Major Lower Limb Amputation in England 2003-2013:
The North/South, Gender and Ethnic Divide

Thesis Submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor of Medicine by

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Abstract

Background: The vast majority (>90%) of the 4000 major amputations undertaken in England every year in people aged 50 and over are related to peripheral arterial disease (PAD). Although it has the same underlying pathology as coronary heart disease similar epidemiological enquiry into inequalities has been lacking.

Aim: To a) describe the prevalence of major lower limb amputation across England in people aged 50-84 highlighting variations across regional, gender and ethnic groups b) determine the influence of geographical location, gender and ethnicity on risk of amputation both with and without revascularisation and c) perform a validation study to compare the sensitivity and specificity of hospital episode statistics database (HES) to hospital records.

Methods: Age standardised prevalence rates of amputation and revascularisation over a six year period (2003-2009) were calculated using HES as the numerator and census data as the denominator. The outcome measures 'amputation with' and 'without' revascularisation were created if the two procedures could be linked and used as a proxy for accessing services. The above to below knee ratio was also calculated. Logistic regression determined the odds of an amputation with and without a revascularisation unadjusted and repeated after controlling for demographic and disease risk factors. Prevalence was then re-calculated over a longer ten year period, 2003-2013, to determine if the patterns highlighted previously remained. To validate HES data, all above knee amputations undertaken in three hospitals over three years had their co-morbidities extracted and compared with the HES database. 90% accuracy was set as the standard.

Results: Between 2003 and 2009, 25 312 amputations and 136 215 revascularisations were undertaken of which 7543 cases were linked. The prevalence rate, per 100 000, of amputation and revascularisation was 26.3 and 141.6 respectively with amputation rates significantly higher in Northern England (North 31.7, Midlands 26.0, South 23.1), men (men 37.0; women 15.9) and the Black community (White 22.2, Black 37.6, South Asian 13.3). The above to below knee amputation ratio was higher in the North (North 1.3:1, Midlands 1.2:1, South 0.9:1) and women (men 1:1 women 1.5:1). The odds of having an amputation with a revascularisation remained significantly higher in the North (OR 1.22; 1.13-1.33) after controlling demographic and disease risk factors. The higher odds in the Black population (OR 1.83; 1.54-2.17) were, however, fully attenuated. The odds of an above knee amputation were lower in men (OR 0.64; .55-.74), diabetics (.44; .55-.74) and those having endovascular only revascularisation (OR 0.82; .75-.90). Between 2003 and 2013, overall major amputation rates fell by 18% but the regional and gender inequalities remained. Rates in diabetics fell at a faster rate than non diabetics in both men (38% vs 24%) and women (43% vs 19%). The sensitivity target for HES co-morbidity codes was only reached by coronary heart disease although HES had specificity of over 90% for all co-morbidities.

Discussion: Major lower limb amputation in England exhibited a North-South, gender and ethnic divide. Despite the overall prevalence falling over the last decade, inequalities remained. These differences were not wholly explained by variations in access, social deprivation or risk factors. A health needs assessment is required to understand and address these variations.

Publications

- **Ahmad N**, Chan C, Thomas GN, Gill P. Ethnic differences in lower limb revascularisation and amputation rates. Implications for the aetiopathology of atherosclerosis? Atherosclerosis 2014; 233:503-507
  Impact factor 3.994

- **Ahmad N**, GN Thomas, Gill P, Chan C, Torella F. Lower limb amputation in England: prevalence, regional variation and relationship with revascularisation, deprivation and risk factors. A retrospective review of English hospital data. J R Soc Med. 2014 Dec;107(12):483-9
  Impact factor 2.118

- **Ahmad N**, GN Thomas, Gill P, Torella F. Endovascular revascularisation is associated with a lower risk of above knee amputation than surgical or combined modalities. Analysis of English hospital admissions over a six year period. Int Angiol 2016;35:498-503
  Impact factor 1.462

- Ahmad N, GN Thomas, Gill P, Torella F. The prevalence of major lower limb amputation in the diabetic and non diabetic population of England 2003-2013. Diab and Vasc Dis Research 2016;13(5):348-53
  Impact factor 2.829

Prize:

- **Ahmad N**, GN Thomas, Gill P, Torella F. Influence of revascularisation modality on risk of an above knee amputations. Charing Cross International Symposium 2015

Declaration

The work presented in this thesis is the author's own work, and has not been presented, nor is currently being presented either wholly or in part for any other degree or qualification

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Synopsis

Background

Major lower limb amputation i.e. above the ankle is a devastating consequence of both diabetes and peripheral arterial disease (PAD). There is significant overlap of these conditions as over 90% of major amputations undertaken in England every year in people over 50 years are related to PAD - half of whom are diabetic. PAD affects the lower limbs, has the same underlying pathology as coronary heart disease and classically presents as intermittent claudication (cramping pain in calves on walking). It can, however, lead to foot ulcers, gangrene, and ultimately amputation.

Most people with PAD die from cardiovascular disease (CVD) i.e. coronary heart disease (CHD) and stroke (CVA). Much of the original research on CVD was stimulated by the high and unequal distribution of mortality across England and ultimately informed national strategies for improved health outcomes. Over the last 25 years, mortality rates from CVD have fallen significantly but inequalities remain as rates are higher in men, older populations, Northern England and South Asians. Similar research and policy into lower limb amputation is lacking.

Relevance of Issue

Major lower limb amputation represents a significant change to a patients' quality of life. It is not only associated with a high mortality rate, but for those who survive, represents a significant cost to the NHS related to both inpatient stay and post operative rehabilitation.

PAD has a prevalence of approximately 20% in those over 50, three quarters of whom are asymptomatic. The rest present with intermittent claudication. Over a five year period, less than one percent go on to have a major amputation. The national prevalence of major lower limb amputation has been reported at 5/100 000 although rates as high as 30/100 000 have been reported in those aged 65-74.

Exploring and understanding the variation in lower limb amputation rates has two benefits. Firstly, it acts as a proxy measure for the management of peripheral arterial disease and secondly, it can inform reduction strategies.

Previous Research and Gaps

There have been sixteen studies determining prevalence of major lower limb amputation in Great Britain. Of these 13 were based in England and studied the population between 1989 and 2010. An overall prevalence of 5/100 000 has been reported from the most recent studies. Rates were higher in men, older populations, diabetics and Northern England. Rates were lower in South Asians.

However, as a result of methodological differences, comparing studies and examining time trends was not possible as the actual rates have been questioned. There were also no national data reporting ethnic variations as they all emanate from single centre experiences. Finally, no studies examining amputation rates have determined the relative contribution of biological, demographic and atherosclerotic risk factors in a multi-variate analysis.

Rationale behind the description of revascularisation, ethnicity, demographic and co-morbidity data

The aim of the research was to provide accurate epidemiological data and describe inequalities surrounding the prevalence of major lower limb amputation in England. Most health inequalities can be ascribed to variation in either the demographic or risk factor profile of a population or their access to services. It is for this reason demographic (age, sex, ethnicity, social deprivation), atherosclerotic risk factors (diabetes, hypertension, hypercholesterolaemia, smoking, history or coronary heart diseases, history of stroke) and evidence of revascularisation was gathered.

The ethnic data analysis was limited to the 'South Asian' and 'Black' groups. South Asians were defined as either 'Indian', 'Pakistani', Bangladeshi' or 'Asian other'. South East Asians i.e. 'Chinese' were excluded. Black was defined as either 'Black African', 'Black Caribbean' or 'Black other'. Analysis was limited to these two groups for three reasons. Firstly, they form the main ethnic minority groups in England, secondly, the numerator and denominator populations used to calculate prevalence i.e. hospital episode statistics (HES) database and the census, used the same method and categories to assign ethnicity and finally previous inequalities research in South Asians had shown high rates of coronary heart disease and low rates of amputation.

Hypothesis

There is no variation in the prevalence of major lower limb amputation across English regional, gender and ethnic groups.

Aims

There were three aims;

1. To determine the prevalence of major lower limb amputation across English regional, gender and ethnic groups.

2. To determine the influence of revascularisation, demography and atherosclerotic disease risk factors on major amputation.

3. To assess the reliability of the health service data used in this research.

Objectives

There were three objectives;

1. To determine the influence of location on the risk of lower limb amputation with and without a revascularisation.

2. To determine the influence of ethnicity on the risk of lower limb amputation with and without a revascularisation.

3. To determine the reliability of the routine government health data used in this research.

The outcome measures for these three objectives were;

Objective 1. The Influence of Location on Lower Limb Amputation:

1.1 To calculate prevalence rates of;

a) Major lower limb amputation
b) Lower limb revascularisation

1.2 To identify a link, if any, between rates of lower limb revascularisation and major amputation across England

1.3 To determine whether regional differences in amputation with or without a revascularisation can be accounted for by differences in the demographic and risk factor profile of patients

Outcome Measures:

1. The prevalence rate, per 100 000, of major lower limb amputation and revascularisation across England

2. The odds of having an amputation with and without revascularisation across England unadjusted and adjusted for demographic and disease risk factors.

Objective 2. The Influence of Ethnicity on Lower Limb Amputation Rates

2.1 To calculate prevalence rates across White, South Asian and Black groups of;

a) Major lower limb amputation
b) Lower limb revascularisation

2.2 To identify a link, if any, between rates of lower limb revascularisation and major amputation by ethnicity unadjusted and adjusted for demographic and disease risk factors.

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2.3 To determine whether ethnic differences, if any, in amputations with or without a revascularisation can be accounted for by differences in the demographic and disease risk factor profile of patients

2.4 To determine the ratio of coronary to lower limb revascularisation across ethnic groups

Outcome Measures:

1. The prevalence rate, per 100 000, of major lower limb amputation and revascularisation in the White, Black and South Asian populations.

2. To calculate the odds of having an amputation with and without a revascularisation across the ethnic groups compared with the majority White British population unadjusted and adjusted for demographic and disease risk factors.

3. The ratio of coronary to lower limb revascularisation in the White, South Asian and Black ethnic groups

Objective 3: The Face Validity of HES Data

To compare procedural and co-morbidity data between HES and hospital records

Outcome Measures:

1. The calculate the sensitivity and specificity of HES data for the following six co-morbidities;
    a. Diabetes
    b. Hypertension
    c. Hypercholesterolaemia
    d. Coronary Heart Disease
    e. Cerebrovascular disease
    f. Smoking

Structure of Thesis

The thesis is written up as one report although the methods and results sections have subdivisions that reflect the aims of the study.

Chapter 1: Introduction

Chapter 1 begins by describing the principals underlying health inequality research and uses cardiovascular disease as an example of outcomes variation by regional, gender and ethnic groups. A background to PAD is then presented followed by a literature review on the prevalence of major lower limb amputation in England. A description of the data sources used for this report is then given followed by the demographic profile of England concentrating on the population studied in this project i.e. 50-84years, by English region, gender and ethnic groups.

Chapter 2: Methods

The method section describes the eight step process used to gain access to the HES database (step 2.1.1-2.1.4), calculate prevalence rates (step 2.1.5), link amputation with revascularisation data (step 2.1.6-2.1.7) and finally perform logistic regression to calculate odds of amputation with and without a revascularisation by geographical location and ethnicity (step 2.1.8). Section 2.2 describes the additional analyses performed and highlights the process of determining the proportion of coronary to lower limb revascularisation by ethnic group (section 2.2.1) and the ten year prevalence (2003-2013) of major amputation and revascularisation across the whole population (section 2.2.2) and then the diabetic population (section 2.2.3).

The final section (2.3) describes a multi-centre audit undertaken to determine the sensitivity and specificity of HES data for coding patient amputation, demographic and co-morbidity data.

Chapter 3: Results

The results are split into 4 sections (3.1-3.4). Section 3.1 describes the prevalence of major lower limb amputation across age, sex and English regions as well as the influence of location on the odds of an amputation with and without a revascularisation (objective 1). Section 3.2 describes the prevalence of major lower limb amputation across ethnic groups and the influence of ethnicity on risk of an amputation with and without revascularisation (objective 2). It also describes the ratio of coronary to lower limb revascularisations in different ethnic groups (objective 2). Section 3.3 describes the 10 year time trends of major (and minor) amputation and revascularisation prevalence from 2003-2013 in the whole (section 3.3.1 to 3.3.4) and diabetic (section 3.3.5) population. Finally, section 3.4 describes the sensitivity and specificity of HES data for coding procedure numbers and co-morbidity (objective 3).

Chapter 4: Discussion

The final chapter summarises the findings of the research, places the research into context, describes the additional knowledge gained and limitations of the research. It finally discusses future research directions.

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List of Abbreviations

Abbreviation	*Title*
AAA	Abdominal aortic aneurysm
Afro-Cab	African-Caribbean
AK	Above knee
AMP	Amputation
ASR	Age standardised rate
BK	Below knee
BMI	Body mass index
BP	Blood pressure
CHD	Coronary heart disease
CI	Confidence interval
CLI	Critical limb ischaemia
CPRD	Clinical Practice Research Database
CRP	C-reactive protein
CVA	Cerebrovascular accident (stroke)
CVD	Cardiovascular disease (combined term for CHD and CVA)
DM	Diabetes mellitus
GLEAS	Global lower extremity amputation study
HC	Hypercholesterolaemia
HES	Hospital episode statistics
HRG	Healthcare Resource Group
ICD-10	International classification of diseases – version 10
IMD	Indices of multiple deprivation
LEA	Lower extremity amputation
NHS	National Health Service
ONS	Office National Statistics
OPCS	Office Population Census Survey
PAD	Peripheral arterial disease
Pak	Pakistani
PR	Proportional rate
QoF	Quality improvement framework
SA	South Asian
SE	Standard error
TASC	Trans-Atlantic Society Consensus
TIA	Transient ischaemic attack
UK	United Kingdom
US	United States
WHO	World Health Organisation

Chapter 1: Introduction

1.0 Concepts behind Health Inequality Research

'the highest standards of health should be within reach of all, without distinction of race, religion, political belief, economic or social condition'

World Health Organisation, 1946[1]

There are many variations in health that are seen across populations and accepted such as older people being generally sicker than the young. However, other variations such as poorer outcomes in socially deprived children are seen but deemed unacceptable. It is these variations i.e. not within the immediate gift of individuals that are deemed unacceptable. Health inequality occurs when such variations are systematic, socially produced and unfair.[1]

The core concept underpinning health inequality research, therefore, is to remove systemic unfairness within the system and promote social justice. However, the term 'health inequality' itself is used to describe examples of both acceptable and non-acceptable variation. Other inter-changeable terms commonly used are variation, disparity and inequity. Although, all these terms essentially describe difference, they do not imply injustice. Clarification is therefore required when using such terms. In this thesis, the term inequality, when used, is simply to describe difference and not imply systemic injustice.

The causes of health outcomes variation is complex. It includes the traditional modifiable and non modifiable causes, but also the social determinants of health. These are described in section 1.1.1.

1.1.1 The social determinants of health

The 'social determinants of health' model (figure 1) describes the multi-factorial causes of ill health and links the biological and social causes. The model itself is a multi-layer framework with the individual at the centre and surrounded by health modifying factors of reducing personal control.

The model acknowledges the responsibility of the individual but incorporates the role of health professionals and government in creating an environment where health is promoted.

Figure 1
The Social Determinants of Health[1]

Policies that seek to improve health outcomes, therefore, need to address these social determinants in addition to the biological and lifestyle factors.

1.1.2 The Health Gap across England

The Office National Statistics (ONS) measured the health gap across England based on occupation from the 2011 census.[2] Social class was split into 7 where class 1 were higher managerial and professional workers e.g. doctors, lawyers and architects and class 7 were workers such as labourers and bar staff. By comparing the health measure 'not good' between classes 1 and 7, the 'health gap' was calculated. Overall, the percentage of men reporting health as 'not good' was 13.7 in class 1 and 30.5 in class 7- the difference of 16.8 is the health gap. Figure 2 describes the health gap by region in men and women. It shows greater health inequality in the North compared with Southern England and in women compared with men.[2]

Health inequality is a major public health and government policy issue. The Marmot report reviewed health inequalities and found that inequality in illness costs the British economy around £32billion each year in productivity losses, £25 billion in lost taxes and welfare payments and £5.5 billion in additional health care costs.[3]

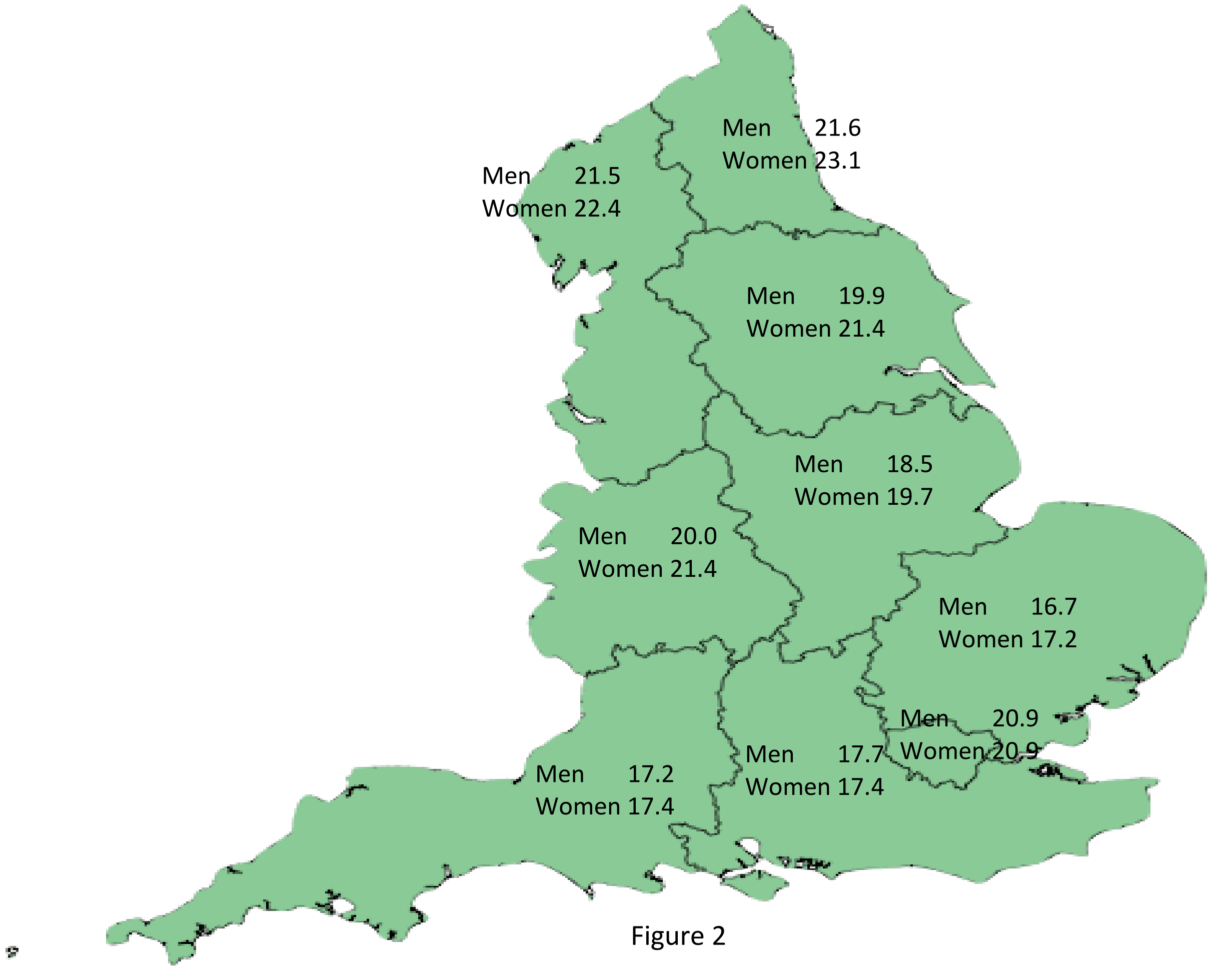


Figure 2

Health Gap between the least and most deprived populations across England; Men and Women based on census 2011[2]

1.2 Health Inequalities in England part 1:

Mortality from Cardiovascular Disease; a blueprint for Peripheral Arterial Disease?

1.2.1 Health Inequalities related to cardiovascular disease

Cardiovascular disease (CVD), the combined term for coronary heart disease (myocardial infarction and angina) and cerebrovascular disease (stroke and transient ischaemic attacks), is one of the conditions most strongly related to health inequalities.[4] Although death rates have declined overall, inequalities across England continue with the burden of morbidity and mortality disproportionately shouldered by groups with the lowest socio-economic status, as well as across geographical areas and ethnic groups.[4]

Understanding the variation surrounding CVD outcomes across English regions and populations is key to understanding variation around peripheral arterial disease (PAD). The two conditions are related by the same underlying disease process i.e. atherosclerosis, risk factors and treatment strategies. Furthermore, most patients with symptomatic PAD die from CVD. Strategies to reduce mortality from CVD involved mapping its epidemiology across England and then developing programs to reduce not only the overall rate but also the inequalities. A similar body of research does not exist for PAD.

The principle of using mortality from CVD as an outcome measure is analogous to a major amputation for PAD. This research aimed to provide an evidence base for inequalities in amputation rates across England and suggest future research directions. The following section describes the epidemiology of CVD across age, sex, regional and ethnic groups. It also presents variations in the risk factors for atherosclerotic disease for these groups.

1.2.2 Coronary Heart Disease

The age specific death rate in men and women between 1996 and 2006 for coronary heart disease (CHD) is shown in table 1. Rates were significantly higher in men compared with women and in older than younger groups. It shows how rates halved over a ten year period. Deaths from CHD and Stoke in those under 75 is of particular interest as these are defined as 'premature deaths' and the particular target of interventions.[5]

Table 1: Age specific death rate, per 100 000, of coronary heart disease between 1996 and 2006; United Kingdom Men and Women[5]

	Men		*Women*	
	1996	2006	1996	2006
45-54	112	72	22	15
55-64	384	194	119	52
65-74	1073	500	465	207

The rates have continued to fall from 2006. The overall age standardised death rate for those under 75 in 2011/2012 in men and women was 63.9 and 19.8 respectively.[6] For all ages, it was 189.9 and 90.3/100 000 in men and women respectively.[6]

1.2.3 Cerebrovascular Disease

The overall death rates for cerebrovascular disease (CVA) i.e. stroke are lower than CHD but the pattern i.e. higher in the older age groups, men and Northern England is the same.

Table 2: Age specific death rate, per 100 000, from Stroke: England and Wales; Men and Women 1996 and 2006[7]

	Men		*Women*	
	1996	2006	1996	2006
45-54	13	15	8	12
55-64	55	35	33	25
65-74	229	134	170	104

The age adjusted mortality rate, per 100 000, of cerebrovascular disease in England for all ages under 75 also continued to fall and in 2011/12 was 105.5 and 46.6 in men and women respectively.[6]

The mortality rate for both men and women was higher in Northern England compared with the South (figure 3).

1.2.4 Variation in the epidemiology of Cardiovascular Disease

1.2.4.1 Incidence

Although a poor measure of incidence, the best available evidence for gender variations in incidence of cardiovascular disease is hospital admissions. Admission for CVD was more common in men than women (men 10% women 6.2%).[6] There are no published data comparing variation in incidence of cardiovascular disease between Northern and Southern England.

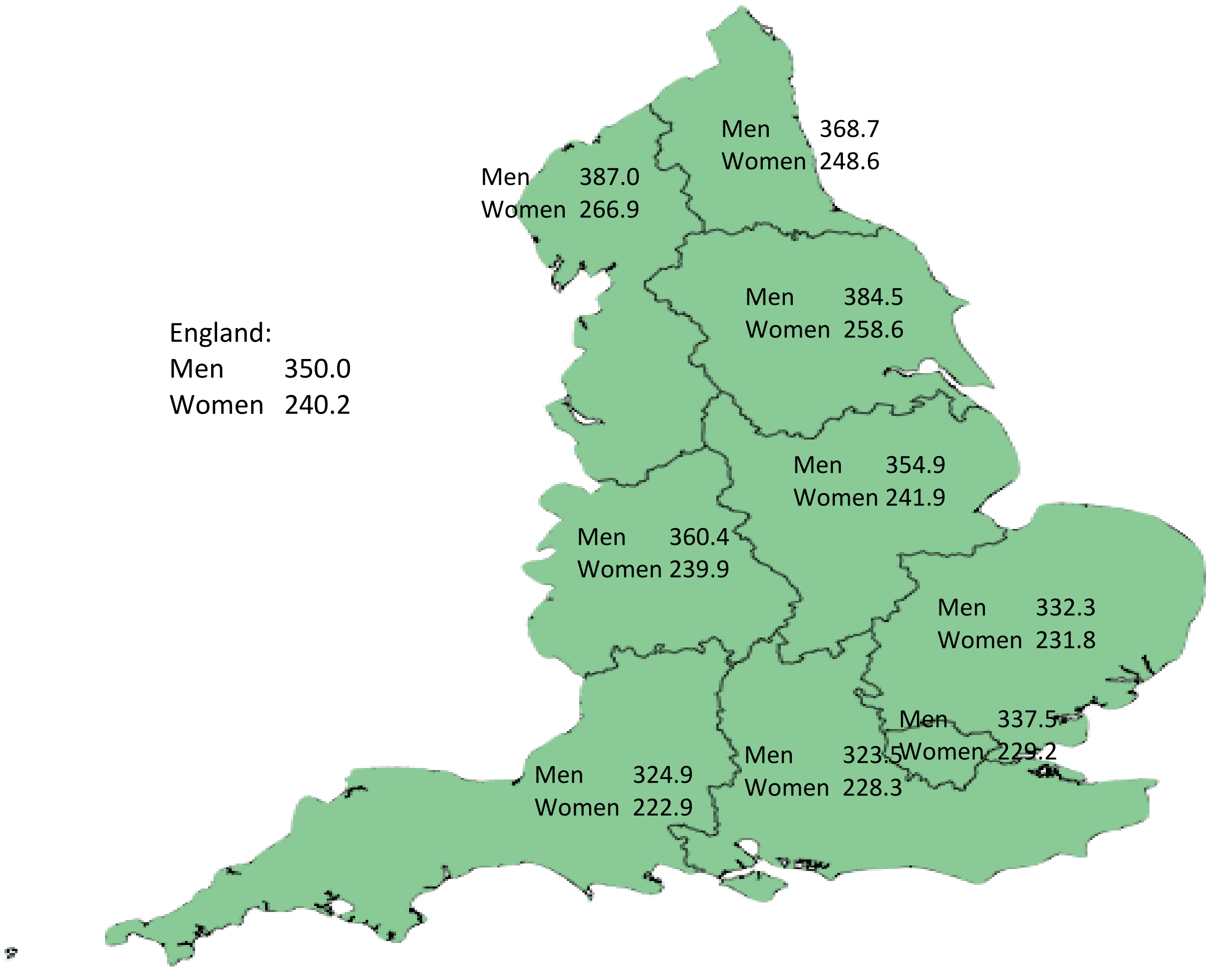


Fig 3

Age Standardised death rate, per 100 000, of Cardiovascular disease by region; Men and Women all ages 2011/12[6]

1.2.4.2 Prevalence

Prevalence of cardiovascular disease has been detailed from the Clinical Practice Research Datalink (CPRD). This is a database covering 8.8% of the UK population registered with a general practitioner. The prevalence of myocardial infarction and stroke was greater in men than women and older compared with younger age groups (table 3).

Table 3: Percentage Prevalence of Myocardial Infarction (MI) or angina and Stroke from General Practitioner Records; England 2013.[6]

	Men		*Women*	
	MI/Angina	Stroke	MI/Angina	Stroke
45-54	2.0	0.9	0.8	0.8
55-64	6.8	2.6	2.4	1.8
65-74	15.1	6.1	6.0	4.1
75+	27.6	14.6	15.7	12.2

Quality and Outcomes Framework (QoF) had led to improved records of patients with cardiovascular disease in GP practices. This has allowed regional variations in prevalence of cardiovascular disease to be explored. The prevalence was higher in Northern England compared with the South (figure 4) .[6]

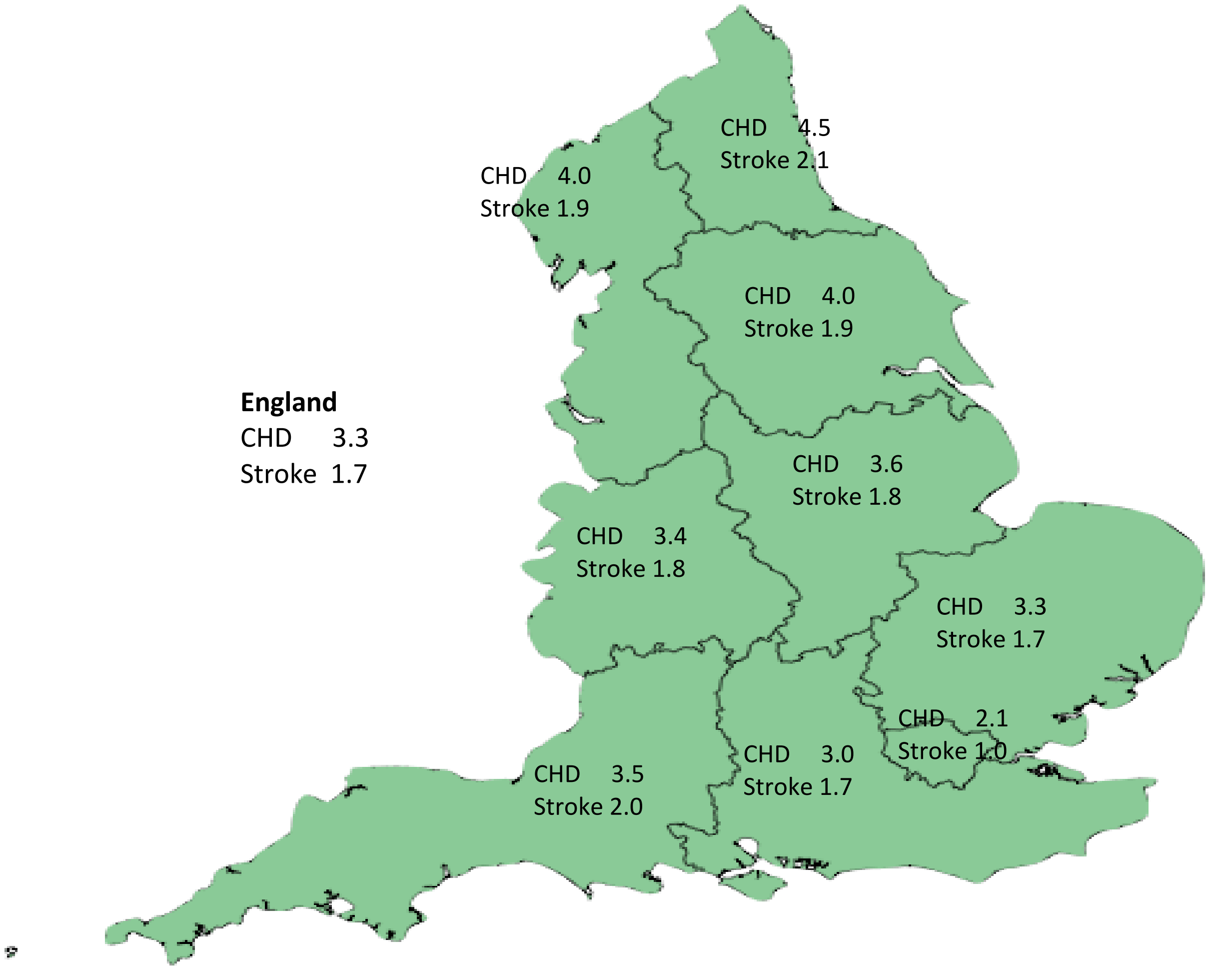


Fig 4

Percentage Prevalence of Coronary Heart Disease (CHD) and Stroke by English Region based on General Practice Data; Men and Women all ages 2012/13[6]

1.2.4.3 Treatment of Cardiovascular Disease

Data describing the variation in cardiovascular risk factors and treatment across England was poorly described.[4] There were no regional, gender or age breakdowns available. The only available data described the cost of treating CVD across England (fig 5).[6]

Treating CVD in England increased from £5.43 billion in 2003/4 to £6.99 billion in 2012/13.[6] There was variation across England and per head of population varied from £113.30 in the East Midlands to £141.5 in the South East. There was, however, no clear pattern - although Southern regions generally spent more than Northern ones. The majority of costs were related to secondary care with higher cost of emergency than elective care. The majority of primary care costs were related to prescribing.[6]

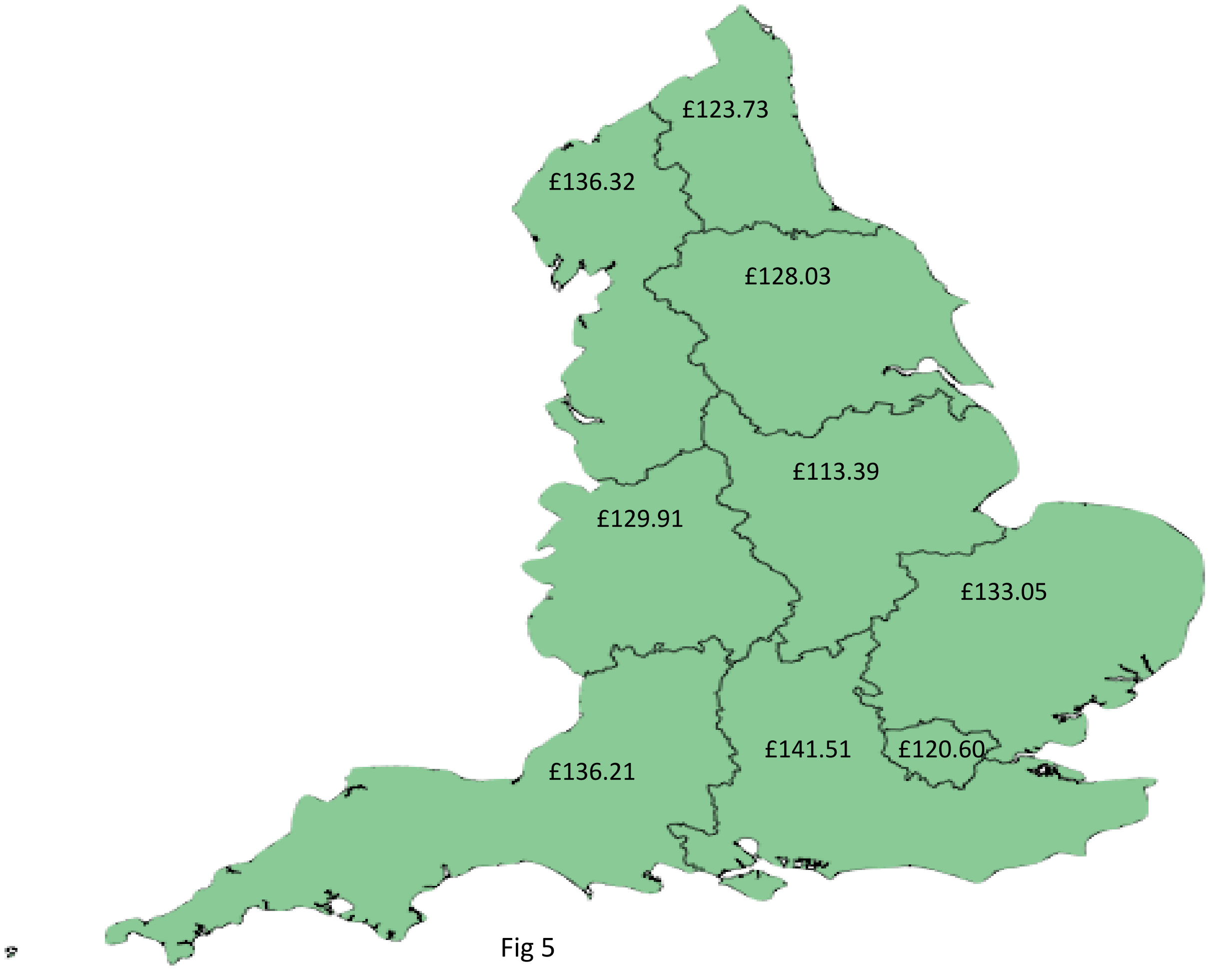


Fig 5

Treatment cost of cardiovascular disease per head of population by English Region: Men and Women all ages 2012/13[6]

1.2.4.4 Variation of Cardiovascular Disease across Ethnic Groups

The variation of CVD across ethnic groups has been the subject of intense study in England. The largest minority groups and the main focus of CVD mortality (as well as the present research) are the 'South Asian' and 'Black' groups. These ethnic categories are standardised and used across government departments and health data. South Asians are self-defined as either 'Indian', 'Pakistani', 'Bangladeshi' or 'Asian other'. They exclude those of far eastern heritage i.e. 'Chinese'. The Black groups are self-defined as 'Black African', 'Black Caribbean' or 'Black other'. A more detailed discussion regarding definitions of ethnicity and how these differ from race along with the demographic profile of all groups in England is discussed in section 1.7.4.

The variation in CVD mortality across ethnic groups is based mainly on the 'ONS longitudinal study'. This study takes a 1% sample of people from the 2001 census and follows up causes of mortality. The mortality rate for CHD and stroke by ethnic group is shown in table 4.[8]

Table 4: Age adjusted death rate, per 100 000, from CHD and stroke by ethnic group and Gender; England and Wales 2006/7.[8]

Ethnic Group	*Sex*	*All ages*		**Under 75**	
		CHD	Stroke	CHD	Stroke
White	Men	149	105	73	34
	Women	71	111	26	31
South Asian	Men	107	128	71	41
	Women	85	109	43	40
Black	Men	49	163	20	65
	Women	35	139	12	37

CHD – coronary heart disease

These data show that compared with the majority White population, South Asian men and women experienced greater rates of death from premature CHD whereas the Black population suffered greater rates of death from premature stroke. Afro-Caribbeans were twice as likely to have a stroke compared with Whites. South Asian men and women were 50% more likely to die from premature CHD than the general population.[8] There were no data on ethnic differences on CHD or stroke rate by English region.

1.2.4.5 Prevalence of atherosclerotic risk factors across ethnic groups

Table 5 describes the distribution of atherosclerotic risk factors across the ethnic groups residing in England based on the Health Survey for England.[9] This is an annual survey undertaken by the government since 1994 and collects data on the nation's health.[10] The data are collected from a representative sample of England from 9400 addresses selected at random from 588 postal code sectors. It collects data from an interview based questionnaire on physical health, lifestyle behaviours, social care, physical measures, mental health and wellbeing.[10] It also collects measurements including blood pressure, anthropometric and analysis of blood and saliva samples, as well as modules of questions on specific issues from year to year. In 2006 it published its Health of the Ethnic Minorities report from where prevalence of several atherosclerotic risk factors across several ethnic minorities was determined.[9]

Approximately one quarter of adult men and women in England smoked with the prevalence ranging from 20% in Indian men to 40% in Bengali men.[9] Smoking among South Asian women was uncommon (<5%) although in Black women levels were similar to men. Generally ethnic groups consumed more fruit and vegetables than the general population. Physical activity levels were generally lower in South Asians and higher in the Black Caribbean compared to the general population. Prevalence of hypertension was higher in the Black population and lower in South Asians compared with the general population. There was, however, heterogeneity, with higher levels in the Black Caribbean compared with the Black African population. Levels of hypercholesterolaemia were lower in all ethnic groups compared with the general population.[9]

The prevalence of diabetes is approximately 4% in men and 3% in women. Levels were more than double in all ethnic groups, particularly Black Caribbean and South Asian men and Black Caribbean and Pakistani women.[9]

Table 5: Distribution of atherosclerotic risk factors by ethnic group in England (all adults >16)[9]

Ethnic Group	Subgroup	Gender	% Smoke	% Diabetes	% Hypertension	% High Cholesterol†	Mean Fruit portions*	% Obesity‡	% High Activity**
General Pop		Men	24	4.3	32	66	3.3	23	37
		Women	23	3.4	29	67	3.6	23	25
South Asian	Indian	Men	20	10.1	33	60	4.2	14	30
		Women	5	5.9	18	53	4.4	20	23
	Pakistani	Men	29	7.3	20	55	4.3	15	28
		Women	5	8.6	15	53	4.0	28	14
	Bangladesh	Men	40	8.2	16	60	3.8	6	26
		Women	2	5.2	19	55	3.6	17	11
Black	African	Men	21	5.0	25	55	3.7	17	35
		Women	10	2.1	19	44	3.8	38	29
	Caribbean	Men	25	10.0	38	51	3.9	25	37
		Women	24	8.4	32	56	3.9	32	31

Data based on
Joint Health Surveys Unit. Health Survey for England 2004; The health of minority ethnic groups and The Stationary Office, London 2006
*Mean fruit portions per day ** high levels of physical activity † High cholesterol (>5.0mmol/l) ‡ BMI >30

1.2.5 Lessons from Cardiovascular Health Inequality Research

The research into cardiovascular disease epidemiology culminated in national strategies to reduce rates and inequalities as well as the development of theories to explain ethic variations.

