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**The epidemiology of cirrhosis and abnormal liver function  
in the general population of the UK**

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Thesis submitted to the University of Nottingham  
for the degree of Doctor of Philosophy

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## **Abstract**

### *Background*

Liver disease is a serious problem both in the UK and globally. While the incidence and mortality from several chronic diseases are decreasing, mortality from liver disease is increasing. As well as the medical sequelae for an individual with liver disease, in the UK the increase in chronic liver disease poses particular problems with respect to increasing hospital admissions, mortality and significant costs to the public both in terms of treatment and in loss of productivity. The increase in society of several risk factors for chronic liver disease, notably alcohol intake, obesity and type 2 diabetes, mean that these problems are likely to increase in the future.

Despite these apparent problems there are surprisingly few reliable sources of data on the occurrence of chronic liver disease (cirrhosis) in the general population of the UK and the rate and consequence of disease progression particularly among ambulatory patients. Nor are there robust estimates of the prevalence of abnormal liver function tests (which may represent undiagnosed liver disease) and their associations with mortality.

This thesis utilises two distinct datasets to examine separate areas of interest in the epidemiology of liver disease in the UK. The first three studies contained within this thesis are concerned with the epidemiology of cirrhosis in the general population of the UK. The second group of three studies focuses on the prevalence of elevated liver function tests in a population of older people in the UK, the demographic, clinical and lifestyle factors associated with such and the mortality following an elevated liver function test.

## *Objectives*

1. To estimate the incidence and prevalence of cirrhosis in the population of the UK
2. To describe the mortality associated with cirrhosis compared with the general population and the disease progression of cirrhosis
3. To estimate the prevalence of elevated liver function tests among people aged 75 and over in the UK
4. To describe the association between elevated liver function test and demographic, lifestyle, clinical characteristics and mortality among people aged 75 and over.

## *Methods*

To examine objectives 1 and 2 I utilised the General Practice Research Database (GPRD) constructing a population based cohort of 4537 subjects with cirrhosis and 44,403 age, sex and practice matched controls. I used Poisson regression to estimate incidence rate ratios and describe trends in alcoholic and non-alcohol-related cirrhosis. Using Cox regression within an historical matched cohort design I estimated the absolute excess mortality rates and hazard ratios for mortality in people with cirrhosis compared to the general population. I described the probability of progressing from one disease state to another.

To examine objectives 3 and 4 I accessed data from one arm of the Medical Research Council (MRC) Trial of Assessment and Management of Older People in the Community, a representative sample of community dwelling people aged 75 and over, totalling 15,308 participants. The prevalence of abnormal liver function was described as the proportion of study participants

with elevated aspartate transaminase, alkaline phosphatase or serum bilirubin. Associations between elevated liver function and demographic, lifestyle and clinical factors were examined using multivariable logistic regression. I determined the absolute mortality rates and hazard ratios for all-cause and cause-specific mortality using a Cox proportional hazards model.

### *Findings*

#### Epidemiology of cirrhosis (GPRD)

These studies have shown an increasing trend in both the incidence and prevalence of cirrhosis in the UK with an estimated 45% increase in incidence of cirrhosis in the 10-year period studied. I estimate that 76 per 100,000 people were living with cirrhosis in 2001. Just over half of all cirrhosis was associated with alcoholism. Disease progression with cirrhosis among this mainly ambulatory population was rapid with a rate of decompensation in people with compensated disease of 5% per year and 1 in 10 dying in the first year following diagnosis. This figure increased to 25% of people dying within one year for those with decompensated disease. Mortality in subjects with compensated and decompensated cirrhosis was 93.4 and 178.0 per 1000 person years compared with only 19.2 per 1000 person years in the general control population. Following adjustment for age and sex people with compensated and decompensated disease were respectively 5 and 10 times more likely to die than the general population.

#### Epidemiology of abnormal liver function tests (MRC cohort)

Abnormalities in liver function were common with roughly 1 in 6 people aged 75 and over having at least one elevated liver enzyme, although most of these elevations were mild. A single elevated measurement of aspartate transaminase was associated with an increased consumption of alcohol and a

lower age in contrast with that of a single measurement of alkaline phosphatase which showed an association with higher age and lower alcohol consumption. An elevated bilirubin measurement was strongly associated with being male. Having a single elevated liver function test was associated with a modest increase in the hazard of death compared with people with normal liver function tests (adjusted hazard ratio for death 1.27 (95% CI[1.19, 1.36])). As well as an unsurprising increase in the hazard ratio for death from liver disease, elevated aspartate transaminase or alkaline phosphatase were both associated with modest increases in the hazard of death from cancer (adjusted hazard ratios of 1.56 (95%CI[1.21, 2.01]) and 1.61 (95%CI[1.39, 1.86]) respectively). Elevated alkaline phosphatase was additionally associated with increases in the hazard of death from respiratory disease (adjusted hazard ratio 1.58 (95%CI[1.32, 1.90])) and cardiovascular disease (adjusted hazard ratio 1.34 (95%CI[1.17, 1.55])).

### *Conclusions*

From my work on the incidence and prevalence of cirrhosis I estimate that a minimum of 31,000 people in the UK are living with cirrhosis, a figure which is likely to rise given increasing trends in the incidence of cirrhosis described in this thesis. The significant mortality and disease progression associated with cirrhosis means that more needs to be done to combat both the incidence and progression of this disease both on an individual and population level.

Elevations in enzymes regarded as reflecting liver function are common in people aged 75 and over and in most people these abnormalities are less than 2x the upper limit of normal for the assays used. These elevations I observed are associated with both a modest increase in all-cause mortality and also with an increase in death due to specific causes. Rather than simply a marker of

liver function the investigation of people with elevated liver function tests, particularly those with severely elevated tests, may lead to the identification of potentially treatable conditions that underlie death.

## **Contributions**

The studies contained within this thesis are based on existing data from two databases – the GPRD and “MRC Elderly”.

### GPRD studies

Joe West had the initial ideas, wrote the grant that funded my salary and obtained the initial extract of all liver disease data. I subsequently extracted data on patients with cirrhosis, performed all of the data management and analysis in the studies included in this thesis. I also conceived the idea to examine the progression of cirrhosis (Chapter 5). Masoud Solaymani-Dodaran provided an introduction to the data format of the GPRD. Joe West, Tim Card and Masoud Solaymani-Dodaran advised on data management, analysis and interpretation of the results. Guruprasad Aithal additionally provided advice on the clinical relevance of the results. Tim Card provided code lists used for the generation of the Charlson index.

### “MRC Elderly” studies

Joe West had the initial idea for these studies. I performed the majority of the data management and all of the data analysis myself. I received help from Richard Atkins of the London School of Hygiene and Tropical Medicine in the preparation of cause of death data. Joe West and Astrid Fletcher advised on data management, analysis and interpretation of the results. Guruprasad Aithal additionally provided advice on the clinical relevance of the results.

