1.42)	0.003	1.22 (1.11 to 1.34)	<0.001
Lower education level	1.20 (1.04 to 1.39)	0.011	1.16 (1.05 to 1.28)	0.003
Model 2				
Male sex	1.32 (1.13 to 1.55)	<0.001	1.39 (1.24 to 1.55)	<0.001
Age per 10 years	2.24 (2.05 to 2.46)	<0.001	2.40 (2.25 to 2.56)	<0.001
Manual social class	1.13 (0.96 to 1.32)	0.131	1.17 (1.05 to 1.30)	0.006
Lower education level	1.07 (0.91 to 1.25)	0.416	1.05 (0.93 to 1.17)	0.428
Current smoker	1.85 (1.50 to 2.26)	<0.001	1.84 (1.58 to 2.13)	<0.001
BMI >30 kg/m²	1.31 (1.07 to 1.58)	0.006	1.53 (1.34 to 1.75)	<0.001
Alcohol intake, units per week	1.00 (0.99 to 1.01)	0.789	1.00 (1.00 to 1.01)	0.805
Physically inactive	1.25 (1.07 to 1.46)	0.004	1.17 (1.05 to 1.31)	0.005
Plasma vitamin C per SD	0.82 (0.76 to 0.89)	<0.001	0.85 (0.80 to 0.90)	<0.001
Model 3				
Male sex	1.32 (1.12 to 1.56)	0.001	1.37 (1.22 to 1.54)	<0.001
Age per 10 years	2.15 (1.95 to 2.37)	<0.001	2.30 (2.15 to 2.46)	<0.001
Manual social class	1.11 (0.95 to 1.31)	0.178	1.15 (1.03 to 1.29)	0.012
Lower education level	1.07 (0.91 to 1.26)	0.383	1.05 (0.94 to 1.18)	0.393
Current smoker	1.88 (1.52 to 2.30)	<0.001	1.86 (1.60 to 2.15)	<0.001
BMI >30 kg/m²	1.30 (1.07 to 1.58)	0.007	1.48 (1.30 to 1.70)	<0.001
Alcohol intake, units per week	1.00 (0.99 to 1.01)	0.828	1.00 (0.99 to 1.01)	0.941
Physically inactive	1.24 (1.06 to 1.45)	0.007	1.16 (1.04 to 1.29)	0.009
Plasma vitamin C per SD	0.83 (0.77 to 0.90)	<0.001	0.86 (0.81 to 0.91)	<0.001
Systolic blood pressure per SD	1.12 (1.03 to 1.21)	0.005	1.13 (1.07 to 1.19)	<0.001
Total cholesterol per SD	0.98 (0.91 to 1.06)	0.607	0.97 (0.92 to 1.03)	0.328

*Charlson Comorbidity Index ≥3 versus Charlson Comorbidity Index ≤2 or no hospital admission.
BMI, body mass index; CVD, cardiovascular disease.

challenging. By using the CCI to define multimorbidity, we were able to show that the chronic diseases defined by the index had considerably higher average length of stay than other conditions requiring hospitalisation and that length of stay increased with higher CCI score. The current population-based study in a defined community was able to assess incident hospital admissions with multimorbidity to enable estimates of 5-year and 10-year rates by age and sex. We were also able to document the relationship between demographic, lifestyle and physiological factors and subsequent hospitalisations for multimorbidity. The EPIC-Norfolk cohort has been followed for 20 years, enabling us to examine the determinants of multimorbidity at two time-points: in mainly middle-aged participants (40–79 years) and mainly old-aged participants (48–92 years) in a subcohort 12 years later after major organisational changes had been made to the National Health Service (NHS). We were also able to examine associations with and without excluding participants with known prevalent conditions at baseline.

While not attempting to examine clusters or pathways of chronic disease, we have identified risk factors that predict any hospital admissions with multimorbidity. It is possible that some factors we observed will be more strongly associated with certain combinations of diseases and others less so. However, the burden of resources experienced by hospitals can best be mitigated by early public health advice, prior to the onset of disease if possible, which can only be general in nature. Our findings are in line with current public health advice such as smoking cessation, a diet containing fruit and vegetables and regular exercise and, given the huge additional burden placed on the

NHS by multimorbidity, should further emphasise the need for public health advice and intervention.

Multimorbidity can be defined in a number of ways, such as disease counts or using various indexes.[39] By restricting the definition to a relatively small subset of chronic conditions such as in the CCI, inevitably some conditions will not be counted. It is notable that the CCI does not include depression or mental health, asthma or respiratory diseases, epilepsy, hypothyroidism, musculoskeletal problems or atrial fibrillation, all common in a primary care setting.[40] In addition to the CCI and other commonly used systems,[41] authors have used many other definitions with variable numbers of underlying conditions and hence the prevalence of multimorbidity varies widely. However, CCI is a widely used measure of multimorbidity.

Since the CCI is weighted to predict mortality, it may be better able to assess health service burden than a simple disease count, since procedures required for higher weighted conditions will generally be more costly. However, it may be less effective as an indicator of multiple long-term conditions. Some chronic conditions such as musculoskeletal and mental health diseases not included in the CCI are nevertheless likely to require long-stay inpatient care. However, increasing CCI had longer hospital length of stay in the present study and this has also been reported in several other studies.[42 43] Medical conditions such as obesity have well-established links to many diseases but, as non-diseases, are not included in the CCI. The use of CCI ≥3 to define multimorbidity classifies a small number of participants with one serious disease with a high CCI weight as multimorbid. However, a sensitivity excluding these people gave virtually identical results. Studies examining the longitudinal predictors of future multimorbidity generally rely on self-reported disease, but our study used the CCI from linked hospital medical coding.

When examining the relationship between lifestyle factors and health outcomes, confounding will always be a limitation. Individuals who smoke, are less physically active and eat a poor diet for example are likely to differ from those with a contrasting lifestyle with respect to other factors relating to the likelihood of future multimorbidity, including their age, sex, lifestyle factors examined in this study and others unknown. However, the associations we report were consistent after multivariable adjustment for other factors. Differential mortality is another possible limitation and would occur for any of the factors examined if participants with an apparently unhealthy characteristic were more likely to have died earlier than those with the contrary healthy characteristic and hence were less likely to use hospital services for the full follow-up period. However, the results for the 5-year follow-up period where very few deaths occurred were consistent with the longer 10-year follow-up period. While it is possible that some participants were multimorbid at baseline, we examined those with and without baseline self-reported major chronic disease.

Comparison with other studies

Estimates of the prevalence of multimorbidity vary widely, partly due to the variety of definitions, number of diseases, weighting and so on used in studies, but range from 55% to 98% in the elderly.[6] Most studies report multimorbidity associated with age and present in more than half of those aged 65 and older.[3 44] Age was strongly associated with future hospitalisation and incident multimorbidity in our study and has been reported to increase hospitalised multimorbidity in elderly patients.[45] Many studies have found that women have a higher rate of multimorbidity than men,[6 44 46–48] but we observed the converse, with male sex strongly predicting future multimorbidity. The use of CCI in the context of prospective hospital admissions rather than cross-sectional multimorbidity in a primary care setting may explain the higher proportion of multimorbid men. Physical-mental comorbidity is reported higher among women in primary care,[49] and mental health, which is not included in the CCI, may be more likely to be treated in a primary care than in an acute hospital setting.

Despite the considerable literature relating to multimorbidity, very few studies have examined the modifiable determinants of incident multimorbidity. Incident cancer and cardiometabolic multimorbidity were examined in a recent multicentre study which included data from the present study[21]; prediagnostic healthy lifestyle behaviours were reported to be inversely associated with the risk. BMI was also reported to be associated with incident cardiometabolic multimorbidity in a pooled analysis of 16 cohort studies.[22] A Finnish study examined incident multimorbidity in both disease-free and those with baseline diabetes and CVD.[24] They reported some similar findings to the present study such as associations with cigarette smoking, physical inactivity and BMI, but associations for low education level and systolic blood pressure were only found in men. Multimorbidity was defined using five common diseases, and time-to-event 10-year follow-up was used rather than a follow-up period approach in this study. Participants in the Finnish cohort were younger than those in EPIC-Norfolk, with the oldest participant 74 years at the end of follow-up against 90 years in the EPIC-Norfolk baseline and 100 years at TP2. Studies using data from an English longitudinal cohort and using self-reported disease counts to define multimorbidity reported associations in physical activity, obesity and low level of wealth and an increased risk of multimorbidity when combined with other lifestyle factors such smoking, obesity and inadequate fruit and vegetable consumption.[25 26] However, they found no association with educational attainment or excess alcohol consumption. Education, which was associated in older participants at TP2 in our study, has been linked to multimorbidity in cross-sectional studies[50] and prospectively.[24] Socioeconomic status was reported to predict the development of multimorbidity throughout the life course in a Scottish longitudinal study.[51] Both educational attainment and occupational social class were attenuated in our study possibly due to the models including plasma vitamin C, also a marker of socioeconomic status. While smoking was a strong predictor, we did not find an association with alcohol drinking. However, other studies in the literature are inconsistent, with some finding no association with cigarette smoking and alcohol consumption in cross-sectional analyses.[1]

Generalisability

While hospital admissions with multimorbidity provide an objective indicator of both health service and individual burden of the condition, studies of hospital admissions in many countries are limited by factors relating to differential accessibility to healthcare such as health insurance, income and healthcare policy. Although not entirely free of differential accessibility, the NHS in the UK, with service free at the point of delivery for all residents, provides an opportunity to examine hospitalised multimorbidity with fewer of these constraints. Healthcare policy and criteria for admission change over time, not least in the UK over the 20-year period of this study, so we examined admissions and risk factors for multimorbidity over two independent time periods using new repeated measures and found consistent results.