1.2.5.1 National Strategies to reduce Cardiovascular Mortality

The reduction in cardiovascular mortality has been the result of a co-ordinated and sustained approach from Government aimed at improving public health.[11-15] These policies had targets which helped to focus the NHS on efforts to reduce mortality. However, despite the reduction, Heart UK[4], reviewing evidence relating to inequalities in cardiovascular disease found inequalities remained and gave recommendations as detailed in table 6.[4] Similar national policies have not been developed for peripheral arterial disease.

Table 6. Practical and Policy recommendations for reducing inequalities in cardiovascular disease[4]

1.	The government should consider the impact on health inequalities when developing domestic policies
2	Public Health England should foster the development of programmes to improve health literacy in CVD management, prepared in conjunction with expert health care professionals and patient relatives
3	Local authorities and clinical commissioning groups must work co-operatively and seamlessly with the NHS Commissioning Board in the delivery of high quality public health services and ensure that hard to reach and lower socio-economic groups have the best opportunities to access them
4	Public Health funding should remain ring fenced and sufficient to enable local authorities, in partnership with CGs and others, to deliver a reduction in health inequalities
5	Heart UK, welcomes the establishment of heath and wellbeing boards and urges then to carefully consider CVD risk, prevention and management as part of their Joint Strategic Needs Assessment and Joint Health and Wellbeing Strategies
6	In addition to life expectancy, Public Health England should measure gaps in risk factors for CVD between different geographic areas and between different social and ethnic groups to provide a more comprehensive picture of inequalities
7	The government should invest in addressing the full range of socio-economic factors that determine health inequalities which will help narrow regional disparities in life expectancy

1.2.5.2 Aetiological research

The ethnic variations in cardiovascular disease, particularly the higher rate of CHD in South Asians and Stroke in the Black population, have led to the development of aetiological theories as well as national strategies.[15-16]

1.2.5.3 Why is CHD more common in South Asians?

The prevalence of traditional risk factors for atherosclerotic disease do not alone account for the increased rate of coronary heart disease in South Asians – although increased prevalence of diabetes and poorer socio-economic status are partial explanations.[16] Some research has suggested an aetiological difference in causation.[17]

Greater levels of metabolic syndrome, particularly glucose intolerance and hyperinsulinaemia and an increased 'dose response' to insulin resistance has been suggested as increased levels of CHD in Asian diabetics compared with European diabetics. This suggested an increased susceptibility to atherosclerosis.[17]

Endothelial dysfunction appears to be at the core of atherosclerosis production of plaques partially through the reduced production of nitric oxide. Nitric oxide has multiple actions in the vasculature including flow dependent vasodilation, inhibition of leucocyte and platelet adhesion and aggregation, anti-proliferative and anti-apoptotic activity and the inhibition of vascular permeability - collectively, these functions are anti-atherosclerotic.[17]

Conditions that predispose to atherosclerosis such as hypercholesterolaemia, diabetes and cigarette smoking lead to endothelial dysfunction and altered production of bioactive molecules such as nitric oxide. As levels of diabetes, particularly insulin resistance, are higher in South Asians, the link between this and atherosclerosis has been examined.[17]

Insulin resistance is defined as resistance to the glucoregulatory actions of insulin. The underlying abnormality is thought to lie at one or more sites along the pathway linking the insulin receptor on the cell membrane to stimulation of glucose uptake via insulin-sensitive GLUT-4 membrane glucose transporters in the cell membrane. Insulin resistance is associated with vascular endothelial dysfunction in humans and there is a close correlation between insulin sensitivity and basal nitric oxide production.[17]

Obesity increases the risk of atherosclerosis. Although levels of obesity as measured by BMI are not different in South Asians, the waist-hip ratio, a measure of central or truncal obesity is higher. Truncal obesity is metabolised differently and is associated with insulin resistance through the release of adipokines e.g. leptin, TNF-α and angiotensin II, all of which influence endothelial function and promote atherogenesis.[17]

1.2.5.4 Why is stroke more common in the Black population?

Greater levels of hypertension are the main explanatory risk factors for higher rates of stroke in the Black population. Guidelines regarding the medical management of hypertension are modified for the Black population to reflect this.[18] The cause for the higher levels of hypertension is not understood and the link between genetic and environmental factors has not been elucidated. One theory is the Afro-caribbean population is more sensitive to salt, increasing the risk of developing high blood pressure.[19] This may be related to different ionic transport mechanisms, renal epithelial sodium channel, rennin-angiotensin-aldosterone system and vasoactive substances. However, at present there is no complete explanation for these differences.[19]

As most research has been conducted in the African-American population, the migration history has been cited as a potential cause. The suggested mechanism is that those that survived the journeys from Africa were those that did not become dehydrated through preserving salt in their kidneys. This has now become a disadvantage and led to hypertension.

1.3 Health Inequalities in England part 2:

Peripheral Arterial Disease and Lower Limb Amputations

1.3.1 Relationship between peripheral arterial and cardiovascular disease

There is considerable overlap between coronary, cerebral and peripheral arterial disease[20] as all three are different presentations of atherosclerosis. The proportion of people with clinically apparent atherosclerotic disease in the coronary, cerebral and lower limb circulations is given below.[21]

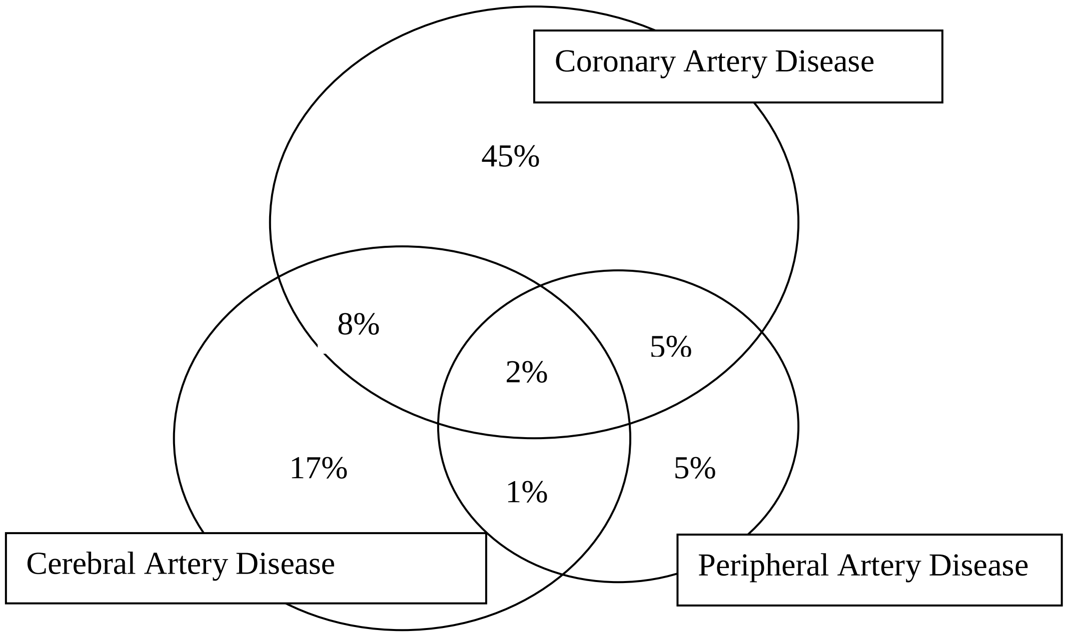


Fig 6
Typical overlap in clinically apparent vascular disease affecting different arterial territories[21]

1.3.2 Risk factors for cardiovascular disease

The risk factors for cardiovascular disease are identical for peripheral arterial disease and can be split into those which are modifiable, non modifiable and existing disease.

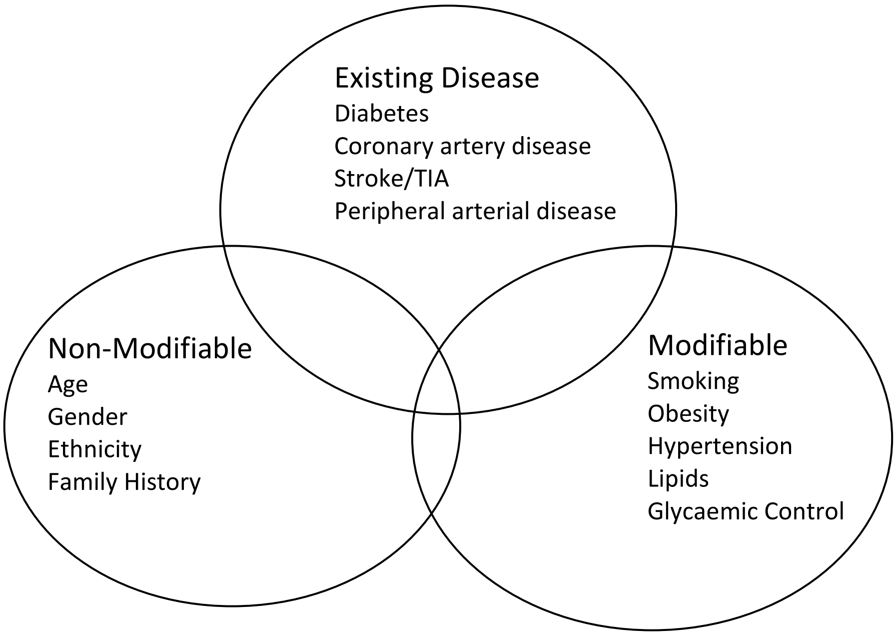


Fig 7

Risk Factors for Cardiovascular Disease[22]

1.3.3 Classification of Peripheral Arterial Disease

PAD is characterised by progressive arterial occlusive disease of the lower extremities.[20] It can be diagnosed based on symptoms - classically intermittent claudication (cramping pain in legs on walking) and signs such as absent peripheral pulses, ulcers, gangrene and amputation. Non invasive diagnosis can also be made using the ankle brachial pressure index. This is a ratio of the blood pressure taken at the arm and the leg (at level of malleoli). A ratio of <0.9 is 95% sensitive and 100% specific for detecting angiogram positive disease.[21]

The world-wide prevalence has been estimated at 3-10% increasing to 15-20% in individuals over 70.[21-25] The ratio of symptomatic to asymptomatic disease is up to one in three with as many as 50% never consulting a doctor.[21] Those with PAD have a three fold increase in risk of mortality from major cardiovascular events (heart attack and stroke) compared to those without PAD.[26-27]

PAD is classified by the Fontaine and Rutherford classification systems and ranges from asymptomatic, through to claudication and finally tissue loss and gangrene.

Table 7: Clinical Categories of Peripheral Arterial Disease. The Fontaine and Rutherford Classifications[22]

Fontaine	*Clinical Description*	*Rutherford*	*Clinical Description*	*Objective Criteria*
I	Asymptomatic	0	Asymptomatic	Normal exercise test
IIa	Mild Claudication Walks>200 metres	1	Mild Claudication	Completes exercise test AP after exercise <50mmHg But AP >25mmHg less than BP
IIb	Moderate to Severe Claudication Walks <200 metres	2	Moderate Claudication	Between categories 1 and 3
		3	Severe Claudication	Can not complete exercise test AP after exercise <50mmHg
III	Ischaemic Rest Pain	4	Ischaemic Rest Pain	Resting AP <40mmHg, Flat or barely pulsatile ankle PVR Toe pressure <30mmHg
IV	Ulceration or Gangrene	5	Minor Tissue Loss- Non Healing Ulcers, focal gangrene and diffuse pedal oedema	Either: Resting AP <60mmHg Flat or barely pulsatile ankle PVR Toe pressure <30mmHg
		6	Major Tissue loss – extending above metatarsal level	Same as category 5

AP: Ankle Pressure; BP: Blood Pressue; PVR: Pulse Volume Reading

1.3.4 Natural history of Peripheral Arterial Disease

The natural history of peripheral arterial disease is shown below.

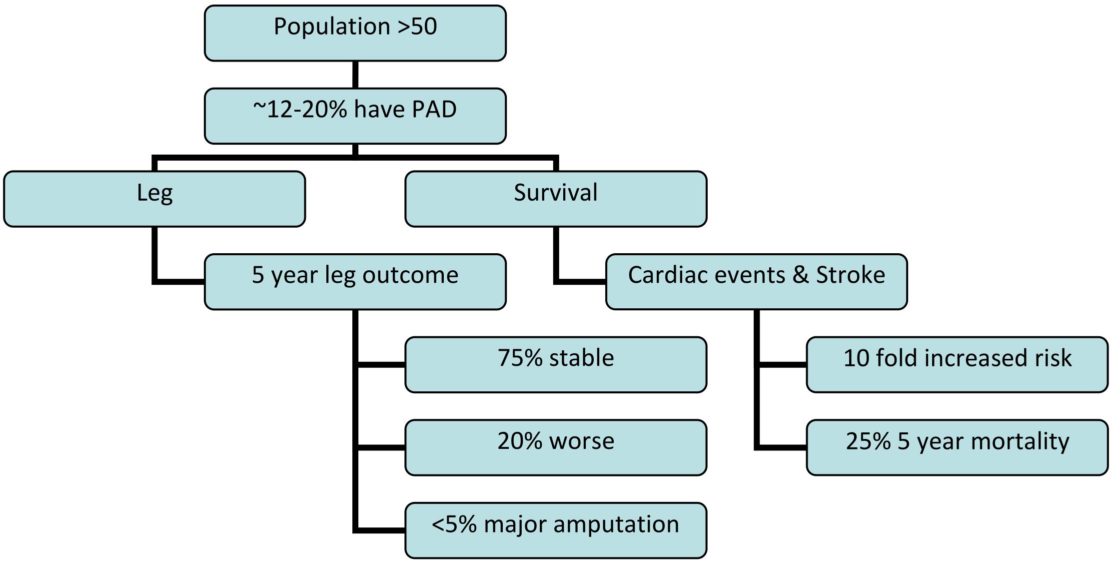


Fig 8

Natural History Peripheral Arterial Disease[28]

1.3.5. Critical Limb Ischaemia – definition, risk factors and epidemiology

Critical limb ischaemia (CLI) is a late complication of PAD with a European prevalence of 500-1000 per million.[21] It is defined as stage 3 and stage 4 in the Fontaine and Rutherford Classification respectively. The progression from intermittent claudication to CLI is related to diabetes (four fold risk), smoking (three fold risk) and hypercholesterolaemia (two fold risk) .[29] Approximately half of all patients with CLI have some form of revascularisation with 40% of those with no reconstructable disease undergoing amputation within 6 months and 20% dying within the same period.[21]

The influence of different risk factors on the progression of PAD into CLI was described by Dormandy et al[20] and is illustrated in figure 9.

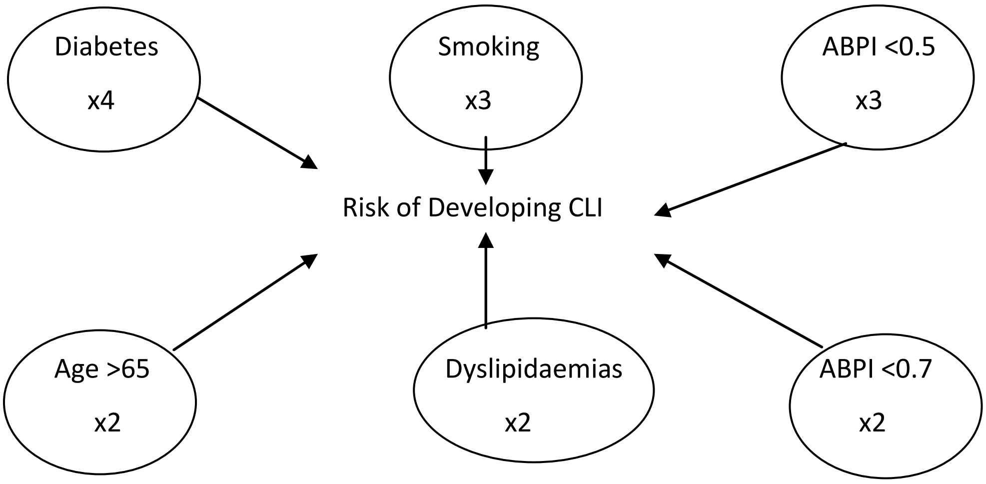


Figure 9

The influence of different risk Factors on the risk of developing Critical Limb Ischaemia[20]

1.3.6 Intervention for Peripheral Arterial Disease

Treatment for PAD can be either interventional or non-interventional. Non interventional strategies use exercise (with risk factor modification) to improve symptoms whereas intervention involves either an endovascular or surgical procedure.

The choice of intervention often takes a patient, limb and lesion approach.[30] Here, the overall condition of the patient, the haemodynamic status of the limb, the desired outcome (limb salvage versus symptom relief) and expected improvement in limb function are all considered.

Generally, supervised exercise therapy is offered to patients with claudication while intervention is reserved for those with critical ischaemia (table 8).

Table 8: Intervention strategies for peripheral arterial disease

Symptom	*Suitable for endovascular*	*Suitable for surgery*	*Strategy*
Claudication (mild/moderate)	Yes	Yes	Exercise therapy
Claudication (severe)	Yes	Yes	Endovascular if failed or unsuitable for exercise therapy
Rest pain/tissue loss	Yes	Yes	Surgery if fit, endovascular if not

1.3.6.1 Supervised Exercise therapy

The outcomes of a randomised trial comparing an exercise program for claudication due to femoro-popliteal disease compared with endovascular or combined treatment showed them to be equally effective in improving walking distance and quality of life.[31] Systematic review of randomised trials has shown consistent results of improved claudication distance following an exercise program with five factors associated with greatest improvements;[32]

- exercise that continued for more than 30 minutes per session
- at least three sessions per week
- walking used as the mode of exercise
- near maximal pain during training used as the claudication pain endpoint
- programme lasting at least six months

Improvements in walking distance of 122% were achieved.[32]

1.3.6.2 Endovascular Revascularisation

There are two types of endovascular techniques; angioplasty and stenting. Both are performed percutaneously as day case procedures under local anaesthetic. They do, however, require co-operative patients.

Angioplasty involves stretching a narrowed segment with a balloon inserted over a wire. A stent is inserted if it is felt that after ballooning a poor result is expected as a stent continues to provide radial force keeping the artery open (fig 10).

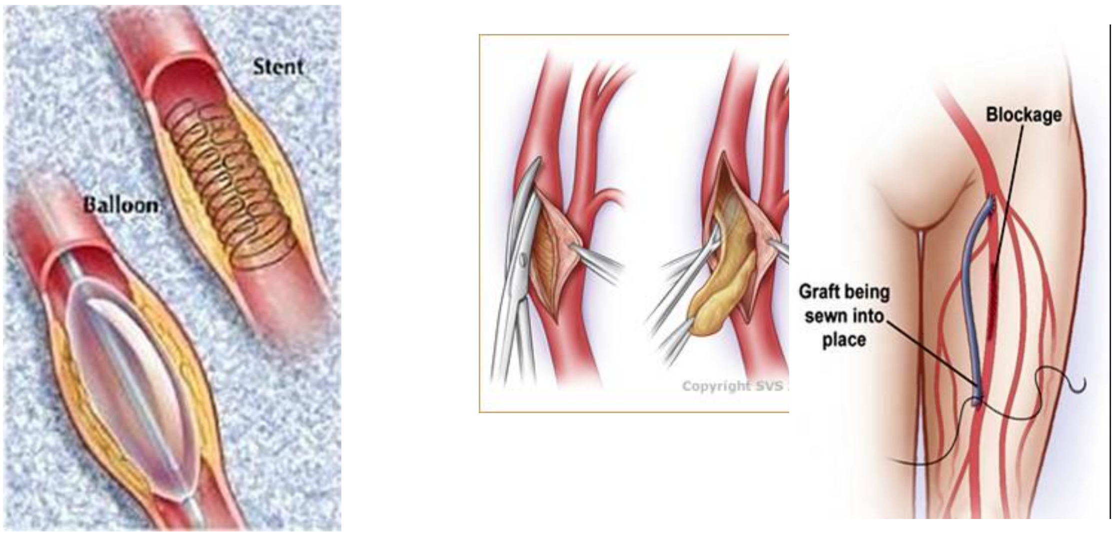


Fig 10
Endovascular and Surgical Techniques for atherosclerotic disease

1.3.6.3 Surgical Revascularisation

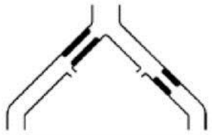
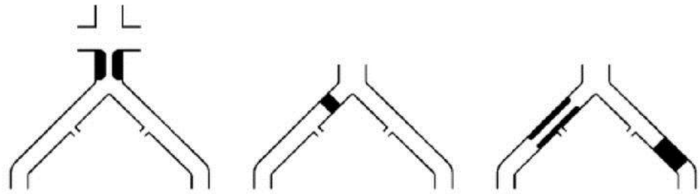
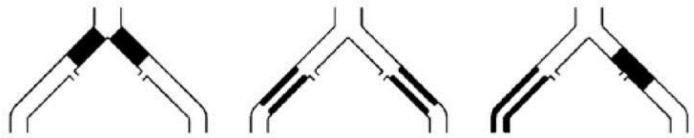
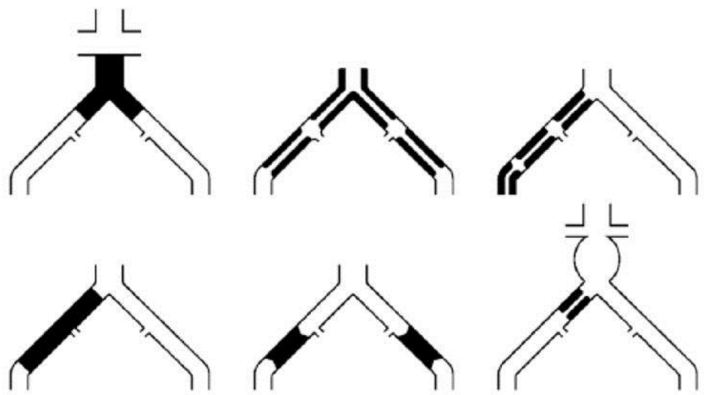
There are two surgical revascularisation techniques. The first is an endarterectomy where the plaque causing the stenosis is removed or a bypass where the occluded segment of artery is bypassed (fig 10). Bypasses are performed using either a native vein or prosthetic graft as a conduit.

1.3.6.4 Choice of endovascular or surgical revascularisation

The Trans-Atlantic, latterly, Inter-Society, Consensus Working Group (TASC) following literature review recently made recommendations for the type of lesion suitable for endovascular and surgical revascularisation (fig 11-13).[30] The lesions were grouped A-D where A represented, the least complex (focal stenosis), and D, the most complex (diffuse occlusive). TASC recommended type A lesions were most appropriately treated with an endovascular strategy and TASC D recommended for surgery. The updated 2015 guidelines additionally classified infra-popliteal disease and reclassified some complex lesions to less complex (TASC C to B) to reflect improved endovascular experience and outcome.[30]

The only randomised controlled trial comparing endovascular versus surgical revascularisation was the BASIL trial. This trial compared outcomes (amputation free survival) in patients with critical ischaemia and disease limited to the femoro-popliteal segment suitable for both endovascular and surgical revascularisation. Here, endovascular intervention was a less morbid procedure with equivalent quality of life outcomes and was significantly less costly than surgery.[33] However, in patients that lived for more than 2 years, there was better survival without a significant difference in amputation free survival.[34] Surgery, after failed angioplasty had a worse prognosis than primary surgery.[32]

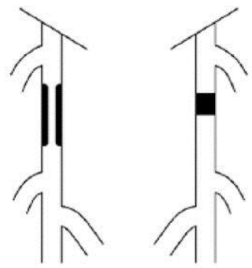
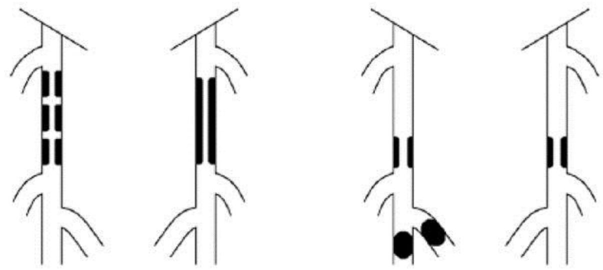
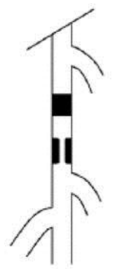
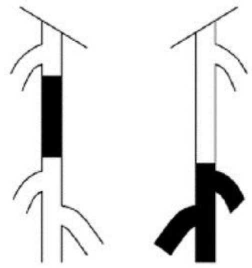
The BASIL II trial is currently underway. It has the same aim as BASIL I but is targeted at infra-popliteal lesions.

TASC A lesions • Unilateral or bilateral CIA stenoses • Unilateral or bilateral single short (≤3 cm) EIA stenosis	
TASC B lesions • Short (≤3 cm) stenosis of the infrarenal aorta • Unilateral CIA occlusion • Single or multiple stenosis totaling 3 to 10 cm involving the EIA not extending into the CFA • Unilateral EIA occlusion not involving the origins of the internal iliac or CFA	
TASC C lesions • Bilateral CIA occlusions • Bilateral EIA stenoses 3 to 10 cm long not extending into the CFA • Unilateral EIA stenosis extending into the CFA • Unilateral EIA occlusion involving the origins of the internal iliac and/or CFA • Heavily calcified unilateral EIA occlusion with or without involvement of the origins of the internal iliac and/or CFA	
TASC D lesions • Infrarenal aortoiliac occlusion • Diffuse disease involving the aorta and both iliac arteries • Diffuse multiple stenoses involving the unilateral CIA, EIA, and CFA • Unilateral occlusions of both CIA and EIA • Bilateral EIA occlusions • Iliac stenoses in patients with AAA not amenable to endograft placement	

TASC A:Primary endovascular TASC B:Endovascular Preferred TASC C:Surgery Preferred TASC:D Primary Surgery

Figure 11.

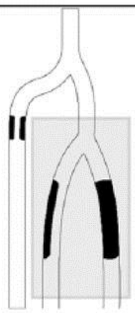
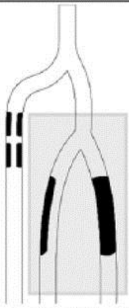
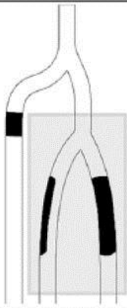
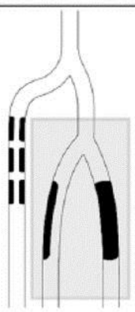
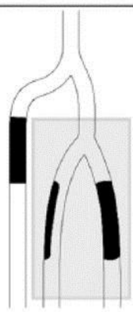
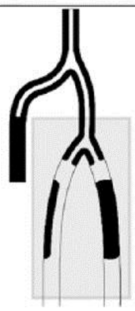
Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) classification of aorto-iliac lesions[30]

TASC A lesions • Single stenosis ≤10 cm in length • Single occlusion ≤5 cm in length	
TASC B lesions • Multiple lesions (stenoses or occlusions), each ≤5 cm • Single stenosis or occlusion ≤15 cm not involving the infrageniculate popliteal artery • Heavily calcified occlusion ≤5 cm in length • Single popliteal stenosis	
TASC C lesions • Multiple stenoses or occlusions totaling >15 cm with or without heavy calcification • Recurrent stenoses or occlusions after failing treatment	
TASC D lesions • Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery) • Chronic total occlusion of popliteal artery and proximal trifurcation vessels	

TASC A:Primary endovascular TASC B:Endovascular Preferred TASC C:Surgery Preferred TASC:D Primary Surgery

Figure 12

Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) classification of femoral popliteal lesions[30]

TASC A lesions Single focal stenosis, ≤5 cm in length, in the target tibial artery with occlusion or stenosis of similar or worse severity in the other tibial arteries.	
TASC B lesions Multiple stenoses, each ≤5 cm in length, or total length ≤10 cm or single occlusion ≤3 cm in length, in the target tibial artery with occlusion or stenosis of similar or worse severity in the other tibial arteries.	 
TASC C lesions Multiple stenoses in the target tibial artery and/or single occlusion with total lesion length >10 cm with occlusion or stenosis of similar or worse severity in the other tibial arteries.	 
TASC D lesions Multiple occlusions involving the target tibial artery with total lesion length >10 cm or dense lesion calcification or non-visualization of collaterals. The other tibial arteries occluded or dense calcification.	

TASC A:Primary endovascular TASC B:Endovascular Preferred TASC C:Surgery Preferred TASC:D Primary Surgery

Figure 13

Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) classification of infra-popliteal lesions[30]

1.3.7 Variation in the Prevalence of Peripheral Arterial Disease across England

The epidemiology of peripheral arterial disease across English regions, gender and ethnic groups as not been as extensively studied as CVD.

1.3.7.1 Age, sex and social class

The only large scale epidemiological study investigating prevalence of peripheral arterial disease in Britain was undertaken in a randomly selected Edinburgh population aged 55-74 in the 1980s.[23] The overall prevalence of claudication among this population was 4.5%.[23] The prevalence increased with age but did not differ between men and women. Prevalence was significantly higher in the lower social classes as measured by higher educational attainment with a prevalence of 5.5% in those only attending school and 2% attending university.[23]

A recent systematic review discussed the global prevalence and risk factors for peripheral arterial disease based on 34 studies measuring PAD as defined as ABPI equal to or less than 0.9.[35] They too found the prevalence of PAD did not differ significantly between men and women in either high or low income countries.[35] Prevalence increased with age and was 6.2% at age 50-54 and 15.9% at age 80-84 in Europe.[35] They estimated that between 2000 and 2010 prevalence rose significantly and increasingly with age. It rose by 12.2% in those aged 50-54 and 52.0% for those aged 80-84.[35]

1.3.7.2 Regional variation of PAD in England

The prevalence of those with a diagnosis of PAD in general practice has been published recently and provided an insight into the varying prevalence of PAD across England.[6] A North/South divide is evident with rates higher in Northern England (fig 14).

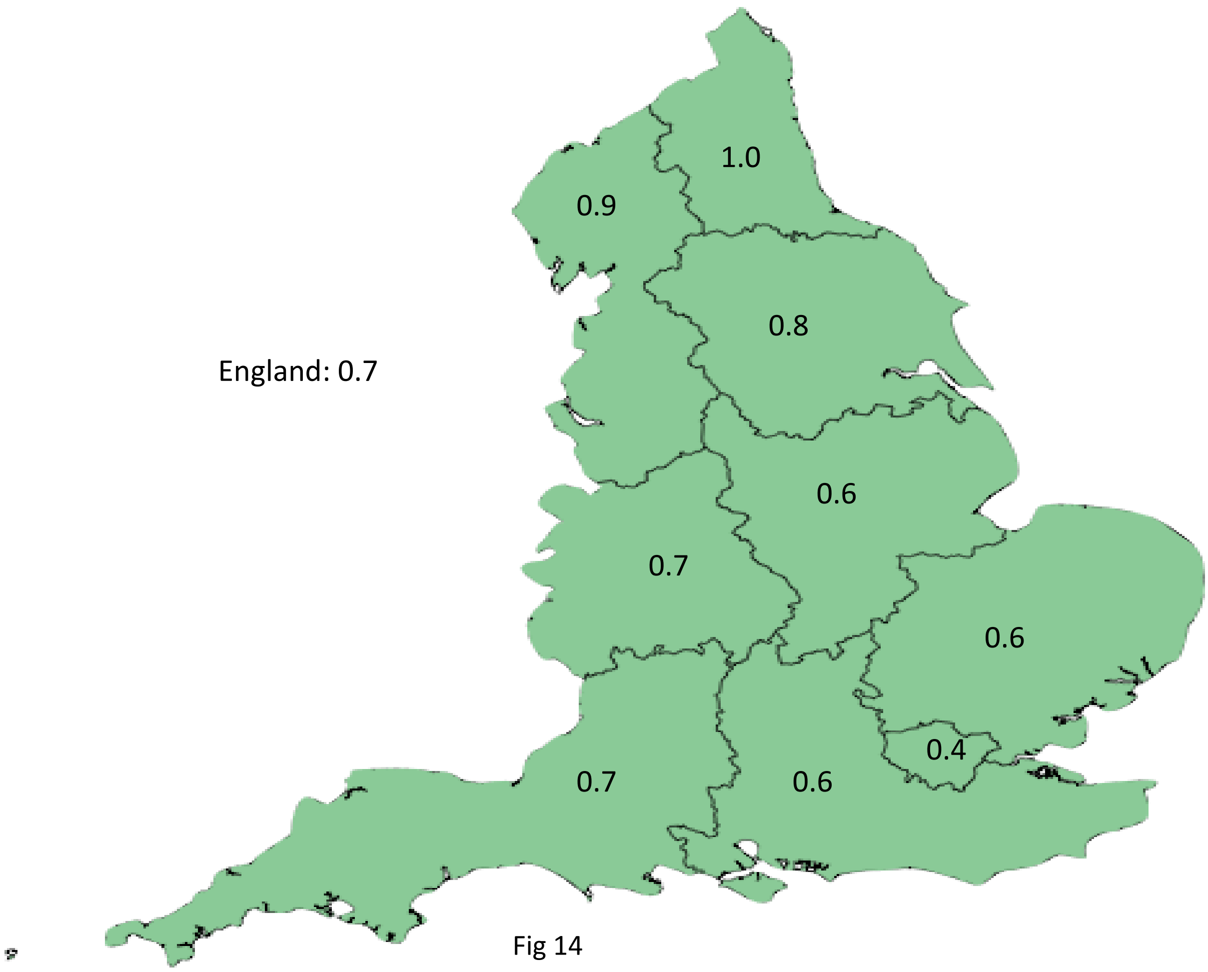


Fig 14

Percentage Prevalence of Peripheral Arterial Disease by English Region (based on General Practitioner Records); Men and Women all ages 2012/13[6]

1.3.7.3 Risk factors for PAD in the general population

Fowkes et al[35] reviewed 14 risk factors for PAD and created a meta-odds ratio based on effect size for risk factors that were investigated by at least three studies using multi-variate analysis. The odds ratios, based on sample sizes varying from 25 000 to 60 000 in Europe, that significantly increased the risk of PAD are detailed in table 9. History of cardiovascular disease (regarded as a evidence of co-existing atherosclerotic disease and not a causal factor for PAD) was 2.55.

Table 9: Risk Factors for PAD based on Meta-odds ratio[35]

	Risk Factor	*Odds ratio*	*Sig.*
Non Modifiable	age (per 10 year increase)	1.75	P<0.05
	male sex	1.43	P<0.05
Modifiable	Hypertension	1.55	P<0.05
	Diabetes	1.88	P<0.05
	Current smoker	2.72	P<0.05
	Former smoker	2.03	P<0.05
	Hypercholesterolaemia	1.19	P<0.05
	Hypertriglyceridaemia	1.26	P<0.05
	CRP	1.82	P<0.05
	BMI (>25mg/m2)	0.96	Not significant
	elevated LDL	1.03	Not significant
	low HDL	0.90	Not significant
	Fibrinogen	1.07	Not significant

1.3.7.4 Ethnic variation of PAD across England

The prevalence of PAD across ethnic groups living in England has been poorly studied.[36] Only one study determined prevalence in 356 South Asian and 216 Black people living in Birmingham.[37] The prevalence based on an ABPI <0.9 in those aged over 45 was 13.2% in South Asians and 10.2% in Blacks.[37]

In South Asians, there was no significant gender difference, but men were more likely to be hypertensive, smokers and diabetic. Men were also more likely to be on statin therapy and antiplatelets than women.[37]

In the Black population, the prevalence was higher in men compared with women (14.9% vs 6.1%). Men were more likely to be smokers, women had a higher BMI.[37] Variables associated with PAD on multivariate logistic regression are shown in table 10.

Table 10: Variables associated with PAD in English South Asian and Black populations [37]

Ethnic Group	*Variable*	*OR*	*Sig.*
South Asians	Age	1.02	Not significant
	Male Sex	2.81	<0.05
	Diabetes	2.14	<0.05
	Smoking	1.72	<0.05
	Systolic BP	1.02	<0.05
Blacks	Age	1.08	Not significant
	Male sex	0.65	Not significant
	Diabetes	1.01	Not significant
	Smoking	2.05	Not significant
	Systolic BP	1.01	Not significant

1.4 Types and causes of non traumatic lower limb amputation

There are two types of lower limb amputation, major and minor. Minor is classified as those below the ankle with major as above. These are shown below.

1.4.1 Minor Amputation

The main types of minor amputation are toe and transmetatarsal (forefoot) amputations.

Fig 15

Types of minor amputation

(left toe amputation, right transmetatarsal amputation)

However, more proximal minor amputations of the foot can be performed. These are either at the level of the proximal metatarsals joints (Lisfranc) or talar joint (Chopart)

1.4.2 Major Lower Limb Amputation

The main major lower limb amputations are below and above knee. Through knee amputations are performed, but rarely.

Figure 16

Types of major amputation (left Below knee, right above knee)

1.4.3 Causes of non traumatic lower limb amputation

The three main, often overlapping, causes of non traumatic lower limb amputation are peripheral arterial disease, diabetes and infection. Over 90% of amputations in people over 50 are related to dysvascularity.[38] Trauma and cancer are causes of major amputation in approximately 5% of cases.[38]

1.4.3.1 Diabetes and amputation

It is estimated that every 20 seconds someone in the world has an amputation related to diabetes.[39] Eighty five per cent of amputations in diabetics are precipitated by foot ulcers with half of these having an ischaemic component.[39] A foot ulcer is a general term to describe a full thickness wound below the ankle in a patient with diabetes, irrespective of duration.[39] The main factors leading to the development of foot ulcers are peripheral neuropathy, minor foot trauma, foot deformity and decreased foot perfusion.[39]

1.4.3.2 Pathology of diabetes and amputation

Sensory neuropathy results in loss of pain, awareness of pressure, temperature sensation and proprioception.[40] This lack of protective sensation leads to minor injuries e.g. ill fitting shoes which progress to ulcers as the initial injury is not felt.

Motor neuropathy, affects the intrinsic muscles of the foot and leg and results in atrophy and weakness. This results in flexion deformities of the toes, an abnormal walking pattern and ultimately instability of the foot. Autonomic neuropathy results in reduced or absent sweat secretion, causing dry skin, cracks and fissures. The combination of motor and autonomic neuropathy alters the biomechanics of the foot leading to increased plantar foot pressures and increased shear forces. This is caused additionally by disturbed collagen metabolism and non enzymatic glycosolation of proteins in the joint tissue and skin leading to joint stiffening.[40]

These changes lead to excess pressure, skin thickening and callus formation. The already abnormal loading is compounded by subcutaneous haemorrhage. The neuropathic bone and joint disease usually affecting the mid or hindfoot (Charcot foot) can cause additional deformity and plantar ulcers.[40]

1.4.3.3 Types of diabetic ulcers

Ulcers caused by increased mechanical stress are usually localised to metatarsal heads or plantar of the first digit, whereas decubitus ulcers are located on the heel. Ischaemic ulcers are usually located on the tips of toes and lateral part of the foot. Interdigit ulcers are usually caused by skin maceration and cracked skin (Fig 17).[40]

Neuropathic Ulcer | Decubitus Ulcer | Interdigit Ulcer | Ischaemic Ulcer

Figure 17
Types of Diabetic Foot Ulcers

Annually, seven percent of diabetics with neuropathic feet develop their first ulcer with 20% of all diabetics developing either a first or recurrent ulcer.[41] Approximately half of all new ulcers occur within two years of a healed ulcer.[40] Ten per cent of ulcers occur in patients who were previously unknown diabetics. Overall, approximately 60% of diabetic foot ulcers are associated with peripheral arterial disease.[40]

1.4.3.4 Diabetes and peripheral arterial disease

The pattern of atherosclerosis in diabetics is different than non diabetics and mainly affects the arteries below the knee.[39] PAD in conjunction with minor trauma may result in neuropathic ulcers. However, because of neuropathy, many diabetics may not have severe rest pain or claudication.