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## Abbreviations used

|        |   |
|--------|---|
| ALP    | Alkaline phosphatase                              |
| ALT    | Alanine transaminase                              |
| AST    | Aspartate transaminase                            |
| BASL   | British Association for the Studies of the Liver  |
| BMI    | Body mass index                                   |
| BSG    | British Society of Gastroenterology               |
| CI     | Confidence interval                               |
| CMO    | Chief Medical Officer                             |
| CTP    | Child-Turcotte-Pug                                |
| DALY   | Disability adjusted life-year                     |
| GGT    | Gamma-glutamyl transpeptidase                     |
| GP     | General Practitioner                              |
| GPRD   | General Practice Research Database                |
| HBV    | Hepatitis B Virus                                 |
| HCV    | Hepatitis C Virus                                 |
| HES    | Hospital Episodes Statistics                      |
| HR     | Hazard Ratio                                      |
| HTA    | Health Technology Assessment                      |
| ICD    | International Classification of Diseases          |
| IgA    | Immunoglobulin A                                  |
| IgG    | Immunoglobulin G                                  |
| IgM    | Immunoglobulin M                                  |
| INR    | Internationalized Normal Ratio                    |
| LFT    | Liver function test                               |
| MELD   | Model for End-Stage Liver Disease                 |
| MHRA   | Medicines & Healthcare products Regulatory Agency |
| MRC    | Medical Research Council                          |
| NAFLD  | Non-alcoholic fatty liver disease                 |
| NHANES | National Health and Nutrition Examination Survey  |
| NHS    | National Health Service                           |
| NHSCR  | NHS Central Registry                              |
| ONS    | Office for National Statistics                    |
| OR     | Odds Ratio  |
| OXMIS  | Oxford Medical Information System                 |
| SMR    | Standardised Mortality Ratio                      |
| UK     | United Kingdom                                    |
| ULN    | Upper limit of normal                             |
| US     | United States                                     |
| UTS    | "up-to-standard"                                  |
| VAMP   | Value Added Medical Products                      |
| WHO    | World Health Organization                         |
| WHR    | Waist:hip ratio                                   |
| YLD    | Years lost with a disability                      |

## **1. Introduction**

This thesis utilises two distinct datasets to examine separate areas of interest in the epidemiology of liver disease in the UK. The first three studies contained within this thesis concentrate on the incidence and prevalence of cirrhosis, an examination of the mortality of people with diagnosed cirrhosis compared with those people in the general population and the progression of this disease. The second group of three studies focuses on the prevalence of elevated liver function tests in a population of older people in the UK, the demographic, clinical and lifestyle factors associated with such and the mortality following an elevated liver function test.

To contextualise these studies this introduction provides a brief consideration of some benefits and pitfalls in the methods of measurement of disease burden and gives an overview of the current burden of liver disease, globally and in the UK. I also describe what is presently known and unknown about the epidemiology of cirrhosis and that of elevated liver function tests in the elderly. Finally, a summary of the content of the subsequent chapters in this thesis is provided.

## **1.1. Measuring the burden of disease**

The burden of disease, or the burden of a specific disease, can encompass a wide range of measures. These include

- the frequency of disease,
- the mortality from disease (and consequent years of life lost),
- the morbidity associated with disease, and
- aspects of societal burden such as the financial and service requirements associated with disease.

This section discusses briefly some relevant issues in measuring the burden of disease particularly with respect to chronic liver disease.

### **1.1.1. Measuring the frequency of disease**

In its crudest form measuring the frequency of a specific disease can be considered as simply counting the number of people with that disease.

Though this may appear, at first consideration, a very easy task it is in fact anything but for the vast majority of diseases.

The two principal ways of considering the frequency of disease in a population are the incidence rate and the prevalence of disease. The incidence rate refers to the identification of new cases of a disease within a determined population over a specified period of time. Prevalence is concerned with the total number of people within a given population who are presently living with the disease of interest. Incidence and prevalence are intrinsically linked with prevalence being a function of incidence and survival time consequent to the acquisition of disease in closed populations. In open populations the prevalence of disease may additionally be affected by migration.

Central to determining either incidence or prevalence are a precise definition of the disease of interest, knowledge of the total population at risk of the disease as well as the means with which to identify people with that disease.

#### **1.1.1.1. The definition of a disease**

Several methods may be employed which in isolation or combination lead to the diagnosis of a particular disease, or indeed the assertion that a particular disease is not present in an individual. These include the identification of histological changes in cell or tissue architecture, the presence or absence of clinical signs and symptoms, and the use of test results, such as laboratory diagnostic tests including blood serology. Frequently such signs, symptoms and tests in isolation are indicative of a disease but are not sufficient to warrant a formal diagnosis. As such the presence of signs and symptoms or positive tests can often be used as a measure of undiagnosed disease. In almost all circumstances to acquire a diagnosis a person must be seen by a health care professional of some sort.

#### **1.1.1.2. Defining the population at risk**

If a person is to acquire a disease at some point in their life they must be at risk of it. It is self-evident that women are not at risk of testicular cancer and any calculation of the incidence or prevalence of testicular cancer would therefore include as its denominator only the total number of men in that population. Similarly, studies of occupational injuries would only include working people within the population at risk.

However, for most diseases it is not possible or practical to identify people who are specifically at risk of the disease. For example, in a disease which requires genetic susceptibility it would be very difficult to exclude from the denominator those people who are not genetically susceptible. Consequently



the vast majority of incidence and prevalence calculations assume that the whole population is at risk of the disease.

Should the population of interest be a geographically determined region then administrative sources of data such as vital statistics (based on birth and death registers) or census data may provide an accurate estimate of the total population 'at risk'. However, if cases of disease are being identified through specific means e.g. presentation at hospital with particular symptoms, then it may not be as clear what the total population at risk is (see section 1.1.1.3).

### **1.1.1.3. Identification of people with disease**

In an ideal world it would be very easy to identify the exact moment of disease onset (or time zero). Particularly with chronic diseases this is far from the case as disease can frequently be present before the onset of any signs or symptoms that would warrant investigation by a health care professional.

Frequently in epidemiological studies the identification of cases of disease is a pragmatic one where the date on which a subject acquires a diagnosis of a particular disease is considered the date of disease onset.

Identifying all people with a particular disease on a truly population-based level is fraught with problems particularly if the diagnosis of disease requires histological confirmation, as is the case with several chronic liver diseases. Clearly it would be impractical and indeed unethical to perform an invasive procedure with attendant risks e.g. liver biopsy on all members of the general population, including those who are otherwise in apparently good health.

Frequently, epidemiological studies are therefore based on populations of 'health-seekers' i.e. people who have for some reason been seen at a hospital or at the community level by a health practitioner, be it for the investigation of particular symptoms, following referral, for a routine health check or for an admission following an acute event. Whilst these study populations may be

representative of the total population of interest there is often likely to be some selection bias in those who are able to seek care.

For all calculations of incidence and prevalence the ideal scenario is a truly population-based approach but this is seldom achieved. However, it may be possible to conduct specific studies on a representative sample of a population, determine clinical signs and symptoms or obtain biological samples for laboratory testing and analysis, and then to extrapolate the results seen from this study population to the general population.

### **1.1.2. Measuring the mortality and morbidity associated with disease**

Ideally once a person has acquired a diagnosis of a particular disease that person would be followed up for life and details regarding morbidity and death associated with the progression of that disease would be recorded and available for analysis.

Concerning morbidity, all aspects of altered health consequent to the acquisition of a disease should be recorded. This would include altered physical health in terms of the clinical manifestation of disease as well as the potential psychological impact of living with a disease.

With respect to mortality it is important to know whether the death of that person is a direct result of the disease in question, whether the disease has been a contributing factor in the death or indeed whether the disease played no part in that individual's demise. It is of benefit to know both the absolute mortality rates and the mortality relative to the general population to understand the effect of that disease on mortality.

### **1.1.3. Measuring the financial and service requirements associated with disease**

In addition to the measurement of morbidity itself it is often desirable to obtain knowledge of the interventions, prescriptions or therapies that are associated with the management of disease and its symptoms as well as the effects of a disease with respect to an individual's ability to go about their everyday life.

In a country like the UK, where the overwhelming majority of healthcare is delivered free at the point of access through the National Health Service (NHS), it is essential that there are adequate estimates of the frequency and cost of treatments associated with a disease. For these figures to be of any real use in terms of the planning of services there must also be accurate estimates of the frequency of disease within a population to enable sufficient resource (personnel, equipment, facilities, in short, money) to be devoted to the treatment of particular diseases. Knowledge of the likely trends in the frequency of a disease is also of paramount importance for future planning requirements.