CONCLUSIONS AND POLICY IMPLICATIONS

We observed in a long-term population-based study that age, male sex and potentially modifiable factors including smoking, BMI, physical inactivity and a diet low in fruit and vegetables predict future incident hospitalised multimorbidity. Multimorbidity is increasingly common among elderly hospital inpatients due in part to improved efficacy of treatments and drugs. While considerable effort is being focused on the progression, disease clustering and treatment of patients with multimorbidity, there has been less attention on the long-term predictors of future incident multimorbidity. This study suggests that modest difference in lifestyle may have the potential to mitigate the future burden of multimorbidity in the population.

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Competing interests RL, SH, K-TK and NW report grants from MRC and CRUK during the conduct of the study.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The work was approved by the East Norfolk and Waveney NHS research governance committee (2005EC07L) and the Norfolk research ethics committee (05/Q0101/191). All participants gave informed signed consent for study participation including access to medical records.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The authors will make the data set available under a Data Transfer Agreement to any bona fide researcher who wishes to obtain the data set in order to undertake a replication analysis. Although the data set is anonymised, the breadth of the data included and the multiplicity of variables that are included in this analysis file as primary variables or confounding factors mean that provision of the data set to other researchers without a Data Transfer Agreement would constitute a risk. Requests for data sharing/access should be submitted to the EPIC Management Committee (epic-norfolk@mrc-epid.cam.ac.uk).

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Study No:

epic

European Prospective Investigation of Cancer

HEALTH AND LIFESTYLE QUESTIONNAIRE

Please answer the following questions about yourself and your health. This is a study to help us to understand the factors that affect our overall health, so there are some questions which may seem unusual. If you feel these are too personal, do not answer them. However, by answering these questions, you will help us to discover links between lifestyles and health.

PLEASE COMPLETE USING BLACK INK/PEN

Your answers will be treated as strictly confidential and will be used only for medical research

Please try to answer every question, even if the answer is 'Don't know'. If you leave boxes blank, we will not be able to assume that you meant 'no' to be the answer.

1. Date of birth

day month year

2. Date completing this questionnaire

day month year

3. Your sex *(Please tick the appropriate box)* Male ☐ Female ☐

4. Please indicate your current marital status by ticking the appropriate box

Single ☐ Married or living as married ☐ Widowed ☐ Separated ☐ Divorced ☐

5. How old were you when you left school? years

Did you have any further education at college or university after you left school? Yes ☐ No ☐

IF **NO**, PLEASE GO ON TO QUESTION 6

IF **YES**, how old were you when you finished this education? years

What did you study?

6. Do you have any of the following qualifications? *(Tick all applicable)*

School Leaving Certificate ☐ Technical College Exams/City & Guilds ☐ Secretarial College Exams ☐

CSE ☐ HND ☐ Teaching Diploma, HNC ☐

GCE "O" level ☐ Completed Apprenticeship ☐ University Degree ☐

Matriculation ☐ Trade Certificates ☐

"A" level, Highers ☐ Other ☐ *describe*

7. Do you have a paid job at present? *(Please tick the appropriate box)* Yes ☐ No ☐

IF **YES**:

What is your current job title?

What do you do in your job?

What does the organisation in which you work make or do?

How many hours do you work each week? hours

Are you a *(Please tick all the appropriate boxes)*

manager ☐ supervisor ☐ foreman ☐ self employed ☐ None of these ☐

IF you have answered **yes** to any of these, how many people are you responsible for in your work?

(If 100 or more, enter 99)

IF YOU ARE NOT EMPLOYED: How would you describe yourself? *(Please tick the appropriate box)*

Housewife (Home duties) ☐

Retired ☐

Unemployed ☐

Student ☐

Other ☐ *describe* ______

When did you last work *(enter year)*? ☐☐☐☐ Never ☐

IF YOU HAVE EVER WORKED:

What was your last job title? ______

What did you do in your last job? ______

What did the organisation in which you worked make or do? ______

Were you a *(Please tick all the appropriate boxes)*

manager ☐ supervisor ☐ foreman ☐ self employed ☐ None of these ☐

IF you have answered **yes** to any of these, how many people were you responsible for in your work? *(If 100 or more, enter 99)* ☐☐

8. If you are not either currently married or living with a partner as if you are married PLEASE GO ON TO QUESTION 9. If you are widowed, PLEASE GO ON TO QUESTION 8a

If you are:

Does your partner have a job at present? Yes ☐ No ☐

IF **YES**:

What is your partner's current job title? ______

What does your partner do in his/her job? ______

What does the organisation in which your partner works make or do? ______

Is your partner a *(Please tick all the appropriate boxes)*

manager ☐ supervisor ☐ foreman ☐ self employed ☐ None of these ☐

IF you have answered **yes** to any of these, how many people is your partner responsible for at work? *(If 100 or more, enter 99)* ☐☐

IF YOUR PARTNER IS NOT EMPLOYED: Is your partner

Housewife (Home duties) ☐

Retired ☐

Unemployed ☐

Student ☐

Other ☐ *describe* ______

When did your partner last work? *(enter year)* ☐☐☐☐ Never ☐

8a. IF HE/SHE HAS EVER WORKED:

What was your partner's last job title? [ ]

What did your partner do in his/her last job? [ ]

[ ]

What did the organisation in which your partner last worked make or do? [ ]

[ ]

Was your partner a *(Please tick all the appropriate boxes)*

manager [ ] supervisor [ ] foreman [ ] self employed [ ] None of these [ ]

IF you have answered **yes** to any of these, how many people was your partner responsible for at work? *(If 100 or more, enter 99)* [ ][ ]

9. Have **you** ever worked in any of the following occupations?

Tick all the occupations you held for at least one year.

- 1.1 Livestock farming [ ]
- 1.2 Arable farming [ ]
  - *Please tick if you ever used* pesticides or herbicides [ ]
- 2. Mines or quarries [ ]
- 3. Foundries [ ]
  - *Please tick if you worked in:*
  - Steel mill [ ]
  - Special alloys [ ]
- 4. Electroplating [ ]
- 5. Chemical industry [ ]
  - *Please tick if you worked in:*
  - Refinery [ ]
  - Dyes [ ]
  - Chemical laboratory [ ]
- 6. Rubber industry [ ]
- 7. Textile industry [ ]
  - *Please tick if you worked in:*
  - Dyeing [ ]
  - Fibre preparation or weaving [ ]
- 8. Leather and tanning industry [ ]
- 9. Shoes or other leather goods [ ]
- 10. Woodworking [ ]
  - *Please tick if you worked in:*
  - Furniture production [ ]
- 11. Metalworking [ ]
  - *Please tick if you worked in:*
  - Turning or other metal engineering [ ]
  - Welding [ ]
  - Painting [ ]
- 12. Shipyards [ ]
- 13. Electrical/electronic industry [ ]
- 14. Glass industry [ ]
- 15. Printing [ ]
- 16. Construction industry [ ]
  - *Please tick if you worked as:*
  - Roofer [ ]
  - Asphalt worker [ ]
  - Demolition worker [ ]
- 17. Transportation [ ]
  - *Please tick if you worked as:*
  - Truck driver [ ]
  - Bus or taxi driver [ ]
- 18. Nuclear industry [ ]
- 19. Paper or pulp production [ ]
- 20. Asbestos cement production [ ]
- 21. Asbestos insulation [ ]
- 22. Cement production [ ]
- 23. Ceramics production [ ]
- 24. Butcher [ ]
- 25. Painter [ ]
- 26. Welder [ ]
- 27. Hairdresser [ ]
- 28. Petrol station worker [ ]
- 29. Car repair worker [ ]
- 30. Bar tender [ ]
- 31. Restaurant worker [ ]
- 32. Medical & Health Services (e.g. nurse, veterinarian, etc) [ ]
- 33. Have you ever worked with any materials which you believe to be hazardous [ ]
  (*Give details* ________________________________)
- 34. NONE OF THE ABOVE [ ]

10. To which of these groups do you consider you belong?

White ☐

Black, Caribbean ☐

Black, other ☐ *(Give details)* ________

Indian ☐

Pakistani ☐

Bangladeshi ☐

Chinese ☐

Other ☐ *(Give details)* ________

11. It is known that some health problems run in families. We have a 'family history' question to help us to find out more about this. If you are adopted or if your parents remarried, it would be better to know about your biological family (i.e. blood relations) for both your parents and your brothers and sisters.