Diabetes is associated with a higher prevalence of PAD and increased risk of adverse outcomes.[40] Of asymptomatic patients with PAD (ABPI <0.9) and diabetes (type 1 or 2), 16% progressed to intermittent claudication, 3% to critical limb ischaemia and 1.6% to major amputation over a six year period.[40]

Patients with diabetes have heavily calcified atherosclerotic arteries and tibial artery occlusive disease. It is for this reason, ABPI readings are artificially high and toe pressures are generally used to assess perfusion. Diabetics also have lower technical success rates after revascularisation, limb salvage and patient survival.[28]

1.4.4 Infection

The incidence of foot infections in diabetic patients is much higher than the general population. The lifetime risk in the general population is 4% whereas in the diabetic population it is 4% annual risk.[42] Diabetics also have a ten fold increase risk of being hospitalized for lower limb infection, with most of these hospitalisations occurring in patients with poor glycaemic control.[42]

The common sequence leading to a foot infection is a foot ulcer (usually neuropathic) acting as a port of entry for bacteria, combined with ischaemia leading to necrosis. About half of all patients with a foot infection will undergo some form of lower extremity amputation, 10% of which will be major.[42] Figure 18 shows a typical diabetic foot ulcer leading to cellulitis (marked area).

Fig 18

Diabetic Foot Infection

(4th digit necrotic ulcer with a marked cellulitic area on dorsum of the foot)

1.5. Literature Review: Major Lower Limb Amputation in England

1.5.1 Summary

There have been thirteen studies describing the prevalence of major lower limb amputation in England published between 1998 and 2012. These are discussed in detail in this section. However, the additional 30 studies outside England have also been reviewed in line with the STROBE[43] guidelines and detailed in the appendix. Of the English studies, establishing time trends is difficult because of methodological differences such as not defining age groups studied, calculating prevalence using different definitions of amputation and denominator populations, variation in the use of age standardisation as well as different methods of presenting results – most did not present age and gender specific rates. It is therefore difficult to establish amputation trends across English regional, gender and ethnic groups. The English studies are described in table 11.

The overall rate of major amputation in England in the general adult population from studies published over the last 15 years was approximately 5/100 000. The rate was significantly higher in diabetics compared with non diabetics (approximately eight times higher), men compared with women (approximately three times higher) and varied approximately 20% across English regions. The rates were also higher in Black non diabetics compared with White non diabetics (three times higher) but lower in Black diabetics than White diabetics (50% lower) and 70% lower in South Asians (diabetics and non diabetics) compared with their White counterparts.

1.5.2 Prevalence of major amputation in England overall

Vamos et al[44] published two studies describing the prevalence of major amputation in England. The first described rates in 1996 and 2005 based on hospital data and found the overall rate in England to have decreased from 7.0 to 4.9/100 000. A subsequent study using similar methodology describing major amputation rates from 2004 to 2008 found the overall rate to have decreased from 7.7 in 2004 to 6.9/100 000 in 2008.[45] Moxey et al[46] described the major amputation rate in England between 2003-2008 using the same data and found it to be 5.1/100 000.

Table 11: Summary of Studies Describing Prevalence of Major Lower limb Amputation in England 2000-2012

Author	*Setting and Study period*	*Aims*	**Prevalence Rate per 100 000**		
			Group (age/sex)	Diabetic	Non Diabetic/ General population
GLEAS 2000[47]	International 10 sites across World, 4 in England 1995-1997	Compare LEA* rates across 10 centres all ages (0-80+) 4 English centres	Rate in 60-79 year olds (age adjusted rate 0-80+))		
			Men		
			Leeds:		80.0 (19.9)
			Leicester:		29.7 (7.2)
			Middlesborough:		121.5 (27.8)
			Newcastle:		74.3 (20.2)
			Women		
			Leeds:		34.6 (10.2)
			Leicester:		19.6 (4.3)
			Middlesborough:		29.2 (8.4)
			Newcastle:		31.4 (8.8)
Rayman 2004[48]	Ipswich 1997-2000 Single centre	Define incidence of LEA in DM, Prospective study	Major LEA	162	4.5
			1997/8	228	6.3
			1998/9	152	4.2
			1999/00	108	3.0
McCaslin 2007[49]	England 1989-2004	Describe national amputation and revasularisation rates in DM and non DM. Compared over individual years	Amputation		
			45-64:	1993:2.3 2004: 1.9	1989: 10.0 2004: 11.5
			65-74:	1996:7.8 2004:(5.0)	1994: 40 2004: 30.9
			75+	1994:11.2 2004:6.5	1989: 60.1 1993: 76.1 2004: 51.5
Canavan 2008[50]	South Tees 1995-2000 Single region	5 year incidence DM and Non DM LEA same area	Major amputation		
			1995/6:		
			1996/7:	310.5	8.7
			1997/8:	190.2	9.6
			1998/9:	132.9	12.4
			1999/2000	272.8	8.1
				75.8	15.3
			M:F ratio DM		
			M:F non DM	2.91	1.41
Vamos 2010[44]	England 1996-2005	Examine time trends LEA (maj and minor) in DM and non DM over 10 yrs. Describe 1 yr mortality post LEA	Major amputation Rate per 100 000	Type 1 1996:1.3 2005:0.7	 1996:7.0 2005:4.9
				Type 2 1996:2.0 2005:2.7	

Author	Setting and Study period	Aims	Prevalence Rate per 100 000		
			Group (age/sex)	Diabetic	Non Diabetic/ General population
Moxey 2010[46]	England 2003-2008	LEA rate across England and English regions and mortality	England		5.1
			NorthWest		6.2
			North East		7.2
			Yorkshire Humber		6.0
			West Midlands		5.1
			East Midlands		4.9
			South West		5.4
			South East		4.4
			London		3.9
			East England		4.4
			Mortality		16.7%
			BK:AK ratio		0.93
Holman 2012[51]	England 2007-2010	Determine incidence DM and non DM LEA across 151 PCTs	Rate per 1000 person years major amputation	0.99	
			Variation major amp acrossPCTs	0.22-2.20	0.01-0.16
			No North/South divide given		

*LEA: lower extremity amputation

1.5.3 Prevalence of major amputation by English Region

Unwin et al, as part of the GLEAS trial (Global Lower Extremity Amputation Study) described major amputation rates in ten cities across the world, with four in England between 1995 and 1997.[47] Their overall age adjusted rate (those aged 0-80) ranged from 29.7/100 000 in Leicester men to 121.5 in Middlesborough, it was lower in women and ranged from 4.3 in Leicester to 10.2 in Leeds.[47]

Canavan et al[50] using the same methodology as the GLEAS trial described the major amputation rate in South Tees between 1995 and 2000. The rate in diabetics reduced from 310.5/1000 in 1995 to 75.8 in 2000. The rate in non diabetics increased from 8.7/100 000 to 15.3 over the same time period.[50]

Rayman et al[48] described the prevalence of major amputation in diabetics and non diabetics in a single centre in Ipswich between 1997 and 2000. Over the three year period, the amputation rate in diabetics reduced from 162 to 109/100 000 and non diabetics from 4.5 to 3.0/100 000.[48]

Moxey et al[46] described the major amputation rate between 2003 and 2008 across the nine English government regions and found the overall rate ranged from 6.2/100 000 in the North West to 4.4/100 000 in the East of England.[46]

Finally, Holman et al[51] described the incidence of major amputation between 2007-2010 by Primary Care Trust (PCT) group. They found major variation across PCTs of 0.01-0.16 rate per 1000 person years.[51]

Describing a consistent pattern of amputation prevalence across England is difficult from the available evidence. A summary is, however, given in section 1.5.4-1.5.7

1.5.4 Prevalence of major amputation by age group

The only study detailing age specific rates of major lower limb amputation in England was McCaslin et al[49] who studied them between 1989 and 2004 in adults over 45. The rate in the 2004 general population aged 45-64, 65-74 and 75+ was 11.5, 30.9 and 51.5/100 000 respectively.[49] The prevalence in the 1989 population was 10.0, 40.0 and 60.1/100 000 respectively.[49] No overall figure or gender/ regional breakdown was given.

1.5.5 Prevalence of major amputation by gender

Gender breakdown of amputation rates was first described by Unwin et al[47] in the GLEAS trial, which reported amputation rates between 1995 and 1997. The overall age adjusted result was approximately two and a half times higher in men compared with women.[47] Canavan et al[50] describing amputation rates in South Tees between 1995 and 2000 found the male to female ratio to be 1.4 in non diabetics and 2.91 in diabetics. Vamos et al[45] describing prevalence between 2004 and 2008 found rates to be 40% higher in male non diabetics and 2.7 times higher in male diabetics compared with female counterparts.

1.5.6 Prevalence of major amputation by diabetic status

Rayman et al[48] described the major amputation rate in diabetics and non diabetics between 1997 and 2000 in Ipswich. The rate in diabetics at the end of the study period was 108/100 000 compared with the non diabetic rate of 3.0/100 000.[48] McCaslin et al[49], however, described the age specific major amputation rate by diabetic status across the whole of England. Surprisingly, the rate was much lower in diabetics where the rate, per 100 000, in 2004 in the 45-64, 65-74 and 75-84 age groups (non diabetics) was 1.9 (11.5), 5.0 (30.9), 6.5 (51.5).[49] The much lower result in diabetics was surprising.

Canavan et al[50] described a five year reduction of amputation by diabetic status between 1995 and 2000 in the South Tees region. At the end of the study period the rate in diabetics was 75.8 compared with 15.3/100 000 in their non diabetic counterparts.[50]

Vamos et al described the amputation rate by diabetic status in 1996 and 2005 using national data.[44] The rate in type 1 diabetes reduced from 1.3 to 0.7/100 000. In contrast type 2 diabetes rose from 2.0 to 2.7/100 000. Again the rate in the general population was similar to McCaslin et al i.e. higher in the non diabetic population but decreased over the same period from 7.0 to 4.9/100 000.[44] The second study by Vamos et al described amputation rates between 2004 and 2008 across England in adults over 17.[45] The rate in diabetics was over ten times higher than non diabetics in 2008 at 102 vs 6.9/100 000 respectively.[45]

1.5.7 Prevalence of major amputation by ethnic group

The reports on ethnic differences in lower limb amputation were limited to five single centre experiences (across three cities) with no national data provided. Table 12 summarises these studies.

Table 12: Summary of Studies Describing Prevalence of Major Lower limb Amputation in England by Ethnic Group 2002-2010

Author	*Setting and Study period*	*Aims*	*Definition of ethnicity*	*Results/100 000 (unless otherwise stated)*		
				Group	Diabetic	Non Diabetic/ General population
Leggetter 2002[52]	London (South East) 1992-1997	Incidence of LEA in Afro-Cab and White	Not given ?ethnicity variable	Major and minor amput >50 yrs		
				White	219	14
				Black	147	47
				Odds ratio Black vs White		
				Men		0.31 (Sig)
				Women		0.97 (NS)
				Odds ratio Men vs women		
				Black		0.86 (NS)
				White		2.66 (sig)
Chaturvedi 2002[53]	Manchester 1992-1997	Determine ethnic distribution of DM amputations in South Asians and Europeans	Patient appearance and parental origin	Odds ratio SA cf European Unadjusted OR		
				Men and women		0.37
				Adjusted for age at diagnosis		
				Asian men		0.33
				Asian women		0.20
Abbott 2005[54]	Manchester, UK 4 years (years not given)	Determine foot ulcer, PAD and amputation rate in diabetics by ethnic group	Patient appearance and parental origin	Percentage DM Hx Foot ulcer		
				White	5.5%	
				Asian	1.6	
				Black	3.0	
					5.1	
				All LEA amputation		
				White	1.3%	
				Asian	0.6	
				Black	1.4	

Table 12 continued: Summary of Studies Describing Prevalence of Major Lower limb Amputation in England by Ethnic Group 2002-2010

Author	*Setting and Study period*	*Aims*	*Definition of ethnicity*	*Results/100 000 (unless otherwise stated)*		
				Group	Diabetic	Non Diabetic/ General population
Hobbs 2006[55]	Birmingham 1997-2002 single institution	Determine incidence of PAD revascularisations and AAA in South Asians Pilot study for PAD prevalence and risk factors	Name analysis program, Asian vs non Asian Asian='Indian', 'Pak', 'Bengali and 'Asian Other'	Major amputation Cases seen (expected) Amp Asian Revas Asian		 6 (19.8) 11 (37.3)
Ndip 2010[56]	UK and USA Manchester and Texas Study year not given	Determine prevalence of lower limb complications in dialysis pts of different ethnic backgrounds	Self reported	% amputation White Hispanic African Asian	 15 20 21 9	

Leggeter et al[52] first reported the combined incidence of major and minor amputation in the Afro-Caribbean population of South East London between 1992 and 1997 using the GLEAS protocol. Here the rate in the non diabetic population was higher in the Black population compared with the White population (14 vs 47/100 000), however, the rate in diabetics was lower in Blacks compared with the White population (219 vs 147/100 000).[52] The rate in South Asians was described by Chaturvedi et al[53] in Manchester between 1992 and 1997. Here, although the prevalence rate was not given, the odds ratio of an amputation in South Asian men and women aged 40-74 was 0.37 compared with the White counterparts.[53] The sex specific age adjusted odds ratio in South Asian diabetic men and women was 0.33 and 0.20.[53]

Abbott et al[54] described the percentage of White, South Asian and Black diabetics attending a diabetes centre in Manchester who had a lower extremity amputation. The rate in the white population was 1.3%, the rate in the Asian and Black population was 0.6 and 1.4% respectively.[54]

Hobbs et al[55] described the actual and expected major amputation rate in South Asians aged over 55 attending a Mosque in Birmingham between 1997 and 2002. Here the amputation rate was 6/100 000 – they expected a rate of 19.8/100 000 applying epidemiological data to their population.[55]

Ndip et al[56] described the percentage of South Asians and Blacks on dialysis with diabetes who have had an amputation in Manchester and Texas, USA. They found no significant ethnic differences although rates were lowest in South Asians (White 15%, African 21% Asian 9%).[56]

1.5.8 Methodological weaknesses of studies

The methodological issues of studies describing amputation rates are summarised in table 13.

The thirteen studies reporting prevalence published between 2000 and 2012 studied populations between 1989 and 2010. Table 13 describes the main methodological weaknesses of these studies. Whilst most studies defined major amputation as those above the ankle, those employing the GLEAS protocol included forefoot amputation in their definition. There was often no description of age groups studied or the denominator population used for calculating prevalence. Results were rarely presented with age and gender specific breakdowns. The overall rate was rarely age standardised. Some used incorrect denominator populations i.e. using amputation numbers from England but using the whole of Great Britain as their denominator.[44,46] It was for this reason, two studies reported a lower amputation rate in diabetics than non diabetics.[44,49]

There are two consequences of these weaknesses. Firstly, lack of comparability has meant that comparison of prevalence over time and across populations is not possible. Secondly, more seriously, wrong results have been presented e.g. Moxey et al[46] presented prevalence as 5.1/100 000 whereas using their methodology it should have been 51/100 000. This is further detailed in section 4.2.

Table 13: Summary of Methodological Weaknesses of Studies Presenting Major Lower Limb Amputation Rates in England (13 studies in total)

Methodological weakness	**Number**	**Studies**
Did not provide time period of study	1	Abbott 2005[54]
Did not define age group studied	7	Leggetter 2002[52] Chaturvedi 2002[53] Rayman 2004[48] Abbott 2005[54] Vamos 2010[44] Moxey 2010[46] Ndip 2010[56]
Definition of major amputation included those below the ankle	7	Unwin 2000[47] Leggetter 2002[42] Chaturvedi 2002[53] Vamos 2010[44] Vamos 2010[45] Abbott 2005[54] Canavan 2008[50]
Did not define denominator population age groups	9	Rayman 2004[48] Abbott 2005[54] Hobbs 2006[55] Canavan 2008[50] Vamos 2010[44] Moxey 2010[46] Ndip 2010[56] Holman 2012[51] Leggetter 2002[52]
Did not provide source of denominator population	3	Rayman 2004[48] Vamos 2010[44] Vamos 2010[45]

Table 13 continued: Summary of Methodological Weaknesses of Studies Presenting Major Lower Limb Amputation Rates in England (13 studies in total)

Methodological weakness	**Number**	**Studies**
Did not age standardise results	7	Leggetter 2002[52] Rayman 2004[48] Abbott 2005[54] Vamos 2010[44] Vamos 2010[45] Moxey 2010[46] Ndip 2010[56]
Did not provide age specific results	*10*	Leggetter 2002[52] Rayman 2004[48] Abbott 2005[54] Hobbs 2006[55] Canavan 2008[50] Vamos 2010[44] Vamos 2010[45] Moxey 2010[46] Ndip 2010[56] Holman 2012[51]
Did not provide gender specific results	10	Leggetter 2002[52] Rayman 2004[48] Abbott 2005[54] Hobbs 2006[55] McCaslin 2007[49] Canavan 2008[50] Vamos 2010[44] Moxey 2010[46] Ndip 2010[56] Holman 2012[51]
Did not provide definition of ethnicity	1	Leggetter 2002[52]

1.6 Data Sources used to Study Major Lower Limb Amputation in England

The present work used national datasets to determine the prevalence of major lower limb amputation in England. The primary sources of data were the Hospital Episode Statistics (HES) database for numerator figures and the census for the denominator population. This section provides background to these databases.

1.6.1 Hospital Episode Statistics (HES)

Hospital Episode Statistics (HES) is a computer database and processes over 125 million inpatient, outpatient and accident and emergency records from English NHS hospitals and NHS patients treated in private hospitals each year.[57] Each horizontal line of data represents a patient admission, linked to a consultant under whom that care was given. Each line is termed a 'finished consultant episode' (FCE), thus individual patients may have several FCEs if they have either multiple admissions in one year or their care was transferred to different consultants during the same admission or a combination of the two. The majority of admissions, however, are patients with a single FCE. For each FCE, HES records clinical, administrative, geographical and demographic information and runs to over 200 columns per FCE. A full list of variables can be found in the appendix.

Data is collected over the financial year. The HES database was started in 1989 following a government report authored by Dame Edith Korner (1921-2000). Prior to this recommendation, only a 10% sample of admissions were collected.[57]

1.6.2 From Patient notes to Hospital Episode Statistics – the data journey

The clinical activity during an admission is eventually transferred to HES after being coded in a standardised manner that involves the translation of medical terminology, as written by clinicians, to describe a patient's diagnosis and treatment into a coded format which is nationally and internationally agreed. Upon discharge from hospital, a clinical coder translates the hospital notes pertinent to the admission into codes using two classification systems, ICD-10[58] for diagnosis and OPCS-4[59] for interventions. This information is added together with administrative and demographic information such as patient age, address and length of stay and is sent securely from the individual hospital's computer system to a national database called the Secondary Uses Database (SUS).[60] Here, the approximately 26 000 codes are grouped into 1500 clinically relevant Healthcare Resource Groups (HRGs) and used by commissioners to pay providers using the Payment by Results system (PbR).[61] The coding process is normally completed within a few days of discharge and submitted to the SUS database on a monthly basis.

Each HRG is a clinically meaningful group of diagnoses and interventions that consume similar levels of NHS resources. They are maintained by the NHS Information Centre (Casemix Service) and produce the grouper software to enable ICD-10 and OPCS-4 codes to be assigned to HRGs.[61] The same grouping logic is included in SUS. There are tariffs for over 1500 HRGs, and were originally based on average cost of services but are now determined by best clinical practice rather than average cost. HRGs provide a currency payment for the average patient. As some patients vary from the average, top ops accommodate these differences. The final tariff received by the provider is multiplied by a nationally determined Market Forces Factor (MFF) to reflect that some care is more expensive in certain parts of the country than others.[61] The provider income under PbR is thus represented as;

Provider income = activity x price x MFF[60]

SUS, having grouped the patient data into HRGs, assigns the relevant tariff and applies any pricing adjustments. Commissioners and providers extract reports from SUS, which they use to compare and financially adjust for the difference between actual activity and the expected contract value. This can result in either an additional payment from the commissioner to the provider if actual is greater than planned for vice-versa.[61]

From the SUS database, the anonymised data are sent through to HES where they are used for planning, monitoring and research purposes.[57]

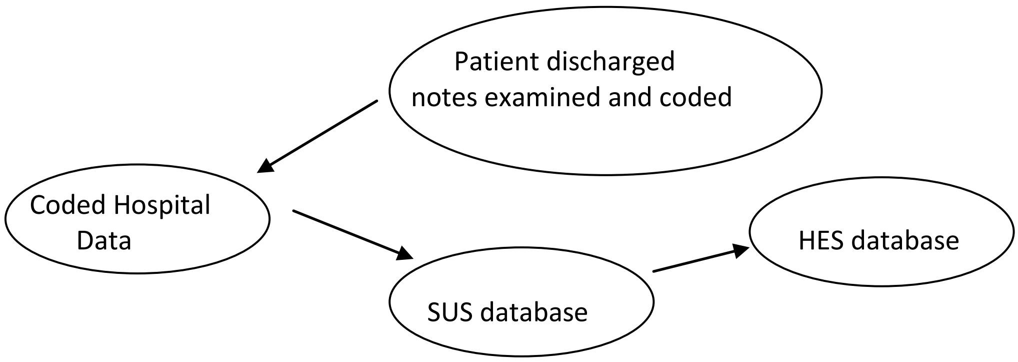


Fig 19
Movement of patient information from hospital notes to the HES database

1.6.3 Process of coding at hospital level

Improved use of Hospital Episode Statistics (HES) for monitoring health and performance was part of the government response to Prof Kennedy reports on cardiac heart surgery at Bristol Royal Infirmary 1994-1995.[62] As a result, improved systems for

HES coding were developed. It is now the responsibility of the Health and Social Care Information Centre (HSCiC) to provide confidence in the quality of coded clinical data.[63] The training for clinical coders is rigorous and provided through accredited Clinical Coding Academies which are run only by the NHS Clinical Classifications Service.[64] Training to become a qualified coder begins with a short training period of up to six week followed by a two year supervised placement and culminates in an exam.[65] After another minimum two year period and exam, a qualified coder can apply to become a trainer or auditor.[65] The qualification is administered through the Institute of Health Records and Information Systems (IHRIM)[66] and an accuracy of over 90% is required to maintain competence.

The clinical information used for coding is based on the 'source document'. This varies from hospital to hospital but is usually the patient's casenotes, but can include discharge summaries, pathology reports and hospital to GP documentation. Despite the rigorous training and assessment of clinical coders, concerns regarding the validity and accuracy of HES exist. The accuracy of coding is reliant upon the clinician providing all the information on the patient's diagnosis and treatment, dated, timed and signed with the clinical coder translating that information in the appropriate coded format to reflect the patient's hospital stay.[67] The coding standard states that clinical coders are not allowed to guess codes, nor can they code a 'query' diagnosis nor is it their responsibility to analyse information outside the admission episode.[67] The responsibility of accurately recording a patient's condition, co-morbidity and medical history and therefore ultimately coding accuracy is the admitting consultant.[67]

1.6.4 ICD-10 and OPCS codes and their use in the HES database

ICD-10[58] is the 10th revision of the International Statistical Classification of Diseases and Related Health Problems, a medical classification list by the World Health Organization (WHO). It contains codes for diseases, signs and symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or disease.

The code set allows more than 14,400 different codes and permits the tracking of many new diagnoses.[58] The codes can be expanded to over 16,000 codes by using optional sub-classifications. It was first endorsed by the Forty-third World Health Assembly in May 1990 and came into use in WHO Member States as from 1994. ICD is currently under revision, through an ongoing Revision Process, and the release date for ICD-11 is 2017.

The Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS)[59] is the procedural classification used by clinical coders within the NHS. The first NHS procedural classification was published in 1987. The fourth revision is currently used.[59]

OPCS-4 is an alphanumeric nomenclature, with a 4 character code system similar to that found in ICD-10. The first character is always a letter. Second, third and fourth characters are always numbers.

1.6.5 How accurate is HES data

Significant concerns regarding HES accuracy have been raised and although these are mainly related to diagnosis[68-70] unreliable clinical coding for common vascular[71] and urological[72] procedures have been described. Several research projects have looked at coding accuracy and a systematic review of these found the median accuracy of primary diagnosis and procedure to be 83%.[73] When comparing studies pre and post introduction of Payment by Results, no significant differences in the overall or procedure coding.[73]

Since the introduction of Payment by Results in 2004, improved data accuracy has gained prominence as poor coding results in care providers not being paid accurately by commissioners. The audit commission has been undertaking yearly audits as part of the Payment by Results Data Assurance Framework and found improved coding error from 9.4% in 2007[74] to 8% in 2013.[75] The financial effect of this error was calculated by the Audit commission where based on 78% of acute trusts in England with a total sample of 18 700 episodes of care (between 38 and 400 episodes per trust) with a financial value of £29.1 million the effect was undercharging commissioners by £100 000.[75] It has also been estimated that inaccurate coding could lead to loss of up to 10% in surgical departments income[118].[76]

There are no data on the accuracy of patient co-morbidity coding within HES.

1.6.6 The Census

The census has been undertaken every ten years since 1801 with the exception of 1941.[77] The date of the last census was Sunday 27th March 2011. It provides a demographic profile of the population of England, Wales, Scotland and Northern Ireland. It provides information that allows government to develop policies, plan and run public services and allocate funding. It is a statutory obligation to make a return and people refusing are liable to prosecution and a fine. Specially trained staff were employed to follow up cases where the householder refuses to make a return.[77]

1.6.7 Strategic aims of the Census

The census is the responsibility of the Office of National Statistics (ONS) with the census reporting through the UK Statistics Authority. The key strategic aims of the census are;[77]

- To give the highest priority to getting the national and local population counts right
- To maximise the overall response and minimise differences in response rates in specific areas and among particular population sub-groups
- To build effective partnerships with other organisations, particularly local authorities, in planning and executing the field operation
- To provide high quality, value for money, fit for purpose statistics that meet user needs and which are as consistent, comparable and accessible across the UK as is possible
- To protect, and be seen to protect, confidential personal census information

1.6.8 Information gathered by the census

Table 14: Information gathered from the census[77]

For households	*For residents in households*
Number and names of all residents whether present or temporary on census night	Name, sex and date of birth Marital status (including civil partnerships*) Relationship to others in household Student status
Tenure of accommodation	Whether or not students live at enumerated address during term time
Type of accommodation and whether it is self contained	Usual address one year ago Country of birth Citizenship (passports held)
Type of landlord	Month and year of entry in UK Intended length of stay in UK
Number of rooms and bedrooms	National identify and ethnic group Religion
Type of central heating	Language General health
Number of cars and vans owned or available	Longstanding illness or disability Provision of unpaid personal care Education and vocational qualifications Second residence Economic activity in the week before the census Time since last employment Employment status Supervisor status Hours worked Job title and description of occupation Name of employer and nature of industry Workplace address Means of travel to work

1.6.9 Cost of the census

The cost of the 2011 census was £450 million.[77] The content of the census was driven principally by the demands and requirements of census statistics, evaluation of previous censuses and guidance of organisation by extensive consultation, through formal advisory committees, topic related working groups, public meetings and via media such as ONS consultation and information papers and the census website.[77]

Forms were primarily delivered by post (95%) to every household in Britain with the form containing questions relating to each person usually resident in the household. The census was carried out with a field force of 30 000 staff with approximately 100 census area managers responsible to the enumeration of an area of 500 000.[77]

1.6.10 Under-enumeration in the census 2001 and 2011

To improve the accuracy of the population, under-enumeration was tackled by the 'One Number Census (ONC) project'.[78] Here, in both 2001 and 2011, the Census Coverage Survey (CCS)[79] estimated the level of under-enumeration and then imputed data based on similar characteristics from those in neighbouring areas.

This consisted of a completely independent survey of a sample from 19 500 postcodes containing 370 000 households from all local authorities from the UK. The CCS was independent of the census with a sample design to take into account the uneven distribution of under-enumeration by a 'hard to count' index. As many calls as needed at varying times of the day were undertaken and a face to face interview was taken. The overall response rate was 92% across the UK. It was deemed the survey succeeded in identifying persons missed by the 2001 census. The results of this study were then added to the main census after detailed quality assurance and extrapolated to provide a more complete picture of the UK population.[79]

The 95% confidence interval of the 2001 census population estimate following the additional CCS study was 0.2% i.e. 104 000 people in England and Wales, 0.3% in Scotland (17 000) and 0.7% (12 000) in Northern Ireland.[79]

1.6.11 Accuracy of Population Estimates

Between the census years, mid year population estimates are created based on births, deaths and net migration. The ONS has produced estimates for each year following the census. The mid year estimate is based on the change from 30th June previous year to 1st July current year. Recent analysis of the method showed the updated 2002-2010 estimates to be fit for practice.[80]

1.7 Demographic profile of England 2011

On census night, Sunday 27th March 2011, the population of the United Kingdom was estimated at 63.2 million[81] an increase of 4.1 million from 2001 (approximately 7%). The population of England was 53 012 456.[81]

1.7.1 Age Structure

The age structure of England (as well as the whole United Kingdom) is changing with an increasing proportion of people in the older age group. The main increases are coming from the post war generation (currently in their 60s) and those born in the 1960s baby boom years (currently in their mid 50s (figure 20).[81]

Whilst the overall population of England increased by 7%, each English region, however, was dynamic. For example, London increased by 11.6% whereas the North East rose by 2.2%. Certain cities saw very high growths e.g. Manchester saw an increase of 19.0%. The age structure of regions also differs, with London having a significantly younger population.

Figure 21, summarised by 'The Guardian' newspaper blog, details the changing population by English region as well as selective age structures.[82]

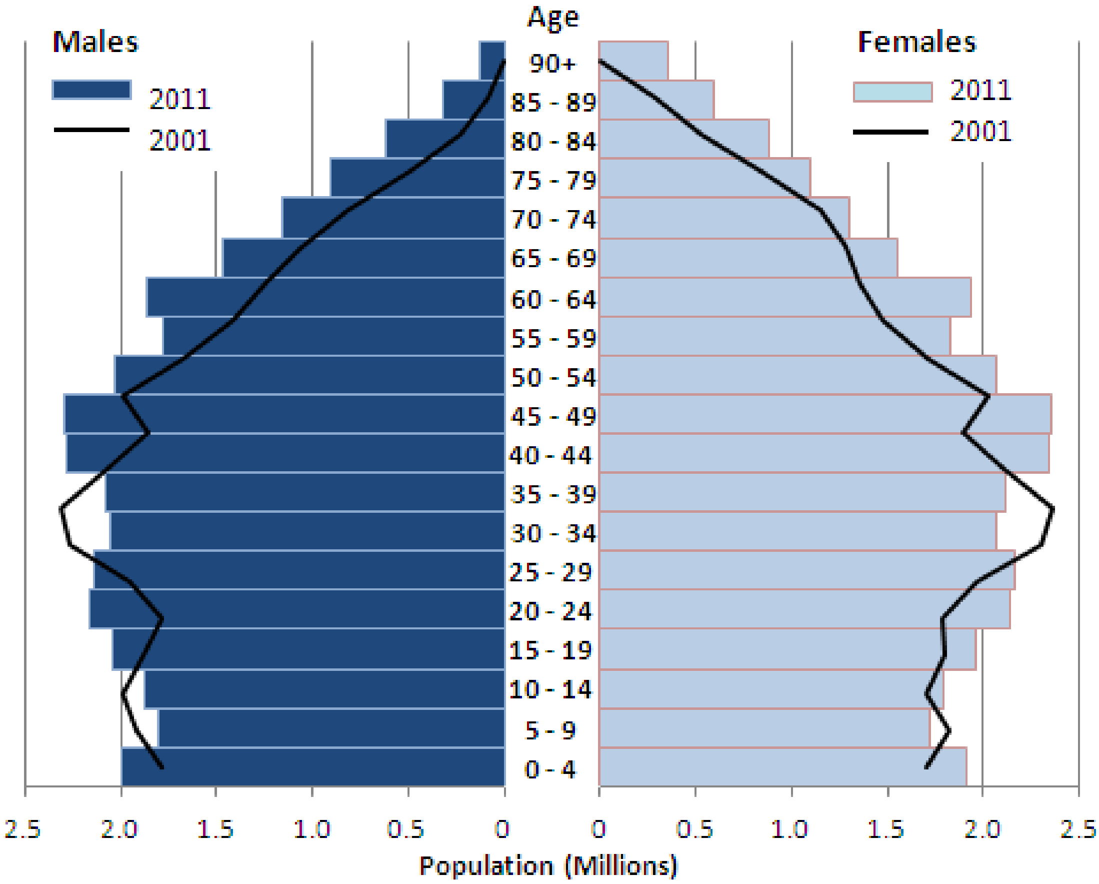


Figure 20

Population Age Structure; England 2011 and change from 2001;

Men and Women[81]

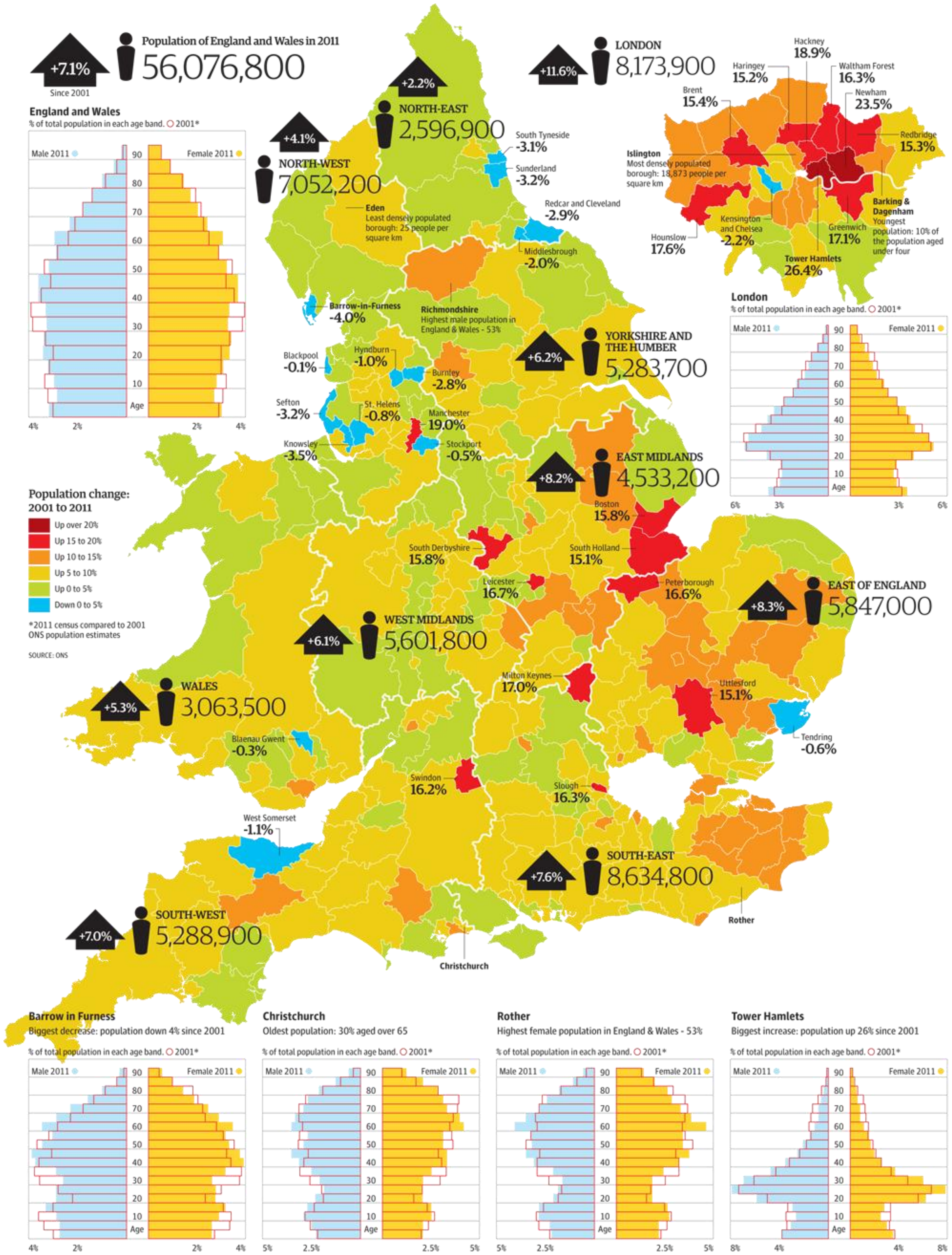


Figure 21

Summary of population change from 2001 to 2011 Census[82]

1.7.2 Median age across English regions

The median age for people living in England is 39.9.[83] The average age of death in England is 78 for a man and 82 for a woman, with an average age expectancy of 18 years from age 65.[83] The focus of this thesis was those aged 50-84. This population comprised 40% of the population of England. Those over 84 comprise 2% of the population and 0.8% of the population over 90.[81] Figure 22 details the median age of those living in each English region and the proportion of those aged 45-84.[81] Those aged 50-84 was not available in a standard published table.

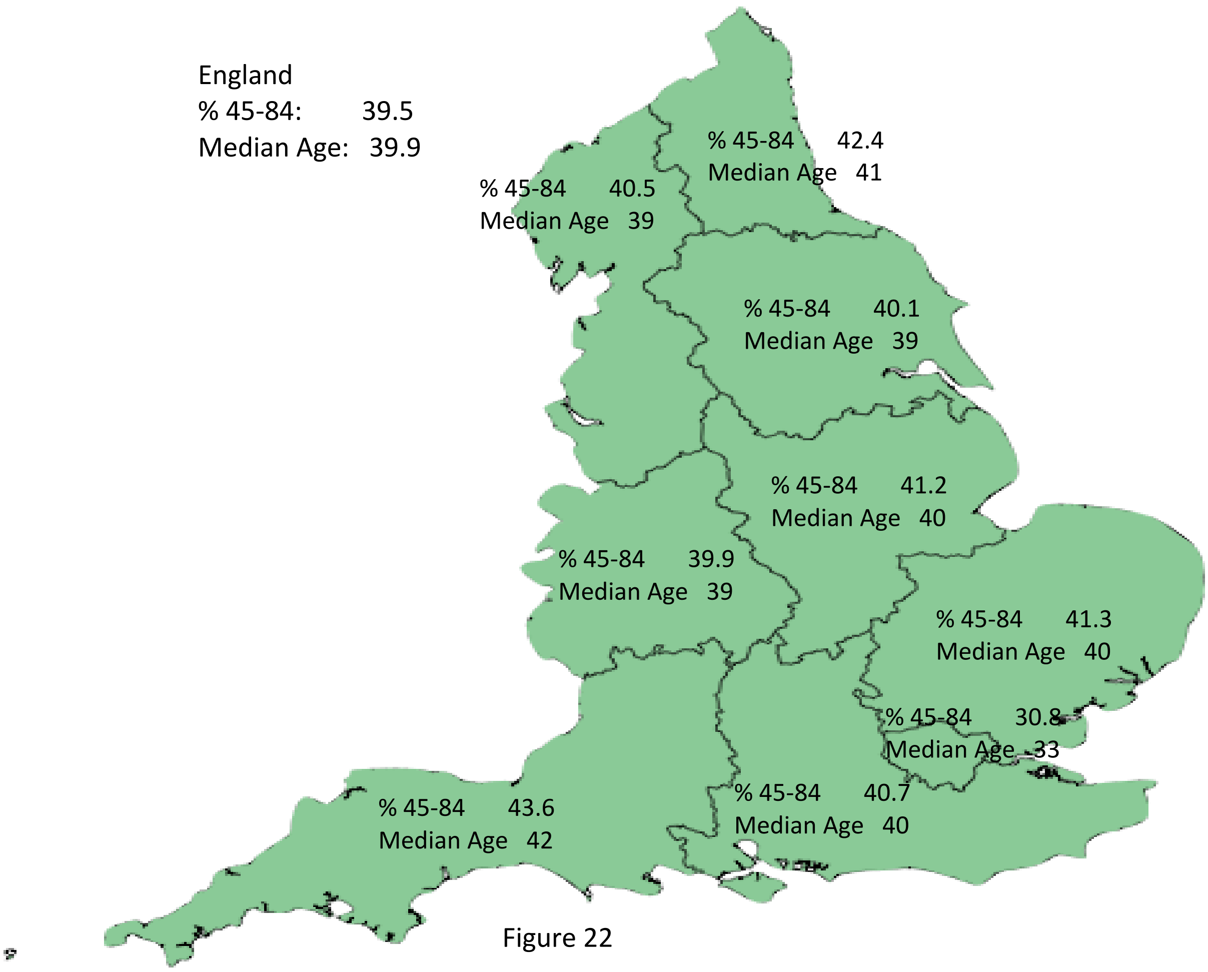


Figure 22

Proportion of population aged 45-84 and median age; England and regions.