In addition, knowledge of the potential loss of productivity of individuals with a specific disease allows the assessment of the economic loss associated with the acquisition of disease. Several specific measures can be calculated including disability adjusted life-years (DALYs) and years lived with a disability (YLD).

### **1.1.4. Data used to measure the burden of disease**

In the vast majority of settings and for the vast majority of diseases there are not sufficiently robust data available regarding the progress of individuals with disease to enable comprehensive assessment of the burden of disease with respect to any of the areas highlighted above. Indeed for most diseases there

are not sufficient data available concerning the incidence of disease, let alone the follow-up of patients with disease.

Notable exceptions to this include the monitoring of particular infectious diseases, for example cases of anthrax or cholera are required, by law, to be reported in the UK, and in many countries cancer, where comprehensive cancer registries exist, many of which can be aggregated to look at supra-national trends.

For other diseases aside from conducting specific bespoke studies there are sources of data which are commonly used to describe some aspects of the burden of disease among particular populations. I will consider the role of vital statistics, such as birth and death registration data, administrative health care data and long-standing surveys.

#### **1.1.4.1. Vital statistics**

Many estimates of the burden of disease rely on the estimation of total population numbers gained from 'vital statistics' i.e. the number of births and deaths (and ideally figures reporting migration) within a particular population.

In many countries where birth and death registration are required by law these numbers are readily obtainable at a national and often at a fairly fine local level. However, in many countries, particularly in the developing world, estimates of total population numbers are more difficult to obtain with any precision.

In addition to the recording of the simple fact and date of these events, in many countries the registration of a birth or death must be accompanied by several pieces of information. For example, in the UK at the time of registering a birth information concerning the sex and birth weight of the child and country of birth of the mother are also collected. When registering a

death in the UK, information regarding the date, place and cause of death, as well as other information such as the occupation of the deceased, is collected. These two data sources are able to be linked together allowing, for example, the examination of trends in infant mortality based on birth weight of child and country of birth of mother.

Used alone, information regarding the cause of death is often used as an estimate of the frequency of disease within a population. For diseases with very high 1-year mortality, such as oesophageal cancer, this is a fairly good way to obtain incidence figures, providing the recording of cause of death includes that particular disease. With chronic diseases such as many liver diseases which people can live with for a very long time this measure will likely lag behind true population estimates of the frequency of disease. Additionally, the recording of cause of death on a death certificate is driven by what an individual doctor believes to be of importance. Though a person may have a long-standing illness, this illness may not have been of direct relevance to the fact of death and hence would not be recorded on the death certificate, leading to underestimates of the true population burden of that disease. For diseases where there are potential stigma attached to the diagnosis, such as liver disease with an aetiology of alcoholism, omission of certain diagnoses on the death certificate may be common in order to alleviate the suffering of the family members registering the death, again leading to underestimates of the true population burden of that disease.

Notwithstanding these limitations the availability of vital statistics is an extremely useful and well-used tool in measuring key population statistics which are readily comparable across nations and time.

### **1.1.4.2. Administrative health care data**

In the course of providing care and treatment to patients in health care settings a significant quantity of data is collected which can potentially be used for epidemiological research and in part to measure the burden of disease. In the UK there are sources of data from both primary and secondary care.

Many practices in the primary care setting contribute data collected as part of the standard delivery of care to bespoke research databases which then allow access to researchers to study particular questions. I have used data from one such database for studies contained within this thesis and discuss the relative merits of such data in detail in Chapter 2.

In secondary care much of the information collected at a hospital level in the UK is available as part of 'Hospital Episodes Statistics' (HES). Each time a patient is admitted to hospital a certain amount of information is collected including the date of admission, demographic information about the patient and diagnostic and procedural codes determined by those administering care. Data on these admissions are often used as estimators of the incidence of disease within the population. As a patient can be seen many times for a single disease unless only the first episode of care a patient receives is counted these figures will inflate estimates of incidence. However, these data remain extremely useful for measuring the burden with respect to the service requirements of a particular disease.

Data collection at a hospital level is not driven by a specific research question eliminating much of the selection bias that may be present in bespoke research studies but limiting data in terms of what is collected. Indeed there are reported issues with the reliability of the recording of diagnoses and

procedures. With respect to the measurement of disease progression and morbidity, differences in surveillance and follow-up will exist in different locations rendering data from individual sites less generalisable than data obtained from the national database, which additionally provides large numbers with which to conduct a study.

#### **1.1.4.3. Surveys**

As a substitute or adjunct to data available from administrative health care data the collection of data through repeated cross-sectional surveys can provide a very valuable resource for the measurement of disease burden within a population. One such example of this, which has been used to great effect, is the National Health and Nutrition Examination Survey (NHANES), which periodically samples the US population. This survey constitutes a nationally representative sample of approximately 5000 people in the US, collecting information regarding risk factors for disease such as obesity, alcohol consumption and environmental exposures, as well as the presence or absence of chronic conditions such as diabetes, cardiovascular disease and kidney disease. All participants additionally attend a physician-led appointment where blood samples and body measurements are taken. A similar survey in the UK exists in the form of the Health Survey for England (HSE) though this is not as comprehensive or well utilised.

Although there are limitations in the usefulness of data gained from cross-sectional surveys, not least the inability to assess the temporal nature of exposure and disease, these surveys nonetheless provide substantial information for the description of the burden of disease in the populations covered and, assuming the sampling has been well carried out, these data can be broadly generalised to the whole population.

Data from other cohort studies with substantial follow-up have been made available to researchers including, in the UK, the 1970 British Cohort Study and the Millennium Cohort Study.

#### **1.1.5. Limitations in the measurement of disease burden**

Although significant quantities of data are collected either routinely or as part of repeated surveys they are either a) not always appropriate for use in measuring the disease burden within a population or b) under-used considering they are available.

In the UK the provision of health care is increasingly concentrated to specialist services with tertiary referral centres for the treatment of particular diseases.

As such, the use of single-centre (or indeed multi-centre) studies is more limited now as these study populations are often no longer representative of the geographic area normally served by that hospital. Rather than rely on traditional 'gold-standard' epidemiology (prospectively identified cohorts with long follow-up) which necessitate a considerable length of time before results are available it is perhaps increasingly more appropriate to utilise aggregated databases that are often available at a national level.



Having briefly discussed how we commonly measure disease I will now describe the burden of liver disease globally and in the UK.

## **1.2. The global burden of liver disease**

Liver disease covers a broad spectrum of diseases including acute and chronic liver diseases. The International Classification of Diseases (ICD-10) includes within the specific section for liver disease (K70-K77) alcoholic liver disease (K70), toxic liver disease (K71), hepatic failure (K72), chronic hepatitis (K73), fibrosis and cirrhosis of liver (K74), inflammatory liver diseases (K75) and other diseases of liver (K76 including fatty liver K76.0). In addition, viral hepatitis (B15-19) and neoplasms of the liver and intrahepatic bile ducts (C22) are classed as liver diseases.

Throughout the world liver disease accounts for a considerable proportion of death, hospital admission, cost and DALYs. The relative contribution of specific liver diseases to the total burden of liver disease varies across the globe. I will briefly consider the global burden of chronic liver disease, viral hepatitis and liver cancer.

### **1.2.1.Chronic liver disease**

The availability of data on chronic liver diseases varies dependent on the research activities and relative importance of chronic liver disease in individual countries or regions. The vast majority of the available data is concerned principally with cirrhosis, which I consider separately in section 1.4.1.

### **1.2.2. Viral hepatitis**

Hepatitis is a general term referring to the inflammation of the liver. There are many different strains of viral hepatitis, the most common globally being hepatitis B and hepatitis C.