Is your mother still alive? Yes ☐ No ☐ Don't know ☐

Please enter here either her present age or the age at which she died ☐☐☐ years

Please put here the cause of her death, if known: ________

Is your father still alive? Yes ☐ No ☐ Don't know ☐

Please enter here either his present age or the age at which he died ☐☐☐ years

Please put here the cause of his death, if known: ________

How many brothers have you had (including those who may have died)? ☐☐

How many sisters have you had (including those who may have died)? ☐☐

Could you please list below some details about your first four brothers and sisters. We would like to know either their present age or, if they have died, the age at which they died. *(Please put M for male and F for female.)*

	Sex	Present age	or	Age at which died	
First brother or sister	☐	☐☐☐		☐☐☐	*Please tick if half brother/sister* ☐
Second brother or sister	☐	☐☐☐		☐☐☐	*Please tick if half brother/sister* ☐
Third brother or sister	☐	☐☐☐		☐☐☐	*Please tick if half brother/sister* ☐
Fourth brother or sister	☐	☐☐☐		☐☐☐	*Please tick if half brother/sister* ☐

First brother or sister — If they have died, please put here the cause of death, if known: ________

Second brother or sister — If they have died, please put here the cause of death, if known: ________

Third brother or sister — If they have died, please put here the cause of death, if known: ________

Fourth brother or sister — If they have died, please put here the cause of death, if known: ________

Have any of your immediate family had any of the following conditions?

(Give the approximate age when the illness first occurred.) (Please put M for male and F for female.)

	Heart attack	Stroke	Diabetes	Osteoporosis	Cancer	None of these
Mother	age	age	age	age	age	
	IF CANCER, describe part of body where it started					
Father	age	age	age	age	age	
	IF CANCER, describe part of body where it started					

PLEASE GIVE INFORMATION FOR SAME BROTHERS AND SISTERS

First brother or sister	age	age	age	age	age	
Male or female	IF CANCER, describe part of body where it started					
Second brother or sister	age	age	age	age	age	
Male or female	IF CANCER, describe part of body where it started					
Third brother or sister	age	age	age	age	age	
Male or female	IF CANCER, describe part of body where it started					
Fourth brother or sister	age	age	age	age	age	
Male or female	IF CANCER, describe part of body where it started					

Has any other member of your family apart from yourself (including children, other brothers and sisters, etc) suffered any serious illnessess (excluding infectious diseases such as measles, mumps, whooping cough, etc).

Give details:

12. For your age how would you rate your general health?

Excellent ☐ Good ☐ Moderate ☐ Poor ☐

13. How satisfied do you feel in general with your life?

Excellent ☐ Good ☐ Moderate ☐ Poor ☐

14. Has the doctor ever told you that you have any of the following?
(please complete all appropriate boxes)

CIRCULATION	Yes	Age first Diagnosed
High blood pressure (hypertension) requiring treatment with drugs *(Hypertension during pregnancy is in the women's section of the questionnaire and should not be included here)*		yrs
High blood cholesterol (hyperlipidaemia)		yrs
Angina		yrs
Heart attack (myocardial infarction)		yrs
Varicose veins		yrs
Migraine, *give details*		yrs
Stroke		yrs
Cardiac arrhythmia/palpitations/irregular heartbeat, *give details*		yrs
Pulmonary embolism		yrs
Deep vein thrombosis		yrs
Other vascular disease, *give details*		yrs

Diabetes
(Diabetes during pregnancy is in the women's section of the the questionnaire and should not be included here) yrs

Thyroid disease, *give details* yrs

EYES	Yes	Age first Diagnosed
Cataract in eye		yrs
Glaucoma (high pressure in eye)		yrs

DIGESTIVE SYSTEM	Yes	Age first Diagnosed
Peptic ulcer, *give details*		yrs
Polyps in the large intestine		yrs
Gallstones		yrs
Have you had your gall bladder removed? *If **yes**, please state at what age*		yrs
Pancreatitis		yrs
Appendicitis		yrs
Liver disease, *give details*		yrs

CHEST/ALLERGIES	Yes	Age first Diagnosed
Hayfever/eczema		yrs
Asthma		yrs
Bronchitis/emphysema		yrs
Allergies, *specify*		yrs

BONES	Yes	Age first Diagnosed
Arthritis, *give details*		yrs
Osteoporosis		yrs
Fracture of the hip		yrs
Fracture of the wrist after age 20		yrs
Fracture of vertebra(e)		yrs

OTHER	Yes	Age first Diagnosed
Tuberculosis, *give details*		yrs
Enlarged prostate		yrs
Insomnia requiring treatment		yrs
Depression requiring treatment		yrs
Other psychiatric illness, *give details*		yrs

TUMOURS

		Yes	Age first Diagnosed
Benign growths (non cancer) *specify site(s)*			yrs
Cancer *specify site(s)*			yrs

Other significant illnesses or operations

Please give details, including age at which it was first diagnosed.

Has the doctor ever told you that you had **ANY** of the health problems listed in question 14 above?

Yes ☐ No ☐ Don't know ☐

15. Have you ever had any pain or discomfort in your chest? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 16

IF **YES**,

Do you get this pain or discomfort when you walk up a hill or hurry? Yes ☐ No ☐ Don't know ☐

Do you get it when you walk at an ordinary pace on the level? Yes ☐ No ☐ Don't know ☐

When you get any pain or discomfort in your chest, what do you do?

Stop ☐ Slow down ☐ Continue at same pace ☐ Don't know ☐

Does the pain go away when you stand still? Yes ☐ No ☐ Don't know ☐

If **YES**, how soon? 10 minutes or less ☐ More than 10 minutes ☐

Have you ever had a severe pain across the front of your chest lasting for half an hour or more? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 16

IF **YES**

Did you talk to a doctor about it? Yes ☐ No ☐ Don't know ☐

If yes, what did he/she say it was?

16. Have you ever had back pain? (Please include back ache caused by gardening, housework, etc.) Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 17

IF **YES**

At what age did you first have it? ☐☐ years old Don't know ☐

Have you had back pain in the last year? Yes ☐ No ☐ Don't know ☐

Do you currently have back pain? Yes ☐ No ☐ Don't know ☐

How long did the most recent episode of back pain last?

- Less than a week ☐
- A week or more, but less than a month ☐
- A month or more but less than three months ☐
- More than three months ☐

Please rate the severity of your most recent episode of back pain *(please circle a number)*

1	2	3	4	5	6	7	8	9	10
not severe									very severe

17. Have you ever been confined to bed for a continuous period of 2 months or more?

Yes ☐ No ☐ Don't know ☐

IF **YES**, was the most recent episode in the last 12 months? Yes ☐ No ☐ Don't know ☐

IF NOT IN THE LAST 12 MONTHS, at what age was the most recent occasion? ☐☐ years old

18. Do you have any problems with the following? If so, please indicate what they are

	Yes	No	Don't know	Problem
Hearing	☐	☐	☐	
Eyesight: Do you wear glasses?	☐	☐	☐	
Do you have any other problems with your eyesight?	☐	☐	☐	

Have you lost any teeth in adult life? Yes ☐ No ☐ Don't know ☐

IF **YES**, how many teeth? ☐☐ Don't know ☐ IF **ALL**, please tick this box ☐

Please give reasons if you can ____________________

19a. In the last week, have you taken any drugs or medicines either prescribed by your doctor or bought from the chemist? *(Please include inhalers, pain killers etc.)*

IF **NO**, PLEASE GO ON TO QUESTION 19b. BELOW Yes ☐ No ☐ Don't know ☐

IF **YES**, please name them

	Name/brand	Dose	Frequency		Name/brand	Dose	Frequency
1)				6)			
2)				7)			
3)				8)			
4)				9)			
5)				10)			

19b. Have you ever taken the following medications continously for three months or more?

	Yes	No	Don't know
Aspirin	☐	☐	☐
Steroid tablets or injections (e.g. cortisone)	☐	☐	☐
Diuretics (e.g. bendrofluazide, frusemide)	☐	☐	☐

20. What is your height? ☐ ft ☐☐ inches Don't know ☐

Approximately how tall were you when you were 20 years old? ☐ ft ☐☐ inches Don't know ☐

How much do you weigh now? ☐☐ stones ☐☐ lbs Don't know ☐

Approximately how much did you weigh when you were about 20 years old? ☐☐ stones ☐☐ lbs Don't know ☐

What is the most you have ever weighed *(excluding pregnancy if you are a woman)*? ☐☐ stones ☐☐ lbs Don't know ☐

What is the least you have ever weighed as an adult? ☐☐ stones ☐☐ lbs Don't know ☐

Have you lost 15 pounds or more in the last 5 years? Yes ☐ No ☐ Don't know ☐

IF **YES**, how did this weight loss occur? *(Please tick as many as apply)* Diet ☐ Exercise ☐ Illness ☐ Don't know ☐

Have you gained 15 pounds or more in the last 5 years? Yes ☐ No ☐ Don't know ☐

What is your chest/bust size? ☐☐ inches Don't know ☐

What is your waist size? ☐☐ inches Don't know ☐

What is your hip size? ☐☐ inches Don't know ☐

What size shoe do you take? Size ☐☐ Wide ☐ Medium ☐ Narrow ☐ Don't know ☐

21a. Have you ever smoked as much as one cigarette a day for as long as a year? Yes ☐ No ☐ *i.e. nonsmoker*

IF YOU HAVE NEVER BEEN A CIGARETTE SMOKER PLEASE GO ON TO QUESTION 21b

IF **YES**:

How old were you when you started smoking regularly? ☐☐ yrs old

Did you smoke at the following ages? If so, how many cigarettes did you smoke each day, and were they usually filter cigarettes?