Men and Women 2011[81]

1.7.3 Deprivation across England

There are several scores available to calculate deprivation. The main score used in England by government is the Indices of Deprivation score (IMD).[84] The IMD scoring system is based on 38 separate indicators organised across seven distinct domains, which are combined using appropriate weights. The domains are income (22.5%), employment (22.5%), health deprivation and disability (13.5%), education skills and training (13.5%), barriers to housing and services (9.3%), crime (9.3%), and living environment (9.3%). IMD scores are calculated for every Lower layer Super Output Area (LSOA). These are homogenous areas of relatively equal size containing approximately 1,500 people. Since their introduction in 2000, IMD scores have been used increasingly by the UK Government to plan public service provision in a variety of sectors, including healthcare.[84] The latest version is 2010.

Average scores across each English region are not available. However, figure 23 highlights that more deprived areas are located in the North of England compared with the South with eight of the ten most deprived areas found in the North West of England.

Figure 23

The English Indices of Deprivation England 2010[85]

1.7.4 Population of England by ethnic group

Table 15 describes the ethnic minority make up according to the 2011 census and the percentage change of ethnic minority groups from the 2001 census. The main ethnic groups and the focus of the thesis were the South Asian and Black populations. They comprised 10.4% of the population of England, an increase of 3.6% from the 2001 census.[86-87]

Table 15: Population by Ethnic Group England 2011 and percentage change from 2001 census[86-89]

		Population 2011	*% 2011 population*	*% change from 2001 Census*
All England		53 012 456	100	+7.3
White				
	British	42 279 236	79.8	+1.1
	Irish	517 001	1.0	- 0.3
	White Traveller**	54 895	0.1	
	White Other	2 430 010	4.6	+1.8
Asian		3 763 900	7.0	+2.4
	Indian	1 395 702	2.6	+0.5
	Pakistani	1 112 282	2.1	+0.6
	Bengali	436 514	0.8	+0.3
	Other	819 402	1.5	+1.0
Black		1 256 614	3.4	+1.2
	African	377 741	1.8	+0.9
	Caribbean	591 016	1.1	+0.0
	Other	277 857	0.5	+0.3
Chinese		379 503	0.7	+0.3
Other*		2 396 192	3.6	+1.4

* includes mixed ** not measured 2001

1.7.4.1 Profile of ethnic groups by English region

The ethnic minorities are clustered in certain areas around England. The majority are in and around London, West Midlands and Yorkshire and the Humber [figure 24].

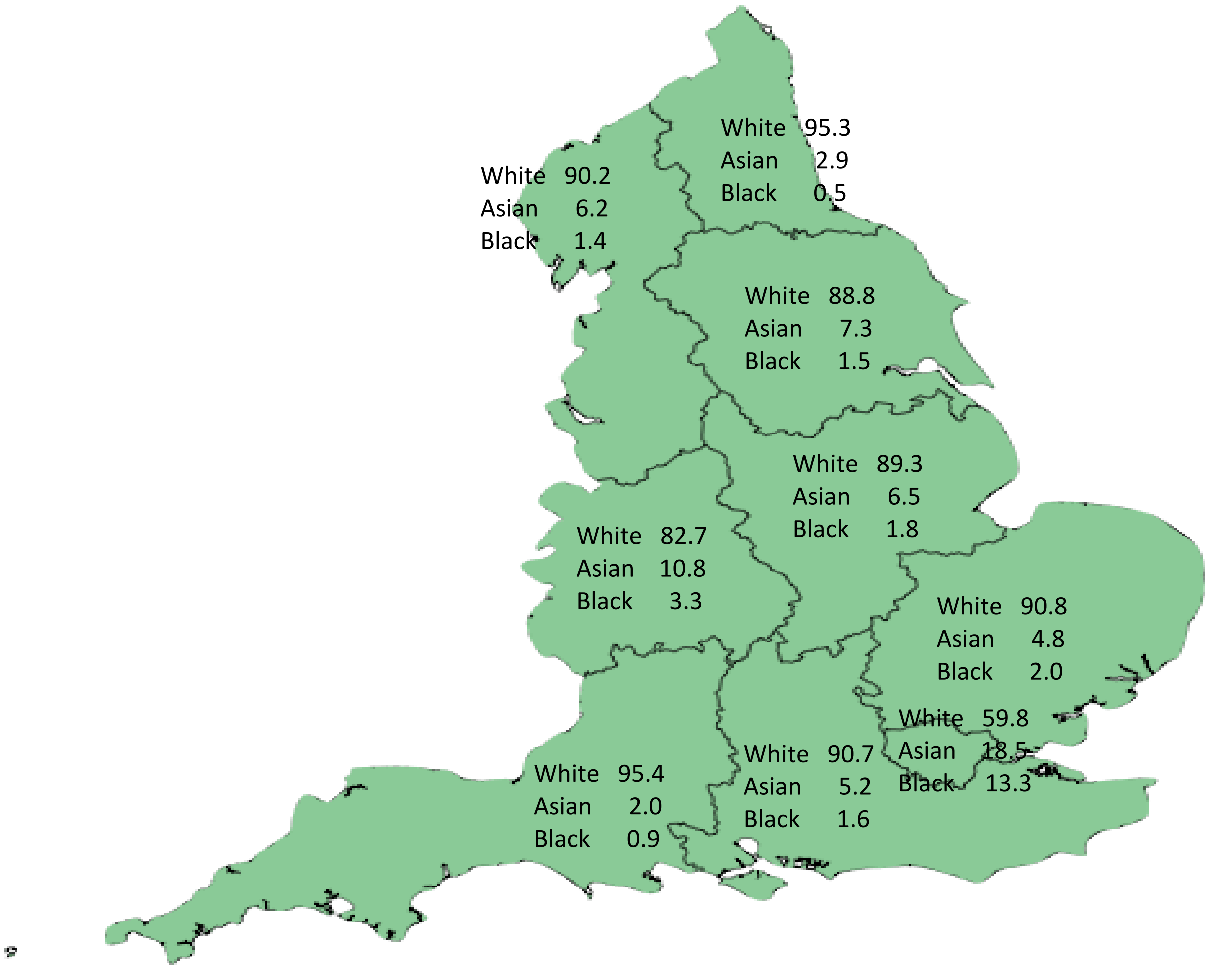


Figure 24
Proportion of Population belonging to Ethnic Minority Group by English Region 2011[88]

1.7.4.2 Median age of Ethnic Minority population in England

The median age of the ethnic groups is different from the majority White British population. The ethnic minorities are generally younger although the White Irish and Black Caribbean population are older (table 16).

Table 16: Median age of ethnic groups in England; Men and Women 2011[90]

	Ethnic Group	*Median Age*
England		39
White	White British	42
	White Irish	53
	White Other	31
Asian	Indian	32
	Pakistani	25
	Bangladeshi	24
Black	Black African	28
	Black Caribbean	40

1.7.4.3 Ethnicity and race as epidemiological variables

The present research determined the prevalence of lower limb amputation across the South Asian and Black ethnic groups. There has been substantial research describing ethnicity and how it differs from race.[91] Both are contested and controversial variables in epidemiology and public health but remain central and of growing interest.[91]

1.7.4.4 Race as an epidemiological variable

Race is a biological concept and related to possessing a limited range of physical factors. Race has been used as a classification system to provide a framework of understanding evolution and examining variation.[91] This concept has been abused in the past to justify inequalities e.g. slavery, colonialism, apartheid, separate education and restriction of medical care.

Racial variation, in theory, helps clarify the genetic and environmental basis of disease. However, physical characteristics such as face shape and colour that were the primary features used to distinguish races have little to do with deeper human traits of intelligence, behaviours, attitudes and the decision making process and so racial classification over the past 150 years has largely failed.[91] Thus, the biological concept of races as subspecies was ill-defined, poorly understood and invalid, however, it is important to understanding the concept of ethnicity.

1.7.4.5 Ethnicity as an epidemiological variable

Ethnicity is a multi-faceted quality deriving from the Greek work 'ethnos' meaning a nation, people or tribe.[91] It relates to groups with shared characteristics including geographical or ancestral origins with particular emphasis on cultural traditions and languages. It is therefore imprecise and fluid.

Ethnicity differs from race, nationality, and migrant status but may include facets of these and is related to the following;[91]

- Shared origins or social background
- Shared culture and traditions which are distinctive, maintained between generations and lead to a sense of identify and group-ness
- A common language or religious tradition

While race and ethnicity are conceptually different, they are overlying concepts that are often used synonymously. Table 17 details the qualities of a good epidemiological variable and how they apply to ethnicity.

Table 17: Ethnicity as an epidemiological variable[91]

Criteria for a good epidemiological variable	***Criteria in relation to ethnicity***
Impact on health in individuals and populations	Ethnicity is a powerful influence on health
Accurately measurable	In most populations, ethnicity is very difficult to assess
Differentiate populations in some underlying characteristic relevant to health e.g. income, childhood circumstance, hormonal status, genetic inheritance or behaviour relevant to health	Huge differences by ethnicity in different ethnic group reflect a rich mix of environmental factors and may also reflect population changes in genetic factors, particularly in populations where migration has been high
Generate testable aetiological hypothesis and/or help in developing health policy and or help plan and deliver health care and/or help prevent and control disease	It is hard to test hypotheses because there are so many underlying differences between populations of different ethnicity.
	Ethnic differences in disease patterns profoundly affect health policy
	Ethnic structure of a population is critical to good decision making
	By understanding ethnic distribution of diseases and risk, preventative and control programmes can be targeted at appropriate ethnic groups

1.7.4.6 The potential benefits of studying ethnic/racial differences in health

Studying ethnic and racial variations in health can, at least, potentially, help understand disease aetiology, tackle inequalities, assess need, make better health plans and direct resource allocation. The focus of race and ethnicity tends to be on those populations with comparatively adverse health outcomes.

1.7.4.7 Short History of Immigration to England

The origins of the peoples of Europe are unclear, however, early Europeans were hunter gatherers from Africa around 50-70 000 years ago with an Inland migration from Asia about 40 to 30 000 years ago. The British Isles were part of the Euroasian landmass around 6500 when the English Channel was formed.[92] Most 'White' people in Britain appear to be from Roman, Viking and Norman invasions[93], Blacks were next to arrive mainly a result of the slave trade with further immigration of Black and South Asians from 1950 onwards mainly to service manual jobs, the NHS and London transport.[94] The table below describes the major events of immigration in to the United Kingdom.

Table 18: Brief History of Immigration into England[92-94]

Year	***Event***
40 000 BC	Modern humans are likely to have arisen some Africa around 200 000 years ago, with the oldest human fossils found in Omo Kibish, Ethiopia. These modern human lefts Africa around 70 000 years ago and eventually replaced the earlier Neandertals. Early Europeans took a route from North Africa, however, modern genetic DNA data resembles peoples of India. This suggests an inland migration from Asia seeded Europe around 40 000 years ago.
6500 BC	The formation of the English Channel led to the British Isles being colonised by the Celts and Pict tribes from modern day Spain and Germany.
250-1066	The Romans, sent a contingent of black legionnaires to stand guard on Hadrian's wall. The Romans quit England in the 5th century with the Germanic tribes becoming the English. The Anglo Saxons from Germany, Denmark and Netherlands then colonised southern England with the Vikings from Scandanavia (Denmark, Norway and Sweden) influencing northern Britain and East Anglia. The Normans, descended from the Vikings who settled in France, with their conquest of 1066 fundamentally changed the direction of England with its government and law. The first Norman king was William the Conqueror.
1500-1800	The middle ages led to increased number of Black people in Britain. These were mainly slaves from Africa. The main merchants were in Liverpool, Bristol, Glasgow and London where slaves were sent to plantations in America.
1800s	Slavery was banned in 1833 with the halt of Black people into Britain. There were some Indian servants brought across by wealthy families with Black and Chinese sailors, mainly abandoned by their owners, putting down roots in port cities. Between 1830-1850 tens of thousands of Irish arrived in Britain, fleeing poverty at home.
World War 1 and II	Hundreds of thousands of men across the Empire fought for England with India alone providing 1.3 millon people, with 60 000 merchant seamen from the sub-continent. Some of these formed small communities in port cities.
Post war-1970s	Significant labour shortages post war led to the encouragement of immigration. 157 000 Polish were the first people encouraged to settle, they were followed by displaced people from Italy, Ukraine and Germany. Many eastern Europeans sought refuge following the establishment of communism. The partition of India in 1947 was the starting point for large scale migration from South Asia. Mass migration to the UK continued over the following years, the NHS and London Transport recruited many men from the Caribbean.

1970s	80 000 Asian Africans expelled from Uganda in 1972, 28 000 with British passports were admitted to the UK. Racial tensions from the pre-ceeding 30 years of migration led to a tightening of immigration rules with 1972 legislation stating British passport holders born overseas could only settle in the UK, if they could prove that a parent or grandparent had been born in the UK. Thus, children born to White families in the former Empire could enter Britain, whereas, their black counterparts could not.
1980s	With the decline of manufacturing and tighter controls on immigration only highly skilled immigration was encouraged. Large numbers of Australians, New Zealanders and South Africans entered the Business and Banking sector with the medical professions entered by South Asians.
1990-2000s	Ethnic conflict in the Balkans and subsequent conflicts in Africa and Middle East have led to increased numbers of Asylum seekers. Changes to EU legislation have recently allowed many Eastern Europeans to work in the UK.

Chapter 2: Methods

2.0 Overview of Methods

This chapter is split into three sections. Section 2.1 describes the process of obtaining access to and analysis of anonymous patient level HES data (summarised in figure 25). Section 2.2 describes additional analyses performed i.e. the ratio of coronary to lower limb revascularisations and prevalence of amputation (both major and minor) in the diabetic and non diabetic population over ten years (2003-2013). Finally, section 3.3 was a multi-site audit to determine the 'face validity' of HES data.

Section 2.1 consisted of eight steps (2.1.1-2.1.8). The process of data acquisition and analysis began by gaining access to HES data (2.1.1), the chosen period for analysis was all finished consultant episodes between 1st April 2003 and 31st March 2009 (2.1.2). The initial database had approximately 90 million rows of data and 200 columns. This was reduced to a manageable size in two steps. Firstly, all major lower limb amputations and revascularisations undertaken in patients aged 50-84 were extracted and placed into two files (2.1.3), variables not of interest were then removed (2.1.4). Prevalence rates were then calculated (2.1.5).

The amputation and revascularisation databases were then merged and, where possible, linked based on the unique HES-ID number (2.1.6). Two dichotomous outcome variables were then created: 'amputation with revascularisation' and 'amputation without revascularisation' (2.1.7). Logistic regression was then performed to determine the influence of ethnicity and location on these two outcome measures (2.1.8).

Section 2.2 describes three additional analyses performed. These were the coronary to lower limb revascularisation ratio by ethnic group (2.2.1), the ten year prevalence of amputation (both major and minor) and revascularisation across England (2.2.2) and the prevalence of major and minor amputation in the diabetic and non diabetic populations (2.2.3).

Finally, section 2.3 was a multi-site audit and compared the data held on the HES database to hospital case notes. It was only possible to determine the 'face validity' of HES as only anonymous data were available thereby only allowing indirect validation i.e. the HES and audit data were not linked. We were thus only able to compare averages and proportions. The sensitivity and specificity of HES coding of the following six co-morbidities was determined; diabetes, coronary heart disease, hypertension, hypercholesterolaemia, cerebrovascular disease and smoking.

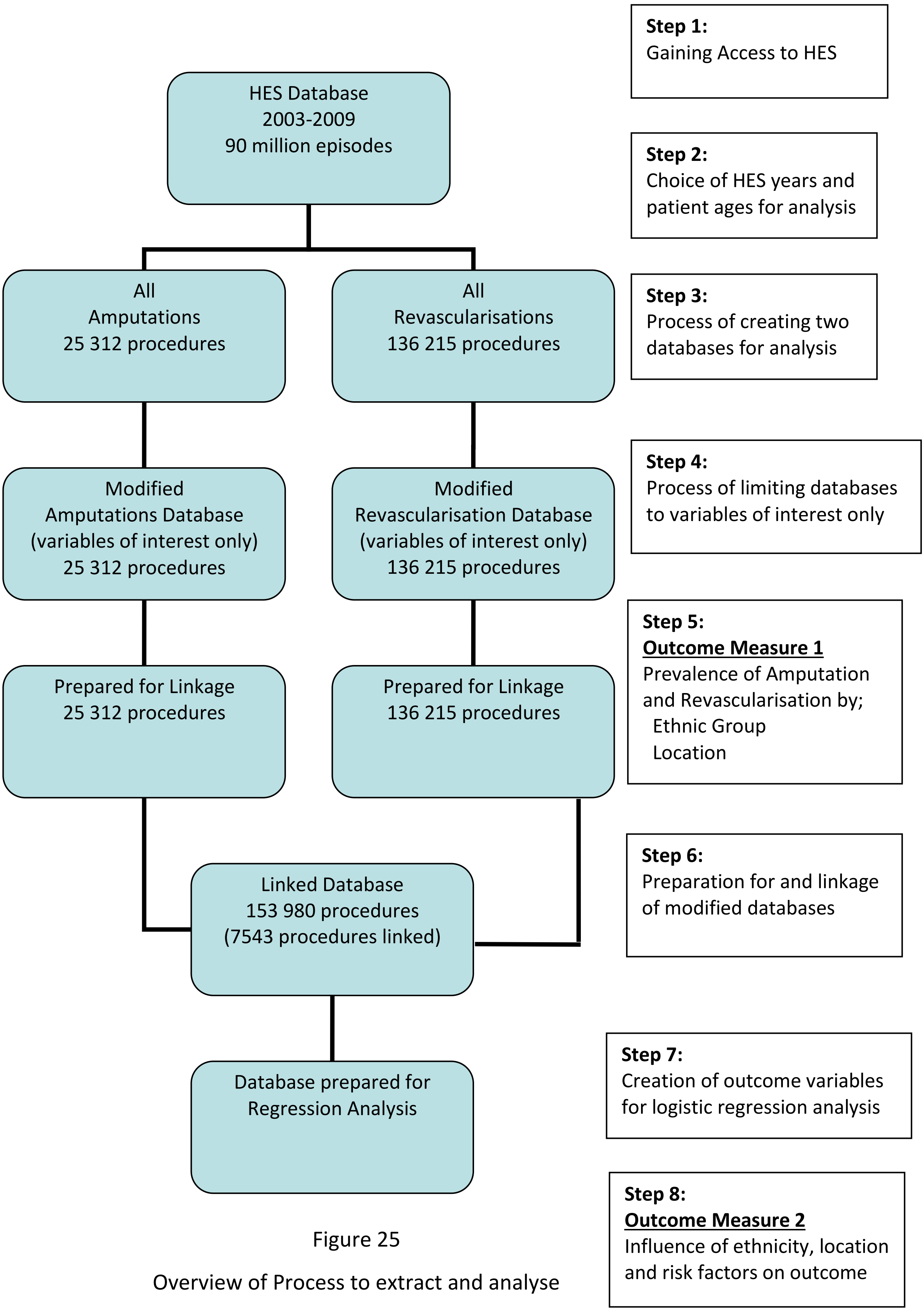


Figure 25

Overview of Process to extract and analyse

Hospital Episode Statistics 2003-2009

2.1.1 Step 1: Process of gaining access to HES data

Access to the HES database was through Public Health England, Liverpool, formally known as the Public Health Observatory. Initial contact was through the Director of the Centre for Public Health with subsequent correspondence through a data analyst to whom the research proposal was submitted. A number of checks were performed and after the conditions of analysis were explained, access to anonymous patient level data was granted. Whilst ethical approval was not formally required as only access to anonymous data was required, I applied as I was initially proposing to store data on a hospital database. Ethical approval was granted by the North Cheshire Research Collaboration 10/H1017/4.

This system has now been modified and only analysis based on aggregated tables provided by Public Health England is allowed i.e. access to patient level data is now not permitted.

Access to the data was granted on the following conditions;

- all analyses to be undertaken on site only
- no HES data to be removed
- all analyses scrutinised to ensure anonymity of patients
- any cells containing less than 6 cases are suppressed

HES data during the period of analysis were held, physically, at the Henry Cotton Building, Webster Street, Liverpool which is part of Liverpool John Moore's University. The data were stored on two giant servers which are held in a temperature controlled room behind a security door. Access to this area is gained after signing in and being escorted through two card controlled security areas. Access to the database was through a stand alone computer terminal. Again this system has changed and access to HES data is only available to analysts who access it through the Health and Social Care Information Centre (HSCiC). Data can still be analysed on the Henry Cotton site.

2.1.2 Step 2: Choice of HES data years and patient age groups for analysis

The sampling frame was limited to patients aged 50-84 and data years 1st April 2003 to 31st March 2009.

This age group was selected because those under 50 are unlikely to have amputations relating to peripheral arterial disease. I chose 84 as the upper cut off for two reasons. Firstly, patients over 84, based on clinical experience, are more likely to have amputations without a revascularisation i.e. often frail, bed bound nursing home residents and secondly, I felt this to be a 'premature amputation'. This definition is analogous to premature death from CHD in those under 75.

Although it was possible to link amputations to diagnosis codes and so retrieve only amputations in those admitted with a diagnosis of peripheral arterial disease, the accuracy of diagnosis codes was not established. Therefore, age group was used as a proxy measure for diagnosis based on clinical experience.

Data up to 31st March 2009 were analysed as they were the latest available at the time of performing the primary analysis. Data from 2003 onwards were used because the ethnic group classification, modified every 10 years for the census, is, in the first two years after change, inconsistently coded as records contained a mixture of 1991 and 2001 ethnicity definitions.

2.1.3 Step 3: Process of creating two databases for analysis

The entire in-patient HES database between 2003 and 2009 contained approximately 90 million episodes of care. In order to allow data manipulation and management, the size of the working database was reduced by creating two smaller databases that were populated with amputation and revascularisation procedures in those aged 50-84. This was followed by reducing the number of variables per episode of care.

The extraction of these two procedures was based on using the OPCS classification. The summarised codes used for retrieving amputations and revascularisations are shown in table 19 and expanded in the appendix.

Three rather than four character procedure codes were used in order to maximise procedure retrieval. This was particularly important for revascularisation codes as they would be used to link with amputations. The procedure codes for revascularisation included imaging codes ie. angiograms and were included as inpatient angiograms are usually done with a view to revascularisation.

HES had 24 operative procedure columns, the most resource intensive procedure is placed in column 1 with subsequent procedures denoted as secondary procedures. Only ten were searched after advice from the data analyst at HES as additional ones would not capture procedures during the time period of interest.

The actual retrieval of data from HES was based on running queries in Microsoft Access. In addition to the procedure codes detailed in table 19, additional search criteria were required to recover cases - these were supplied by the data analyst. The final query used to return major lower limb amputations is shown in table 20.

Table 19: OPCS procedure codes used to extract amputation and revascularisation procedures from the HES database

Procedure	***Area***	***Code***	***Description***
Amputation	Leg	X09	All leg amputations (above ankle)
Endovascular	Aorta	L26	Percutaneous angioplasty/stent of aorta
	Iliac	L54	Percutaneous angioplasty/stent of Iliac artery
	Femoral	L63	Percutaneous angioplasty/stent of femoral/popliteal artery
	Other	L66	Other therapeutic transluminal operations/stent on artery
Surgery	Iliac	L50	Other emergency replacement of iliac artery
		L51	Bypass of iliac artery (vein or prosthesis)
		L52	Reconstruction of iliac artery (endarterectomy)
	Femoral*	L58	Emergency bypass of femoral artery
		L59	Bypass of femoral artery (vein or prosthesis)
		L60	Reconstruction of femoral artery (endarterectomy)
		L62	Other open operation on femoral artery
		L65	Revision of reconstruction of artery

*Includes popliteal and distal vessels

Table 20: Search criteria used by Microsoft Access to retrieve amputation cases from HES

	Variable	***Syntax****	***Name***	***HES groups***
1	Epistat	Like '3'	Episode Status	1=unfinished 3=finished
2	soal	Like 'E*'	Lower Super output area	E=England W=Wales There are 32 482 output areas classed using a unique 6 digit tag
3	Classpat	Not In (3,4)	Class of Patient	1=ordinary admission 2=day case admission 3=regular day attender 4=regular night attender 5=mother and babies using only delivery facilities 8=not applicable (other maternity event)
4	Yr	2003-2008		
5	Startage	Between 50 and 84	Age at start of episode	
6	Oper_01	Like 'X09*'	Operation	Primary operation
7	Oper_02	Like 'X09*'	Operation	Secondary procedure
8	Oper_03	Like 'X09*'	Operation	Secondary procedure
9	Oper_04	Like 'X09*'	Operation	Secondary procedure
10	Oper_05	Like 'X09*'	Operation	Secondary procedure
11	Oper_06	Like 'X09*'	Operation	Secondary procedure
12	Oper_07	Like 'X09*'	Operation	Secondary procedure
13	Oper_08	Like 'X09*'	Operation	Secondary procedure
14	Oper_09	Like 'X09*'	Operation	Secondary procedure
15	Oper_10	Like 'X09*'	Operation	Secondary procedure

*Search criteria 1-5 were linked with the AND command and 6-15 linked with the OR command.

The query returned all major leg amputations (above ankle), undertaken in patients aged between 50 and 84 between April 2003 and March 2009. Only amputations that were performed in England, on inpatients and ‘finished’ (discharged from the consultant under whom amputation was performed) were retrieved.

The amputations were initially returned into an Excel spread sheet but then transferred into SPSS (version 19) for data manipulation and analysis.

In order to retrieve endovascular and surgical revascularisation procedures, the same queries as 1-5 were used but had the operation codes set as; Like ‘L26*’ or like ‘L53*’ or like ‘L63*’ or like ‘L66*’ or like ‘L51*’ or like ‘L52*’ or like ‘L59*’ or like ‘L60*’ and repeated with OR command for oper_02 to oper_10. These are detailed in the appendix.

The two search strategies retrieved 25 312 amputations and 136 215 revascularisations. The next stage involved reducing variables within each database to the ones pertinent to analysis.

2.1.4 Step 4: Process of limiting databases to variables of interest only

HES collects 201 variables per episode, although not all are required to be completed for all admissions e.g. maternity codes. The variables pertinent to analysis were those relating to patient demography and co-morbidity. These are listed below;

Demographic variables:

- Age
- Sex
- Ethnic group
- Government region of residence (location)
- Social class

Co-morbidity variables;

- Diabetes
- Hypertension
- Hypercholesterolaemia
- History of coronary heart disease
- History of cerebrovascular disease
- Smoking

Table 21 details the demographic variables, their original HES coding and subsequent recoding that was used to facilitate analysis.

Table 21: Demographic variables in HES and subsequent recodes used for analysis

Demographic Variable	*HES variable name*	*HES codes*	***Recoded Groups***
Age	Startage	Calculated age in cell (based on date of birth and date of episode started)	1=50-54 2=55-59 3=60-64 4=65-69 5=70-74 6=75-79 7=80-84
Sex	Sex	Male/female	1=male 2-female
Ethnic group	ethnos	A=British (White) B=Irish (White) C=Any other White background D=White and Black Caribbean (mixed) E=White and Black African (mixed) F=White and Asian (mixed) G=Any other mixed background H=Indian (Asian or Asian British) J=Pakistani (Asian or Asian British) K=Bangladeshi (Asian or Asian British) L=Any other Asian background M=Caribbean (Black or Black British) N=African (Black or Black British) P=Any other Black background R=Chinese (other ethnic group) S=Any other ethnic group Z=Not stated X=Not known	1=White British 2=White Non British (B+C) 3= Asian (H+J+K+L) 4=Black (M+N+P) 9=all other ethnic groups
Government Office Region of Residence	resgor	A= North East B= North West C= Merseyside (until 1998/9) D= Yorkshire & Humber E= East Midlands F=West Midlands G=East of England H=London J=South East K=South West S=Scotland U=No fixed above W=Wales X=Foreign (including IOM) Y=unknown Z=Northern Ireland	1=North East 2=North West 3=Yorkshire and Humberside 4=East Midlands 5=West Midlands 6=East England 7=South East 8=London 9=South West
Social Class	IMD04_decile	Decile group of deprivation	1=Most deprived 2=Second most deprived 3=Third most deprived 4=Fourth most deprived 5=Least deprived

Age was categorised into 5 year age bands to allow calculation of age specific rates and age standardisation. The multiple ethnic categories were recoded into four. White British was the standard comparative ethnic group. 'All Asian' was formed by combining Indian, Pakistani, Bangladeshi and Asian other. 'All Black' was formed by combining Black African, Black Caribbean and Black Other. 'White non British' was formed by the amalgamation of the groups 'White Irish' and 'White Other'. Numbers and rates for each amalgamated and component group were calculated but only presented if they contained six or more cases.

HES groups the actual IMD score into deciles in line with the Office of National Statistics, which, for ease of reference were combined to form quintiles of deprivation. This part of the analysis was performed by the Public Health Analyst and I simply merged the IMD score to the patient's LSOA .

The coding and recoding of co-morbidities was complex. The co-morbidities retrieved were diabetes, hypertension, hypercholesterolaemia, coronary heart disease, cerebrovascular disease and smoking (table 22). These were selected as they are the major risk factors for atherosclerosis and (apart from hypercholesterolaemia) part of the 38 codes which hospital coders are required to seek out and code as part of coding standards. The summarised codes used to extract these co-morbidities from HES are shown below and expanded in the appendix.

Table 22: Summarised ICD-10 codes used for extracting Co-Morbidity data from HES (expanded codes in Appendix)

Assigned Re-code	***Co-morbidity***	**ICD-10 code**
1	Diabetes	E10-E14
2	Hypertension	I10-I13
3	Hypercholesterolaemia	E78
4	Coronary Heart Disease	I20-I25
5	Cerebrovascular Disease (stroke and TIA)	I63-I67 and G45
6	Smoking	F17 and Z72

HES has 20 columns within which co-morbidities are recorded and all 20 were searched culminating in six dichotomous co-morbidity variables (yes/no).

Once the database variables were reduced and recoded to include only those relevant to analysis, prevalence rates were calculated.

2.1.5 Step 5: First Analysis – Outcome measure 1

Calculation of prevalence rates (crude and age adjusted) and confidence intervals

Prevalence rates for both amputation and revascularisation procedures used HES data as the numerator with the denominator population derived from the Office National Statistics (ONS) mid year population estimates. Crude rates were calculated using the combined number of procedures over the six year period as the numerator with the denominator derived by combining the mid year population estimates between 2003 and 2008. The 2010 modified estimated denominator population was used. Denominator populations for both ethnic group and governmental region were available online and both databases i.e. census and HES used the same groups.

The nine governmental regions were split into North (North West, North East, Yorkshire & Humber), Midlands (East and West Midlands) and South (East of England, London, South East, South West) for statistical purposes. Proportional rates were derived by determining the ratio of the age adjusted rate to the reference population. For regional variations, the national rate was the reference source with the 'White British group used to explore ethnic variations.

The age adjusted rate was calculated using the direct method and standardised to the 2001 population structure for England and Wales and based on the distribution of the 50-84 year old population. The process involved calculating the age specific rate for each 5 year age band (50-84) which was then weighted by the appropriate population proportion in line with standard techniques. The sum of these weighted rates was the age standardised rate. Confidence intervals were determined by calculating of sum of the variance of each age specific rate. The formulas used are shown in table 23.

Table 23: Formulas used to derive crude and age standardised rates and confidence intervals

Description	***Formula***
Age specific rate, per 100 000 for each age band	R = (N/P)*100 000
Weighted age specific rate	X = W*R
Age Standardised Rate (ASR)	ASR = sum of weighted age specific rates
Variance	V = 10^5x10^5 x Nx(W^2/P^2)
Sum of Variance	All age specific variances added
Standard Error of age specific rate	SE = √variance
Confidence Intervals of ASR	ASR $\pm$ 1.96 x SE(ASR)

where: N = observed number of cases

P = denominator population

R = Age Specific rate per 100 000 persons per year

W = Proportion of the standard population (England and Wales) in each age group

X = Weighted age specific rate.

V = Variance of the age specific rate.

ASR = age standardised rate

The population weights applied to men and women is shown below.

Table 24: Population weights applied to each 5 year age band for age standardisation

Age	***Males***	***Females***	***Combined***
50-54	0.2288	0.2067	0.2171
55-59	0.1927	0.1744	0.1830
60-64	0.1617	0.1488	0.1549
65-69	0.1427	0.1370	0.1397
70-74	0.1223	0.1299	0.1263
75-79	0.0948	0.1171	0.1066
80-84	0.0570	0.0862	0.0724

In order to illustrate the calculation process used for crude and age adjusted prevalence, an example of the prevalence, per 100 000 (95% confidence intervals), of amputations in Asian men is given. This calculation was repeated for all regions and ethnic groups

Table 25: The calculation of crude and age adjusted prevalence of amputations; Asian males aged 50-84; England 2003-2009

Age	*Number of Procedures*	*Population*	*Crude Rate/100 000*	*Weight*	*Weighted Rate*	*Variance*	*Age Standardised Rate and CI*
50-54	27	413,100	6.54	0.23	1.50	0.0828	
55-59	30	269,700	11.12	0.19	2.14	0.1532	
60-64	46	200,900	22.90	0.16	3.70	0.2980	
65-69	41	203,800	20.12	0.14	2.87	0.2011	
70-74	38	149,500	25.42	0.12	3.11	0.2543	
75-79	32	81,500	39.26	0.09	3.72	0.4331	
80-84	11	36,700	29.97	0.06	1.71	0.2653	
Total	225	1,355,200			18.75	0.0828	18.8± 2.6

2.1.5.1 Calculation of Proportional Rate (PR) and Confidence Intervals (CI)

The prevalence rate in each ethnic group was compared with that of the White British group and expressed as a proportion of this rate. The Eurocentric approach to analysis was taken to highlight rates in the minority groups. Regional rates were then expressed as a proportion of the national average. The 95% confidence interval for each proportion was calculated by altering the actual rate by the same proportion it represented. The calculation of the proportional rate for Asian and White British males is given below.

Table 26: The calculation of proportional rates; Age adjusted proportional rate: Asian to White British men aged 50-84; England 2003-2009.

Description	***Calculation***
1.Prevalence and confidence interval, per 100 000; Asian Male Amputation Rate	18.8 $\pm$ 2.6 (16.2-21.3)
2. Prevalence and confidence interval, per 100 000; White British Male Amputation Rate	32.1 $\pm$ 0.5 (31.5 – 32.6)
3. Proportional rate; Asian Males to White British Males	(18.8/32.1)*100 = 58.6
	(2.6/18.8) = 0.14
4. CI Ratio Asian Males (of Asian Male rate)	58.6$\pm$(58.6*0.14) = 58.6 $\pm$ 8.21=
95% Confidence Interval of Asian PR	58.6 $\pm$ 51-66

Once the actual and proportional prevalence of amputations and revascularisations for every ethnic and geographical group was calculated, the two stage process of setting up a database to allow logistic regression analysis began. This involved merging the amputation and revascularisation files (step 6) and then creating outcome variables based on linked cases (step 7).

2.1.6 Step 6: Linkage of Amputation and Revascularisation databases

The process of linking cases began by creating a variable within the amputation database called ‘amputation’ and similarly ‘revascularisation’ within the revascularisation database. Every cell within that column was labelled as amputation or revascularisation respectively. Then every column in both databases was renamed with either an ‘a’ and ‘v’ prefix to denote whether its origin was the amputation or revascularisation database.

Each row in the database represented a patient and so had a unique HES ID. It was this unique identifier that would form the basis of linking the two databases in SPSS through the 'MERGE' command. Thus, where amputations and revascularisations occurred and the HES-ID matched, the revascularisation columns would be added to the same row as amputations. Where revascularisations did not match amputations, these rows were added to the bottom of the database and would populate the 'v' set of columns i.e. the 'a' set of columns would remain empty.

The amputations database containing 26 312 procedures and revascularisations containing 136 215, were merged and 7543 amputations (29.8%) were successfully linked to a revascularisation.

2.1.7 Step 7: Creation of Outcome variables for regression analysis

Following merger, two outcome variables were created using a two stage process. Firstly, the 'amputation' and 'revascularisation' columns created prior to merging were recoded in the merged database into dichotomous variables i.e. amputation; yes/no or revascularisation; yes/no.

There were three possible combinations of these dichotomous amputation and revascularisation columns;

1. Amputation=Yes; Revascularisation=Yes
2. Amputation=Yes; Revascularisation=No
3. Amputation=No; Revascularisation=Yes

These corresponded to the following outcome measures;

1. Amputation with revascularisation
2. Amputation without revascularisation
3. Revascularisation no amputation

The two outcome measures of interest (1 and 2) were created using the 'RECODE IF' command in SPSS.

The ethnic and location variables of the amputation and revascularisation columns were recoded so that the 'ethnic' and 'location' variables were carried out in patients who had the same ethnic classification or had both procedures undertaken in the same region.

2.1.8 Step 8: Second Analysis: Outcome Measure 2;

Influence of ethnicity, location and risk factors on outcome

The two primary outcome measures 'amputation with revascularisation' (yes/no) and 'amputation without revascularisation' (yes/no) were the dependent variables.

The forward step entry method was used to enter the predictor variables with demographic (age, sex and social class) and disease risk factor variables (diabetes, hypertension, hypercholesterolaemia, coronary heart disease, cerebrovascular disease and smoking) entered in blocks. As the primary interest was outcomes based on location and ethnicity, these variables were entered individually first to calculate unadjusted odds. They were then re-entered after demography and risk factors to calculate adjusted rates.

Thus, the process for predicting the relationship of ethnicity to 'amputation with revascularisation' was completed by entering ethnicity alone (unadjusted odds), then block entry of demographic variables (adjusted for demography) and finally block entry of risk factors. The process was repeated for the outcome, 'amputation without revascularisation'

The analysis was performed this way to ascertain the relative effect of demography and risk factors on outcome. This was thought important to generating intervention strategies and assessing the role of government and clinicians in effecting change.

All predictor variables were categorical and defined in SPSS as either 0 or 1 (where 1 was positive) or if there were more than 2 categories e.g. location, ethnicity, age group and social class, the first variable i.e. North West, White British, 50-54 and most deprived were the indicator variables.

2.2.1 Determining coronary to lower limb revascularisation ratio

The prevalence of coronary revascularisation was determined using the same age and time definitions as lower limb revascularisation. The definitions used for endovascular and surgical coronary procedures are summarised in table 27 and expanded in the appendix.