#### **1.2.2.1. Hepatitis B**

Hepatitis B, caused by the hepatitis B virus (HBV) is believed to have infected 2 billion of the world's population.<sup>1</sup> Most adult patients will recover from the infection but approximately 5-10% of people will not clear the virus. The prevalence of hepatitis B varies considerably across the globe with chronic HBV infection endemic (defined as greater than 8% of the population being carriers) in some areas of south-east Asia, sub-Saharan Africa, the Amazon Basin, part of the Middle East, central Asian Republics and some countries in eastern Europe (see Figure 1-1). Areas of low endemicity (carriers represent less than 2% of the population) include North America, Western and Northern Europe, Australia and part of South America with the rest of the world being classed as intermediate endemicity (carriers representing between 2 and 8 % of the population).

The principle route of transmission depends on the level of endemicity in a country, with mother-to-child transmission the most frequent method in areas of higher endemicity. In areas of lower endemicity more common transmission routes include high-risk sexual activity, blood transfusion in countries without donor screening, needle sharing and sometimes, although relatively rarely, through exposure to blood products in health care settings.

An estimated 350 million people worldwide are carriers of the HBV, often asymptomatic but frequently developing into chronic hepatitis, cirrhosis and/or liver cancer.

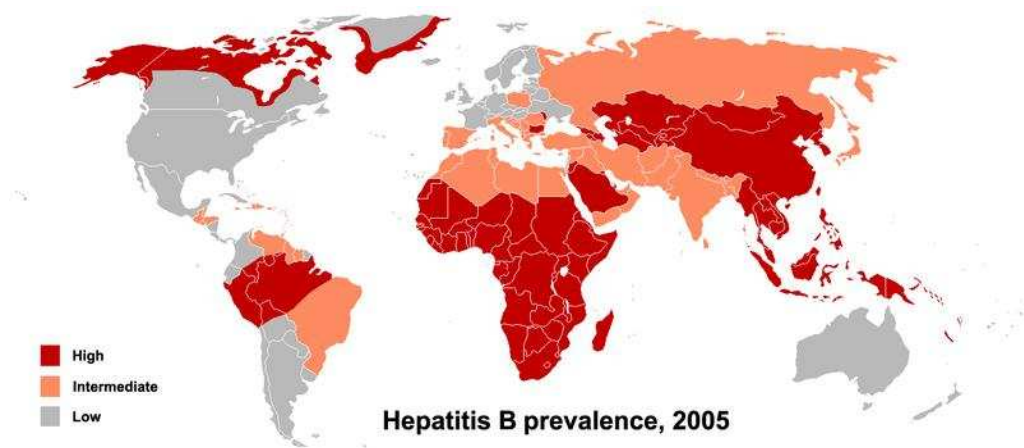


Figure 1-1 Global Hepatitis B prevalence, 2005.

#### **1.2.2.2. Hepatitis C**

Hepatitis C, caused by the hepatitis C virus (HCV), was identified in 1989, previously having been referred to as non-A non-B hepatitis. HCV is much less common than HBV with an estimated 3% of the world's population being infected.<sup>2</sup> HCV is more evenly distributed across the world than HBV but there remains substantial variation in the prevalence (see Figure 1-2).

The principle routes of transmission are through needle sharing, transfusion of unscreened blood products and, principally in areas of high endemicity, mother-to-child transmission.

Incidence of HCV is believed to be declining thanks to donor blood screening and needle-exchange programmes. As with HBV, most cases of HCV are asymptomatic so precise estimation of the prevalence is very difficult. HCV can progress to chronic hepatitis, leading to cirrhosis and liver failure in approximately 10-20%.<sup>2 3 4</sup>

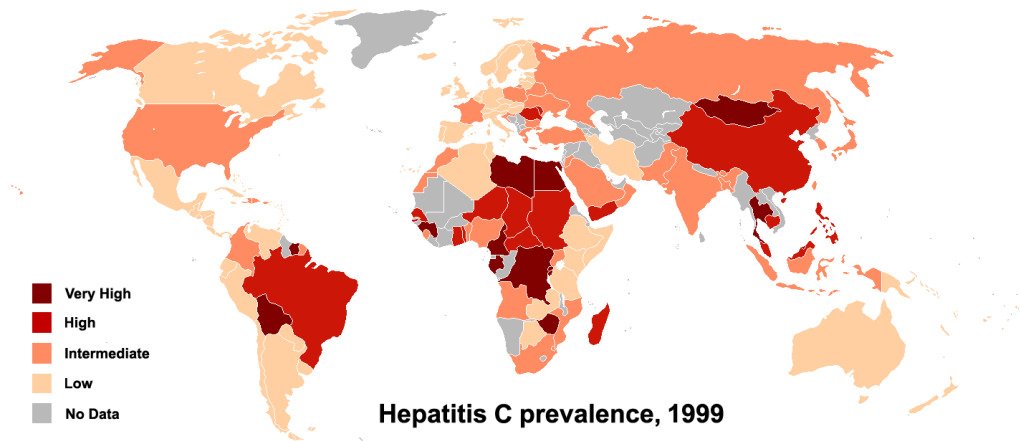
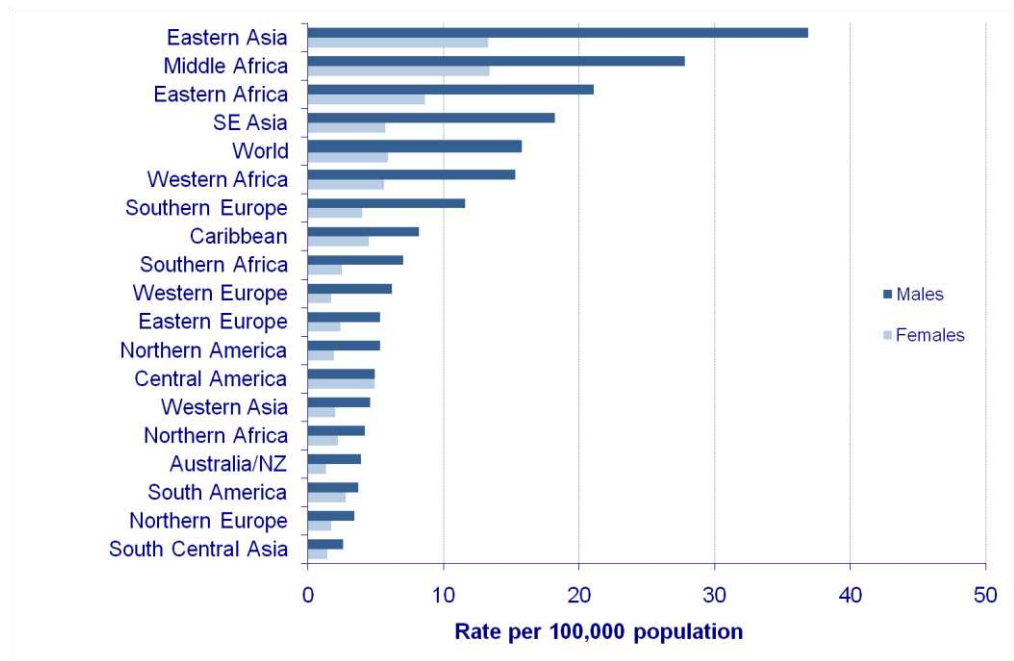


Figure 1-2 Global Hepatitis C prevalence, 1997.

### **1.2.3. Liver cancer**

An estimated 632,000 cases of liver cancer occur every year across the globe.<sup>5</sup> Liver cancer ranks as the 6<sup>th</sup> most common cancer worldwide and the third most common cause of death from cancer worldwide.<sup>6</sup> The number of new cases of liver cancer is highest in the Western Pacific region (an estimated 386,000 in 2004) accounting for over three fifths of all cases whilst age-standardised incidence rates are highest for Eastern and South-East Asia and Middle and Eastern Africa (see Figure 1-3).