Age 20	Cigarettes per day ☐☐☐	Filter ☐	No filter ☐	Non smoker ☐
Age 30	Cigarettes per day ☐☐☐	Filter ☐	No filter ☐	Non smoker ☐
Age 40	Cigarettes per day ☐☐☐	Filter ☐	No filter ☐	Non smoker ☐
Age 50	Cigarettes per day ☐☐☐	Filter ☐	No filter ☐	Non smoker ☐

21b. Do you smoke cigarettes now? Yes ☐ No ☐

IF **YES**: How many cigarettes do you smoke each day? ☐☐☐

Do you usually smoke filter cigarettes? Yes ☐ No ☐ Don't know ☐

Do you usually smoke low tar cigarettes? Yes ☐ No ☐ Don't know ☐

How deeply do you inhale? Deeply into the lungs ☐ A little ☐ Not at all ☐

If you have stopped smoking, how old were you when you gave up? ☐☐ yrs old

21c. Do you smoke cigars? *(Please tick one box)* Currently ☐ In the past ☐ Never ☐ Don't know ☐

Do you smoke a pipe? *(Please tick one box)* Currently ☐ In the past ☐ Never ☐ Don't know ☐

22. Have you modified your diet in the past year? Yes ☐ No ☐ Don't know ☐

(Tick all appropriate reasons.)

Overweight/obesity ☐

Diabetes ☐

High blood cholesterol ☐

High blood pressure ☐

Allergies, e.g. skin rash ☐

Stomach problems, e.g. ulcer or gastritis ☐

Bowel problems, e.g. irritable bowel or diverticulitis ☐

Concern over a family history of illness ☐

Concern over eating a healthy diet ☐

Other ☐ *(give details)* ____________

23. Do you follow any particular diets? *(See below for examples)* Yes ☐ No ☐ Don't know ☐

(Tick all appropriate reasons.)

Low fat ☐

Low salt ☐

Low saturated fat ☐

Diabetic ☐

Weight reduction ☐

Gluten free ☐

Vegetarian ☐

High fibre ☐

Vegan ☐

Other ☐ *(give details)* ____________

24. Have you taken any vitamins, minerals or other food supplements taken regularly during the past year (such as vitamin C, vitamin D, iron, calcium, fish oils, primrose oil, beta carotene etc.) *(List brand and daily dose, if known)*

Yes ☐ No ☐ Don't know ☐

	Name/brand	Daily Dose
1).		
2).		
3).		
4).		
5).		

25. How often do you eat the following foods?

	Never	Seldom	Once a week	2-4 times a week	5-6 times a week	Once or more daily	Don't Know
Fresh fruit (e.g. apples, oranges, pears)							
Green leafy vegetables (e.g. cabbage, broccoli)							
Other vegetables (e.g. peas, carrots, beans, tomatoes)							
Oily fish (e.g. herring, salmon, sprats, pilchards, mackerel)							
Other fish (e.g. cod, tuna, haddock)							
Chicken							
Meat (e.g. chops, roasts, stews)							
Meat products (e.g. sausages, ham, beefburgers)							
Eggs							
Cheese							
Wholemeal/brown bread							

26. How many cups of these beverages do you usually drink in a day?

	Cups *If none put "0"*	milk *Tick if added*	sugar
Caffeinated coffee, instant			
Caffeinated coffee, ground			
Decaffeinated coffee, instant			
Decaffeinated coffee, ground			
Tea			
Decaffeinated tea			
Herbal tea			
Milk, full fat (e.g. in cocoa, but not including milk in coffee or tea)			
Milk, low fat or skimmed (as in milk above)			

27. Please indicate your total milk intake, including milky drinks, milk in drinks and on breakfast cereal, etc. at different ages, by ticking the appropriate boxes. From this we may be able to learn whether it is more important to drink milk as a teenager than, say, in your forties.

	None	Up to 1/2 pt weekly	More than 1/2 pt/week, less than 1/2 pt/day	1/2 pt - 1 pt daily	More than 1pt daily	Don't know
As a teenager						
20-44 yrs old						
45 yrs to present						

28. Are you a non-drinker/teetotaller now? Yes ☐ No ☐ Don't know ☐

Have you ever drunk alcohol in the past? Yes ☐ No ☐ Don't know ☐

IF YOU HAVE NEVER DRUNK ANY ALCOHOL, PLEASE GO ON TO QUESTION 29.

When you were aged 20, about how many alcoholic drinks did you have each week?

	Put "0" if none		Tick if less than one drink a week
Beer, cider or lager		pints each week	Occasional
Wine		glasses each week	Occasional
Sherry or fortified wine		glasses each week	Occasional
Spirits - whisky,gin, brandy, liqueurs etc.		glasses (singles) each week	Occasional

When you were aged 30, about how many alcoholic drinks did you have each week?

	Put "0" if none		Tick if less than one drink a week
Beer, cider or lager		pints each week	Occasional
Wine		glasses each week	Occasional
Sherry or fortified wine		glasses each week	Occasional
Spirits - whisky,gin, brandy, liqueurs etc.		glasses (singles) each week	Occasional

At present, about how many alcoholic drinks do you have each week?

	Put "0" if none		Tick if less than one drink a week
Beer, cider or lager		pints each week	Occasional
Wine		glasses each week	Occasional
Sherry or fortified wine		glasses each week	Occasional
Spirits - whisky,gin, brandy, liqueurs etc.		glasses (singles) each week	Occasional

29. How many times a day do you eat, including meals, snacks, biscuits with coffee breaks, etc. ☐☐ times

30. We would like to know the type and amount of physical activity involved in your work.
(Please tick what best corresponds to your present activities from the following four possibilities:)

Sedentary occupation. You spend most of your time sitting (such as in an office) ☐

or

Standing occupation. You spend most of your time standing or walking. However, your work does not require intense physical effort (e.g., shop assistant, hairdresser, guard, etc.) ☐

or

Physical work. This involves some physical effort including handling of heavy objects and use of tools (e.g. plumber, cleaner, nurse, sports instructor, electrician, carpenter, etc.) ☐

or

Heavy manual work. This involves very vigorous physical activity including handling of very heavy objects (e.g., docker, miner, bricklayer, construction worker, etc.) ☐

31. In a typical week during the past 12 months, how many hours did you spend on each of the following activities? *(Put "0" if none.)*

Walking, including walking to work, shopping and leisure	In summer	☐☐ hours per week
	In winter	☐☐ hours per week
Cycling, including cycling to work and during leisure time	In summer	☐☐ hours per week
	In winter	☐☐ hours per week
Gardening	In summer	☐☐ hours per week
	In winter	☐☐ hours per week
Housework such as cleaning, washing, cooking, child care,		☐☐ hours per week
Do it Yourself		☐☐ hours per week
Other physical exercise such as keep fit, aerobics, swimming, jogging,	In summer	☐☐ hours per week
	In winter	☐☐ hours per week

32. In a typical week during the past year did you practise any of these activities vigorously enough to cause sweating or a faster heartbeat? Yes ☐ No ☐ Don't know ☐

IF **YES**, for how many hours per week in total did you practise such vigorous physical activity? *(Put '0' if none)* ☐☐ hours per week

33. In a typical day during the past 12 months, how many floors of stairs did you climb up? *(Put "0" if none)* ☐☐ floors per day

We would like to ask some general questions which may help us to identify people who could be protected against disease. Please answer the following if you can.

34. Were you a premature baby? Yes ☐ No ☐ Don't know ☐

Do you know what you weighed at birth? ☐☐ lbs ☐☐ oz Don't know ☐

How was your general health as a child? Excellent ☐ Good ☐ Moderate ☐ Poor ☐

35. Do you consider yourself naturally Left handed ☐ Right handed ☐ Both right and left handed ☐

With which hand do you usually write? Left hand ☐ Right hand ☐

36. What was your natural hair colour at the age of 20 years?

Brown/brunette ☐ Blonde ☐ Black ☐ Red ☐ Other ☐

What is your skin colouring? Fair ☐ Medium ☐ Dark ☐

Do you suffer from loss of hair on your head resulting in bald patches? Yes ☐ No ☐ A little ☐

IF **YES**, please indicate where the loss is Receding front ☐ Top back (on crown) ☐ Both ☐

37. What is the colour of your eyes?

Blue ☐ Brown ☐ Hazel ☐ Other ☐ *specify* ________ Don't know ☐

Green ☐

Two different sections follow, one for women, one for men. Please complete only the section that applies to you.