Table 27: Summarised HES codes for Coronary Revascularisation

Procedure	***Code***	***Description***
Coronary Angioplasty	K49	Transluminal balloon angioplasty of coronary artery
Coronary stenting	K75	Transluminal angioplasty and insertion of stent into coronary artery
Coronary bypass graft	K40	Saphenous vein replacement of coronary artery
	K41	Other autograft replacement of coronary artery
	K43	Prosthetic replacement of coronary artery
	K44	Other replacement of coronary artery
	K45	Connection of thoracic artery to coronary artery

2.2.2 Ten year amputation and revascularisation prevalence 2003-2013

Upon completion of the 2003-2009 data analysis, a bespoke request to Public Health England was placed to retrieve the number of amputations (major and minor) and revascularisations (endovascular and surgical) between 2003 and 2013. I was supplied with tables containing aggregated data. Although, requested ethnicity and diabetes data was not supplied. Changing prevalence by ethnic group over ten years could, therefore, not be calculated. The 2003-2009 was used to determine the proportion of amputees with diabetes and applied to the 2013 population prevalence data.

To include minor amputations and procedures on stumps, the following additional codes were requested.

Table 28: OPCS procedure codes used to extract both major and minor amputation and revascularisation procedures from the HES database

Procedure	***Area***	***Code***	***Description***
Amputation	Leg	X09	All major leg amputations
		X10	Transmetatarsal amputation
		X11	Toe amputation
Endovascular	Aorta	L26	Percutaneous angioplasty/stent of aorta
	Iliac	L54	Percutaneous angioplasty/stent of Iliac artery
	Femoral	L63	Percutaneous angioplasty/stent of femoral/popliteal artery
	Other	L66	Other therapeutic transluminal operations/stent on artery
Surgery	Iliac	L50	Other emergency replacement of iliac artery
		L51	Bypass of iliac artery (vein or prosthesis)
		L52	Reconstruction of iliac artery (endarterectomy)
	Femoral*	L58	Emergency bypass of femoral artery
		L59	Bypass of femoral artery (vein or prosthesis)
		L60	Reconstruction of femoral artery (endarterectomy)
		L62	Other open operation on femoral artery
		L65	Revision of reconstruction of artery

2.2.3 Calculating prevalence of amputations in the diabetic population 2003-2013

Prevalence rates, per 100 000, were calculated using HES data as the numerator with the denominator population derived from the Office National Statistics (ONS) mid year population estimates.[86-87] The denominator diabetic population was calculated by applying the age specific prevalence of diabetes to census estimates from the national Health and Lifestyle survey for England 2003-2012.[95] This is an annual government run survey since 1991 collecting information on physical health, lifestyle behaviours, social care, physical measures, mental health and well being. The age specific non diabetic population was derived by removing the diabetic population from the whole population. The number of major amputees who were diabetic was based on co-morbidities coded in the HES database using the ICD-10 code of diabetes (E10-E14). I applied the same proportions of major amputees with diabetes to those who had minor and amputation procedures.

Table 29: Percentage of Major Amputees and England population with Diabetes

		Percentage of Population with Diabetes			
		2003		**2013**	
Gender	***Age***	***Amputees****	**England****	**Amputees***	**England****
Men	50-64	47.3	8.1	52.6	12.0
	65-74	48.8	11.9	52.2	17.3
	75-84	38.1	10.0	50.4	17.5
	All	44.7	10.0	51.8	15.6
Women	50-64	51.8	4.7	45.5	8.9
	65-74	42.7	8.4	44.7	11.0
	75-84	29.5	8.9	38.4	12.9
	All	38.3	7.3	42.0	10.9

*Amputees: Percentage of major amputees with diabetes based on HES data
**England: Percentage general population with diabetes based on Health and Lifestyle Survey[95]

Table 30: Number of procedures and denominator populations used for calculations

		2003				2013			
		Major	Minor	Stump†	Population	Major	Minor	Stump	Population
Diabetic									
Men	50-64	421	500	161	351 994	467	804	241	568 140
	65-74	522	493	128	234 644	515	697	156	403 298
	75-84	390	304	57	117 240	446	582	102	230 178
	Total*	1 333	1 280	337	748 980	1 429	2 081	497	1 307 436
Women	50-64	157	298	51	210 193	150	307	64	432 148
	65-74	185	289	42	185 102	166	305	48	276 463
	75-84	204	192	24	151 585	205	285	34	216 243
	Total*	548	729	107	611 667	518	882	142	985 927
Non Diabetic**									
Men	50-64	470	557	179	3 993 606	421	724	217	4 166 360
	65-74	547	517	135	1 737 156	472	638	143	1 927 902
	75-84	633	493	93	1 055 160	438	572	100	1 085 123
	Total*	1 650	1 584	416	6 740 820	1 330	1 936	462	7 073 564
Women	50-64	147	278	47	4 262 007	179	367	76	4 423 452
	65-74	248	387	57	2 018 498	206	378	60	2 236 837
	75-84	489	459	59	1 551 615	328	457	55	1 460 057
	Total*	882	1 174	173	7 767 333	716	1 217	195	8 059 273

*Total: based on percentage of population with/without diabetes not sum of relevant column
** Non diabetic: based on removing diabetic population from whole population
† stump procedure: all procedures on major amputation stumps including re-amputation to a higher level

2.3.1 Determining the Face Validity of HES Data

In order to determine the 'face validity' of HES, its data relating to three hospitals was compared with clinical notes from the same hospitals. Patients undergoing the same procedure over the same three year time period were compared to determine the accuracy of procedure numbers, demography (age, sex) and the sensitivity and specificity of six cardiovascular co-morbidities, namely, coronary heart disease, hypertension, diabetes, hypercholesterolaemia, cerebrovascular disease and smoking.

The study was based in the North West of England, and sourced data from two teaching and one district general hospital. All three serve a predominately inner city urban population of similar sized catchments although one of the teaching hospitals generally served a more deprived population.

Upon gaining approval from the audit departments of all three participating hospitals, a retrospective review of patients aged between 50 and 84 who underwent an above knee amputation between 1st April 2006 and 31st March 2009 was performed. We determined the accuracy of data should be 90% inline with national standards.

The individual hospital theatre record systems were searched to extract the patients of interest. In line with the coding standard, diagnosis of co-morbidity was based primarily on a doctor diagnosis written in the patient case notes pertinent to the admission generating the amputation. If not confirmed in the case notes, then all parts of the hospital record including clinic letters and previous hospital admissions were searched as it was assumed that no patient was cured of their condition. Notes subsequent to the admission were not searched as a new diagnosis could have occurred. If no diagnosis could be determined based on hospital notes, then medications used specifically for conditions were searched for as well as operations linked to certain co-morbidities. These are listed in table 31 along with the ICD-10 codes used to retrieve co-morbidities from the HES database. These risk factors were chosen as they were the common ones for peripheral arterial disease, and all, apart from hypercholesterolaemia, are part of 38 co-morbidities that must be searched for and coded.

It was only possible to determine the 'face validity' of the HES database. This term was used as identifiable patient level HES data was inaccessible and so data from the audit and the HES database could not be matched. It was therefore not possibly to perform any meaningful statistical testing such as percentage agreement or Cohens Kappa.

Only averages and proportions between the two datasets were assessed. Hospital data were used as the reference dataset to calculate sensitivity and specificity for co-morbidities. Differences in the proportion of people with co-morbidities between HES and patient notes was analysed using Pearson chi square test.

Table 31: Criteria used to Diagnostic Patient Co-morbidity

Chronic Condition	**HES Code**	**Case note Definition**
Diabetes	E10 – E14	Doctor diagnosis of; Type 1 (Insulin) Type 2 (non insulin dependant) Type 3(other types e.g. Malnutrition related) On following medication; Insulin, oral glycaemics e.g. Metformin, Glizlazide, Blood test Following surgical procedure Pancreas transplant, total pancreatectomy
Hypertension	I10 - I13	Doctor diagnosis
Hypercholesterolaemia	E78	Doctor diagnosis, blood test
Coronary heart disease	I20 – I25	Dr diagnosis of any of following; Angina, Myocardial infarction Congestive cardiac failure Left ventricular heart failure Cardiac arrest Any surgical procedure; Coronary artery angioplasty Coronary artery bypass On following medication GTN spray, other nitrates, ivrabadine Coronary intervention (any)
Cerebrovascular disease	I63 – I67 and G45	Doctor diagnosis of; Transient Ischaemic Attack Stroke, amauraosis fugax Any surgical procedure: Carotid endarterectomy
Smoking	F17, Z72	Documented social history On nicotine replacement therapy Stopped smoking within 1 year

Chapter 3: Results

3.0 Overview of Results

The results section is split into four sections. Section 3.1 describes the North/South, regional and gender divide in the amputation and revascularisation rate based on 2003-2009 data. It then statistically determines the contribution of demographic and disease risk factors on the risk of any major amputation (both with and without revascularisation) and then specifically on the risk of an above knee amputation.

Section 3.2 describes the prevalence of amputation and revascularisation by ethnic group and the influence of ethnicity on the risk of a major amputation both with and without a revascularisation. It then describes the proportion of coronary to lower limb revascularisation by each ethnic group.

Section 3.3 brings the 2003-2009 results up to date and describes the yearly prevalence of major amputation and revascularisation from 2003-2013. It additionally describes the minor amputation rate across regional, gender, age and diabetic groups.

Section 3.4 describes the sensitivity and specificity of co-morbidity coding in HES data.

<u>Section 3.1 Summary: North/South, Regional and Gender divide 2003-2009</u>

The overall age standardised prevalence rate of amputations and revascularisations in England for those aged 50-84 was 26.3/100 000 and 141.6/100 000 respectively. Rates were approximately double in men than women for both amputations (37.0 vs 15.9/100 000) and revascularisations (197.4 vs 90.7/100 000). Regionally, the rates, per 100 000, of amputations and revascularisation were higher in Northern England: North 31.7 and 182.1; Midlands 26.0 and 121.3; South 23.1 and 124.9 respectively. Within each region, amputations and revascularisations varied by approximately 40% and 60% respectively.

The mean age of amputees was 70.6 years, 68.5% were men and 28.6% were from the most deprived areas. The commonest disease risk factors were diabetes (44%), hypertension (39%) and coronary heart disease (23%). Amputees from Northern England had higher levels of coronary heart disease and smoking, Southern amputees had greater levels of diabetes.

On multi-variate analysis, risk of an amputation with a revascularisation was significantly higher in Northern England compared with the Midlands even after controlling for demographic and disease risk factors.

Overall, more above than below knee amputations were performed in England (ratio AK:BK; 1.1:1), with again higher ratios in Northern England (1.3:1) than the South (0.9:1). On multi-variate analysis risk of an above knee amputation, however, was not associated with location of treatment. Risk was increased with revascularisation and was higher with both surgical and combined surgical and endovascular modalities. Risk was lowest when endovascular was used as sole treatment modality.

Section 3.2 Summary: The Ethnic Divide 2003-2009

There were significant variations in the prevalence of amputation and revascularisation by ethnic group. Compared with the majority White British population, the Black population had significantly higher rates of amputation. Rates were significantly lower in South Asians. Rates of revascularisation were significantly lower in both Black and South Asians. The excess risk of amputation without a revascularisation in Blacks was fully attenuated by controlling patient demography and risk factors whereas excess risk remained for amputation with a revascularisation.

The lower prevalence of limb revascularisation in South Asians was associated with much higher levels of coronary revascularisation, whereas in all other groups there was an approximately even split between revascularisation of the two arterial territories.

Section 3.3: Bring it all up to date; Changing prevalence 2003-2013

The ten year analysis of HES data demonstrated the prevalence of major amputation to have decreased by approximately 18% whereas minor amputation rates rose by a similar amount. Revascularisation rates have risen overall by 23% with greater rises in surgical (52%) than endovascular interventions (15%). Age, gender and regional variations of both major and minor amputation have remained largely unchanged. The North of England continues to have the highest rate of amputation as well as the highest AK:BK ratio; men continue to have double the amputation rate of women, who in turn continue to have a much higher AK:BK ratio than men. Further, a reduction in amputation rates is not seen in the youngest 50-64 year old age group. Amputation rates in diabetics have fallen at a faster rate than non diabetics but remain six times higher. The rise in minor amputations appears to be driven by non diabetic men.

Section 3.4 Summary: Validity of HES data

The validation study determined the sensitivity and specificity of HES and used the national standard of 90% as the reference point. HES was found to be accurate for procedure numbers and patient demography and have high specificity for co-morbidities. However, HES was only sensitive (>90%) for coronary heart disease. The sensitivity for diabetes was 77%.

3.1.1 The North/South Divide– descriptive statistics

Over the study period, 1st April 2003-31st March 2009, there were approximately 90 million in-patient hospital episodes. From this sampling frame 25 312 major lower limb amputations and 136 215 revascularisations among patients aged between 50 and 84 were performed (table 32).

Table 32: Number of Major Lower Limb Amputations and Revascularisations; England 2003-2009; Men and Women

	England	***North***	***Midlands***	***South***
Number Amputations	25312*	8981	4969	11 358
Number Revascularisations	136 215	51 784	23 163	61 268
Above knee amputations	12 240	5074	4207	2959
Below knee amputations	10 778	3961	3598	3219
AK:BK ratio	1.1:1	1.3:1	1.2:1	09:1
Total Population	52 234 000	14 844 000	9 936 000	27 454 000

* Major amputations includes through knee and hip disarticulations

The overall age standardised prevalence rate of amputations and revascularisations in England for those aged 50-84 was 26.3/100 000 and 141.6/100 000 respectively. Regionally, the rates, per 100 000, of major amputation and revascularisation was higher in Northern England: North 31.7 and 182.1; Midlands 26.0 and 121.3; South 23.1 and 124.9. These figures as well as the proportional prevalence in relation to the national average (England=100) and their corresponding 95% confidence intervals are shown in figure 26.

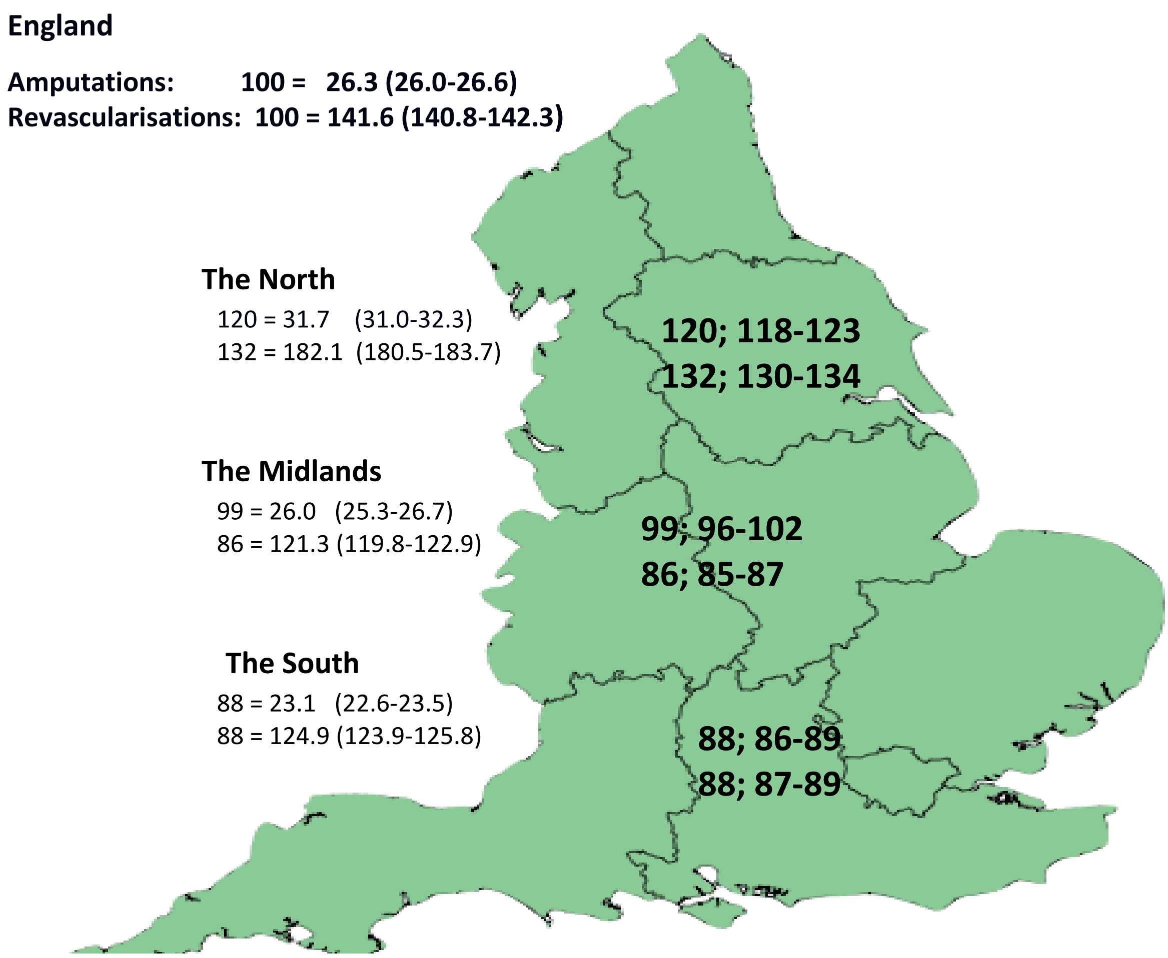


Figure 26

Proportional Prevalence (relative to national average; England=100) of Amputations (upper value) and Revascularisations (lower value) (Inside Map) with Actual Rates (Outside map); Males and Females: England 2003-2009

A gradient across England is evident with the North undertaking procedures at a rate that is above the national average whereas the reverse is true for the South. The Midlands undertook amputations in line with the national average but have a below average revascularisation rate. This North/South divide is evident across all age groups (Fig 27 and 28)

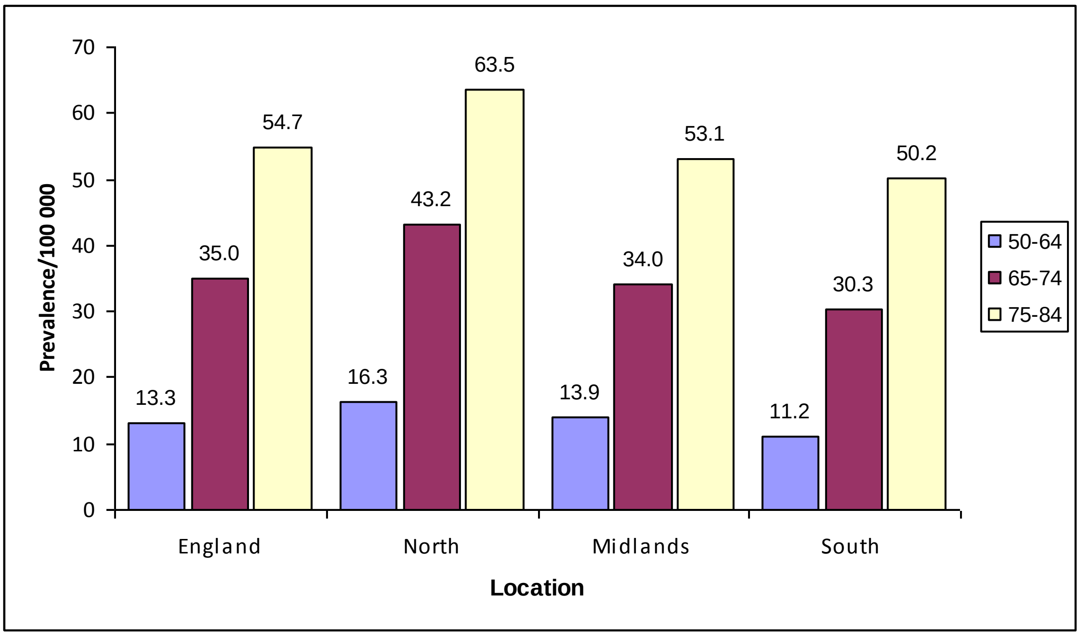


Fig 27
Age specific prevalence, per 100 000, major lower limb amputations:
Males and females; England 2003-2009

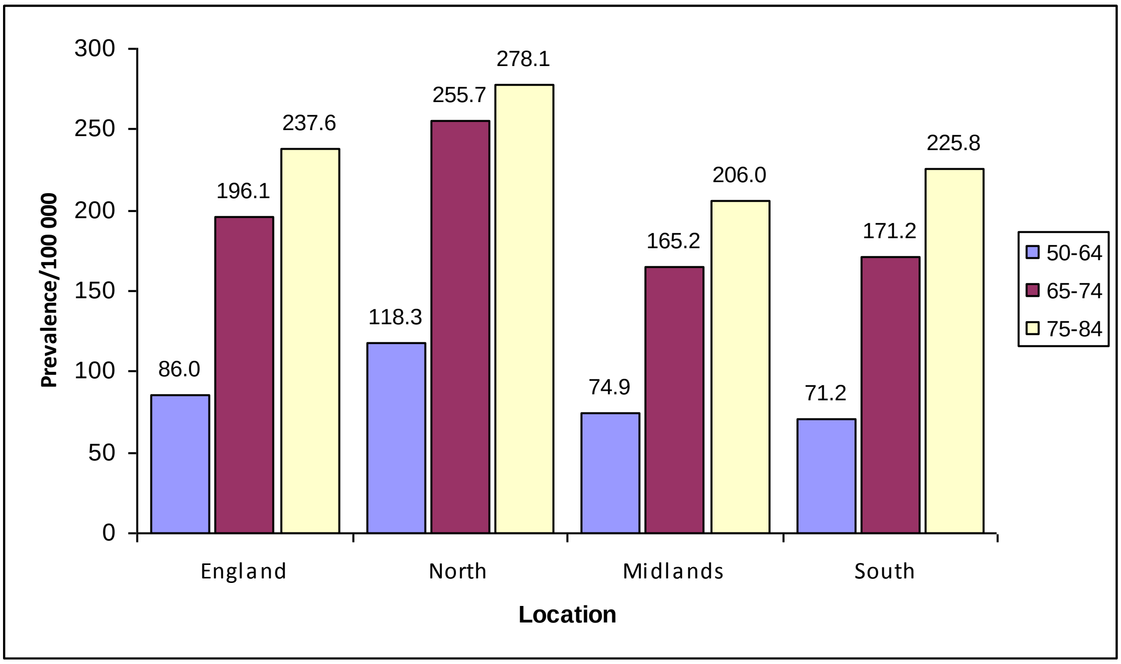


Fig 28
Age specific prevalence, per 100 000, lower limb revascularisation:
Males and females; England 2003-2009

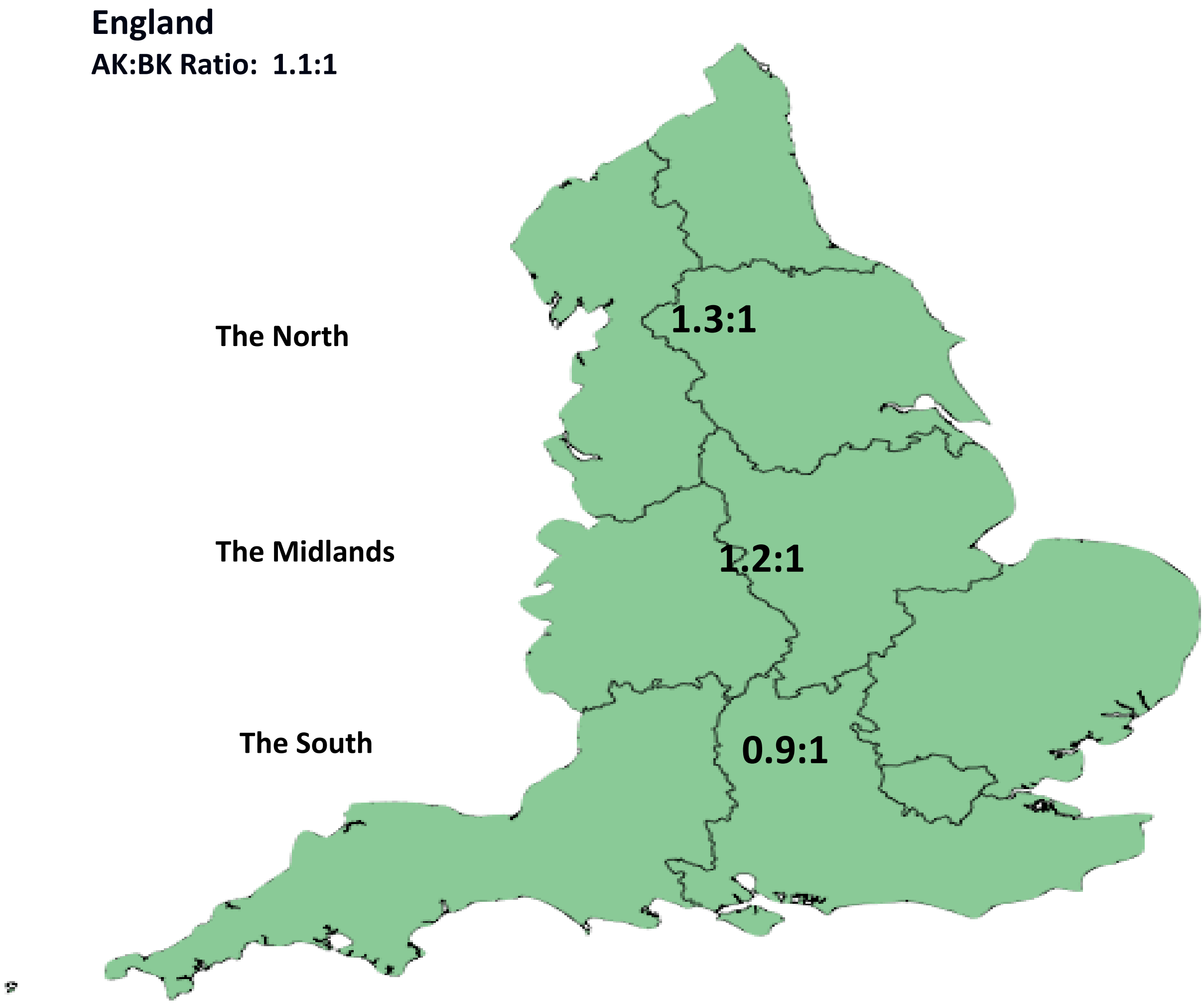


Figure 29

Ratio of Above (AK): Below Knee (BK) Amputation in North and South England;

Males and Females: England 2003-2009

The higher overall amputation rate in the North is matched by a greater above to below knee amputation ratio (fig 29).

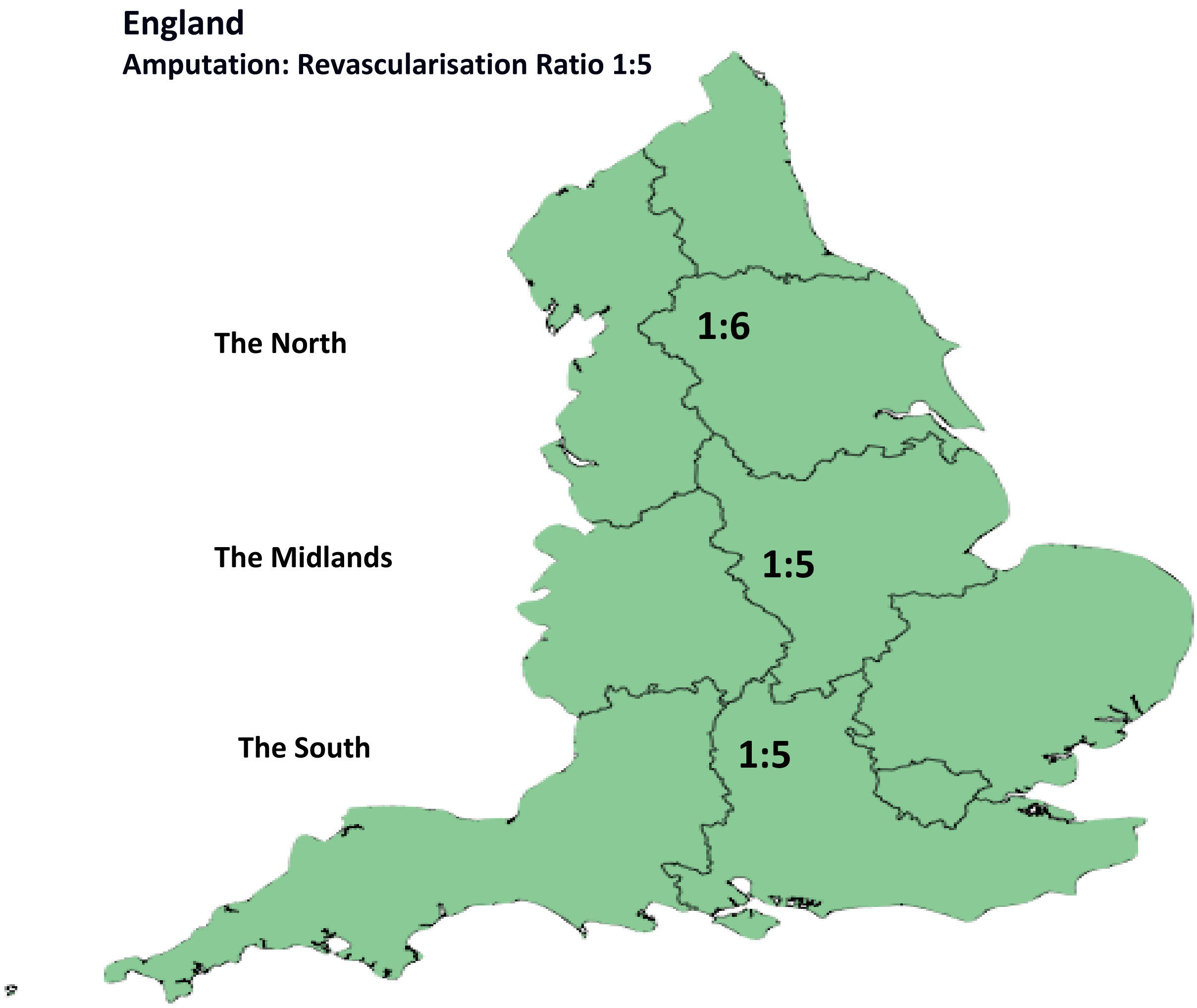


Figure 30

Ratio of Amputations to Revascularisation in North and South England;

Males and Females: England 2003-2009

The higher amputation rate in the North is matched by a greater revascularisation rate as shown by the amputation to revascularisation ratio (fig 30).

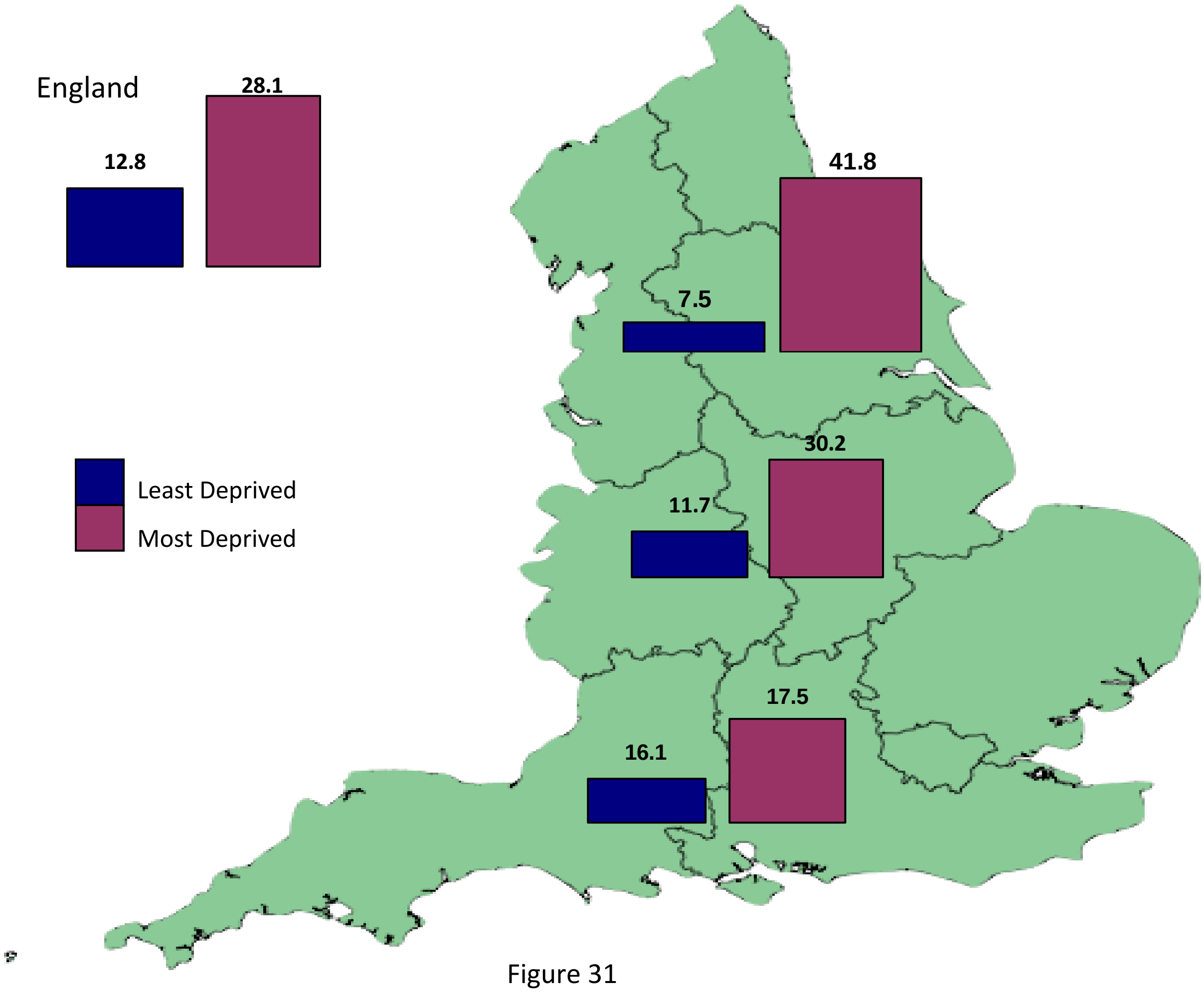


Figure 31

Percentage Proportion of amputees from the most and least deprived areas:

North and South England: Males and Females; 2003-2009

The demographic profile of amputees varies across England. A far greater proportion of Northern amputees come from the most deprived areas compared with the South (figure 31).

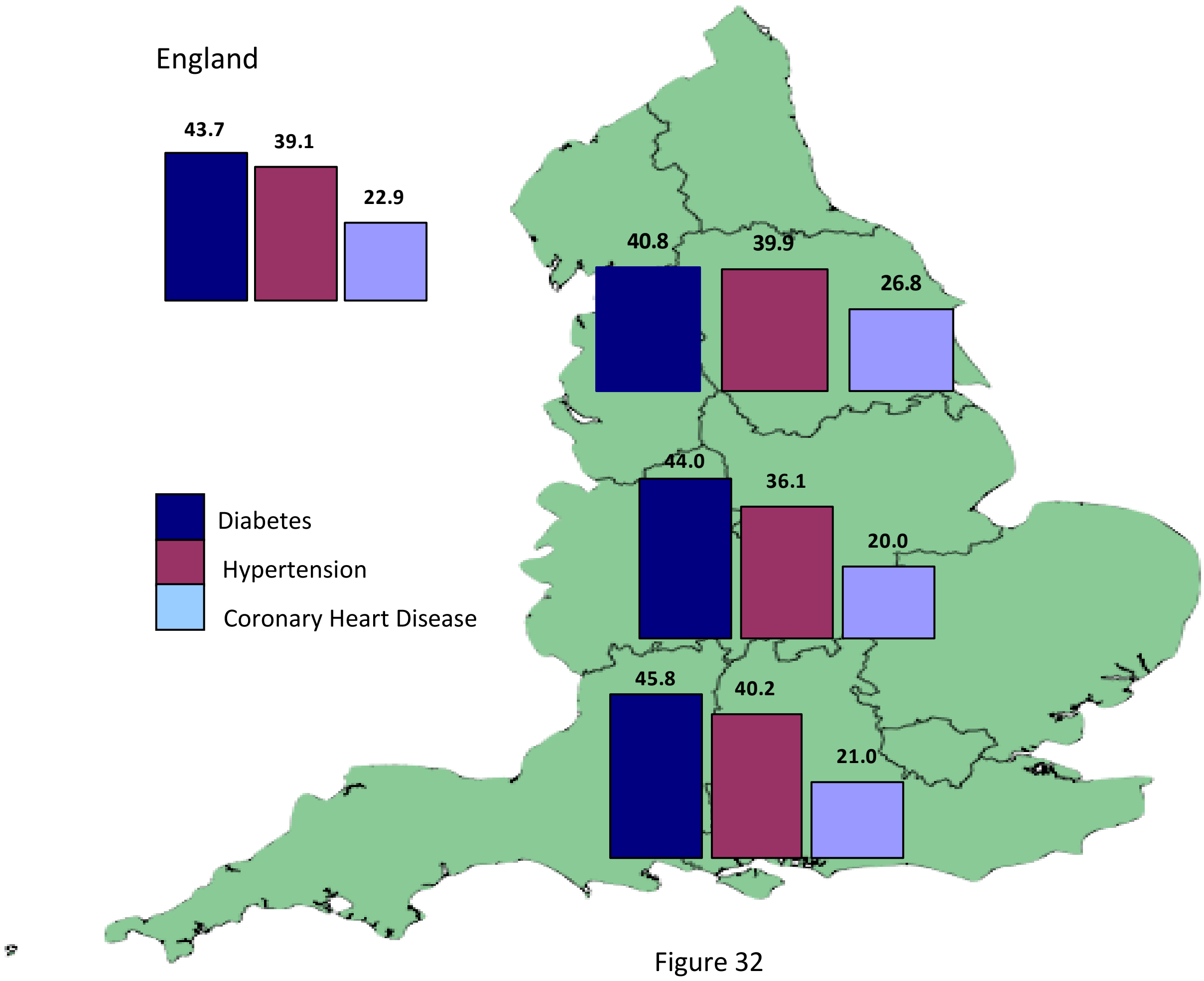


Figure 32

Proportion of amputees with Diabetes, Hypertension and Coronary Heart Disease: North and South England: Males and Females; 2003-2009

Northern amputees, had greater levels of coronary heart disease whereas Southern amputees had greater levels of diabetes. The proportion with hypertension was similar across England (figure 32).

Table 33: Demographic and risk factor profile of amputees by geographical location

		England	*North*	*Midlands*	*South*
Demography	Mean Age	70.6	70.4	70.4	70.8
	% Least deprived	12.8	7.5	11.7	16.1
	% Most deprived	28.1	41.8	30.2	17.5
Risk Factors					
	% Diabetes	43.7	40.8	44.0	45.8
	% Hypertension	39.1	39.9	36.1	40.2
	% Hypercholesterolaemia	8.6	9.1	6.3	9.5
	% Coronary Heart Disease	22.9	26.8	20.0	21.0
	% Cerebrovascular disease	3.3	3.2	3.6	3.3
	% Smoking	8.9	12.2	5.0	8.2

In addition to the highlighted demographic and co-morbidities in figures 31 and 32, table 33 demonstrates the average age and proportion of amputees with hypercholesterolaemia, cerebrovascular disease and smoking. The mean age of amputees was similar across England, with more Northern amputees smoking. The levels of risk factors recorded in HES, particularly, smoking and cerebrovascular disease was surprisingly low.

3.1.2 The Regional Divide

Within the broad North/South divide there were regional variations. The highest amputation rates in the North were seen in the North East. Rates were higher in the East compared with the West Midlands. The lowest rates in the South were seen in the East of England.

The risk factor profile of amputees also followed this broad pattern although amputees from the West Midlands had a worse profile than East Midlands. London amputees had a risk factor profile similar to Northern amputees.