**Figure 1-3 Age-standardised liver cancer incidence rates, by region and sex, 2002 estimates.**

from Ferlay J. GLOBOCAN 2002. IARC CancerBase No.5, Version 2.0

### **1.3. Liver disease in the UK**

The focus on liver disease in the UK is now principally concerned with chronic liver disease (including hepatocellular carcinoma), particularly chronic liver disease relating to increasing alcohol consumption, and, to a slightly lesser extent, HCV.

In the first decade of the 21<sup>st</sup> century there have been several documents published concerning the increasing problem of liver disease in the UK. Foremost was a chapter from the Annual Report of the Chief Medical Officer (CMO) for England in 2001 highlighting the problem of liver cirrhosis, particularly at younger ages.<sup>7</sup> Subsequent to this were four not insubstantial reports each concerning, at least in part, the burden of liver disease in the UK.<sup>8 9 10 11</sup>

The appointment of a National Clinical Director for Liver Disease in January 2010 would indicate that liver disease is considered a significant challenge to the NHS in the 21<sup>st</sup> Century.<sup>12</sup>

I will briefly consider the national burden of chronic liver disease, viral hepatitis, liver cancer and the demand for liver transplants.

### **1.3.1. Chronic liver disease**

Estimates of the burden of chronic liver disease are largely based on mortality statistics and to a lesser extent on hospital admission statistics.

I will briefly summarise the five reports mentioned in section 1.3.

The report from the CMO highlighted a 3-fold increase in deaths from chronic liver disease (which it subsequently refers to as cirrhosis) over the period 1970-2000, with an 8-fold increase seen in men aged 35-44 and a 7-fold increase in women of the same age based on death certification data.<sup>7</sup> The most likely reason for this increase, according to this report, is the higher level of alcohol consumption in the UK over the same period. The report also briefly considers the role of viral hepatitis (particularly HCV) as an important cause of cirrhosis.

The second report, entitled 'The epidemiology and health care burden of chronic liver disease', commissioned by the British Liver Trust and the Foundation for Liver Research, published in December 2004 and included an examination of current knowledge of the epidemiology of several chronic liver diseases utilising data from mortality statistics, hospital episode statistics, cancer registry statistics and viral hepatitis notifications from the Health Protection Agency.<sup>8</sup> Analyses were limited to simple examination of time trends in mortality from particular diseases and admissions to hospital from these diseases and, in general, showed an increase in the burden of chronic liver disease. Again, considerable focus was given to the observed increase in alcohol consumption contemporaneously with an increase in mortality from liver disease.

In January 2006, a report prepared for the CMO by the Department of Health's Quality Strategy Team 'Liver Disease: a scoping study into the nature and burden of the disease' again provided a limited description of the burden of liver disease based on mortality statistics, data from the General Household Survey and the World Health Organization, as well as a brief summary of the current provision of liver services in the UK.<sup>9</sup> This report highlighted the lack of evidence about the incidence, nature and progression of liver disease in the United Kingdom.

The fourth report to consider was commissioned by the British Society of Gastroenterology (BSG) and published in February 2007.<sup>10</sup> 'Gastroenterology services in the UK. The burden of disease, and the organisation and delivery of services for gastrointestinal and liver disorders: a review of the evidence.' included a section on the incidence of liver diseases and mortality from liver disease based on a systematic review of the available literature and an examination of mortality statistics, with similar conclusions to the above reports, and a further consideration of the level of service provision in the UK.

The fifth report of note, 'A Time to Act: Improving liver health and outcomes in liver disease' published in 2009, prepared by the British Association for the Study of the Liver (BASL) and the BSG's Liver Section presented the national plan for liver services in the UK.<sup>11</sup> This report highlighted the potential preventability of much of the chronic liver disease affecting the UK, through alcohol harm reduction strategies, identification and reduction in transmission of HCV and through decreasing the prevalence of obesity.

In 2008 a paper summarised the trends in UK hospital admissions with a code for chronic liver disease and mortality rates based on death certification data

for all patients with a mention of liver disease.<sup>13</sup> Both hospital admissions and mortality from chronic liver disease were seen to increase over the period of 1989-2002.

There are, of course, many individual studies considering the burden of specific chronic liver diseases and the progression and mortality associated with such. However, a detailed examination of each of these diseases is beyond the scope of this thesis. A consideration of the epidemiology of cirrhosis is given in section 1.4.1.

### **1.3.2. Viral hepatitis**

In the UK there is a low prevalence of active carriers of viral hepatitis with roughly 0.3% and 0.4% of the population infected with HBV and HCV respectively.<sup>1 14</sup>

However, there is considerable uncertainty surrounding the prevalence of these two viral hepatitises as so many patients whilst infected remain asymptomatic.

The reported increase in the prevalence of HBV is believed to be largely driven by immigration from areas of high endemicity.<sup>11</sup> The prevalence of HCV is reported to be lower in more recent birth cohorts, perhaps due to a decreased risk of infection in younger generations following the advent of blood screening and changes in injecting drug-users' habits.<sup>15</sup> Progression with HCV to cirrhosis in the UK is estimated at 12% (95% CI [6%, 22%]) over 20 years.<sup>16</sup>

### **1.3.3. Liver cancer**

Figures from Cancer Research UK based on the cancer registrations of England, Scotland, Wales and Northern Ireland show an incidence of liver cancer in the UK in 2006 of 3193 new cases, accounting for just over 1% of all new cancers in the UK<sup>17</sup> placing liver cancer as the 18<sup>th</sup> most common cancer in the UK. Between the years 1975 and 2006 the age-standardised incidence rates of liver cancer in Great Britain have increased nearly 3-fold, from 1.4 to 3.9 per 100,000 person years.<sup>17</sup>

### **1.3.4. Liver transplant**

Figures from the UK NHS Blood and Transplant Authority show 607 liver transplants in 2008/09 with a further 338 on the active transplant list at 31 March 2009.<sup>18</sup> For all patients on the transplant list, the most common reason for a liver transplant in the UK is cirrhosis (49% of all transplant patients) with metabolic and hereditary chronic liver diseases accounting for the majority of the remainder. (Personal Communication, UK NHS Blood and Transplant Authority, March 2010)

## **1.4. Rationale behind the studies in this thesis**

### **1.4.1. Cirrhosis**

#### What is cirrhosis?

Cirrhosis is a chronic liver disease defined anatomically as a diffuse process with fibrosis and nodule formation.<sup>19</sup> Its causes are myriad and it is considered the end point of most chronic liver diseases. Principle aetiologies are viral hepatitis, alcohol, autoimmune disorders such as autoimmune hepatitis and primary biliary cirrhosis, and metabolic disorders including haemochromatosis and Wilson's disease. Recent studies have suggested the progression of non-alcoholic fatty liver disease (NAFLD) to steatohepatitis, fibrosis and cirrhosis.<sup>20</sup> Frequently the aetiology of cirrhosis is unknown with such cases being commonly referred to as 'cryptogenic' cirrhosis. The aetiology of cirrhosis differs across the world, with alcohol representing a more common cause of cirrhosis in much of the Western world.