FOR WOMEN ONLY

38F. How old were you when you had your first menstrual period?

☐☐ yrs old   Don't know ☐   Never ☐

39F. When you were in your mid thirties how many days were there between the start of one menstrual period and the start of the next? *(Ignore times when you were pregnant, breastfeeding or taking an oral contraceptive ("the pill")).*

Usually 24 days or less	☐	Irregular	☐
Usually 25 to 26 days	☐	No menstrual cycles	☐
Usually 27 to 29 days	☐	Used the pill continuously	☐
Usually 30 to 31 days	☐	Don't know	☐
Usually 32 or more days	☐		

40F. Are you still menstruating?   Yes ☐   No ☐   Don't know ☐

IF **YES**

Do you take the pill?   Yes ☐   No ☐

Do you take hormones for the treatment of menopause?   Yes ☐   No ☐

How many periods have you had in the last 12 months?

1-3 ☐   4-5 ☐   6-9 ☐   10+ ☐

IF **NO**

How old were you when you stopped having your periods?   ☐☐ years old

Have you had any periods during the last 12 months?   Yes ☐   No ☐   Don't know ☐

IF YES, how many periods have you had in the last 12 months?

1-3 ☐   4-5 ☐   6-9 ☐   10+ ☐

What was the date of the start of your last 'natural' menstrual period? *Don't record date if you were using hormone replacement therapy.*

Date ☐☐ / ☐☐ / ☐☐   Don't know ☐

Day   Month   Year

41F. Have you ever been pregnant?   Yes ☐   No ☐   Don't know ☐

IF **YES** PLEASE GO ON TO QUESTION 42F

IF **NO**

Have you ever tried to become pregnant?   Yes ☐   No ☐   Don't know ☐

PLEASE GO ON TO QUESTION 48F

42F. Have you ever had high blood pressure (hypertension) during pregnancy?

Yes ☐   No ☐   Don't know ☐

IF **YES**, please record the year(s)   Year ☐☐☐☐   Year ☐☐☐☐   Year ☐☐☐☐

43F. Have you ever had diabetes during pregnancy?   Yes ☐   No ☐   Don't know ☐

IF **YES**, please record the year(s)   Year ☐☐☐☐   Year ☐☐☐☐   Year ☐☐☐☐

44F. Have you had any children? Yes ☐ No ☐

IF **YES**, FILL IN ONE LINE FOR EACH CHILD YOU HAVE HAD.

IF TWINS OR TRIPLETS, FILL IN ONE LINE PER CHILD.

	Date of Birth: day / month / year	Boy (*Tick as applicable*)	Girl	Number of weeks breastfed, even if only occasional (*Put "0" if not breastfed, "1" if yes, but less than 1 week*)
1.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
2.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
3.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
4.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
5.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
6.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
7.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
8.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
9.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐
10.	☐☐ / ☐☐ / ☐☐	☐	☐	☐☐☐

45F. Have you had any stillbirths? Yes ☐ No ☐ Don't know ☐

IF **YES**, please record the year(s) Year ☐☐☐☐ Year ☐☐☐☐ Year ☐☐☐☐

46F. Have you had any miscarriages? Yes ☐ No ☐ Don't know ☐

IF **YES**, please record the year(s) Year ☐☐☐☐ Year ☐☐☐☐ Year ☐☐☐☐

Year ☐☐☐☐ Year ☐☐☐☐ Year ☐☐☐☐

47F. Have you had any other pregnancies which lasted for less than 28 weeks?

Yes ☐ No ☐ Don't know ☐

IF **YES**, please record the year(s) Year ☐☐☐☐ Year ☐☐☐☐ Year ☐☐☐☐

If ectopic, please tick ☐ ☐ ☐

48F. Have you ever used oral contraceptives or "the pill"? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 49F

IF **YES**

How old were you when you first used the pill? ☐☐ years old

For how long altogether did you use the pill? ☐☐ Years ☐☐ months

Are you currently on the pill? Yes ☐ No ☐

Do you know what brand name you last used? ____________

If you are not currently on the pill, how old were you when you last used it? ☐☐ years old

49F. Have you ever used a coil or "IUD" (intra-uterine device)? Yes ☐ No ☐ Don't know ☐

IF **YES**

Do you have a coil or IUD at present? Yes ☐ No ☐ Don't know ☐

50F. Have you ever received any Hormone Replacement Therapy (HRT)? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 52F

IF **YES**,

Are you currently taking this treatment? Yes ☐ No ☐ Don't know ☐

Why did you take it? Treatment for hot flushes/menopausal symptoms ☐

Osteoporosis ☐

Other reasons ☐ *Give details* ____________________

How old were you when you started this treatment? ☐☐ yrs old

For how long have you taken this treatment? ☐☐ yrs ☐☐ mths

Do you know what brand name you last used? ____________________

51F. In what form did you take Hormone Replacement Therapy? *(Tick those which apply)*

By mouth (pill form) ☐

By implantation under the skin ☐

By adhesive pads on the skin ☐

By injection ☐

By cream (vaginal or skin) ☐

Are these the only hormonal drugs you have ever taken? Yes ☐ No ☐ Don't know ☐

52F. Have you ever seen a doctor because of fertility problems? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 53F

IF **YES**

Has a doctor ever told you that you were infertile? Yes ☐ No ☐ Don't know ☐

Has a doctor ever told your partner that he was infertile? Yes ☐ No ☐ Don't know ☐

Have you ever been treated with drugs for infertility? Yes ☐ No ☐ Don't know ☐

Have you ever had surgery for infertility? Yes ☐ No ☐ Don't know ☐

53F. Have you had a hysterectomy (womb removed)? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 54F

IF **YES**

At what age? ☐☐ yrs old

Why did you have a hysterectomy *(Tick those which apply)*?

Complications of pregnancy ☐

Cancer ☐

Endometriosis ☐

Abnormal bleeding not due to any of above ☐

Fibroid or cyst ☐

Contraception ☐

Prolapsed uterus/urine incontinence ☐

Don't know ☐

None of above ☐

54F. Have you had an operation to remove one or both ovaries? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 55F

IF **YES**

At what age? ☐☐ years old

Were one or both ovaries removed? One ☐ Both ☐ Don't know ☐

55F. This may seem to duplicate part of an earlier question. We would still be grateful if you would answer it fully so that we are absolutely certain that we have not missed information about this important problem.

Have you had benign breast disease? *(please tick one)* Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 56F

IF **YES**, *please tick those which apply*

Cyst ☐

Mastitis ☐

Benign lump (not cancer) ☐

Other, *please specify* ________ ☐

Have you ever had breast cancer? *(please tick one)* Yes ☐ No ☐ Don't know ☐

IF **YES**, please give year it was diagnosed ☐☐☐☐

56F. What is your cup size (A, B, C, D, DD) ☐☐ Don't know ☐

57F. How would you rate your body hair growth on the following areas:

Facial hair ("moustache type")	Little ☐	Some ☐	Heavy ☐
Legs	Little ☐	Some ☐	Heavy ☐

THANK YOU VERY MUCH FOR ANSWERING THESE QUESTIONS

FOR MEN ONLY

38M. Has a spouse or partner ever been pregnant by you? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 39M

IF **YES**, have you ever had any live born children? Yes ☐ No ☐ Don't know ☐

IF **NO**, PLEASE GO ON TO QUESTION 39M

IF **YES**,

How many boys have you had? ☐☐

How many girls have you had? ☐☐

39M. Have you had a vasectomy? Yes ☐ No ☐ Don't know ☐

IF **YES**, at what age? ☐☐ years old

40M. Do you have any of the following urinary symptoms?

	Yes often	Yes occasionally	No	Don't know
Difficulty starting to pass urine	☐	☐	☐	☐
Discomfort on passing urine	☐	☐	☐	☐
Slow urine stream	☐	☐	☐	☐

THANK YOU VERY MUCH FOR ANSWERING THESE QUESTIONS

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The World Health Organization

3HC
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Study Number:

European Prospective Investigation of Cancer

www.epic-norfolk.org.uk

HEALTH QUESTIONNAIRE

Thank you for taking part in EPIC. Please answer the following questions about yourself and your health. This is a study to help us understand the factors that affect our overall health and maintain good health as we get older.

Sometimes it helps researchers to ask the same questions at different times, so we would be grateful if you could answer them. If you feel any of the questions are too personal, do not answer them.

Your answers will be treated as strictly confidential and will be used only for medical research. Your name does not appear on this questionnaire.

Please try to answer every question, even if the answer is 'Don't know'. If you leave boxes blank, we will not be able to assume that you meant 'no' to be the answer.