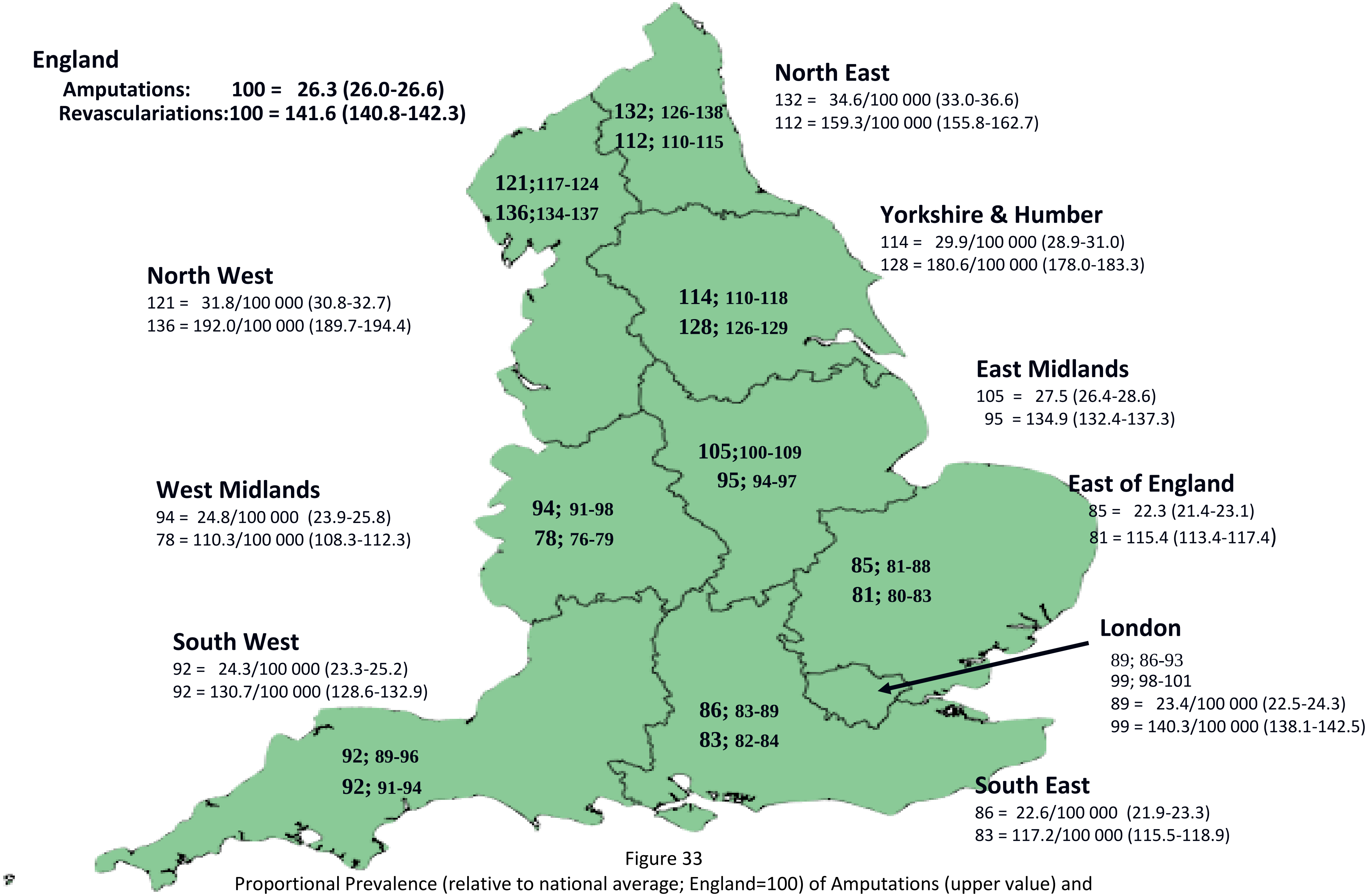


Figure 33
Proportional Prevalence (relative to national average; England=100) of Amputations (upper value) and Revascularisations (lower value) (Inside Map) with Actual Rates (Outside map);
Males and Females combined: England 2003-2009

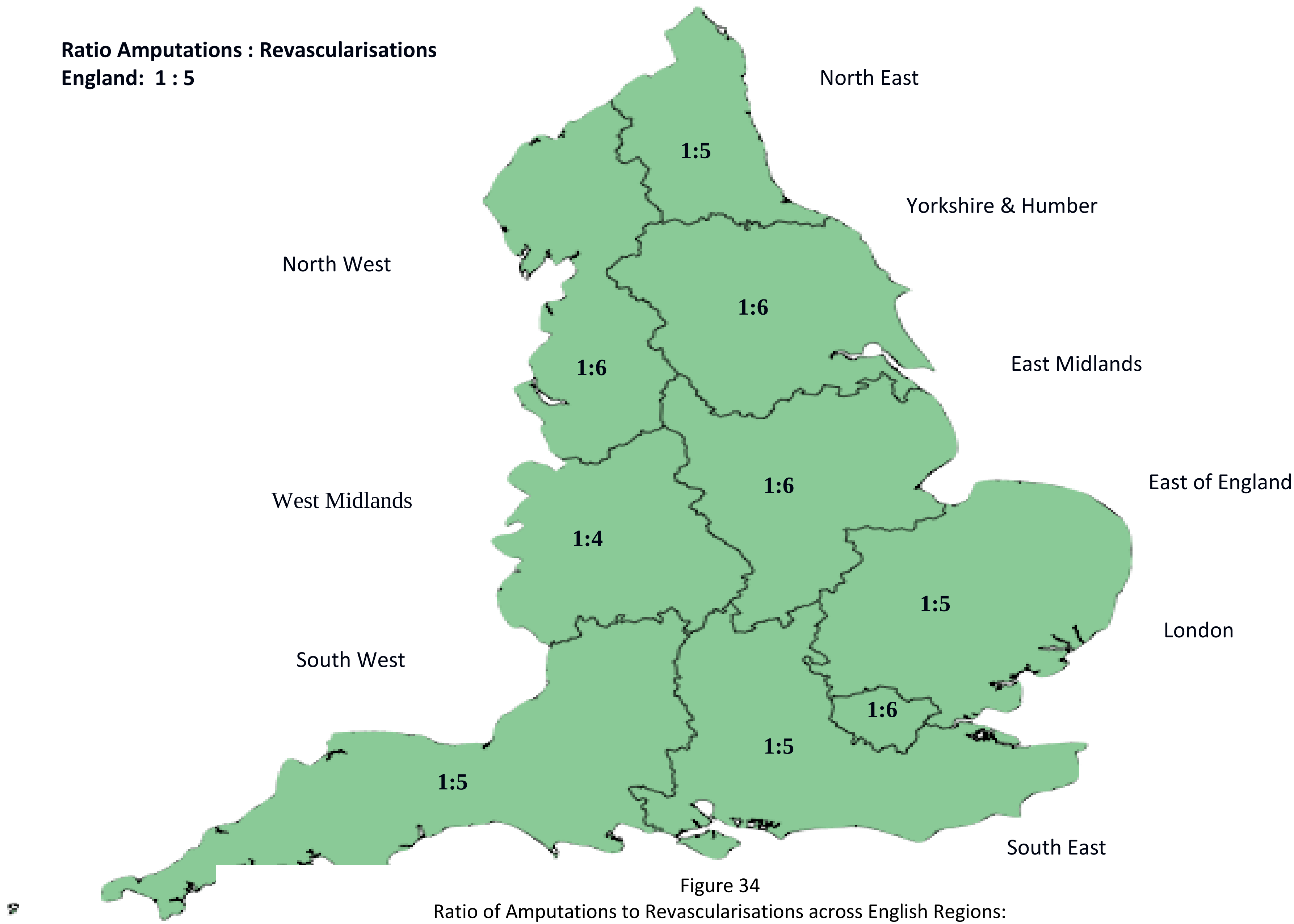


Figure 34
Ratio of Amputations to Revascularisations across English Regions:
Males and Females 2003-2009

Ratio Above to Below Knee Amputation
England: 1.1:1

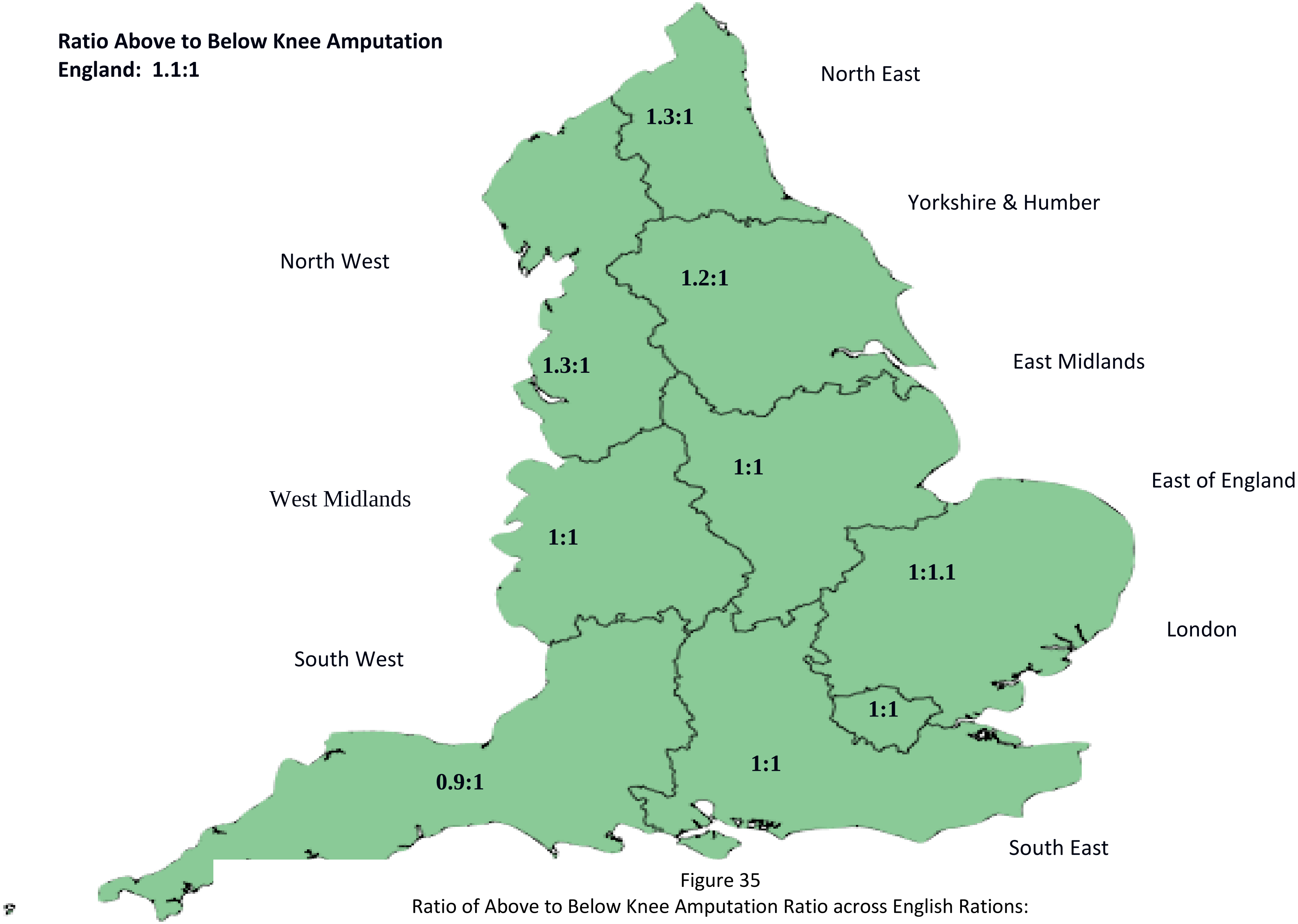


Figure 35
Ratio of Above to Below Knee Amputation Ratio across English Rations:
Males and Females 2003-2009

Table 34: Distribution of risk factors among amputees across English regions; males and females; England 2003-2009

	Mean Age	*Most deprived*	*DM*	*BP*	*HC*	*CHD*	*CVA*	*Smoke*
The North	**69.1**	**41.8**	**40.8**	**39.9**	**9.2**	**26.8**	**3.2**	**12.2**
North West	68.8	43.5	41.8	41.5	8.5	28.3	2.8	14.6
Yorkshire & Humber	69.3	35.7	40.5	36.9	7.9	24.0	3.5	6.7
North East	69.1	46.1	40.0	41.2	11.1	28.1	3.4	15.2
The Midlands	**68.9**	**30.2**	**44.1**	**36.1**	**6.4**	**20.0**	**3.6**	**5.1**
West Midlands	68.6	37.0	45.3	38.5	7.1	20.3	4.4	5.5
East Midlands	69.2	23.3	42.8	33.7	5.6	19.7	2.8	4.6
The South	**69.6**	**17.5**	**45.8**	**40.3**	**9.5**	**21.1**	**3.3**	**8.2**
South West	70.0	13.3	46.4	37.6	6.6	22.0	3.3	7.2
South East	69.2	11.3	44.2	36.3	9.0	20.8	3.5	8.6
London	69.2	32.3	47.0	44.7	15.2	18.6	4.0	8.1
East of England	69.8	12.9	45.5	42.4	7.0	22.8	2.4	8.7
England	**69.3**	**28.1**	**43.7**	**39.1**	**8.6**	**22.9**	**3.3**	**8.9**

DM: Diabetes; BP: hypertension; HC: hypercholesterolaemia; CHD: coronary heart disease; CVA: cerebrovascular accident (stroke); smoke: smoker

3.1.3 The Gender Divide – descriptive statistics

The prevalence of both amputation and revascularisation is approximately double in men than women. This pattern was consistent across North and South England (table 35), each region (table 36) and age group (fig 36 -39).

Table 35: Age Adjusted Prevalence, per 100 000 (95% confidence intervals), of Amputation and Revascularisation by English Region and Sex; 2003-2009

	Males		Females	
	Number	**Prevalence**	**Number**	**Prevalence**
Amputations: England	**17341**	**37.0 (37.1-38.2)**	**7967**	**15.9 (15.5-16.2)**
North	6273	46.5 (45.3-47.6)	2708	18.2 (17.6-18.9)
Midlands	3450	37.4 (36.1-38.6)	1519	15.4 (14.6-16.2)
South	7618	32.3 (31.6-33.1)	3740	14.6 (14.1-15.0)
Revascularisations: England	**90693**	**197.4 (196.1-198.7)**	**45522**	**90.7 (89.9-91.5)**
North	34 009	251.5 (248.8-254.2)	17 775	119.5 (117.7-121.2)
Midlands	15 789	171.1 (168.4-173.8)	7394	75.0 (73.3-76.8)
South	40 915	174.5 (172.8-176.2)	20 353	79.9 (78.4-80.6)

Table 36: Age Adjusted Prevalence, per 100 000 (95% confidence intervals), of Amputation and Revascularisation by English Region and Sex; 2003-2009

	Males		Females	
	Number	**Prevalence**	**Number**	**Prevalence**
Amputations: England	**17341**	**37.0 (37.1-38.2)**	**7967**	**15.9 (15.5-16.2)**
North East	1250	50.8 (48.0-53.6)	544	20.0 (18.3-21.7)
North West	2988	47.1 (45.4-48.8)	1253	17.9 (16.9-18.9)
Yorkshire and Humber	2035	43.4 (41.5-45.3)	911	17.7 (16.6-18.9)
East Midlands	1617	38.7 (36.8-40.6)	744	16.9 (15.6-18.1)
West Midlands	1833	36.3 (34.6-38.0)	775	14.2 (13.2-15.2)
East of England	1692	31.2 (29.7-32.7)	805	13.9 (12.9-14.8)
London	1670	33.2 (31.6-34.7)	829	14.8 (13.8-15.8)
South East	2424	31.4 (30.2-32.7)	1225	14.5 (13.7-15.3)
South West	1832	34.1 (32.5-35.7)	881	15.1 (14.1-16.1)
Revascularisations: England	**90693**	**197.4 (196.1-198.7)**	**45522**	**90.7 (89.9-91.5)**
North East	5512	223.9 (218.0-229.9)	2754	101.0 (97.2-104.8)
North West	16650	261.9 (257.9-265.9)	9030	129.1 (126.5-131.8)
Yorkshire and Humber	11847	251.8 (247.2-256.3)	5991	116.1 (113.2-119.1)
East Midlands	7786	186.8 (182.7-191.0)	3786	86.0 (83.2-88.7)
West Midlands	7983	158.2 (154.7-161.7)	3608	66.2 (64.0-68.4)
East of England	8655	160.6 (157.2-164.0)	4228	73.4 (71.1-75.6)
London	10053	200.0 (196.0-203.9)	4925	87.6 (85.1-90.0)
South East	12462	162.4 (159.6-165.3)	6367	75.9 (74.0-77.8)
South West	9745	182.3 (178.6-185.9)	4833	83.2 (80.8-85.5)

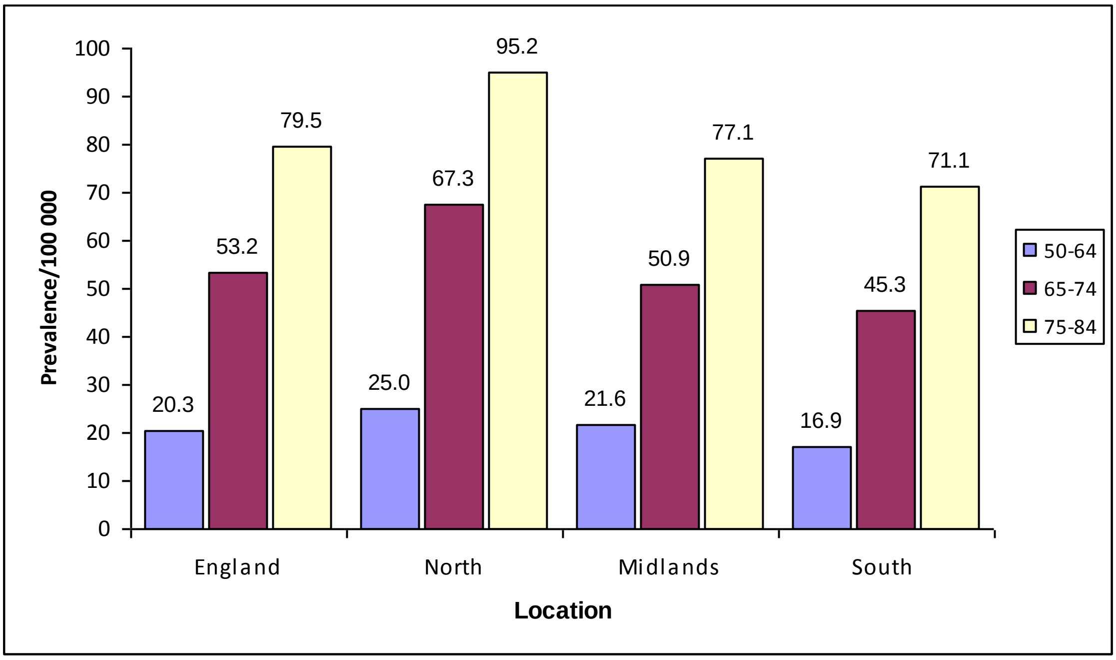


Figure 36

Age specific prevalence, per 100 000 of amputations: males; England 2003-2009

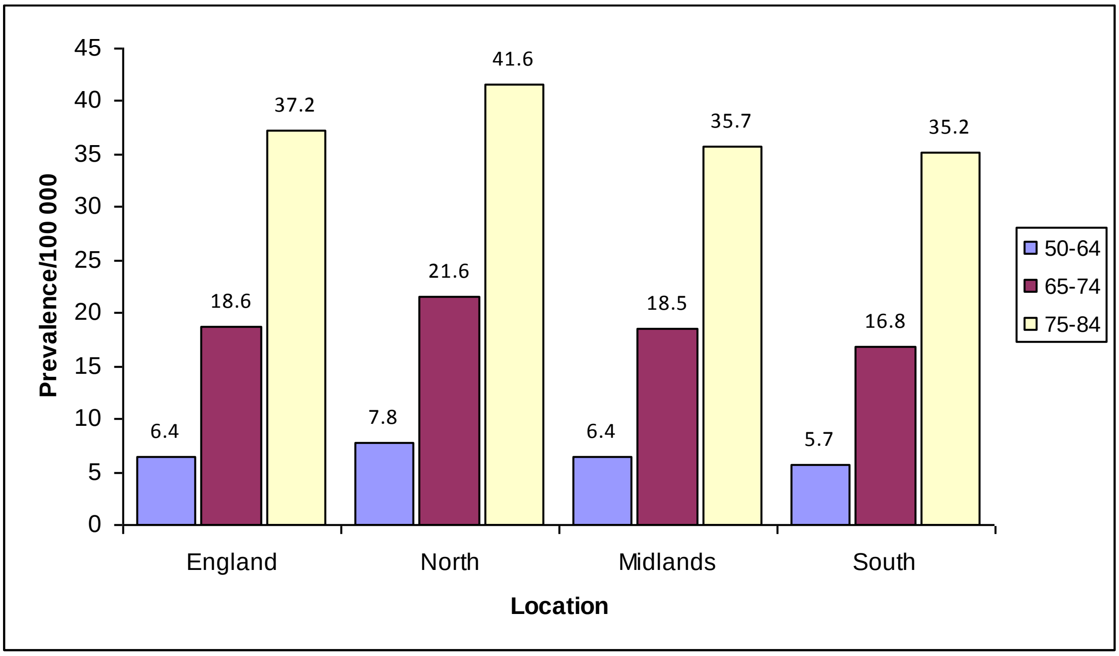


Figure 37

Age specific prevalence, per 100 000 of amputations: females; England 2003-2009

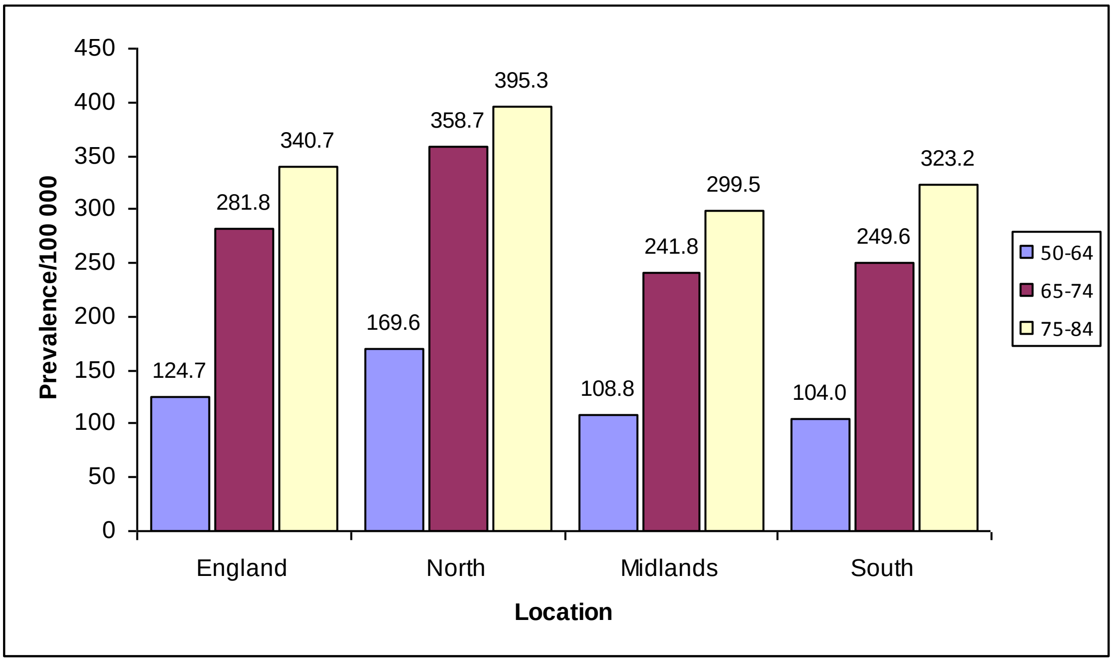


Figure 38
Age specific prevalence, per 100 000 of revascularisations: males;
England 2003-2009

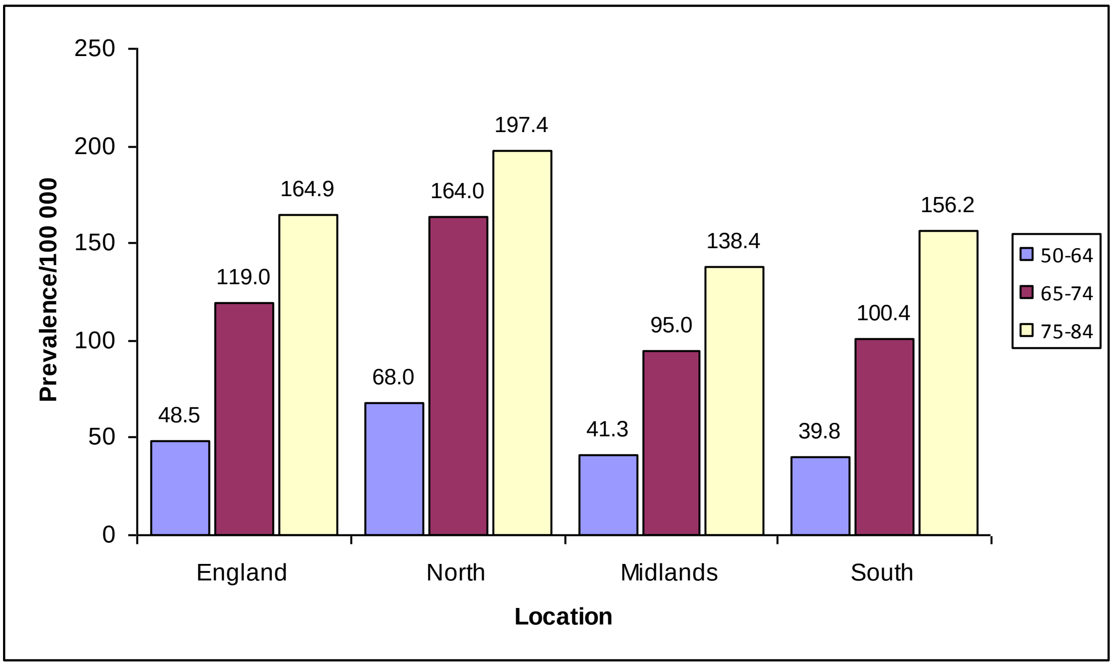


Figure 39
Age specific prevalence, per 100 000 of revascularisations: Females
England 2003-2009

Female amputees were generally older, less deprived, and had lower levels of all risk factors except hypertension (table 37).

Table 37: Percentage distribution of risk factors among of amputees; males and females: England 2003-2009

		England	*North*	*Midlands*	*South*
Males					
Demography	Mean Age	69.3	69.1	68.9	69.6
	Least deprived	12.3	7.4	10.4	16.0
	Most deprived	29.4	42.9	31.7	18.0
Risk Factors	Diabetes	47.1	44.6	48.5	48.7
	Hypertension	37.7	38.4	34.0	39.0
	Hypercholesterolaemia	8.8	9.1	6.3	10.0
	Coronary Heart Disease	25.8	30.0	22.1	24.1
	Cerebrovascular disease	3.3	3.0	3.9	3.4
	Smoking	10.3	13.4	6.0	10.0
Females					
Demography	Mean Age	71.9	71.7	71.9	72.1
	Least deprived	13.4	7.6	13.1	16.2
	Most deprived	26.8	40.6	28.7	16.9
Risk Factors					
	Diabetes	40.4	36.9	39.5	42.8
	Hypertension	40.5	41.4	38.2	41.5
	Hypercholesterolaemia	8.4	9.2	6.3	9.0
	Coronary Heart Disease	20.0	23.6	17.9	18.0
	Cerebrovascular disease	3.3	3.5	3.3	3.2
	Smoking	7.5	11.0	4.1	6.3

3.1.4 The North/South, Regional and Gender divide: Analytical Statistics

We were able to match 7543 amputations (29.8%) to a revascularisation. Table 38 demonstrates the effect of patient demography and co-morbidity on the odds of having an amputation with and without a revascularisation. Increased odds of having an amputation associated with a revascularisation were seen with increasing age, male sex and all risk factors except diabetes. Social deprivation had no effect on amputation with or without revascularisation.

The odds of an amputation both with and without revascularisation by geographical location are shown in table 39. Relative to the Midlands, the odds of having an amputation without revascularisation is significantly lower in the North of England. There was no significant difference between the Midlands and the South. Within each region, using the North West as the standard, the odds of having an amputation with a revascularisation was significantly lower in all regions except Yorkshire and Humber where there was no significant difference.

Thus, the higher rate of amputation in the North, matched by a higher rate of revascularisation translated into a reduced risk of amputation without a revascularisation.

The risk of an amputation, both with and without revascularisation, did not increase with social deprivation.

Table 38: Multi-variable logistic Regression; Odds of Amputation with and without Revascularisation by Risk factor

		Amputation alone (n=17 765) OR (95% CI)	Amputation with Revascularisation (n=7 543). OR (95% CI)	Sig
Age group	50-54 (standard)			
	55-59	0.79 (.67-.92)	1.27 (1.09-1.49)	<.001
	60-64	0.67 (.58-.78)	1.49 (1.29-1.73)	<.001
	65-69	0.66 (.57-.76)	1.52 (1.32-1.76)	<.001
	70-74	0.65 (.56-.74)	1.55 (1.34-1.79)	<.001
	75-79	0.71 (.62-.81)	1.42 (1.23-1.64)	<.005
	80-84	0.81 (.70-.94)	1.24 (1.07-1.43)	<.001
Gender	Male sex	.94 (.88-1.00)	1.07 (1.00-1.14)	.051
Deprivation	Most deprived (standard)			
	Second most deprived	1.02 (.95-1.11)	0.98 (.90-1.06)	.562
	Third most deprived	1.05 (.97-1.14)	0.95 (.87-1.04)	.245
	Fourth most deprived	1.07 (.97-1.16)	0.94 (.86-1.03)	.171
	Least deprived	0.93 (.85-1.03)	1.07 (.97-1.18)	.153
Risk Factors	Diabetes	1.34 (1.26-1.42)	0.75 (.70-.79)	<.001
	Hypertension	0.68 (.64-.72)	1.48 (1.39-1.57)	<.001
	High cholesterol	0.50 (.46-.52)	1.98 (1.81-2.17)	<.001
	Coronary heart disease	0.70 (.66-.75)	1.43 (1.34-1.52)	<.001
	Stroke	0.93 (.80-1.08)	1.08 (.93-1.25)	.340
	Smoker	0.49 (.49-.53)	2.05 (1.88-2.23)	<.001

Table 39: Unadjusted and Adjusted odds of location predicting amputation with and without revascularisation

	Unadjusted		Adjusted for Demography*		Adjusted for demographic and disease risk factors**	
	OR (95% CI)	**Sig.**	**OR (95% CI)**	**Sig.**	**OR (95%CI)**	**Sig.**
Amputation Alone (n=17765)						
North West (standard)						
North East	1.31 (1.16-1.48)	<.05	1.27 (1.12-1.44)	<.05	1.32 (1.17-1.51)	<.05
Yorkshire & Humber	1.10 (1.00-1.22)	<.05	1.10 (0.99-1.22)	.071	1.00 (0.90-1.11)	.996
West Midlands	1.46 (1.31-1.63)	<.05	1.44 (1.29-1.61)	<.05	1.25 (1.12-1.41)	<.05
East Midlands	1.62 (1.45-1.81)	<.05	1.58 (1.40-1.77)	<.05	1.34 (1.19-1.51)	<.05
South West	1.42 (1.28-1.58)	<.05	1.36 (1.22-1.52)	<.05	1.24 (1.10-1.39)	<.05
South East	1.50 (1.36-1.54)	<.05	1.32 (1.19-1.46)	<.05	1.24 (1.12-1.38)	<.05
London	1.19 (1.07-1.32)	<.05	1.17 (1.05-1.30)	<.05	1.15 (1.03-1.29)	<.05
East of England	1.45 (1.30-1.62)	<.05	1.38 (1.23-1.55)	<.05	1.29 (1.15-1.46)	<.05
Relative to Midlands						
Northern England	0.72 (.66-.77)	<.05	0.72 (.67-.78)	<.05	0.82 (.75-.89)	<.001
Southern England	0.88 (.81-.95)	<.05	0.87 (.80-.94)	<.05	0.95 (.88-1.03)	.218
Amputation and Revascularisation (n=7543)						
North West (standard)						
North East	.79 (.70-.90)	<.05	.79 (.70-.89)	<.05	.75 (.66-.86)	<.05
Yorkshire & Humber	.90(.82-1.00)	.057	.91(.82-1.01)	.071	1.00 (.90-1.11)	.996
West Midlands	.69 (.62-.77)	<.05	.69 (.62-.78)	<.05	.80 (.71-.89)	<.05
East Midlands	.63 (.56-.71)	<.05	.63 (.56-.71)	<.05	.75 (.66-.84)	<.05
South West	.71 (.64-.80)	<.05	.73 (.66-.84)	<.05	.81 (.72-.91)	<.05
South East	.75 (.68-.83)	<.05	.76 (.69-.84)	<.05	.81 (.72-.89)	<.05
London	.85 (.76-.95)	<.05	.86 (.77-.96)	<.05	.87 (.77-.97)	<.05
East of England	.71 (.64-.80)	<.05	.72 (.65-.81)	<.05	.77 (.69-.87)	<.05
Relative to Midlands						
Northern England	1.40 (1.29-1.51)	<.05	1.39 (1.28-1.50)	<.05	1.22 (1.13-1.33)	<.001
Southern England	1.14 (1.05-1.23)	<.05	1.16 (1.07-1.25)	<.05	1.05 (.97-1.14)	.218

*Age, sex, social class (defined by IMD quintile)
** Diabetes, hypertension, hypercholesterolaemia, coronary, cerebral vascular disease and smoking

The risk of an above knee amputation was lower in men, diabetics and those having endovascular only revascularisation (table 40). The risk was higher in women, those having a coronary or cerebrovascular event and having either surgical or a combined endovascular and surgical revascularisation. The risk did not increase with social deprivation or living in the North of England.

When only patients having revascularisation were analysed, endovascular treatment was again associated with lower odds of an AK amputation compared to surgery or combined surgical and endovascular treatment after adjustment for confounders (table 41).

Table 40: Multi-variable regression analysis for above knee amputation

Group	*Co-variates*	*Risk of Above knee Amputation*	
		OR (95% CI)	p value
Age group	50-54 (standard)		
	55-59	.83 (.59-1.18)	.301
	60-64	1.23 (.89-1.70)	.218
	65-69	1.19 (.86-1.63)	.288
	70-74	1.22 (.89-1.68)	.208
	75-79	1.04 (.76-1.42)	.824
	80-84	1.25 (.91-1.73)	.170
Gender	Male sex	.64 (.55-.74)	<.001
Deprivation	Most deprived (standard)		
	Second most deprived	.87 (.73-1.04)	.121
	Third most deprived	.79 (.65-.96)	.015
	Fourth most deprived	.96 (.78-1.17)	.686
	Least deprived	.82 (.66-1.02)	.075
Risk Factors	Diabetes	.44 (.39-.50)	<.001
	Hypertension	.94 (.82-1.07)	.357
	Hypercholesterolaemia	1.00 (.82-1.21)	.972
	Coronary heart disease	1.28 (1.10-1.47)	.001
	Stroke	1.90 (1.33-2.71)	<.001
	Smoker	1.13 (.94-1.36)	.185
Revascularisation	No revascularisation (standard)		
	Only endovascular	.82 (.75-.90)	<.001
	Only surgical	1.16 (1.07-1.25)	<.001
	Endovascular and Surgical	1.24 (1.09-1.40)	.001
Location	Midlands (standard)		
	Northern England	1.10 (.92-1.32)	.304
	Southern England	.86 (.72-1.04)	.117

Table 41: Multi-variable regression analysis for above knee amputation using endovascular revascularisation as sole treatment modality

Control Group	*Co-variate*	*Risk of Above knee Amputation*	*Sig.*
		OR (95% CI)	
Surgical only revascularisation	Endovascular alone*	.71 (.61-.79)	<.001
Endovascular and surgical revascularisation	Endovascular alone*	.67 (.58-.78)	<.001

* Adjusted for demographic and disease risk factors

3.2 The Ethnic Divide 2003-2009

The proportional prevalence of amputations and revascularisations in the main ethnic groups, relative to the White British group are shown figure 40. The combined male and female proportional prevalence of amputation relative to the majority White British population was 40% lower in South Asians, 19% higher in the White non British population, and, 69% higher in Blacks. Although revascularisation rates were significantly higher in the White non British group, they were significantly lower in both the Black and Asian groups.

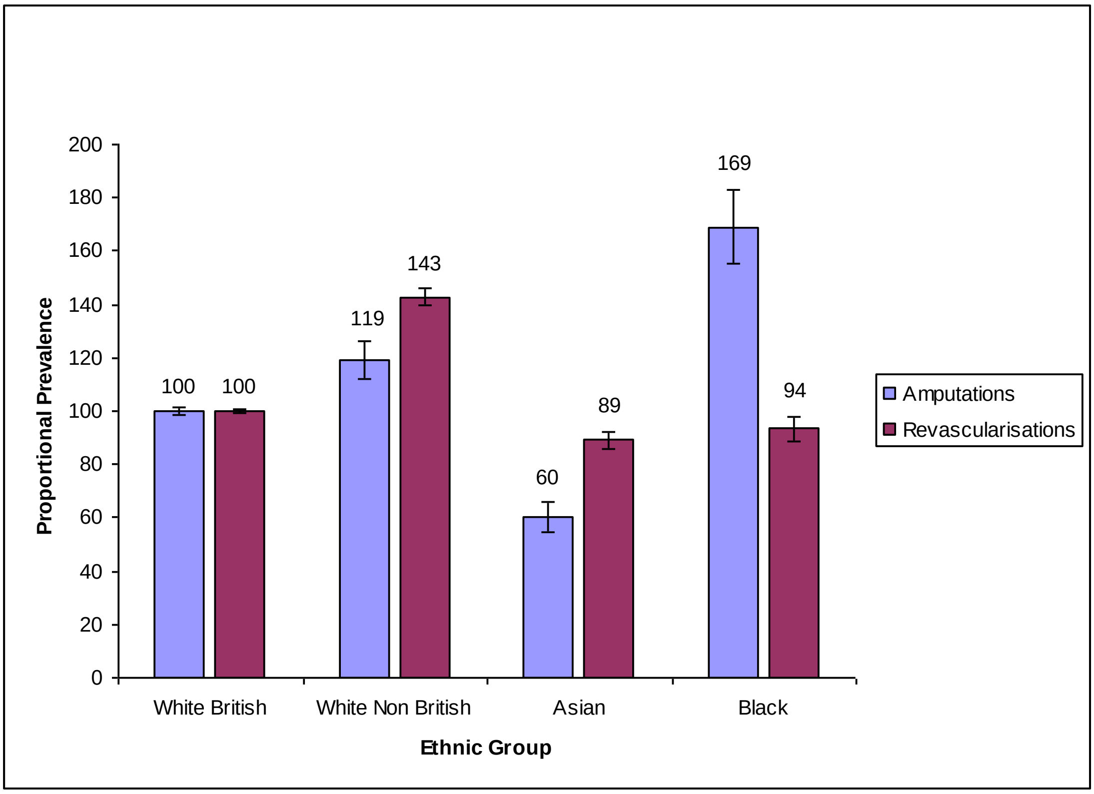


Figure 40
Age Adjusted Proportional Prevalence (95% confidence intervals) of Amputation and Revascularisation by Ethnic Group; Males and Females; England 2003-2009

There is, however, heterogeneity within these broad groups. Within ethnic sub-groups, Indian Asians have a higher amputation rate and a lower revascularisation rate compared with Pakistani Asians and Black Caribbeans have higher rates of amputation and revascularisation compared with Black Africans.

The gender difference observed in the general population was replicated in ethnic groups. However, the gap between minority men and women is three times wider (table 40). The exception was Black women, both African and Caribbean, whose rates more closely match their male counterparts.

Ethnic classification was, however, missing in 15% of amputations and 17% of revascularisations.