#### Diagnosis of cirrhosis

The diagnosis of cirrhosis is often based on a combination of clinical, ultrasound, biochemical and histological findings but liver biopsy is still considered the 'gold-standard' for the diagnosis of cirrhosis.<sup>21</sup> A liver biopsy carries with it some procedural risks, including bleeding, considerable discomfort for the patient and even a small risk of death,<sup>22 23</sup> so several other non-invasive methods for diagnosis are being more commonly employed and evaluated. These include transient elastography (Fibroscan), magnetic resonance elastography and combinations of ultrasound CT and MRI.<sup>24 25</sup>

### Disease progression and treatment

Cirrhosis in the absence of complications is referred to as compensated cirrhosis but following the appearance of ascites, oesophageal variceal bleeding, encephalopathy or jaundice is considered to be decompensated. Cirrhosis has until recently been considered irreversible, but this concept is no longer absolute as regression of fibrosis can be seen and 'reversal' of cirrhosis has been reported.<sup>26 27 28 29 30 31</sup> The principle aim for therapies in patients with cirrhosis is to slow the rate of progression which would lead eventually to liver failure or death. Treatments are few and are mostly focussed on the removal of the aetiologic agent(s), the suppression of hepatic inflammation, inhibition of hepatic stellate cell activation and then therapeutic strategies for the common sequelae of cirrhosis including the early detection of hepatocellular failure, hepatocellular carcinoma, fluid retention, encephalopathy and prevention or treatment of oesophageal varices and oesophageal bleeding.

### Global burden of cirrhosis

The global burden of cirrhosis of the liver is significant, accounting for an estimated 800,000 deaths (1.3%) worldwide in 2004 according to the World Health Organization (WHO) ranking it as the 18<sup>th</sup> highest cause of death.<sup>5</sup> In Europe, it is estimated to have contributed to 3.1 million DALYs (2.0% of total DALYs), ranking it as the 9<sup>th</sup> leading disease burden. Estimates of the years lived with a disability (YLD) for cirrhosis of the liver are as high as 3.79 million based on population estimates for 2000.<sup>32</sup>



### UK burden of cirrhosis

In contrast to much of Western Europe, America and Australasia, where mortality from cirrhosis has remained constant or in decline, mortality from cirrhosis in the UK has tripled across the last few decades.<sup>7 33</sup> Although this increase is considerable the age-standardised mortality rates in England and Wales remain lower than those in most other countries studied, with the notable exceptions of Canada, Greece, and the Scandinavian countries (excepting Denmark).<sup>33</sup> Much of the increase in mortality from cirrhosis seen in the UK is attributed to the increase in alcohol consumption in the UK.<sup>7 34 35</sup> The commonly used definition for cirrhosis when examining mortality statistics includes codes for alcoholic liver disease (K70), chronic hepatitis (K73) as well as codes for fibrosis and cirrhosis of the liver (K74). In 2008, 1.3% of all deaths of people aged 25 years or over in England and Wales were attributed to these codes (K70, K73 and K74) according to death certification information.<sup>36</sup>

Despite the significant apparent burden of cirrhosis globally and the observation of an increasing trend in cirrhosis mortality in the UK there is little contemporary data surrounding the frequency of cirrhosis in the population of the UK, the mortality associated with a diagnosis of cirrhosis and the progression of the disease.

#### **1.4.1.1. Incidence and prevalence of cirrhosis in the UK**

Most reports examining the burden of cirrhosis in the UK concentrate on figures derived from death certificate information referring to a combination of chronic liver disease and cirrhosis (ICD-9 571 and ICD-10 K70, K73 and K74). As discussed above (section 1.1.4.1) there are significant limitations of mortality statistics to measure the burden of disease within a population, particularly a chronic disease such as cirrhosis. In addition, the inclusion of other chronic liver diseases which may not yet have developed into cirrhosis could lead to an overestimate in the burden of cirrhosis itself at a population level. These opposing potential misclassification biases mean estimates of incidence based on these mortality statistics are unlikely to be valid.

Despite the observed 3-fold rise in mortality from chronic liver disease the last studies to truly try to look at the incidence of cirrhosis in the population of the UK were reported nearly 30 years ago.<sup>37 38</sup>

The study by Saunders et al reported in 1981 presented a summary of data collected over 18 years in the 1960s and 1970s concerning patients aged 15 years and over identified to have cirrhosis from a single hospital in west Birmingham and from Coroner's post-mortem reports.<sup>37</sup> The incidence of cirrhosis was reported as 10.3 per 100,000 population. Though probably representative of the population served by this hospital, these figures are not generalisable to the rest of the UK as the West Midlands region has a higher than average mortality from liver disease compared with the general population of the UK.<sup>39</sup> In addition, 11.3% of the subjects in this study were identified as 'incident' cases as a result of incidental findings at post-mortem examination.

Information provided by Hislop in the form of a letter to the British Medical Journal in 1981 reports an incidence of cirrhosis of 14.6 per 100,000 population over the period of 1975-9.<sup>38</sup> Unfortunately I could not find a full publication of these results and the methods of data collection are unclear leaving the validity of these results questionable.

A third study reporting the incidence of cirrhosis on the islands of Lewis and Harris off the north-west coast of Scotland reported an incidence of 5.5 per 100,000 population based on only 12 patients with confirmed cirrhosis between 1977 and 1982.<sup>40</sup>

These wide estimates of incidence, mostly based on data from over 30 years ago and studies with varied methodology, provide considerable uncertainty to the present burden of cirrhosis in the UK. With this absence of contemporary studies on the incidence of cirrhosis we also have little idea as to future trends in mortality and we are unable to project the level of service provision required for treatments associated with the progression of cirrhosis, including liver transplantation and oesophageal banding.

### **1.4.1.2. Mortality experience of patients with cirrhosis**

Whilst there are several studies which report the number of people who die with a recording of cirrhosis on their death certificate and the trends in such data there is little information about the mortality experience of patients with cirrhosis. We also have little idea of the comparative mortality experience of people with cirrhosis with reference to the general population.

The most recent estimate of survival in patients with cirrhosis in the UK comes from a regional study based on data from 1968-1999.<sup>41</sup> This study considered all patients in the Oxford Regional Health Authority who were admitted to hospital for any chronic liver disease (ICD-10 codes K70, K73, K74 and K76; ICD-9 and ICD-8 code 571) comprising 8192 patients across the whole period. The standardised mortality ratio (SMR), compared to mortality in the Oxford regional population, was 16.3 in the first year. The inclusion of only hospitalised patients will likely lead to an overestimate in the SMR as these patients requiring hospital admission are likely to be patients with more severe disease. As discussed above the inclusion of patients with other chronic liver diseases, not just specifically cirrhosis, may introduce some error into the estimates of mortality, though without knowledge of the relative mortality experience of patients with different liver diseases it is not possible to know in which direction this may change the point estimate of mortality. Additionally, it has been shown that the use of population death rates for comparators in mortality studies leads to an overestimate in the mortality risk suggesting an internal comparison group would be more appropriate.<sup>42</sup>

Other estimates of mortality in patients with cirrhosis in the UK come from much older studies. In the same study examining incidence Saunders et al

report the 5-year survival of patients with alcoholic cirrhosis, 36%, and non-alcohol related cirrhosis, 14%.<sup>37</sup> An earlier study, also from Birmingham, covering patients with cirrhosis in a single hospital between 1959-64 reports similarly low 5-year survival figures of 14.4% after first admission to hospital, again with patients with alcoholic cirrhosis having a better prognosis (5-year survival of 20% compared with 5.1% for patients with cryptogenic cirrhosis).<sup>43</sup>

There have been varying estimates in the mortality associated with a diagnosis of cirrhosis provided from other countries within Europe and the USA, all of which were based on hospitalised patients.

Perhaps the most commonly referenced figures in the literature looking at the mortality experience of patients with cirrhosis are those based on 1155 consecutive patients admitted to a single hospital in Sicily during the 1970s and 1980s which reported 6-year survival of 54% and 21% in patients with compensated and decompensated cirrhosis respectively.<sup>44</sup>

In Denmark between 1995 and 2006 a hospital cohort of 14,976 patients with cirrhosis described a 1-year survival of 65.5% and 5-year survival of 37.5%.<sup>45</sup>

This study was not able to categorise patients into severity of disease and additionally did not report the hazard ratios for mortality compared with their matched control cohort. Previously these same authors had reported SMRs for patients hospitalized with cirrhosis compared with the general population of 32.3 for the first year following diagnosis and 5.7 thereafter.<sup>46</sup>

Two papers considering the experience of patients from the 1950s and 1960s report survival varying from less than 50% in the first year following diagnosis in Malmo, Sweden<sup>47</sup>, to 60% in Brisbane, Australia.<sup>48</sup> Neither of these studies reported comparisons with a general population cohort.