A GENERAL

(Please write in or tick (✓) the box as appropriate)

1. Today's date ☐☐/☐☐/**2 0**☐☐

2. Date of birth ☐☐/☐☐/**1 9**☐☐

3. Sex — Male ☐ Female ☐

4. Current marital status — Single ☐ Married (or living with a partner) ☐ Widowed ☐ Separated ☐ Divorced ☐

5. Do you have a paid job at present? — Yes ☐ No ☐ Don't know ☐

If **YES**, is this job full time? — Yes ☐ No ☐ Don't know ☐

6. Are you currently retired from your main occupation? — Yes ☐ No ☐ Don't know ☐

If **YES**, in which year did you retire? ☐☐☐☐

7. If you are retired what was your **main** reason for giving up work?

Reached retirement age ☐ Ill health ☐ Enough money ☐ Redundancy ☐ Voluntary Retirement ☐ Other reason ☐

B LIFESTYLE

The next few questions are about your lifestyle as this can influence your general health.

8. Do you currently smoke cigarettes? — Yes ☐ No ☐

9. If you have stopped smoking, how old were you when you gave up? ☐☐ years old — Don't know ☐

IF YOU DO SMOKE,
how many cigarettes do you usually smoke each day? ☐☐☐ cigarettes a day — Don't know ☐

10. Do you currently smoke cigars? — Yes ☐ No ☐

11. Do you currently smoke a pipe? — Yes ☐ No ☐

12. Do you live in a household where other people smoke? — Yes ☐ No ☐ Don't know ☐

13. Are you a non-drinker/teetotaller now? — Yes ☐ No ☐ Don't know ☐

14. Have you ever drunk alcohol in the past? — Yes ☐ No ☐ Don't know ☐

15. Did you drink alcohol in the last week? — Yes ☐ No ☐ Don't know ☐

If **YES**, during the last week, how many of the following alcoholic drinks have you consumed? *(Please enter the number of drinks you had each day.)*

	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Beer, cider or lager (half pints)							
Wine (glasses)							
Sherry or fortified wine (glasses)							
Spirits (whisky, gin, brandy, liqueurs etc.) single measures							
How many of these were consumed during a meal?							

16. We would like to know the type and amount of physical activity involved in your work. (Please tick (✓) what best corresponds to your present activities from the following four possibilities.)

Sedentary occupation. You spend most of your time sitting (such as in an office). ☐

or

Standing occupation. You spend most of your time standing or walking. However, your work does not require intense physical effort (e.g. shop assistant, hairdresser, guard, etc.). ☐

or

Physical work. This involves some physical effort including handling of heavy objects and use of tools (e.g. plumber, cleaner, nurse, sports instructor, electrician, carpenter, etc.). ☐

or

Heavy manual work. This involves very vigorous physical activity including handling of very heavy objects (e.g. docker, miner, bricklayer, construction worker, etc.). ☐

17. In a typical week during the past year, how many hours did you spend on each of the following activities? (Put '00' if none.)

Walking, including walking to work, shopping and leisure	In summer	☐☐	hours per week
	In winter	☐☐	hours per week
Cycling, including cycling to work and during leisure time	In summer	☐☐	hours per week
	In winter	☐☐	hours per week
Gardening	In summer	☐☐	hours per week
	In winter	☐☐	hours per week
Housework such as cleaning, washing, cooking, child care		☐☐	hours per week
Do it Yourself		☐☐	hours per week
Other physical exercise such as keep fit, aerobics, swimming, jogging	In summer	☐☐	hours per week
	In winter	☐☐	hours per week

18. In a typical week during the past year did you do any of these activities vigorously enough to cause sweating or a faster heartbeat? Yes ☐ No ☐ Don't know ☐

If **YES**, for how many hours per week in total did you practice such vigorous physical activity? (Put '00' if none.) ☐☐ hours per week

19. In a typical day during the past year, how many flights of stairs did you climb up? (Put '00' if none.) ☐☐ flights per day

20. TV or Video viewing (Please put a tick (✓) on **every** line.)

Hours of TV or video watched per day	Average over the past year					
	None	Less than 1 hour a day	1 to 2 hours a day	2 to 3 hours a day	3 to 4 hours a day	More than 4 hours a day
On a weekday before 6 pm						
On a weekday after 6 pm						
On a weekend day before 6 pm						
On a weekend day after 6 pm						

21. Computers, including computer games (Please put a tick (✓) on **every** line.)

Hours spent at a computer per day (at work or home)	Average over the past year					
	None	Less than 1 hour a day	1 to 2 hours a day	2 to 3 hours a day	3 to 4 hours a day	More than 4 hours a day
On a weekday before 6 pm						
On a weekday after 6 pm						
On a weekend day before 6 pm						
On a weekend day after 6 pm						

22. Do you regularly join in the activities of any of these organisations? (Please tick(✓) all that apply)

Political parties ☐
Trade unions (including student unions) ☐
Environmental groups ☐
Parent-teacher association or school association ☐
Tenants' or residents' group or neighbourhood watch ☐
Education, arts, music or singing group (including evening classes) ☐
Charity, voluntary or community group ☐
Group for elderly or older people (e.g. lunch club) ☐
Youth group (e.g. scouts, guides, youth club) ☐
Women's Institute or Townswomen's Guild or Women's group ☐
Social club (including working men's club, Rotary club) ☐
Sports club, gym, exercise or dance group ☐
Other group or organisation ☐
OR No, I don't regularly join in any of the activities of these organisations ☐

23. Please indicate when you take part in any of the following activites by ticking the appropriate box(es)

	Once a year or less	Several times a year	Several times a month	Several times a week	Every day or almost every day
Listening to radio					
Reading newspaper					
Reading magazines					
Reading books					
Playing games such as cards, chess					
Crosswords					
Puzzles					

C HEALTH AND WELLBEING

24. In general would you say your health is? (Please tick (✓) **one** box)

Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor ☐

25. Compared to one year ago, how would you rate your health in general now?
(Please tick (✓) **one** box)

Much better now than one year ago ☐
Somewhat better now than one year ago ☐
About the same ☐
Somewhat worse than one year ago ☐
Much worse now than one year ago ☐

26. For your age in years, how do you think you look?
(Please tick (✓) **one** box)

Much younger ☐
A little younger ☐
About your age ☐
A little older ☐
Much older ☐
Don't know ☐

27. For your age in years, how do you feel? (Please tick (✓) **one** box)

Much younger ☐
A little younger ☐
About your age ☐
A little older ☐
Much older ☐
Don't know ☐

28. What is your current weight? ***(if known)***

☐☐ stones ☐☐ lb or ☐☐☐ kg Don't know ☐

29. If you have lost more than 5 kg (10 lb) in the last five years,
how did this weight loss occur? (Please tick (✓) **all** that apply)

Not applicable ☐ Diet ☐ Exercise ☐ Illness ☐

Other *(please specify)* ________ Don't know ☐

30. Do you wear glasses/contact lenses? Yes ☐ No ☐ Don't know ☐

If **YES**, for what reason? Distance ☐ Reading ☐ Distance and reading ☐

Other *(please specify)* ________

31. If you wear glasses/contact lenses for reading, at what age
(other than in childhood) did you start wearing them? ☐☐ years old Don't know ☐

32. Do you have any other problems with your eyesight? Yes ☐ No ☐ Don't know ☐

If **YES**, please indicate what they are. ________

33. How good is your eyesight for seeing things at a distance, like recognising a friend across the street *(using glasses or corrective lens if you usually wear them)*?
(Please tick(✓) **one** box)

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

34. How good is your eyesight for seeing things up close, like reading ordinary newspaper print *(using glasses or corrective lens if you usually wear them)*? (Please tick (✓) **one** box.)

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

35. Have you ever had an eye operation? Yes ☐ No ☐ Don't know ☐

If **YES** – Please specify.

36. Do you have a relative with eye disease or eye problems? Yes ☐ No ☐ Don't know ☐

If **YES** – Please specify.

37. Are you having any treatment or medication (e.g. eye drops) for any eye conditions? Yes ☐ No ☐ Don't know ☐

If **YES** – Please specify.

38. Do you have any problems with hearing? Yes ☐ No ☐ Don't know ☐

If **YES** – Please specify.

39. How good is your hearing *(using a hearing aid if you usually wear one)*? (Please tick (✓) **one** box.)

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

40. How difficult do you find it to follow a conversation if there is background noise, such as TV, radio or children playing *(using a hearing aid if you usually wear one)*?

No difficulty ☐ Some difficulty ☐ Much difficulty ☐ Unable to do this ☐

41. When you go on a trip away from your home, like a trip to a shop, restaurant, or visits to friends, how often do you purposely limit the amount of walking you have to do?

Always ☐ Often ☐ Sometimes ☐ Rarely ☐ Never ☐

The next questions ask about difficulties you may have walking a quarter of a mile because of a health problem. By health problem we mean any long-term physical mental or emotional problem or illness.

42. By yourself and without using any special equipment, how much difficulty do you have walking for a quarter of a mile?

No difficulty ☐ Some difficulty ☐ Much difficulty ☐ Unable to do this ☐

43. If you have difficulty, or are unable to walk for a quarter of a mile, what are the symptoms that cause this difficulty?

	The Main Symptom (please tick (✓) **one** box **only** in this column)	Other Symptoms (tick (✓) as many boxes as necessary in this column)
Chest pain	☐	☐
Fatigue/too tired	☐	☐
Shortness of breath	☐	☐
Tremor(s)	☐	☐
Pain in leg or foot	☐	☐
Swelling in leg or foot	☐	☐
Incontinence or fear of incontinence	☐	☐
Seeing difficulty	☐	☐
Hearing difficulty	☐	☐
Confusion	☐	☐

Question 43 continued on next page

43. *Continued*.