Table 42: Number and Age Adjusted Prevalence of Amputations and Revascularisations by Ethnic Group; men and women aged 50-84: England 2003-2009

	Males		Females	
	Number	Rate/100 000 (95%CI)	Number	Rate/100 000 (95%CI)
Amputations: England	**17,341**	**37.7 (37.1-38.2)**	**7,967**	**15.9 (15.5-16.2)**
White British	13,496	32.1 (31.5-32.6)	6,109	13.2 (12.9-13.5)
White Non British$	736	40.7 (37.8-43.7)	305	14.7 (13.0-16.3)
All Asian*	225	18.8 (16.2-21.3)	77	7.4 (5.6-9.3)
All Black†	258	42.7 (37.3-48.0)	172	32.3 (26.7-37.8)
Missing Ethnicity	2,501 (14%)		1,240 (16%)	
Ethnic Subgroups				
Irish	160	16.8 (14.2-19.5)	54	4.0 (2.8-5.2)
White Other	576	66.4 (60.9-71.8)	251	20.2 (17.4-23.0)
Indian	141	21.8 (18.1-25.5)	43	7.7 (5.1-10.2)
Pakistani	51	17.5 (12.5-22.5)	19	6.9 (3.4-10.4)
African	178	23.8 (15.8-31.9)	126	25.3 (14.8-35.9)
Caribbean	38	40.4 (34.2-46.6)	29	31.8 (25.8-37.7)
Revascularisations: England	**90,693**	**197.4 (196.1-198.7)**	**45,522**	**90.7 (89.9-91.5)**
White British	67,777	161.6 (160.4 - 62.8)	34,141	74.3 (73.5-75.1)
White Non British$	2905	244.3 (237.1-251.5)	1515	101.2 (96.9-105.5)
All Asian*	1781	145.3 (138.3- 152.3)	617	57.1 (52.2-62.0)
All Black†	817	132.6 (123.3-141.9)	508	83.9 (76.0-91.8)
Missing Ethnicity	15 100 (17%)		7702 (17%)	
Ethnic Subgroups				
Irish	701	125.1 (117.8-132.4)	363	50.0 (45.7-54.2)
White Other	2204	374.5 (361.5-387.6)	1152	155.7 (148.0-163.4)
Indian	840	128.6 (119.6-137.7)	310	50.1 (44.1-56.1)
Pakistani	517	167.5 (152.6-182.4)	174	66.6 (55.6-77.6)
African	545	99.5 (81.5-117.6)	329	63.5 (48.0-79.1)
Caribbean	144	122.2 (111.6-132.9)	98	75.9 (67.2-84.5)

* Includes Indian, Pakistani, Bangladeshi and Asian Other

† Includes Black African, Black Caribbean and Black Other

$ Includes 'White Irish' and 'White other'

Table 43 explores the risk factor profile of amputees from the different ethnic groups. The White non British group resemble the majority White British group whereas Asians and Blacks differ widely. Asians were generally younger, more deprived and had greater levels of risk factors, particular diabetes, hypertension and coronary heart disease compared with the majority population. Blacks had a similar proportion of diabetes to Asians but much greater levels of deprivation and hypertension.

Table 43: Distribution of Risk Factors among Amputee Ethnic Groups; Males and Females aged 50-84: England 2003-2009

Males	*Risk Factor*	*England*	*White British*	*White Non British*	*Asian*	*Black*
Males	**Number**	**17341**	**13496**	**736**	**225**	**258**
	Median Age	70	70	70	65	71
	% Least deprived	12.3	12.3	12.1	7.1	1.9
	% Most Deprived	29.4	29.1	34.0	34.7	54.3
	% Diabetes	47.1	46.9	46.9	72.4	63.6
	% Hypertension	37.7	38.0	41.2	40.4	55.8
	% High Cholesterol	8.8	8.8	12.2	9.3	14.0
	% History of CHD	25.8	26.7	25.4	32.9	17.1
	% History of Stroke	3.3	3.1	3.9	5.8	8.5
	% Smoker	10.3	10.4	12.5	5.3	8.1
Females	**Number**	**7967**	**6109**	**305**	**77**	**172**
	Median Age	74	74	74	68	72
	% Least deprived	13.4	13.4	7.9	9.1	4.7
	% Most Deprived	26.8	26.4	36.7	40.3	48.3
	% Diabetes	40.4	39.6	38.0	68.8	77.3
	% Hypertension	40.5	39.7	45.6	54.5	61.6
	% High Cholesterol	8.4	7.9	13.4	15.6	19.8
	% History of CHD	20.0	20.2	20.0	35.1	18.6
	% History of Stroke	3.3	3.2	5.2	2.6	7.0
	% Smoker	7.5	8.0	8.9	.0	1.2
Total	**Number**	**25312**	**19605**	**1041**	**302**	**430**
	Median Age	72.0	72.0	72.0	66.5	71.3
	% Least deprived	12.8	12.8	10.0	8.1	3.3
	% Most Deprived	28.1	27.8	35.3	37.5	51.3
	% Diabetes	43.7	43.3	42.5	70.6	70.4
	% Hypertension	39.1	38.8	43.4	47.5	58.7
	% High Cholesterol	8.6	8.4	12.8	12.5	16.9
	% History of CHD	22.9	23.4	22.7	34.0	17.8
	% History of Stroke	3.3	3.1	4.6	4.2	7.8
	% Smoker	8.9	9.2	10.7	2.7	4.7

Table 44: Unadjusted and increasingly adjusted odds for amputation with and without revascularisation by ethnic group (relative to White British)

	Unadjusted		Adjusted for Demography*		Adjusted for demographic and disease risk factors**	
	OR (95% CI)	Sig.	**OR (95% CI)**	Sig.	**OR (95%CI)**	Sig.
Amputation Alone (14938)						
White non British	.83 (.77- .90)	.000	.84 (.77-.91)	.000	.86 (.79-.94)	.001
Asian	.68 (.59-.78)	.000	.68 (.59-.79)	.000	.54 (.46-.62)	.000
Black	1.63 (1.43-1.85)	.000	1.45 (1.27-1.66)	.000	1.07 (.93-1.23)	.359
Amputation and Revascularisation (6634)						
White non British	.91 (.82-1.02)	.112	.88 (.78-.99)	.033	.88 (.78-.99)	.034
Asian	.54 (.43-0.68)	.000	.54 (.43-.68)	.000	.46 (.36-.58)	.000
Black	1.83 (1.54-2.17)	.000	1.67 (1.40-1.99)	.000	1.35 (1.13-1.61)	.001

* Age, sex, social class
** Diabetes, hypertension, hypercholesterolaemia, coronary heart disease, cerebrovascular disease, smoking

The odds of having an amputation with and without a revascularisation as compared with the majority White British group are shown in table 44. The odds of having an amputation without a revascularisation are significantly lower in the White non British group. The risk is even lower in South Asians and reduces further after controlling disease risk factors. The much higher odds of amputation without a revascularisation in Blacks is fully attenuated after controlling demography and disease risk factors.

A similar picture among the ethnic groups is seen for amputations with a revascularisation. However, the excess risk seen in Blacks is not fully attenuated by demographic and disease risk factors.

Figure 41 illustrates the proportion of lower limb revascularisation to coronary revascularisation in each ethnic group and England as a whole. There is an even split in England which remains essentially true for all ethnic groups except Asians. Here, the proportion of coronary revascularisation significantly exceeds lower limb revascularisation.

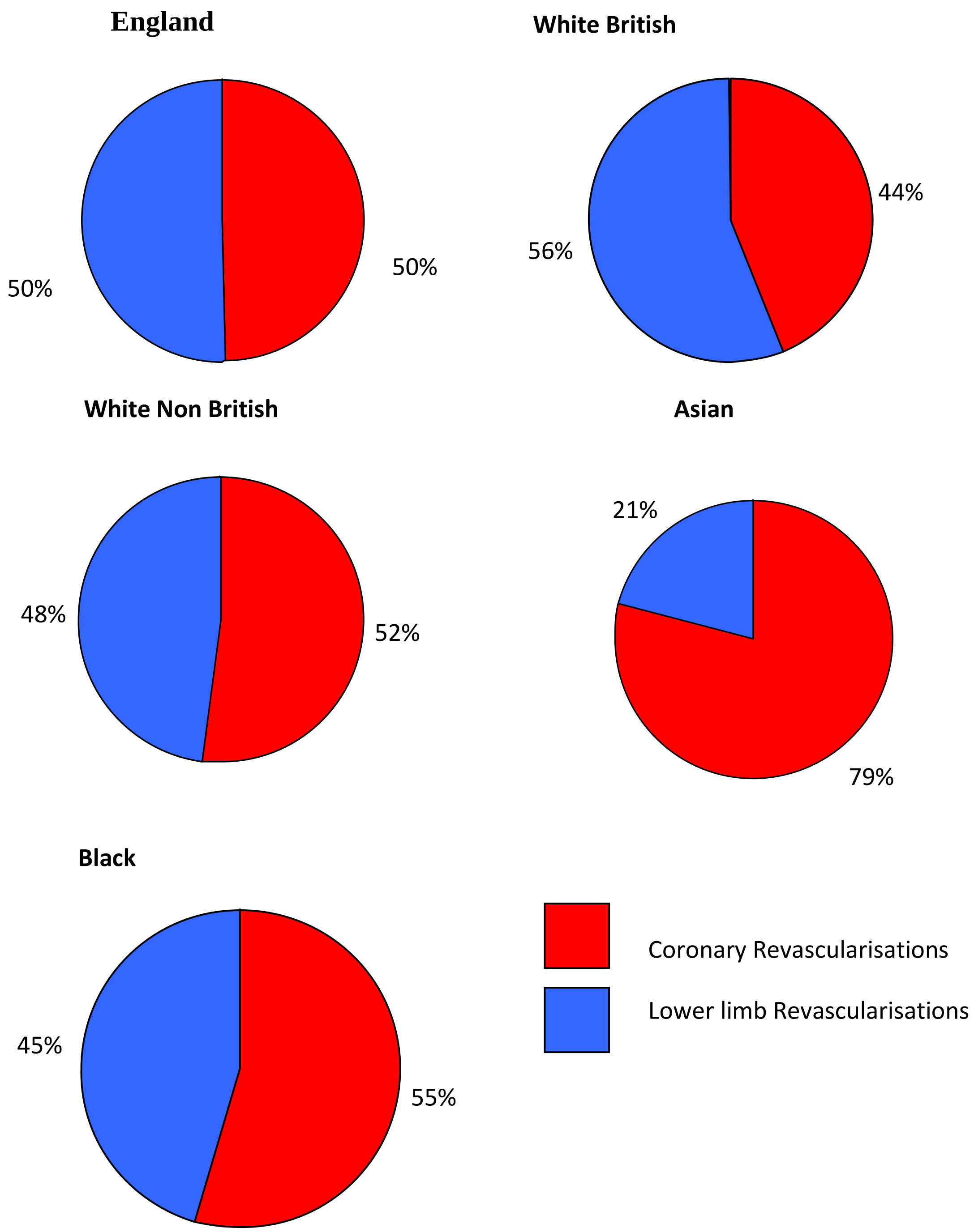


Figure 41
Ratio of Coronary to Lower Limb Revascularisation;
Males and Females aged 50-84 by Ethnic Group; England 2003-2009

3.3 Bringing it all up to date: Amputation and Revascularisation 2003-2013

Ten year period prevalence; England 2003-2013

Between 1st April 2003 and 31 March 2013, there were 42 294 major lower limb amputations (22 645 above knee; 19 658 below knee) and 355 545 revascularisations (endovascular 288 148; surgical 67 397). The overall ten year age-adjusted period prevalence, per 100 000, for those aged 50-84 in England was 25.6 and 215.2 for major amputation and revascularisation, respectively. Major amputation rates were more than double in men than women (36.7 vs 15.4) and higher in Northern compared with Southern England (North 31.4; Midlands 30.8; South 23.1). The above to below knee amputation ratio was 1.2:1 and was higher in women (men 1:1; women 1.5:1) and Northern England (North 1.3:1; Midlands 1.1:1; South 1.1:1).

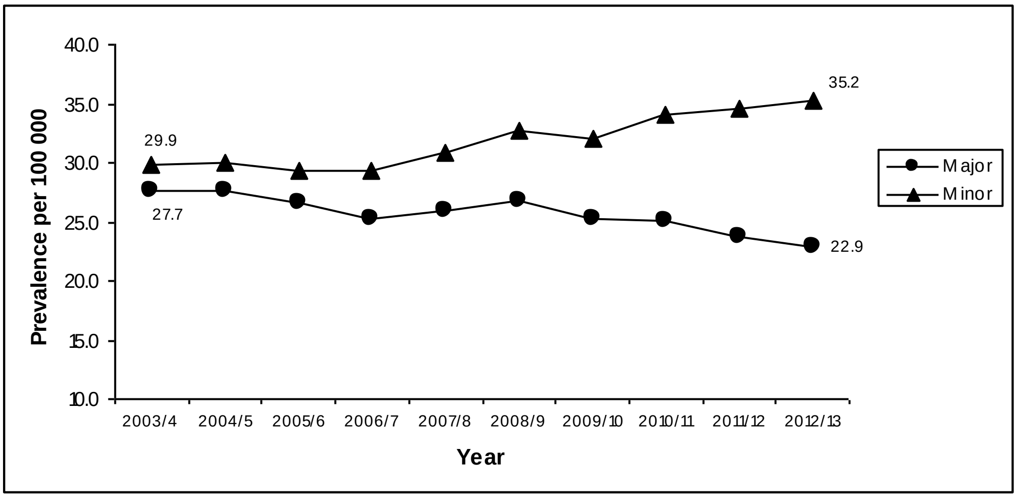
The prevalence, per 100 000, of revascularisation showed a similar pattern with rates higher in men (men 286.3; women 174.0) and Northern England (North 271.9; Midlands 243.5; South 193.7).

The 2003-2013 pattern of inequalities, was, therefore, similar to the 2003-2009 data.

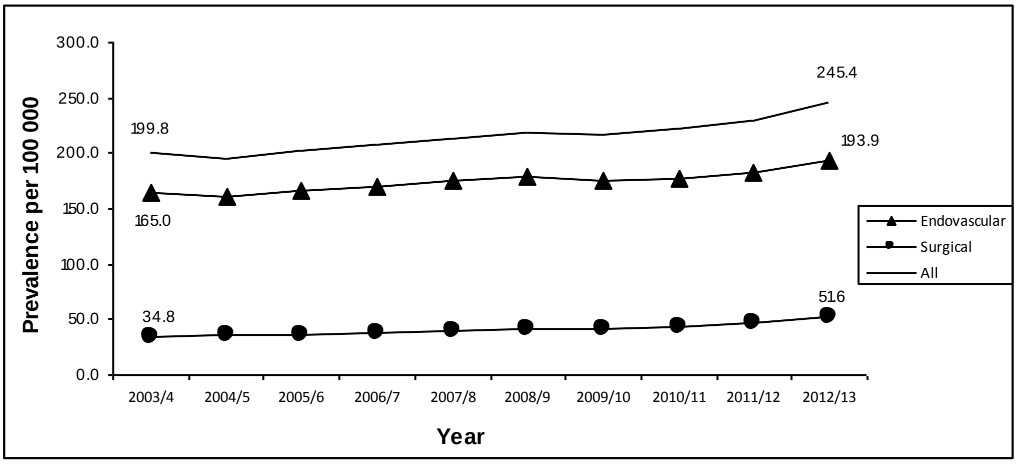
Minor amputations as well as procedures on amputation stumps were collected from the 2003-2013 data. There were 52 525 minor amputations and 11 218 procedures on amputation stumps. The prevalence, per 100 000, of minor amputation and stump procedures was 31.8 and 6.8, respectively. Minor amputation rates were again double in men than women (men 41.0, women 22.5) and higher in Northern compared with Southern England (North 37.0; Midlands 33.8; South 29.0). Stump procedures were three times higher in men than women (10.5 vs 3.4) and the same across England (North 7.1; Midlands 7.8; South 7.1).

3.3.1 Changing prevalence over time: England 2003-2013 (Fig 42)

Figure 42 (a and b) illustrates the yearly age adjusted prevalence of amputation (major and minor) and revascularisation from 2003 to 2013 respectively. It shows the prevalence, per 100 000, of major amputation to have reduced by almost 20% (27.7 to 22.9), whereas minor amputations have increased by a similar amount (29.9 to 35.2/100 000). Revascularisations have also increased by 20% (199.8 to 245.4), although surgical revascularisations have risen at double the rate of endovascular revascularisations (surgery 52% rise, 34.0 to 51.6: endovascular 18% rise; 165.0 to 193.9).



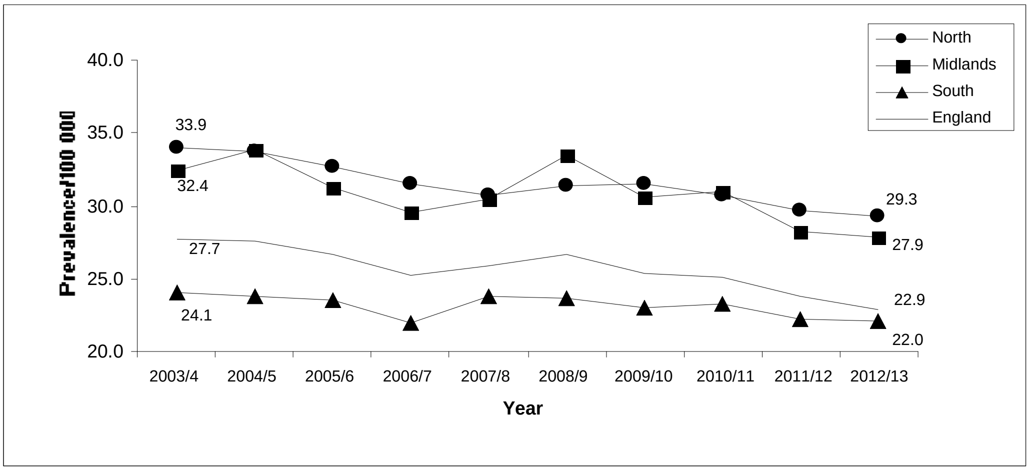
42a
Age adjusted major and minor lower limb amputation prevalence rate; men and women aged 50-84: England 2003-2013



42b
Age adjusted lower limb endovascular and surgical revascularisation prevalence rate; men and women aged 50-84: England 2003-2013

3.3.2 North/South changes 2003-2013 (Fig 43)

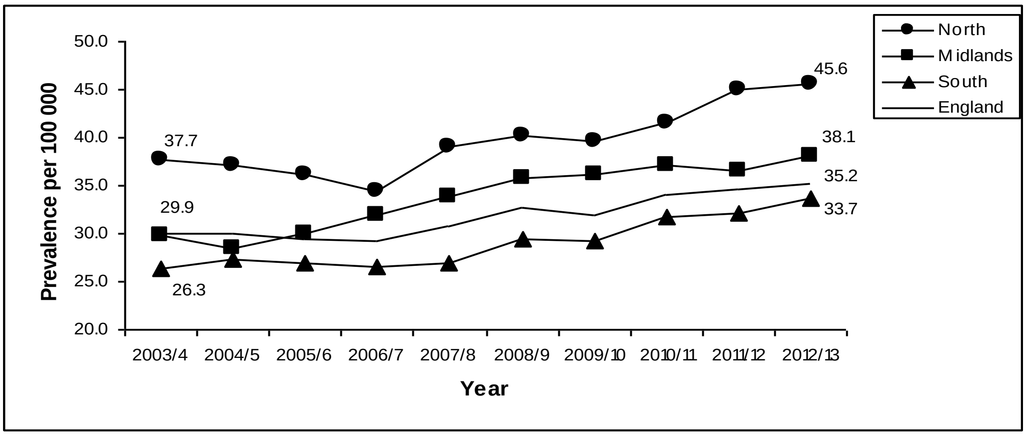
Although rates of major amputation have reduced in all English regions, the North/South divide remains unchanged. Prevalence rates have fallen by approximately 14% in the North (33.9 to 29.3) and Midlands (32.4 to 27.9) and 9% in the South (24.1 to 22.0) over the last ten years.



43a

Age adjusted major lower limb amputation rate by English region; men and women aged 50-84: England 2003-2013

Minor amputation rates have increased across all English regions with the North/South divide again remaining unchanged. Rates have risen by 28% in the South (26.3 to 33.7) and Midlands (29.9 to 38.1) and 21% in the North (37.7 to 45.6).

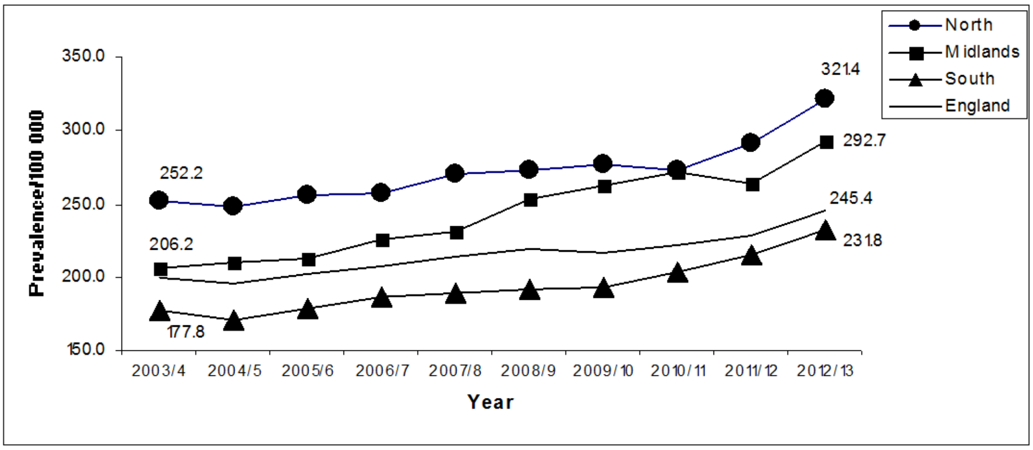


43b

Age adjusted minor lower limb amputation rate by English region;

men and women aged 50-84: England 2003-2013

The higher amputation rate in the North is associated with an increase in revascularisation rates. Rates have risen by 27% in the North, 30% in the South and 42% in the Midlands (North 252.2 to 321.4; South 177.8 to 231.8; Midlands 206.2 to 292.7) over the last ten years.



43c

Age adjusted lower limb revascularisation rate by English region;

men and women aged 50-84: England 2003-2013

Table 45: Percentage change in major and minor amputation rates by English region; males and females 2003-2013

		2003		*2013*		*Percentage Change*	
		Major	Minor	Major	Minor	Major	Minor
North		*33.9*	*37.7*	*29.3*	*45.6*	*-13.6*	*+21.0*
	North East	34.6	72.5	34.1	86.3	-1.4	+19.0
	North West	31.8	28.0	30.1	33.8	-5.3	+20.7
	Yorkshire Humber	29.9	32.7	25.5	39.9	-14.7	+22.0
Midlands		32.4	29.9	27.9	38.1	-13.9	+27.4
	West Midlands	24.8	27.5	22.2	35.9	-10.5	+30.5
	East Midlands	22.3	27.4	23.6	32.6	-5.8	+19.0
South		24.1	26.3	22.0	33.7	-8.7	+28.1
	East of England	22.3	23.5	21.6	29.6	-3.1	+26.0
	London	23.4	23.7	20.7	27.4	-11.5	+15.6
	South East	22.6	27.2	24.2	39.3	+7.1	+44.5
	South West	24.3	30.4	21.1	36.7	-13.2	+20.7
England		27.7	29.9	22.9	35.2	-18.3	+17.7

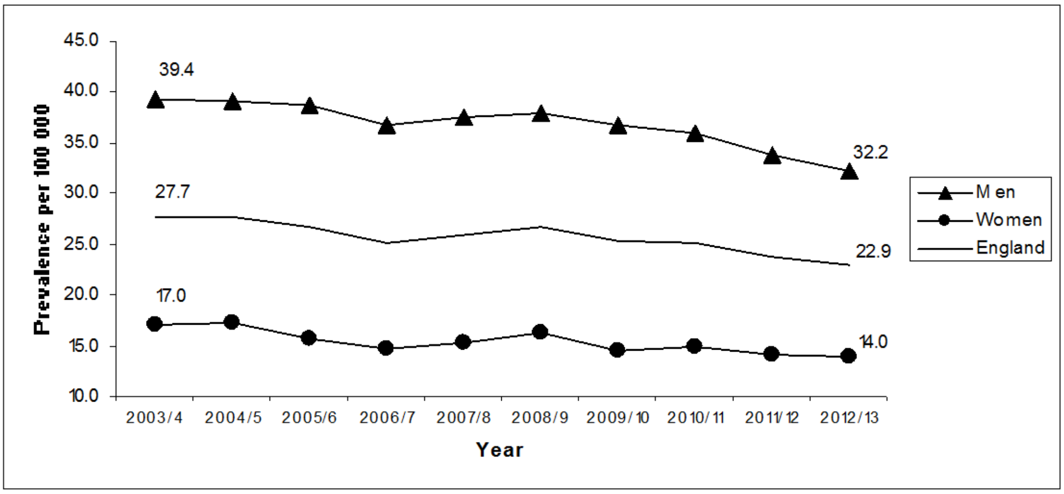
Table 46: Changing ratios of above to below knee amputation and endovascular to surgical by English region; men and women 2003-2013

		2003		*2013*	
		AK:BK	Endo:Surg	AK:BK	Endo:Surg
North		1.3:1	4.4:1	1.4:1	3.5:1
	North East	1.3:1	6.5:1	1.4:1	4.6:1
	North West	1.3:1	3.7:1	1.5:1	2.9:1
	Yorkshire Humber	1.2:1	4.5:1	1.2:1	4.0:1
Midlands		1.1:1	5.2:1	1.1:1	4.3:1
	West Midlands	1.1:1	4.4:1	1.1:1	3.1:1
	East Midlands	1.1:1	6.9:1	1.3:1	6.5:1
South		1.1:1	4.9:1	1.1:1	3.7:1
	East of England	1.1:1	4.8:1	1.0:1	3.4:1
	London	1.0:1	4.9:1	1.0:1	4.5:1
	South East	1.1:1	4.7:1	1.3:1	3.8:1
	South West	0.9:1	5.1:1	0.9:1	3.2:1
England		1.2:1	4.7:1	1.2:1	3.7:1

AK:BK above knee to below knee ratio; Endo: Surg endovascular to surgical ratio

3.3.3 Gender changes 2003-2013 (Fig 44)

The reduction in major amputation rates has affected men (39.4 to 32.2) and women (17.0 to 14.0) equally as rates have fallen in both groups by approximately 18%. The disparity, therefore, is unchanged and rates remain approximately double in men compared with women (Fig 44a).

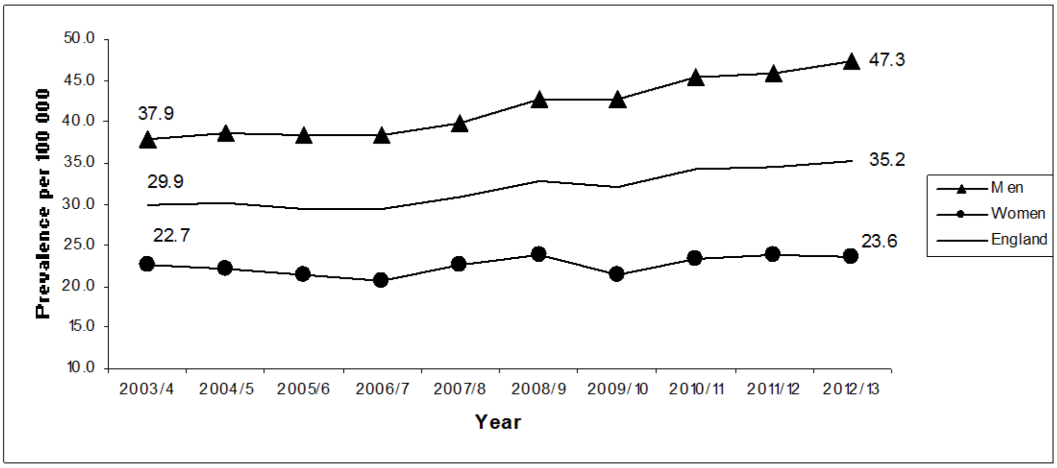


44a

Age adjusted major lower limb amputation rate by sex;

men and women aged 50-84: England 2003-2013

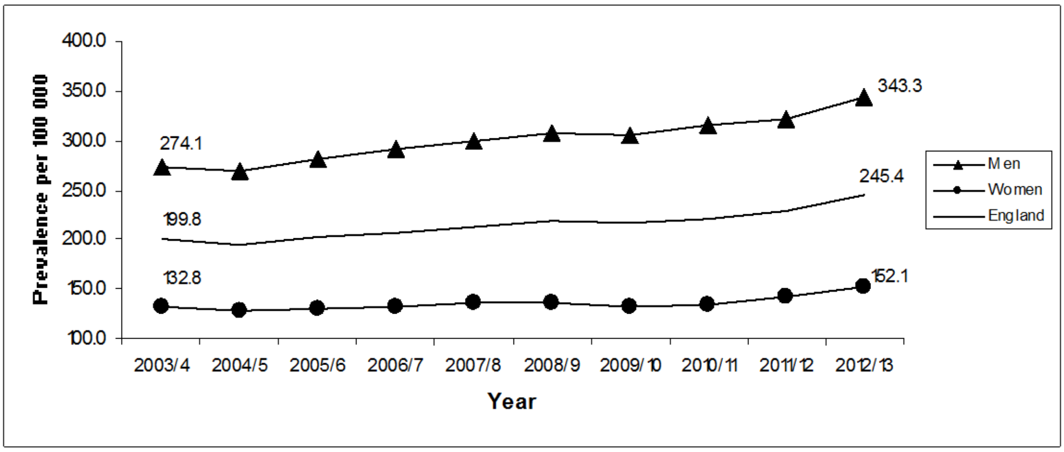
However, the gender disparity in minor amputation rates has increased. Rates in men have increased by approximately 25% (37.9 to 47.3) but only risen by 4% in women (22.7 to 23.6) (Fig 44b).



44b

Age adjusted minor lower limb amputation rate by sex;
men and women aged 50-84: England 2003-2013

The disparity in revascularisation rates has also increased as rates have risen by 25% in men (274.1 to 343.3) and 15% in women (132.8 to 152.1) (fig 44c).



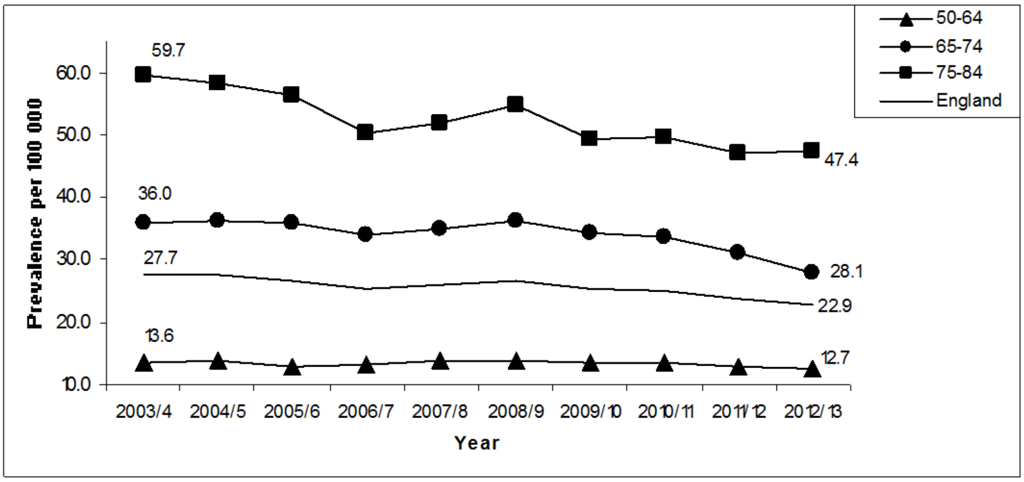
44c

Age adjusted lower limb revascularisation rates by sex;

men and women aged 50-84: England 2003-2013

3.3.4 Age Changes 2003-2013 (Fig 45)

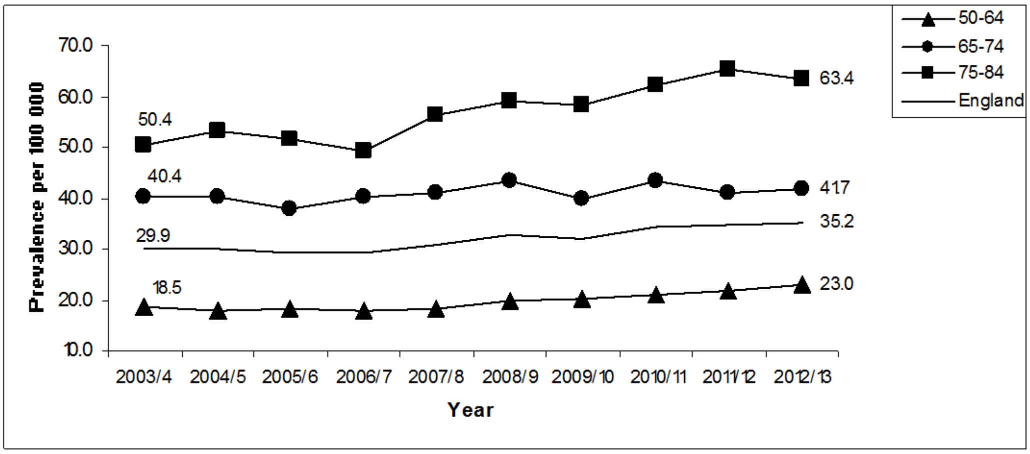
The reduction in major amputation rates has not affected all age groups equally (Fig 45a). The reduction is only 7% in the youngest 50-64 year age group (13.6 to 12.7) and approximately 21% in both the 65-74 (36.0 to 28.1) and 75-84 year age groups (59.7 to 47.4).



45a

Age adjusted major lower limb amputation rate by age group; men and women aged 50-84: England 2003-2013

Minor amputation rates have increased in all age groups but not at similar rates (Fig 45b). Rates have increased by 20% in both the youngest (18.5 to 23.0) and oldest age groups (50.4 to 64.4) but remained essentially unchanged in the 65-74 year age groups (40.4 to 41.7). Disparities have therefore reduced between the two youngest age groups and increased between the two oldest age groups.

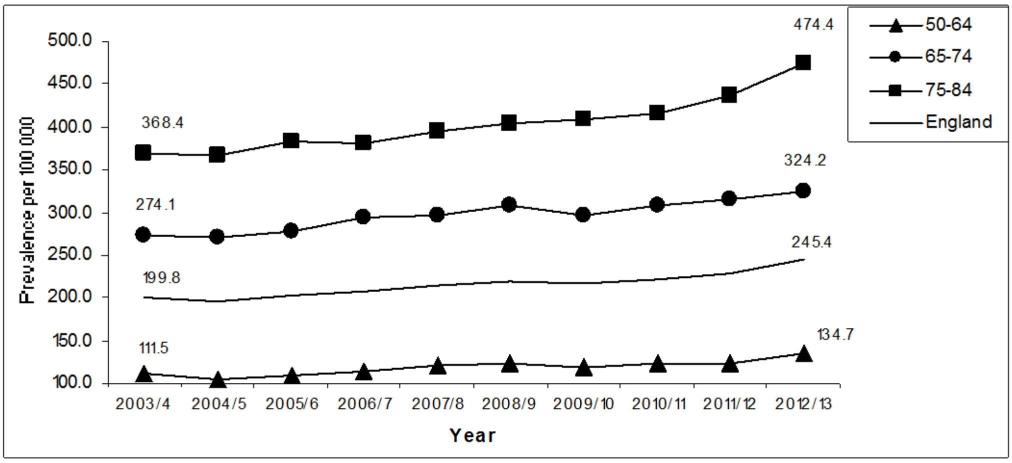


45b

Age adjusted major lower limb amputation rate by age group;

men and women aged 50-84: England 2003-2013

Revascularisation rates have increased by approximately 15% in both the 50-64 (115.5 to 134.7) and 65-74 year age groups (274.1 to 324.2) but rose 22% in the oldest 75-84 year old age group (368.4 to 474.4) (Fig 45c).



45c

Age adjusted lower limb revascularisation rates by age-group;

men and women aged 50-84: England 2003-2013

3.3.5 Changes in amputation prevalence amongst diabetics 2003-2013 (tables 47 and 48)

The prevalence of amputation, both major and minor is decreasing in diabetics at a faster rate than non diabetics.

Table 47: Prevalence, per 100 000, and percentage change of major amputation in the diabetic and non diabetic population England 2003-2013

	Age group	***2003***		**2013**		**% Change**	
		DM*	Non DM	DM	Non DM	DM	Non DM
Men	50-64	119.7	11.8	82.2	10.1	- 31.3	- 14.4
	65-74	222.3	31.5	127.8	24.5	- 42.5	- 22.2
	75-84	332.4	60.0	193.6	40.4	- 41.8	- 32.7
	All	180.5	24.6	111.8	18.7	- 38.0	- 24.0
Women							
	50-64	74.9	3.4	34.6	4.1	- 53.8	+ 20.6
	65-74	99.9	12.3	60.1	9.2	- 39.8	- 25.2
	75-84	134.9	31.5	94.6	22.5	- 29.8	- 28.6
	All	92.8	11.0	52.7	8.9	- 43.2	- 19.1

* DM: Diabetic; Non DM: not diabetic

Table 48: Prevalence, per 100 000, and percentage change of minor amputation in the diabetic and non diabetic population England 2003-2013

	Age group	***2003***		**2013**		**% Change**	
		DM*	Non DM	DM	Non DM	DM	Non DM
Men	50-64	142.0	13.9	141.5	17.4	- 0.4	+ 24.6
	65-74	210.1	29.8	172.8	33.1	- 17.7	+ 11.2
	75-84	259.0	46.8	252.7	52.7	- 2.4	+ 12.8
	Standardised to England 2011	178.5	23.3	167.2	27.1	- 6.3	+ 16.3
Women							
	50-64	141.9	6.5	71.0	4.1	- 50.0	- 37.8
	65-74	155.9	19.2	110.4	9.2	- 29.2	- 52.1
	75-84	126.7	29.6	131.8	22.5	+ 4.0	- 24.0
	Standardised to England 2011	142.9	14.2	92.9	14.9	- 35.0	+ 4.8

3.4 Validation of HES Data

A total of 178 and 191 patients were retrieved from hospital audit and HES database respectively. We were unable to retrieve hospital notes in 38 cases across the three sites and although did not have their co-morbidity data, included their demographic profiles for analysis. There were no significant differences in the mean age or sex distribution between the two sources (table 49). There were no significant differences in the proportion with hypertension or coronary heart disease. However, the proportions of diabetes, hypercholesterolaemia, cerebrovascular disease and smoking were significantly lower in HES data compared to hospital data (table 49).

HES was found to have high sensitivity for coronary heart disease but was sub-standard for diabetes, hypercholesterolaemia, cerebrovascular disease and smoking (Table 50). However, it had high specificity for all conditions (table 50). Of importance is the variation that existed in coding accuracy between individual hospitals. There was variation in the coding of both procedures and co-morbidities. Two of the three hospitals performed fewer amputations than recorded in HES. Hypertension and coronary heart disease were coded accurately in two of the three hospitals, only one coded diabetes accurately and all three coded hypercholesterolaemia, cerebrovascular disease and smoking poorly (table 50).