Thus, most of our knowledge on the mortality experience of people with cirrhosis is from a few highly selected populations which may not be broadly representative of the whole population of people with cirrhosis, particularly with the absence of ambulatory patients. Previous studies have also been unable to take into account comorbid conditions and the aetiology and severity of cirrhosis itself. Indeed in a recent health technology assessment (HTA) systematic review it was claimed that existing data suggest that there is no excess mortality in those patients with compensated disease compared with the general population for the purposes of the cost-effectiveness analysis carried out.<sup>49</sup> Differences in the aetiology of cirrhosis in different countries may also render these estimates of mortality inappropriate for a UK cohort of patients with cirrhosis. There is clearly a need for contemporary estimates of the mortality experience of patients with cirrhosis within the UK, compared with a valid comparison cohort from the general population.

### 1.4.1.3. Progression with cirrhosis

Knowledge of the progression of disease is of natural interest to both physicians and patients alike wishing to understand the likely risks of subsequent morbidity and mortality associated with a diagnosis of cirrhosis.

At an individual level and near the end stage of liver disease there are scoring systems commonly used to rank patients in order of risk of death and to enable identification of patients suitable for transplantation.

Two commonly used prognostic models in liver disease are the Child-Turcotte-Pugh (CTP) classification<sup>50</sup> and the Model for End-Stage Liver Disease (MELD) score.<sup>51</sup> The CTP score is a combination of five clinical measures of liver disease, each graded 1, 2 or 3. These are total bilirubin, serum albumin, internationalized normal ratio (INR), presence and severity of ascites and the presence and severity of hepatic encephalopathy. Limitations of the CTP score have led to the increasing use of the MELD score, a calculation combining serum bilirubin, serum creatinine and INR measurements using the following formula:

$$\text{MELD} = 3.78 [\ln \text{ serum bilirubin (mg/dL)}] + 11.2 [\ln \text{ INR}] + 9.57 [\ln \text{ serum creatinine (mg/dL)}] + 6.43$$

Several modifications have been suggested to improve the measurements of current MELD components and the incorporation of other measurements, including coagulopathy, renal dysfunction and serum sodium, have also been suggested to improve the accuracy of the score's ability to predict survival.<sup>52</sup>

The development of these scores primarily as a tool for identifying patients suitable for transplant may also mean that their utility as a score for cirrhosis itself may not be as valid as individual prognostic markers.<sup>53</sup> Some studies have examined prognostic factors specifically in cirrhosis using complex

regression models including 46 and 174 variables,<sup>54 55</sup> while there is a wide literature base of studies examining one or more individual prognostic factors. Whilst these scores are undoubtedly useful to clinicians in assessing the survival probability of an individual patient the complicated nature of the calculation and component parts may not be as readily comprehensible to patients themselves. As such, it is useful to have some knowledge of the progression of cirrhosis based on clinical symptoms which are easily understood by patients and clinicians alike and which do not necessitate laboratory tests.

Current knowledge of the progression of cirrhosis as a whole based on stage of disease is limited to a single centre study in Sicily, Italy from 1970s-80s,<sup>55</sup> and a recent study of hospitalised patients with alcoholic cirrhosis in Denmark.<sup>56</sup> Other studies have considered the prognosis of patients with cirrhosis once they have acquired certain symptoms such as oesophageal varices,<sup>57</sup> or variceal bleeding.<sup>58 59 60</sup> Whilst the more recent of these studies may provide useful information on the likely progression for patients with a diagnosis of cirrhosis they were all based on hospitalised patients only, some in populations with quite different risk factor prevalences to the UK, and were not able to examine the progression of disease based on severity and aetiology.

Understanding the contemporary disease progression in people with cirrhosis is key to determining the prognosis, health needs and burden of disease consequent upon having this serious condition.



### **1.4.2. Liver function tests**

Several markers of liver function are included as part of standard laboratory blood tests which in the UK are frequently requested both in primary and secondary care. Standard blood tests which may be bracketed under the nomenclature of 'liver function tests' (LFTs) include serum bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), albumin, prothrombin time (INR) and gamma-glutamyl transpeptidase (GGT). None of these are truly specific in the measurement of liver function and as such the label of 'liver function test' is perhaps a little misleading. Nonetheless, these tests are useful on the diagnostic pathway and also as a prognostic tool. Additional tests that may be ordered on suspicion of liver disease may include several measurement of immunoglobulins (IgG, IgA, IgM), antimitochondrial antibody (AMA, used in the diagnosis of primary biliary cirrhosis), antinuclear antibodies (ANA, used in the diagnosis of autoimmune hepatitis), alpha-1 antitrypsin (used in the diagnosis of alpha-1 antitrypsin deficiency), caeruloplasmin (used in the diagnosis of Wilson's disease) and viral marker tests e.g. antibodies for the HBV and HCV.

I will focus the remainder of this section on a discussion of three commonly used 'liver function tests' namely aminotransferases (particularly AST), ALP and bilirubin.

#### Aminotransferases (ALT and AST)

ALT is a cytosolic enzyme present in the liver, and to a lesser extent in the heart and skeletal muscles. AST is a mitochondrial enzyme which is present in large quantities in the heart, skeletal muscle and kidney and also in the liver.

Variations in the serum prevalence of ALT and AST are indicative of the early stages of viral hepatitis, as well as other liver insults or injuries including alcohol abuse, autoimmune hepatitis, non-alcoholic steatohepatitis, haemochromatosis, Wilson's disease and alpha-1 antitrypsin deficiency. Non-hepatic causes of elevations in ALT or AST include coeliac disease, striated muscle disorders, some endocrine diseases (hyperthyroidism and Addison's disease) as well as glycogen storage diseases.<sup>61</sup> Often the ratio of the two enzymes is used in the diagnosis of alcoholic hepatitis and cirrhosis.

### Alkaline phosphatase (ALP)

Alkaline phosphatase is an enzyme present in the liver and bile ducts. Elevations in ALP are common in cholestatic diseases (such as primary sclerosing cholangitis and primary biliary cirrhosis) but as ALP is also particularly concentrated in some other tissues (such as bones, placental tissue and in the kidneys) the specificity of ALP as a 'liver function test' is not very high. Elevations of ALP can occur in a wide variety of other diseases including Paget's disease and other bone disorders, with malignant tumours, in renal disease as well as natural elevations being seen during pregnancy. A simultaneous elevation in GGT would suggest a problem of liver origin.

### Bilirubin

Bilirubin is a product of haemoglobin catabolism. An increase in serum bilirubin can be as a result of additional bilirubin production, decreased hepatic uptake or decreased conjugation (occurring within the liver). Elevations in unconjugated bilirubin can indicate haemolysis or familial abnormalities of bilirubin metabolism such as Gilbert's syndrome. Elevations in conjugated bilirubin are more indicative of congenital hyperbilirubinaemias such as Dubin-Johnson syndrome and Rotor's syndrome.<sup>62</sup>

Although these 'liver function tests' are performed frequently in both primary and secondary care the prevalence and consequences of these standard markers of liver disease have been ill-described in the UK making the interpretation of them difficult, particularly in the case of an isolated elevation in one of these tests.

A finding of an elevation of serum aminotransferase, ALP and / or bilirubin may be used as an indication of potential liver disease with subsequent follow-up or more invasive testing probable in such patients although specific guidance is not available in the UK.