	The Main Symptom (please tick (✓) **one** box **only** in this column)	Other Symptoms (tick (✓) as many boxes as necessary in this column)
Difficulty concentrating	☐	☐
Memory problems	☐	☐
Unsteady on feet or balance problems	☐	☐
Lightheaded or dizziness	☐	☐
Fear of falling	☐	☐
Anxiety or fear	☐	☐
Some other problem or symptom	☐	☐

44. How many times have you fallen to the ground in the **past year**? *(Include falls where any part of your body above the ankle hit the floor or ground, and falls which occurred on stairs.)* (Please tick (✓) the box)

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 or more ☐

45. If you had any falls, as a result of the **WORST** fall, were you injured? Yes ☐ No ☐

46. As a result of your **WORST** fall, how many days did you cut down on normal activity? ☐☐ days

47. How many times were you seen by your doctor or did you go to hospital because of a fall in the past year?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 or more ☐

48. Have you ever had any joint replacements, eg a hip or a knee replacement? Yes ☐ No ☐

49. Which joints have you had replaced?

	Right leg	Left leg
Hip	☐	☐
Knee	☐	☐

50. If you had a hip replacement, why was it replaced?

Arthritis ☐ Fracture ☐ Both arthritis and a fracture ☐ Other reason ☐

51. How would you rate your pain when you are walking on a flat surface for each of the following:
(Please rate your pain during the past month from 0 – 10, where 0 is no pain and 10 is severe or excruciating pain, as bad as you can imagine)

In your BACK?

0 1 2 3 4 5 6 7 8 9 10
no pain…………………………………………………… Severe or excruciating pain

In your HIPS?

0 1 2 3 4 5 6 7 8 9 10
no pain…………………………………………………… Severe or excruciating pain

In your KNEES?

0 1 2 3 4 5 6 7 8 9 10
no pain…………………………………………………… Severe or excruciating pain

In your FEET?

0 1 2 3 4 5 6 7 8 9 10
no pain…………………………………………………… Severe or excruciating pain

52. Many people have trouble with their bladder as they grow older. In the past year, have you had any problems with losing control of your urine because you could not get to the toilet quickly enough?

Yes ☐ No ☐ Don't know ☐

IF **YES**, how often does this occur?

Daily or nightly ☐
Several times a week ☐
Once a week ☐
Less than once a week ☐
Rarely ☐

53. Do you ever limit your activity because of difficulty holding your urine? Yes ☐ No ☐ Don't know ☐

54. Have you noticed tremor or shakiness in your hands? Yes ☐ No ☐ Don't know ☐

If **YES**, when is this most obvious? When active ☐ When relaxed ☐ Don't know ☐

55. Do you have any difficulty in getting started when you walk? Yes ☐ No ☐ Don't know ☐

If **YES**, is this due to joint problems such as arthritis? Yes ☐ No ☐ Don't know ☐

56. Do you have any difficulty with getting out of a chair? Yes ☐ No ☐ Don't know ☐

If **YES**, is this due to joint problems such as arthritis? Yes ☐ No ☐ Don't know ☐

57. Has your walking become slower? Yes ☐ No ☐ Don't know ☐

58. Has your handwriting changed in the last few years? Yes ☐ No ☐ Don't know ☐

If **YES**, has it become Smaller? ☐ Bigger? ☐ Don't know ☐

59. Have you had any serious illnesses or operations in the past 3 years?

Yes ☐ No ☐ Don't know ☐

If **YES**, was this due to either cancer? Yes ☐ No ☐ Don't know ☐

or heart disease? Yes ☐ No ☐ Don't know ☐

60. Have you ever been diagnosed as having Parkinson's disease? Yes ☐ No ☐ Don't know ☐

61. Are you currently taking any of the following medication? (Please tick (✓) boxes)

Medication to lower your blood pressure	Yes ☐	No ☐	Don't know ☐
Medication to lower your cholesterol	Yes ☐	No ☐	Don't know ☐
Medication for diabetes	Yes ☐	No ☐	Don't know ☐
Aspirin	Yes ☐	No ☐	Don't know ☐
Steroid tablets or injections (e.g. cortisone)	Yes ☐	No ☐	Don't know ☐

62. In the last week please list below any drugs or medicines you have taken, either prescribed by your doctor or bought from the chemist (Please include inhalers, antacids, laxatives, pain killers, HRT, etc. but not vitamins, food supplements etc.)

Name *(Please list **full** name)*	How many at a time?	How often?

63. In the last week, have you taken any vitamins, food supplements etc? Yes ☐ No ☐ Don't know ☐

(Please name any vitamins, minerals or other food supplements taken on each day of last week **as in the example below**.)

Brand	Name (Please list **full** name)	Amount taken per day – number of pills, capsules or teaspoons.	Tick (✓) box(es) to show which day(s) supplement was taken last week.						
			M	T	W	T	F	S	S
Healthcrafts	Multivitamins with iron and calcium	1 tablet	✓		✓		✓	✓	

Example

64. The following questions are about activities you might do during a typical day.
Does your health now limit you in these activities?
If so, how much? (Please tick (✓) **one** box on **each** line.)

	Yes, limited a lot	Yes, limited a little	Not limited at all
Vigorous activities, such as running,lifting heavy objects, participating in strenuous sports	☐	☐	☐
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐
Climbing **one** flight of stairs	☐	☐	☐
Bending, kneeling or stooping	☐	☐	☐
Walking **more than one mile**	☐	☐	☐
Walking **half a mile**	☐	☐	☐
Walking **one hundred yards**	☐	☐	☐
Bathing or dressing yourself	☐	☐	☐

65. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health.** (Please tick (✓) **one** box in **each** line.)

Cut down on the **amount of time** you spent on work or other activities	Yes ☐	No ☐
Accomplished less than you would like	Yes ☐	No ☐
Were **limited** in the **kind** of work or other activities	Yes ☐	No ☐
Had **difficulty** performing the work or other activities (for example, It took extra effort.)	Yes ☐	No ☐

66. During the **past 4 weeks**, have you had any of the following problems with your work **or**
other regular daily activities **as a result of any emotional problems** (e.g. feeling depressed or anxious)? (Please tick (✓) **one** box in **each** line.)

Cut down on the **amount of time** you spent on work or other activities	Yes ☐	No ☐
Accomplished less than you would like	Yes ☐	No ☐
Didn't do work or other activities as **carefully** as usual	Yes ☐	No ☐

67. During the **past 4 weeks**, to what extent have your physical health or emotional problems interfered with your normal social activities with family, neighbours, or groups? (Please tick (✓) **one** box.)

Not at all ☐ Slightly ☐ Moderately ☐ Quite a bit ☐ Extremely ☐

68. How much **physical** pain have you had in the **past 4 weeks**? (Please tick (✓) **one** box.)

Not at all ☐ Slightly ☐ Moderately ☐ Quite a bit ☐ Extremely ☐

69. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)? (Please tick (✓) **one** box.)

Not at all ☐ Slightly ☐ Moderately ☐ Quite a bit ☐ Extremely ☐

70. These questions are about how you feel and how things have been with you during the **past 4 weeks**.
(Please give the answer that is closest to the way you have been feeling, for each item.)

(Please tick (✓) **one** box in **each** line.)	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?						
Have you been a very nervous person?						
Have you felt so down in the dumps that nothing could cheer you up?						
Have you felt calm and peaceful?						
Did you have a lot of energy?						
Have you felt downhearted and low?						
Did you feel worn out?						
Have you been a happy person?						
Did you feel tired?						

71. During the past 4 weeks, how much of the time have your physical health or emotional problems interfered with your social activities (like visiting friends, relatives etc.)? (Please tick (✓) **one** box.)

- All of the time ☐
- Most of the time ☐
- Some of the time ☐
- A little of the time ☐
- None of the time ☐

72. How **TRUE** or **FALSE** are each of the following statements for you?
(Please tick (✓) **one** box on **each** line.)

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
I seem to get sick a little easier than other people					
I am as healthy as anybody I know					
I expect my health to get worse					
My health is excellent					

The next questions ask about difficulties you may have doing certain activities because of a health problem. By 'health problem' we mean any long-term physical, mental or emotional problem or illness (not including pregnancy).

73. By yourself, and without using any special equipment, how much difficulty do you have with the following? (Please tick (✓) **one** box on **each** line.)

	No difficulty	Some difficulty	Much difficulty	Unable to do
Preparing your own meals?				
Biting and chewing on hard foods such as a firm apple?				
Standing up from an armless straight chair?				
Standing or being on your feet for about 2 hours?				
Sitting for about 2 hours?				
Reaching up over your head?				
Using your fingers to grasp or handle small objects?				