Table 49. Comparison of demographic and co-morbidity variables between HES and hospital records

	All 3 Hospitals			Hospital 1			Hospital 2			Hospital 3		
	Hospital	**HES**	**Sig.***	**Hospital**	**HES**	**Sig.***	**Hospital**	**HES**	**Sig.***	**Hospital**	**HES**	**Sig.***
No	178	191		49	58		59	52		70	81	
Mean age	70.8	70.8		71.7	71.5		68.2	70		72.4	70.9	
Median age	71	71.2		70	71.5		70	70		73	72	
Males (%)	133 (74.7)	138 (72.3)	.592	41 (83.7)	45 (77.6)	.430	42 (71.2)	37 (71.2)	.997	50 (71.4)	56 (69.1)	.759
Females (%)	45 (25.3)	53 (27.7)	.592	8 (16.3)	13 (22.4)	.430	17 (28.8)	15 (28.8)	.997	20 (28.6)	25 (30.9)	.759
Diabetes (%)	88 (49.4)	68 (35.6)	.007	19 (38.8)	11 (19.0)	.023	39 (66.1)	18 (34.6)	.001	30 (42.9)	39 (48.1)	.520
Hypertension (%)	91 (51.1)	82 (42.9)	.115	24 (50.0)	29 (50.0)	.916	31 (52.5)	16 (30.8)	.021	36 (51.4)	37 (45.7)	.481
High Cholesterol (%)	47 (26.4)	20 (10.5)	< .001	9 (18.4)	4 (6.9)	.070	18 (30.5)	7 (13.5)	.032	20 (28.6)	9 (11.1)	.007
Coronary Heart Disease (%)	66 (37.1)	67 (35.1)	.690	14 (28.6)	22 (37.9)	.307	30 (50.8)	19 (36.5)	.130	22 (31.4)	26 (32.1)	.930
Cerebrovascular disease (%)	32 (18.0)	5 (2.6)	< .001	7 (14.3)	3 (5.2)	.107	10 (16.9)	1 (1.9)	.008	22 (31.4)	1 (1.2)	< .001
Smoking (%)	86 (48.3)	22 (11.5)	< .001	22 (44.9)	2 (3.4)	< .001	46 (88.5)	10 (19.2)	< .001	22 (31.4)	10 (12.3)	.004

HES: Hospital episode statistics, *: Pearson chi square $p < 0.05$

Table 50: Sensitivity and specificity of co-morbidity codes between hospital records and HES data

		Sensitivity (95% CI)	Specificity (95% CI)
	Diabetes	77.3% (67.1-85.5)	100% (95.9-100)
	Hypertension	90.1% (82.1-95.4)	100% (95.8-100)
Overall	High Cholesterol	42.6% (28.3-57.8)	100% (97.2-100)
	Coronary Heart Disease	100% (94.5-100)	99.1% (95.1-99.9)
	Cerebrovascular disease	15.6% (5.3-32.8)	100% (97.5-100)
	Smoking	25.6% (16.8-36.1)	100% (96.0-100)
	Diabetes	57.9% (33.5-79.7)	100% (88.3-100)
	Hypertension	100% (85.6-100)	80.0 % (59.3-93.1)
Hospital 1	High Cholesterol	44.4% (14.0-78.6)	100% (91.1-100)
	Coronary Heart Disease	100% (76.7-100)	77.1%(59.9- 89.6)
	Cerebrovascular disease	42.9% (10.4-81.3)	100%(91.5-100)
	Smoking	9.1 % (1.4-29.2)	100% (87.1-100)
	Diabetes	46.2% (30.1-62.8)	100% (83.0-100)
	Hypertension	51.6% (33.1-69.8)	100%(87.5-100)
Hospital 2	High Cholesterol	43.8%(19.8-70.1)	100%(91.3-100)
	Coronary Heart Disease	63.3% (43.9-80.1)	100% (87.9-100)
	Cerebrovascular disease	10.0%(1.7-44.5)	100% (92.7-100)
	Smoking	21.7%(11.0-36.4)	100%(75.1-100)
	Diabetes	100% (88.3-100)	77.5% (61.5-89.1)
	Hypertension	100% (90.2-100)	97.1% (84.6-99.5)
Hospital 3	High Cholesterol	45.0% (23.1-68.5)	100% (92.8-100)
	Coronary Heart Disease	100% (84.4-100)	91.7% (80.0-97.6)
	Cerebrovascular disease	4.6% (0.8-22.9)	100% (92.5-100)
	Smoking	45.5% (24.4-67.8)	100% (92.5-100)

HES: Hospital episodes statistics, CI: confidence interval

Chapter 4: Discussion

4.0 Principle findings – overall summary

This research analysed all English hospital admissions over two time periods and described inequalities in the prevalence of major lower limb amputation and revascularisation. The first, between 2003 and 2009, calculated the six year period prevalence and then explored patient level data to understand differences related to location, gender and ethnic group. The second dataset, 2003-2013, calculated yearly prevalence over a longer time period and assessed whether patterns identified in the earlier time period persisted. It additionally identified variations in the prevalence of minor amputation. Overall, 42 000 major and 52 000 minor amputations along with 355 000 revascularisations were analysed.

The prevalence of both major amputation and revascularisation varied significantly across regional, gender and ethnic groups. The prevalence of both procedures was significantly higher in Northern England compared with the South and in men compared with women. In the Black population, the rates of major amputation were significantly higher but the revascularisation rate significantly lower than the White population. In South Asians, prevalence of both procedures was significantly lower.

Between 2003 and 2013, the major amputation rate declined and the revascularisation rate (particularly surgical) rose. However, regional and gender inequalities remained. Rates of major amputation in diabetics reduced at a faster rate than non diabetics but remained six times higher. The minor amputation rate rose at a similar rate to the fall in major amputations.

4.1.1 North/South variations

What was already known	*What this study added*
Variation existed in overall amputation rates across both English regions and Primary Care Trusts.	1. Described a definite North/South divide with rates of major amputation higher in Northern regions. 2. Greater proportion of major amputations in the North were above knee. 3. Significantly more revascularisations performed in the Northern regions.

The North of England had a higher prevalence of both overall and above knee amputations. Allied to this was a higher revascularisation rate. There was, however, heterogeneity across England with amputation and revascularisation rates varying by up to 50 and 60% respectively. Of Northern regions, the North East had the highest amputation rate and the lowest revascularisation rate (albeit above the national average). The North West had the highest revascularisation rate in the country as well as the second highest amputation rate. In the Midlands, the East has rates of amputation and revascularisation that were significantly higher than the West Midlands (although broadly in line with the national average). The West Midlands itself had the lowest revascularisation rate and below average amputation rates. Within Southern regions, the South West and London had higher rates, although still significantly below the national average. The picture in London is unique. It had a significantly higher revascularisation rate compared with other Southern regions (although in line with the national average) yet had an amputation rate that was ten percent below the national average.

Although the overall prevalence of major amputation and above to below knee ratio was higher in the North, being treated in the North was not an independent predictor of an above knee amputation.

4.1.2 Gender variations

What was already known	***What this study added***
The prevalence of amputation in men was approximately double that of women.	1. This pattern was consistent across all English regions, age and ethnic groups. 2. Black women had an amputation rate greater than Black men. 3. Women had a much higher proportion of above knee amputations. 4. The major amputation rate over the last ten years had reduced in men and women at the same rate. 5. The prevalence of minor amputation in men had risen at a faster rate than women.

The prevalence of both amputations and revascularisations was approximately double in men with this difference observed across all English regions and ethnic groups (except Black women). However, a far higher above to below knee amputation ratio was seen in women. Female gender was an independent predictor of an above knee amputation.

Over the last ten years the prevalence of major amputation has decreased in both men and women but the above to below knee amputation ratio has remained unchanged. The gender inequality therefore remains. However, inequality has widened for minor amputations as rates have increased in men at a faster rate than women.

4.1.3 Ethnic Variations

What was already known	*What this study added*
1. Rates of amputation in British Black population was greater than the White population. 2. Rates of amputation in South Asians was lower than White counterparts.	1. Provided national not single centre data. 2. Black Caribbeans experienced much higher rates than Black Africans. 3. Higher rates in Blacks was associated with low revascularisation rates. 4. Higher risk of amputation with no revascularisation in Blacks explained by worse demographic and risk factor profile. 5. Distribution of coronary and lower limb revascularisation was equal among ethnic groups except South Asians where disproportionately more coronary revascularisations were performed.

Compared with the majority White population, the Black population had a significantly higher major amputation but not revascularisation rate. This translated to a significantly higher risk of an amputation without a revascularisation. However, on multi-variate analysis, this higher risk was fully attenuated by demographic and cardiovascular risk factors.

In South Asians, however, the prevalence was significantly lower for both major amputation and revascularisation procedures. A disproportionately high coronary to lower limb revascularisation was also seen in South Asians, whereas a more equal distribution was seen in Black and White groups.

4.1.4 Diabetic Variations

What was already known	***What this study added***
Prevalence of major amputation in diabetics was eight times higher than non diabetics	1. Half of all major amputees were not diabetic. 2. Rates of major amputation in diabetics reduced to six times over a ten year period. 3. Amputation rate in non-diabetics reduced at a slower rate than diabetics. 5. The rise in minor amputations was driven by non-diabetic men.

Among those aged 50-84 in the general population, the prevalence of diabetes is 16% in men and 11% in women and 51% and 42% among male and female amputees. The prevalence of diabetes in all groups has increased by approximately 5% over the last ten years.

The rate of major amputation in the diabetic population has reduced by approximately 40% over the last ten years yet remains six times higher than non diabetics. The rate of minor amputation has also decreased in diabetics but increased in non diabetics with marked gender variations. The rising prevalence of minor amputation overall appears to be driven by non diabetic men (men 16% women 5%), particularly those aged 50-64 where a 25% rise was seen.

4.1.5 Risk factors for an above knee amputation

What was already known	***What this study added***
Use of multi-variate analysis incorporating patient demography and atherosclerotic risk factors to assess the influence of revascularisation modality on amputation level in England not known.	1. Increased risk of an above knee amputation associated with female gender, history of coronary or cerebrovascular disease and surgical revascularisation. 2. Reduced risk associated with being male, diabetic and endovascular revascularisation. 3. Age, social deprivation and living in the North did not increase risk of an above knee amputation.

Above knee amputations were a potential marker of poor care. We found a greater above to below knee amputation ratio in the North of England, women, non diabetics and those having both surgical and endovascular revascularisations. To assess the contribution of these factors, we performed a multi-variate analysis and controlled for social and disease risk factors.

The risk of an above knee amputation was independent of all cardiovascular risk factors except coronary heart and cerebrovascular disease. Risk was, however, higher in women and those who had only surgical or combined endovascular and surgical revascularisation. Risk was lowest when endovascular revascularisation was used as sole revascularisation modality. An increased risk of an above knee amputation was not seen in those living in the North of England or belonging to the most deprived population.

4.1.6 Influence of social deprivation on amputation risk in England

What was already known	*What this study added*
No study has identified the contribution of social deprivation to risk of a major amputation in England in a multi-variate analysis.	1. Social deprivation does not independently increase the risk of an above knee amputation or any major amputation with or without a revascularisation. 2. Social deprivation does partly explain the higher risk of an amputation both with and without revascularisation in the Black population.

The social determinants of health were accounted for by using the 'index of social deprivation' score. The proportion of amputees from the poorest social group was much higher in Northern compared with Southern England and in men compared with women. However, on multi-variate analysis, increasing social deprivation did not independently increase risk of an amputation with or without a revascularisation or an above knee amputation. However, it did contribute to the higher risk of amputation in the Black population.

4.1.7 Changing prevalence over a ten year period 2003-2013

What was already known	***What this study added***
1. Overall prevalence of major amputation in England is approximately 5/100 000.	1. 5/100 000 is an understatement as prevalence is approximately 26/100 000.
2. No epidemiological data regarding amputation prevalence in England from 2008 onwards.	2. Direct comparison across age, gender, region, diabetic status and time now possible
3. Multiple epidemiological studies, spanning over 20 years are not comparable because of different methodologies and reporting styles.	3. Major amputation reduced by 18%.
	4. Minor amputations increased by 18%.
	5. Revascularisations increased by 20%.
	6. Despite overall reductions in major amputations, regional, gender and diabetic inequalities remain
	7. Rise in minor amputations driven by non diabetic men.

The ten year analysis of English hospital data has shown the prevalence of major amputation to have decreased by approximately 18% with minor amputation rates increasing by a similar amount. Revascularisation rates overall have increased by 20% although a greater rise was seen in surgical revascularisations (endovascular rise 18%, surgical rise 52%). However, age, gender and regional variations of both major and minor amputations have remained largely unchanged. The North of England continued to have the highest rate of amputation as well as the highest AK:BK ratio; men continued to have double the amputation rate of women, who in turn continued to have a much higher AK:BK ratio than men. Further, a reduction in amputation rates is not seen in the youngest 50-64 year old age group.

4.1.8 Accuracy of HES data

What was already known	*What this study added*
1. HES data accuracy for primary procedure and diagnosis was approximately 83%. 2. Sensitivity and specificity of HES co-morbidity coding was not known. 3. National target for coding accuracy was 90%.	1. Provided sensitivity and specificity of common HES co-morbidity codes. 2. HES was highly specific for co-morbidities. 3. HES is only sensitive (>90%) for coronary heart disease. 4. The sensitivity of diabetes coding in HES is 77.3% with specificity of 100%.

The accuracy of procedural, demographic and co-morbidity data held on the HES database was compared with patient records across three sites in the North West of England. Although differences across sites existed, overall, HES was within recommendations of accuracy (>90%) for both the actual number of procedures performed and the age and sex of patients. With regard to co-morbidity, HES was highly sensitive for coronary heart disease, but was sub-standard for the sensitivity of hypertension, diabetes, hypercholesterolaemia, cerebrovascular disease and smoking. HES, was, however, highly specific for all these co-morbidities.

4.2 Results in relation to other studies

4.2.1 Methodological weaknesses of studies

Five studies have used HES data to describe prevalence of major amputation over the last 25 years.[44-46,49,51] Of these, two were similar to the present study in methodology but not results.[46,49] These, along with other international studies were reviewed by Jeffcoate and van Houtum[96] in 2004 and brought up to date by Moxey et al in 2011.[97] However, the comparability of prevalence rates presented in these studies to each other as well as our own is limited because of differences in numerator and denominator definitions and use of age standardisation. For example, eight studies defined major amputation as above the ankle[44-46,48,50-51,55-56] whereas six included forefoot[47,50-54] and eight have either not defined their denominator population or age group[44,48.50-52,54-56] or used the wrong population[49] altogether. The present study defined the numerator and denominator population and presented both age specific and age adjusted rates. The two review articles[96,97] summarised many national and international prevalence studies but the latter published in 2011[97] did not include the first major study, published in 2007, to present amputation rates across the whole of England by age group.[49]

4.2.2 National rate

The national prevalence of major amputation in England has been reported to be around 5/100 000[44-46] i.e. much lower than the 25/100 000 in the present report. Of these studies, only Moxey et al[46] presented sufficient methodological data to allow comparison.

Moxey et al[46] reported the five year period prevalence (2003-2008) of both major and minor amputation using HES and census data across England and its regions but only included those with an admission diagnosis of 'peripheral vascular disease'. Although they returned a similar number of procedures over comparable time periods to our study, they reported a prevalence rate that was five times lower. The dissimilar rates can be explained by methodological differences. Firstly, their rates were actually per 10 000 and not per 100 000, secondly, their denominator was the whole of the United Kingdom (including children) whereas their numerator was only England (age groups studied not given). Thirdly, they used only one year population data (2008) and not five year averages and finally they did not age standardise their result. Using their reported numerator data but more accurate denominator population, the overall prevalence could have been reported in the region of 60/100 000.

4.2.3 English Region

The GLEAS trial[47] reported major and minor amputation rates (major amputation included forefoot) across a number of English cities (as well as globally) between 1995 and 1997 using a very accurate multi-source capture/recapture technique. Their age specific rates in men and women in the 60-79 year old age group may be cautiously compared with our 65-74 year old region specific prevalence for the corresponding English city. Similar to McCaslin et al[49] a general decrease can also be demonstrated in the major amputation rate over two decades in Northern England both in men, (Leeds GLEAS 80.0, Yorkshire & Humber 56.4; Middlesborough GLEAS 84.9; North East 72.0) and women (Leeds GLEAS 36.4, Yorkshire & Humber 19.3; Middlesborough GLEAS 29.2, North East 21.8). However, a consistent decrease can not be demonstrated in minor amputations in either men (Leeds GLEAS 80.0, Yorkshire and Humber 68.3; Middlesborough 65.4; North East 149) or women (Leeds GLEAS 40.1, Yorkshire and Humber 30.8; Middlesborough 31.1; North East 67.1). Their age adjusted rate can not be compared with our study as they included the total population (including children) for calculating LEA rates and age adjusted rates to the European population.

4.2.4 Gender

Age and gender specific rates have only previously been reported in the GLEAS trial.[47] They showed a consistent pattern of excess amputations in men. We additionally report a greater proportion of major amputation in women being above knee. A similar finding was recently reported from the United States.[98] The reasons for this are unknown especially as the prevalence of PAD is similar in both men and women[35-37] although men in the Framingham study were twice as likely to develop intermittent claudication.[99] The prevalence of diabetes is also slightly higher in men compared with women.[95] A potential explanation is that women were slightly older in our study and are known to have worse outcomes than men following revascularisation, particularly infection.[100-101]

4.2.5 South Asians

These were people of 'Indian', 'Pakistani', 'Bangladeshi', or 'Asian other' origin. They are known to have a greater incidence[102], prevalence[103] and mortality[104] from coronary heart disease which appears to be related to greater levels of atherosclerosis risk factors, particularly diabetes.[16] The lower levels of PAD interventions reported in this study is therefore surprising but may be explained by variations in the profile of either patients or the disease.

Asians are generally younger than the majority population with the proportion aged 50 and over only 15% (Whites 37%).[105] The competing risk of coronary heart disease and potential higher mortality may explain lower PAD in this ethnic group. However, recent Scottish data suggested incidence of myocardial infarction although higher in South Asians, particularly Pakistanis, does not translate into higher rates of mortality.[106] The higher coronary rates occurring within a younger population may potentially increase the time on disease modifying drugs e.g. statins. Lower rates of intervention may also be a result of either disparities in service utilisation as has been found in coronary heart disease revascularisation[107] or the 'salmon effect'. This is when the elderly first generation return to their home country in their retirement resulting in these diagnoses and outcomes not showing up in UK statistics.[91]

Evidence for a difference in presentation of atherosclerosis is limited. Chaturvedi et al[108] showed that for a given level of coronary artery calcification, Asians had less femoral artery calcification than Whites. Lower levels of PAD have also been used to explain fewer diabetes related amputations.[109] Chow et al[110] showed that hypercholesterolaemia and diabetes was particularly associated with carotid atherosclerosis in Asians than Australian Whites with the protective effect of HDL not apparent in Asians. There have been no studies describing the prevalence of revascularisation of coronary vessels in relation to lower limb vessels for different ethnic groups. The present study is the first to report a disproportionate ratio of coronary to lower limb revascularisation in South Asians (79% vs 21%) compared with the 50/50 split observed in England overall.

4.2.6 Black

This population was self defined as 'Black African', 'Black Caribbean', and 'Black Other'. Our study has shown this group to have higher rates of major leg amputation with lower rates of revascularisation than the White and South Asian populations. This is especially true of Black women where rates of amputation were 2.4 times greater than White British women. Earlier UK studies, combined the African and Caribbean populations and determined the prevalence of diabetes related lower limb amputation to be lower than Europeans with a relative risk of 0.67.[52] All studies describing ethnic variations in England were single centre experiences. The lower rates in these areas may, therefore, be a result from improved pockets of local services within the National Health Service or recruiting from mainly Black African populations.

We found heterogeneity within the Black population with higher rates in Black Caribbeans than Black Africans. This may be related to Caribbeans being much older than the Africans (Caribbean median age 40, African 28).[90] However, the higher odds of amputation with no revascularisation for the whole Black population, were fully attenuated by demographic and disease risk factors. This suggested the higher rates were not related to ethnicity. However, the odds of having an amputation with a revascularisation remained significantly higher than the White population after controlling for these factors. The reasons for this are unclear, but more failed revascularisations may be a result of more aggressive popliteal trifurcation disease in this population[111] or barriers to accessing care.

Most data regarding Black and White amputation differences come from the United States. These are not directly comparable with the UK as health care systems differ and studies have not provided definitions of Black and White. This latter point is a common theme in much comparative ethnic health research.[91] However, important differences have been found which are consistent with our results.

Resnick et al[112] measured incidence of amputations by following up a cohort of the National Health and Nutrition Examination Survey between 1971 and 1992. They found the age adjusted proportional incidence of all lower extremity amputations in Blacks compared with Whites to be higher at 2.78. However, the higher rates were attenuated after controlling for education, hypertension and smoking, suggesting the higher rates were related to socio-economic factors and not directly ethnicity. This is in contrast to Collins et al[113] and Criqui et al.[114]

Collins et al[113] found race to be an independent predictor for amputation in patients with peripheral vascular disease after controlling for diabetes. Criqui et al[114] also found Black ethnicity was a strong and independent risk factor of peripheral vascular disease amputations after controlling for diabetes, hypertension and body mass index. Neither of these two studies controlled for socio-economic factors. This was in contrast to the present study.

4.2.7 Age specific rate

The age specific rates in this report allow cautious comparison with those of McCaslin et al.[49] Whilst acknowledging differences in the definition of major amputation, amputation capture techniques and age groups, amputation rates over a 20 year period can be investigated.

McCaslin et al[49] defined major amputation as including stump procedures with revascularisations excluding supra-inguinal procedures, their amputation prevalence from the early 1990s in the 45-64, 65-74 and 75+ age groups was approximately 10, 40 and 76/100 000 (data extracted from graphs not tables) respectively. This suggests that amputation rates have risen in the youngest age groups by 30% but decreased by approximately 25% and 60% in the 65-74 and 75+ age groups respectively compared with our study. In contrast, revascularisation rates have increased substantially in the same period with a 75% rise in the youngest age groups and a twenty fold increase in the older age groups (driven mainly by the rise in endovascular procedures). They did not report gender specific rates.

4.2.8 Diabetes status

Epidemiological data regarding the prevalence of major and minor amputation in diabetics gives a consistent picture of higher rates in diabetics. Diabetes UK, has reported that approximately 135 amputations in England are occurring in diabetics every week and that with good diabetes care up to 80% of these can be prevented.[115] This overall amputation figure is similar to ours (108 amputations performed weekly in diabetics in 2012-2013). Our data suggests the prevalence of major amputation to be reducing in diabetics but still remaining six times that of non diabetics. We have, however, found the rising rate of minor amputations to be driven by non diabetic men.

4.2.9 HES data accuracy

Significant concerns regarding HES accuracy have been raised but these relate mainly to diagnosis.[68-70] Burns et al's[73] systematic review found the median accuracy of primary diagnosis and procedure to be 83%. When comparing studies pre and post introduction of Payment by Results, no significant differences in overall or procedure coding were found. Only Wright et al[117] examined the accuracy of co-morbidity codes and agreed with our finding that coronary heart disease was accurate when compared with general practice and hospital records. We could not find any other co-morbidity investigated in detail beyond the Audit Commission which made a general statement that the coding error for secondary diagnosis (potentially co-morbidity) was 15% with an inter-quartile range of 7.4% to 8.5%.[75]

4.3 Strengths and limitations of research

There were several limitations to the study. Some of these limitations were a product of the dataset used e.g. missing ethnic status and therefore unalterable, whereas others were related to methodology e.g. limiting analysis to those aged 50-84 and not excluding amputations secondary to trauma and cancer. A summary of the strengths and limitations is described in the table below with a detailed analysis of these limitations provided thereafter.

Strengths	*Limitations*
1. Very large dataset.	1. Analysis limited to those aged 50-84.
2. Numerator and denominator populations defined.	2. Indication for procedures not defined.
3. Age and gender specific as well as overall adjusted rates presented.	3. Only one third of amputations linked to a revascularisation with linkage not based on laterality or temporality and included primary/repeat amputations and 'diagnostic' revascularisations.
4. Descriptive and analytic statistics undertaken on HES data.	4. Limited co-morbidities used in analysis.
5. Inequalities explored using both social and disease risk factors.	5. 17% ethnic group data 'Missing'.
6. Assessment of HES data quality made.	6. Concepts of competing risk not explored.
	7. Prevalence of diabetes in minor amputees based on prevalence in major amputees.
	8. HES validation not based on direct linkage with many missing case notes.
	9. Use of forward step wise logistic regression multi-variate modelling relies on computer to choose best subset of variables to control

4.3.1 Choice of age-groups 50-84 (limitation 1)

These age cut-offs were chosen in order to capture the majority of amputations undertaken for PAD. The prevalence of PAD in those under 50 is very low. The cut off of 84 was chosen because the average life expectancy in England is 78 for a man and 82 for a woman and 18 years from age 65.[83] We further felt that major amputations in those over 84 were more likely to be done for palliative reasons. The excluded population i.e. aged over 84 comprise 2% of the population, approximately 350 000 - half of whom are over 90.[81] The number within each English region is therefore extremely low. Whilst including this population would have made the dataset complete, its exclusion has not significantly altered the regional, gender and ethnic inequalities that were the focus of the report.

In retrospect, I would change the methodology and include the whole population i.e. all ages. This would have provided a complete picture of amputations and provide insights into inequalities at the extremes of age.

4.3.2 Clinical Indication for amputation (limitation 2)

All amputations i.e. trauma and cancers were included in the analysis. It was assumed the majority of those performed in the chosen age group 50-84 were for PAD. Only five per cent of major amputations in this age group were for these additional causes.[38]

Although it was possible to include only amputations with a diagnosis of 'peripheral arterial disease' as done by Moxey et al[46], this was not done. This was based on a recent systematic review that showed primary diagnosis in HES to be only 83% accurate.[73] It was, therefore, felt providing 'all amputations' and assuming 5% were trauma/cancer as opposed to limiting amputations based on a diagnosis which is only 83% accurate was more reliable. This additionally increased the number of amputations that could be linked to a revascularisation.

Ultimately, the strategy of identifying amputations primarily related to PAD by age group and not indication was only 14% lower than Moxey et al[46] over a similar time period i.e. within the margin of error. It was, therefore, assumed the strategy only minimally affected the numerator used to calculate prevalence and did not affect the conclusions regarding inequalities in any meaningful way.

However, again, I would not repeat this methodology. I would instead calculate 'cause specific' and 'all cause' amputation rates thereby allowing a 'cleaner' prevalence report.

4.3.3 Linkage of amputation and revascularisation procedures (limitation 3)

The linking of only a third of amputations with a revascularisation was surprising.
One explanation of the poor linkage was the methodology used. It is possible that many more amputations had revascularisations but were done outside of the six year time frame of the study. The ability to link the two procedures was, however, maximised by using procedure codes such as 'diagnostic angiogram' and not just therapeutic procedures. Despite the low linkage rate, a similar proportion has been reported in by others [117] including Moxey et al[46] who found 60% of patients having a major amputation did not have a revascularisation within the preceding three years.

Further, the temporal linkage between amputation and revascularisation is not complete as individual patients were not tracked over time. As such, scenarios such as failed revascularisation resulting in amputation followed by subsequent re-amputation without a revascularisation potentially count as two separate patients with only one amputation linked to a revascularisation. This may occur if unique identifiers were not correctly assigned to the same patient on every admission and may result in inaccuracies relating to the number and linkage of procedures. The linkage was also not based on laterality i.e. side of amputation and revascularisation. This was again to maximise linkage of procedures especially as there was no data on accuracy of this variable.

As procedures were not linked temporally or by laterality, the outcome measure ‘amputation with’ and ‘without revascularisation’ was interpreted as a measure of access to services rather than a measure of quality of service i.e. we have not interpreted these outcome measures as ‘primary amputation’ and ‘failed revascularisation’ respectively. However, very cautious interpretation in this way is possible.

In order to provide a ‘cleaner’ interpretation of the linked variables, I would have performed an additional sub-analysis based on linking the amputations with a similar sided revascularisation occurring within the previous three years. This would have provided an indication of quality of outcome.

4.3.4 Limited co-morbidities used in analysis (limitation 4)

The choice of co-morbidities was based on those that are risk factors for peripheral arterial disease. We additionally searched for those co-morbidities that are part of the diagnoses coders are obliged to search for and code[118] although adverse outcomes are associated with other co-morbidities not searched for e.g. renal failure. With respect to renal failure, it is not a risk factor for PAD per se and is not on the obligatory coding list, although ‘dialysis dependent’ renal failure is.[118] We included all the risk factors for PAD as outlined in the recent meta-analysis[30] but excluded the biochemical factors e.g. CRP as they are not coded in the HES database.

4.3.5 Missing data in ethnic classification (limitation 5)

The ethnic classification used in this study has weaknesses relating to both completion and validity. 15% of amputees had their ethnicity classification missing. Further, the validity of this variable is unknown i.e. do those labelling themselves as 'British Asian/Pakistani' consistently label themselves as such. This is important as ethnicity labelling is fluid, context dependant[119] and, therefore, potentially influences the numerator and denominator populations used to calculate rates. However, the completion criteria both for the census and HES data i.e. self completed questionnaire is the gold standard and both use the same categorical variables. Therefore, there is little that can be done to alter the validity beyond acknowledging it when interpreting data.

Changing ethnic groups seems unlikely as extensive research spanning several years was conducted to find a question form that was both acceptable and practical for defining ethnicity.[120] Field trials of the question used found it to perform consistently well and be robust.[120] Thus, validity has been established and unalterable, completion, however, is more challenging.

The total number of amputees with a missing ethnic group was greater than the total number of amputations performed in all minority groups. This has the potential of introducing bias. Methods have been used to impute ethnicity data based on likelihood. An example is the 'Nam Pechan' computer program which assigns South Asian ethnicity based on name. It has an acceptable sensitivity (80%) and specificity (62%).[121] An additional method to assign ethnicity is based on the assumption that people of similar ethnic origin live in the same area. Here ethnicity is imputed based on matching demographic data. This was not available as we did not have patient post code. There were no amputations performed in any ethnic group other than 'White British' in the audit. No comment can therefore be made on accuracy.

4.3.6 Concept of competing risk (limitation 6)

The lower prevalence of amputation in South Asians may be a result of competing risk. The main competing risk is that of coronary heart disease i.e. the higher prevalence and higher mortality may result in fewer cases of peripheral arterial disease and thus amputations. Although, mortality rates were not investigated, the higher incidence of myocardial infarctions in South Asians does not appear to be matched by a higher mortality rate.[106] However, it is not known whether being on disease modifying drugs such as anti-platelets or statins following a coronary event (which occurs earlier in South Asians) is a contributing factor. Another potential reason for the lower rates in South Asians is the 'Salmon effect.' This is where elderly South Asians return to their 'home countries' in their latter years to retire and thus do not show up on English statistical data. Again, there is little beyond anecdotal evidence to support this theory.[91] Furthermore, peripheral arterial disease is often symptomatic prior to CHD and the similar prevalence of PAD in this group support the suggestion that the lower amputation rate may be related to a lower prevalence of this disease.

4.3.7 Prevalence of diabetes in minor amputees extrapolated from major amputees (limitation 7)

The prevalence of diabetes among minor amputees was based on applying the prevalence from major amputees. This was done because access was not given to patient level data for minor amputees. Although requested, the diabetes status for the aggregated data on minor amputees was not provided. Further, due to funding cuts, bespoke analysis are now not being performed by Public Health England and so this can not now be investigated without funding. The prevalence of diabetes in minor amputees may, therefore, be inaccurate.

4.3.8 HES validation not based on direct linkage with patient notes (limitation 8)

This sub-study had significant limitations. Firstly, the calculations of sensitivity and specificity were based on averages and proportions of the whole dataset rather than individual records. There was, however, no other way to perform our analysis as HES data were anonymised. Secondly, the missing hospital notes could potentially lead to overestimation of HES accuracy. Thirdly, the sample was based on a single relatively simple procedure limited to one part of England. This limits the ability to generalise or look at trends over time. Finally, the data are somewhat historical and may not reflect current coding accuracy.

Although, it was not possible to link HES data with hospital notes directly, indirect linking based on ordered demographic profile is a method that could have been employed. Here, a reasonable deduction is made based on the gender and age of patients along with the date of procedure. We did not employ this method as we did not have date of procedure - only year.

Despite the historical nature of these data and its collection methodology, we have for the first time described the sensitivity and specificity of common co-morbidities associated with a common procedure across multiple sites. Furthermore, the procedure code accuracy was in line with the recent Audit commission data accuracy report.[75]

4.3.9 Use of forward stepwise entry logistic regression modelling (limitation 9)

Binary logistic regression was used because the outcome variables were dichotomous and categorical i.e. amputation 'with' and 'without' revascularisation (yes/no) and above knee amputation (yes/no). All predictor variables were also categorical.

This method was used because the analyses were exploratory and none of the assumptions for this method were violated. The data were large, did not assume a linear relationship between actual dependant and independent variables (although assumes a linear relationship of the log values), did not assume a normal distribution for the dependant variables or the errors and variation around the regression line (homoscedasticity).[122] Nevertheless, using the standard method as determined by SPSS has been criticised even though the stepwise method places variables into the model based on most significant coefficients.[123]

The main criticism of such a strategy is that there is no reason to expect that such methodology will select the best possible subset of variables to control.[123] This may result in important confounders not ending up in the final model leading to poor sensitivity.[123] Further, there is no standard method to present logistic regression data.[122] The odds ratios were presented along with the 95% confidence interval to aid interpretation and provide a 'handle' on model fit. Alternatives could have been to provide additional statistical values such as the Cox & Snell, Hosmer –Lemeshow and Negelkerke, Wald and -2log likelihood.

4.4 Implications of Research

This research was hypothesis generating and, as such, not definitive. It, can not, therefore, provide reasons for the regional, gender and ethnic inequalities identified. However, it can provide insights and suggestions for future research strategies. There are essentially four implications for the research. These are how future epidemiological research should present results, what the public health priorities regarding amputation rates should be, possible research direction into the biology of atherosclerosis and the implication of HES coding variability.

Area	*Implication*
Presentation of Epidemiology data	Future studies should standardise definitions of amputation level and present age and gender specific rates along with the age standardised rate. Studies should follow the STROBE guidelines.
Public Health Priorities	Inequalities surrounding amputation rates continue and the following should be addressed; 1. The higher amputation rate in Northern England 2. The higher amputation rate in men 3. The higher AK:BK ratio in women 4. The rising minor amputation rate in non diabetic men 5. The higher amputation rate in diabetics 6. The higher amputation rate in the Caribbean population
Biology of atherosclerosis	The suggestion that atherosclerosis potentially affects different parts of the arterial tree in women and South Asians suggests a biological basis for variation.
HES coding accuracy	Demographic and procedural data recorded in HES is accurate. Co-morbidity coding is highly specific but not sensitive. Cautious interpretation of differences in outcome is required as inaccuracies in HES are not uniformly spread across English hospitals.

4.4.1 Presentation of Results

Despite 13 studies publishing prevalence of major amputation spanning 25 years in England, it was not possible to compare prevalence rates over this time period. This was because of varying definitions of amputation, denominator population and method of presenting data. Future comparison would be facilitated by standardising definitions and presenting age and gender specific rates as well as the overall age adjusted rate.

It is suggested that minor amputations are regarded as those below the ankle with major amputation defined as above. Age and gender specific results should be in ten year age bands and further delineated by diabetic status.

4.4.2 Public Health Priorities

It is suggested the following inequalities are seen as public health priorities;

1. To reduce the higher amputation rate in Northern England
2. To reduce the higher AK:BK ratio seen in women
3. To reduce the rising minor amputation rate in male non diabetics
4. To reduce the higher overall amputation rate in diabetics
5. To reduce the excess amputations in the Black population

Holman et al[51] suggested that wide geographical variations within an equitable health care system pointed to key differences in the organisation or delivery of health care for amputees, particularly diabetics. This research informs this debate in two ways. Firstly, the provision of accurate epidemiological data, and, secondly, the suggestion that the higher rate of amputation in the North is not related to poorer access to services or greater social deprivation.

A suggestion for the higher observed amputation rate in the North is the quality, availability and access to services in primary care leading to late presentation in secondary care. Further work in these areas should allow the development of a targeted strategy. One example of health promotion to a hard to reach group is the British heart foundation strategy targeting middle aged men using Barnsley football team ('Hearty Lives Fit Red Project').[124] A three year evaluation has shown reduced waist lines, weight and blood pressures. The support of the local football was crucial as they not only provided facilities but also incentives e.g. match tickets.

4.4.3 Biology

Many studies determining ethnic variation have suggested this to be a proxy marker for genetic variation. This seems unlikely as the genes that code for phenotypic appearance are not known to be linked to atherosclerosis. Further, the changing prevalence of atherosclerotic disease in the developing (rising rates) and developed (reducing) world suggest environmental changes play a much larger part. Further, in the present study the higher rate of amputation in the Black population was essentially explained by the demographic profile of these patients.

The only finding in the research suggesting a biological basis for variation was the coronary to lower limb revascularisation ratio in South Asians and the higher AK:BK ratio in women. To determine whether there is any genetic basis to this, an incidence study is first required.

4.4.4 HES coding data

Whilst the standard for coding accuracy was being met for demographic and procedural data (albeit limited to above knee amputations), it was not for diagnosis and co-morbidity codes. This had two implications. Firstly, studies that have extracted amputations limited to a diagnosis to 'peripheral arterial disease' or 'diabetes' in an attempt to describe 'clean' epidemiology are potentially missing around 15% of cases.

Secondly, the wide variation in error as noted by the Audit Commission[75], Burns et al[73] and our own confidence intervals suggested inaccuracy was not uniformly spread across data sites. Such assumptions have been made, for example, when interpreting volume/outcome data and the conclusion that lower volumes in some centres were related to poorer outcomes.[125] Our data show that some hospitals perform fewer procedures than coded by HES and vice versa, thus calculations regarding outcome are potentially using incorrect denominator procedures. Poorer outcomes may, therefore, be a reflection of poor coding rather than actual performance especially as procedure numbers have been shown to vary between HES and other specialist databases.[68,126] We therefore suggest detailed analysis of variation in coding practice should be undertaken particularly when analysing outcomes using large datasets.

4.5 Conclusion and Future Work

4.5.1 The North/South divide and reasons for it

This study has shown there to be significant variation in the prevalence of major lower limb amputation across England with a clear North/South divide. Rates of major amputation were higher in the North with this higher rate seen across all age and gender groups. A greater proportion of amputations in the North were also above knee.

The reasons for the higher rate in the North were not clear. However, poorer access to services is unlikely as the North had higher revascularisation rates. This was reinforced by multi-variate analysis which showed there to be no significant difference in the risk of an amputation with a revascularisation across England. Finally, social class and living in the North of England were not independent predictors for an above knee amputation.

It was therefore reasonable to suggest the higher overall and above knee amputation rate in the North was not related to accessing revascularisation services, social class or living in the North.

The divide may therefore be related to factors not studied in this report. These include, patients in the North presenting at a later stage in their disease, differences in the treatment choices made by clinicians and patients, and the quality and outcomes of services provided.

4.5.2 The Gender Divide and reasons for it

The prevalence of amputation was greater in men compared with women. This pattern was repeated across all English regions and ethnic groups. The exception was Black women where rates were similar to Black men. Women, overall, however, also had far more above than below knee amputations. The reason for this is unclear but may be related to a ether different patterns of atherosclerotic disease i.e. more aorto-iliac disease.

4.5.3 The Ethnic Divide and reasons for it

Major amputation rates differ significantly across ethnic groups. Compared with the White British population, the Black population had a significantly higher rate and South Asians a significantly lower rate. However, there was heterogeneity. The prevalence in Black Caribbeans was higher than Black Africans with rates higher amongst Indian compared with Pakistani South Asians.

The higher rate in the Black population appeared to be explained by a poorer demographic and risk factor profile. However, among South Asians, the picture was more complex.

The risk factor profile in South Asians, especially the higher rate of diabetes has been used to explain the higher risk of coronary heart disease. However, they do not explain the lower amputation risk. Further, the preponderance for South Asians to have coronary rather than lower limb revascularisation (whereas a more even spread among other ethnic groups was seen) raises the possibility that atherosclerotic disease preferentially affected the coronary vessels. This varying ethnic distribution may, therefore, have a genetic basis.

4.5.4 Future Work

Future research should aim to address the inequalities surrounding regional, gender and ethnic groups as well as the overall rate. A strategy would be to address inequalities within one region and use this as an evidence base for a national strategy.

Within this population the following three stage program could be developed and implemented;

1. Health needs assessment
2. Design and implementation of strategy
3. Evaluation of strategy.

The health needs assessment would obtains background information on service provision (both services available and user views of these services) and epidemiological data on amputation rates across regional, gender and ethnic groups. The services provided (quality and usage) and amputation rates are then modelled. This will highlight patterns and particularly gaps in service provision/uptake and amputation rates.

A strategy based on this local information is developed, implemented and finally evaluated. The lessons learned from this study can then be an evidence base for a national strategy.

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