D MOOD

The next few questions are about your mood which is something that can also influence your general health

74. In the past **10 YEARS** have there been times when you felt sad, depressed for **TWO WEEKS** or **MORE** in a row? Yes ☐ No ☐

75. In the past **10 YEARS** have there been times when you have lost interest in most things like your work or activities that usually give you pleasure, for **TWO WEEKS** or **MORE** in a row? Yes ☐ No ☐

IF YES continue IF NO go to question 81

For the next few questions, please think of the **MOST RECENT TWO WEEK** episode **during the past 10 YEARS** when these feelings of sadness, depression or loss of interest were worst.

76. During that time did the feelings of being sad or depressed, or loss of interest usually last? (Please tick (✓) **one** box.)

- All day long ☐
- Most of the day ☐
- About half the day ☐
- Less than half the day ☐

77. During those two weeks or more, did you feel this way? (Please tick (✓) **one** box.) Every day ☐ Almost every day ☐ Less often ☐

78. During those two weeks or more did you? (Please tick (✓) **YES** or **NO**.)

Gain or lose weight without trying?	Yes ☐	No ☐
Have more trouble falling asleep than you usually do, or sleeping too much?	Yes ☐	No ☐
Feel tired out or low on energy all the time?	Yes ☐	No ☐
Feel unable to sit still and have to keep moving or the opposite feeling – feeling slowed down and having trouble moving?	Yes ☐	No ☐
Feel guilty or ashamed of yourself for something you did or thought?	Yes ☐	No ☐
Feel inferior or worthless?	Yes ☐	No ☐
Lose confidence in yourself?	Yes ☐	No ☐
Have trouble concentrating, thinking, or making decisions?	Yes ☐	No ☐
Think a lot about death, either your own, someone else's, or suicide?	Yes ☐	No ☐

People differ in how much their day to day activities are affected when they feel sad, depressed or lose interest in the things that they normally enjoy. The next questions are about how you were affected by this experience and these feelings during this same time that you have just described.

79. During those two weeks (or more), how much did these feelings and experiences **interfere with your life** (so much that it kept you from working, including such things as housework, children, and other activities or from seeing friends or relatives)?

Often ☐ Sometimes ☐ Rarely ☐ Never ☐

80A. Thinking about the last **10 years** when did this **MOST RECENT TIME** in your life start when you felt sad, depressed or had lost interest in things? (Please tick (✓) one month, if possible, and complete year)

Jan ☐ Feb ☐ Mar ☐ April ☐ May ☐ June ☐
July ☐ Aug ☐ Sep ☐ Oct ☐ Nov ☐ Dec ☐

19………….(show year) 20………….(show year)

80B. Is it still going on? Yes ☐ No ☐

IF NO

80C. About when did this **MOST RECENT TIME** end? (Again please tick (✓) one month, if possible, and complete year)

Jan ☐ Feb ☐ Mar ☐ April ☐ May ☐ June ☐
July ☐ Aug ☐ Sep ☐ Oct ☐ Nov ☐ Dec ☐

19………….(show year) 20………….(show year)

81. Have you in the past **10 YEARS** been particularly anxious, worrying more than you needed to about things for **SIX MONTHS or longer**? Yes ☐ No ☐

IF YES continue **IF NO GO TO QUESTION 89**

For the next few questions, please think of the **MOST RECENT** time in the **last 10 YEARS** when you worried a lot more than most people who were in the same situation, for **SIX MONTHS or longer**?

82. During this time did you worry?

- Every day ☐
- Just about every day ☐
- Most days ☐
- About half the days ☐
- Less than half the days ☐

83. During this time did you have **different worries** on your mind at the same time? Yes ☐ No ☐

84. During this time how often did you find it **difficult to control** your worry?

Often ☐ Sometimes ☐ Rarely ☐ Never ☐

85. During this time how often was your worry so strong that you **couldn't put it out of your mind** no matter how hard you tried?

Often ☐ Sometimes ☐ Rarely ☐ Never ☐

86. During this time did you **tell a doctor** about these feelings or take any medication? Yes ☐ No ☐

87. During this time did you **seek help** from anyone else, like a minister, or a friend, or did anyone suggest that you seek help? Yes ☐ No ☐

88A. About when did this **MOST RECENT TIME** start when you were nervous or anxious, worrying more than you needed to about things?
(Please tick (✓) one month, if possible, and complete year)

Jan ☐ Feb ☐ Mar ☐ April ☐ May ☐ June ☐
July ☐ Aug ☐ Sep ☐ Oct ☐ Nov ☐ Dec ☐

19.............(show year) 20.............(show year)

88B. Is it still going on? Yes ☐ No ☐

IF NO

88C. About when did this **MOST RECENT TIME** end?
(Again please tick (✓) one month, if possible, and complete year)

Jan ☐ Feb ☐ Mar ☐ April ☐ May ☐ June ☐
July ☐ Aug ☐ Sep ☐ Oct ☐ Nov ☐ Dec ☐

19.............(show year) 20.............(show year)

89. Do you usually see a solution to problems and difficulties that other people find hopeless?
Yes, usually ☐ Yes, sometimes ☐ No ☐

90. Do you usually feel that the things that happen to you in your daily life are hard to understand?
Yes, usually ☐ Yes, sometimes ☐ No ☐

91. Do you usually feel that your daily life is a source of personal satisfaction?
Yes, usually ☐ Yes, sometimes ☐ No ☐

E HOUSEHOLD CIRCUMSTANCES

The next few questions are about your household circumstances. They will provide us with extra information on factors which influence health. If you do not wish to answer them please move on to the next section.

92. In general, would you say you (and your family living with you) have:
More money than you need ☐ Just enough money ☐ Not enough money ☐

93. How often does it happen that you do not have enough money to afford the kind of food or clothing you/your family should have?
Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always ☐

94. How much difficulty do you have in meeting payment of bills?
None ☐ Very little ☐ Slight ☐ Some ☐ Great ☐ Very great ☐

95. Think of the ladder below as representing where people stand in the UK.

At the top of the ladder are the people who are best off – those with the most money, the most education and the most respected jobs. At the bottom of the ladder are the worst off – those with the least money, least education, and the least respected jobs or no job. The higher up you are on this ladder, the closer you are to the people at the very top; the lower you are, the closer you are to the people at the very bottom.

Where would you place yourself on this ladder?
Please place a large **X** on the ladder where you think you stand at this time of your life, relative to other people in the UK.

F YOUR FAMILY

We would now like to ask a few questions about your family as we have done in the past.

96. Were you your mother's first born child? Yes ☐ No ☐ Don't know ☐

97. Have any of your immediate family had any of the following conditions?
(Give the approximate age when the illness first occurred.)
(Please put **M** for male and **F** for female.)

	M/F	Alzheimer's	Dementia	Serious Memory Problems	None of these
Mother		age ☐☐	age ☐☐	age ☐☐	☐
Father		age ☐☐	age ☐☐	age ☐☐	☐
First brother or sister	☐	age ☐☐	age ☐☐	age ☐☐	☐
Second brother or sister	☐	age ☐☐	age ☐☐	age ☐☐	☐
Third brother or sister	☐	age ☐☐	age ☐☐	age ☐☐	☐
Fourth brother or sister	☐	age ☐☐	age ☐☐	age ☐☐	☐

THANK YOU VERY MUCH FOR ANSWERING THESE QUESTIONS

The next few questions are very personal. We realise that many people may not wish to complete them. However, we feel that there is a great deal to be learned from them. Please leave them out if you would prefer to.

FOR MEN ONLY

98. On average, in the last year, how many times did you have an erection?

- Never ☐
- Less than once weekly ☐
- More than once weekly, less than once daily ☐
- Once or more daily ☐

99. On average, in the last year, how many times did you have an ejaculation?

- Never ☐
- Less than once weekly ☐
- More than once weekly, less than once daily ☐
- Once or more daily ☐

100. How would you rate your sex drive:

In your thirties	1	2	3	4	5	6	7	8	9	10
(Please circle a number)	low sex drive .... high sex drive									
Now	1	2	3	4	5	6	7	8	9	10
(Please circle a number)	low sex drive .... high sex drive									

101. Do you have any of the following urinary symptoms?

	Yes often	Yes Occasionally	No	Don't know
Difficulty starting to pass urine	☐	☐	☐	☐
Discomfort on passing urine	☐	☐	☐	☐
Slow urine stream	☐	☐	☐	☐

THANK YOU VERY MUCH FOR ANSWERING THESE QUESTIONS

FOR WOMEN ONLY

102. How would you rate your sex drive:

In your thirties	1 2 3 4 5 6 7 8 9 10
(Please circle a number)	low sex drive .... high sex drive
Now	1 2 3 4 5 6 7 8 9 10
(Please circle a number)	low sex drive .... high sex drive

103. Have you ever taken Hormone Replacement Therapy (HRT)?

Yes ☐ No ☐ Don't know ☐

IF YES

104. Are you currently taking Hormone Replacement Therapy (HRT)?

Yes ☐ No ☐ Don't know ☐

105. If you are no longer taking Hormone Replacement Therapy (HRT), at what age did you stop?

☐☐ years old Don't know ☐

THANK YOU VERY MUCH FOR ANSWERING THESE QUESTIONS

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