One study in the UK examined the records of all patients from a single centre in the UK with an abnormal liver function based on a test requested from their GP.<sup>63</sup> Of 342 patients with an elevated LFT (a single measurement of ALT, ALP or GGT twice the upper limit of normal) just under half (157 patients (46%)) had initially not been considered to warrant further investigation. The authors invited these patients for subsequent tests which diagnosed liver disease in 97 (62%) of these patients. The remaining 195 patients from the original sample had their liver function test repeated with only 38% showing spontaneous resolution of the abnormal test results. Other studies from outside of the UK have reported high levels of liver disease in patients with persistently raised LFTs but who are otherwise asymptomatic.<sup>64 65</sup>

A report from the Department of Health's Quality Strategy Team (January 2006) recommended 'providing guidance to general practitioners on the use and interpretation of liver function tests'.<sup>9</sup> Current consensus opinion in the UK suggests that patients should be investigated only if abnormalities persist for between 3 and 6 months.

As the data I examined for chapters 7-9 only include measurements of AST, ALP and bilirubin for the remainder of this section when I refer to LFTs I am principally concerned with the measurement of serum AST, ALP and bilirubin only. As these data are also only concerned with people aged 75 and over I have tried to report studies specific to populations of older people. As this is a rapidly growing sector of the UK population who may be undergoing several tests as part of routine care for other conditions the quantification of the prevalence of abnormal LFTs, the association with demographic, lifestyle and clinical factors as well as subsequent mortality is of particular interest to clinicians who will be treating these patients.

#### **1.4.2.1. Prevalence of elevated liver function tests**

Information on the prevalence of elevated LFTs in the UK is surprisingly lacking. The only study I could find that specifically addressed the issue of prevalence of elevated LFTs in a UK population is the recent publication from McLernon and colleagues which examines LFTs in a population of adults of all ages from Scotland.<sup>66</sup> This study reports 21.7% of all study participants having at least one abnormal LFT with 7.0% having an elevated AST, 10.4% an elevated ALP and 7.1% an elevated bilirubin. Unfortunately this sample is unlikely to be representative of the general population as subjects were identified based on having already had a LFT recorded in primary care. As this is likely to include patients undergoing investigations for suspected liver disease these results cannot be widely generalised.

Other estimates of the prevalence of elevated LFTs come from outside of the UK and are often based on highly selected populations. Conflicting estimates from studies focussing on healthy employed workers place the range of elevated AST as low as 4.2% in Maryland, US<sup>67</sup> or as high as 21.8% in German construction workers<sup>68</sup> with a further study from the US placing the estimate of the prevalence of elevated AST at 14.9%.<sup>69</sup>

One study from America which identified patients who had had at least one healthcare encounter in the year 1995 estimated a prevalence of elevated AST of 13%. Again, as these patients are likely to include those who are sicker than the general population and therefore seeking health care this figure is probably an overestimate of the true population prevalence of elevated AST. Further studies from the USA using survey data from NHANES, a more representative sample of the population, have shown a much lower prevalence than that seen in the UK study, with 3.7% and 4.9% of

the population aged 20 or over having an elevated measurement of AST in 1988-1994 and 1999-2002 respectively.<sup>70 71</sup>

Fewer studies considered elevations in ALP and bilirubin. The study of a working population from Maryland, US reported a prevalence of elevated ALP of 5.9% and of elevated bilirubin of 8%.<sup>67</sup>

I did not identify any studies looking specifically at this problem in a population of older people.

Differences in the distribution of various risk factors, the prevalence of different liver diseases in these populations, the definitions of normal and abnormal tests as well as the methodological limitations in the selection of study populations mean that we are without a valid estimate of the prevalence of elevated LFTs in a UK population.

### **1.4.2.2. Associations with elevated liver function tests**

Knowledge of the clinical, demographic and lifestyle factors that are associated with elevations in LFTs is crucial in the management of patients who may present with an elevated LFT.

It is important to know whether patients with elevated LFTs are a particular group of people (aside from whether they have liver disease) in order that we can potentially target the groups of people in whom further follow-up may be appropriate and also to aid in the understanding consequent to the identification of a person with elevated LFTs, particularly if there are specific comorbidities that are associated with elevations in LFT.

Many studies have looked at the association of certain 'risk factors' for elevated LFTs. Often these include the examination of elevated transaminases (either an elevation of ALT or AST) so it is not possible to determine what an elevation of one of these enzymes may be associated with. Markedly different associations have been shown, both in magnitude and indeed in some cases in the direction of the association. In addition, there is little consistency in the definition of abnormality employed in these myriad studies making comparisons and extrapolations to other populations difficult.

In the recent study from Scotland, an elevated measurement of ALP was associated with a statistically significant lower risk of several comorbidities (ischaemic heart disease, diabetes, respiratory disease and cancer) but with an increased risk of biliary disease.<sup>66</sup> However there were no statistically significant associations seen between transaminase elevations and these comorbidities studied. This is in contrast to the data from NHANES which

show an increased prevalence of type 2 diabetes and hypertension in patients with elevated transaminases as well as associations with younger ages, increasing BMI and being male<sup>70</sup> and data from Germany where elevated AST was associated with hypertension, ischaemic heart disease, hyperlipidaemia and higher BMI.<sup>72</sup> Of specific interest appears to be the association between abnormal LFTs and diabetes. Several papers have reported elevations of transaminases being associated with existing diabetes or the development of diabetes.<sup>68 72 73 74</sup>

There are again conflicts in the literature surrounding the association of elevated LFTs with alcohol consumption. Whilst three studies have reported an association between increasing alcohol intake and elevated transaminases,<sup>68 71 75</sup> another found no association between drinking 3 or more units per day and elevated LFTs.<sup>69</sup>

Differences in populations, definitions of abnormality and indeed the lack of consistency between these studies' findings leave a substantial gap in our knowledge of the associations between elevated LFTs and clinical, demographic and lifestyle factors. I was not able to find any papers that looked at the associations between elevated liver function tests and other characteristics specifically in a population of older people.



### **1.4.2.3. Mortality associated with liver function tests**

Few studies have assessed the association between elevated LFTs and mortality in the general population as opposed to populations with known liver disease. Most of these studies have been performed in selected populations not broadly representative of the general population.

The only study to attempt to describe the relationship between elevated LFTs and mortality in the UK on a population-based level is the study by McLernon et al, described above.<sup>66</sup> This study reported statistically significant associations between elevated LFTs (transaminases, ALP and bilirubin) with increased all-cause mortality. Although moderate in absolute terms (for example, mildly elevated ALP (defined as elevated ALP between 1 and 2.5 times the upper limit of normal) was associated with a hazard ratio of 1.8 for all-cause mortality) the authors reported a higher risk of death with increasingly abnormal transaminases and ALP. The increased risk of death from liver disease specifically was markedly higher with hazard ratios of 3.8 and 5.4 for mildly elevated ALP and transaminases respectively.

A relatively recent study from the USA reported similar increased risks of death with elevated transaminases and a comparable 'dose-response' effect.<sup>76</sup> The study population was selected based on subjects who had had a healthcare encounter in a small geographically defined region of Minnesota and had at least 2 years of follow-up. Not all patients had their LFTs measured and as with the study in Scotland these populations are likely to include a significant proportion of subjects who were being actively investigated for liver disease meaning results cannot be widely generalised to the general population.

Two further studies from working populations in Germany and South Korea report markedly higher risks of death with elevated AST than the two studies described above.<sup>68 75</sup> Arndt and colleagues report a 3-fold increased relative risk of death from all causes in construction workers with an elevated AST, where Kim et al. report relative risks of mortality of 5.6 and above for increasing levels of abnormal AST. Indeed even within accepted normal limits subjects with a higher AST measurement than baseline (<20 IU/l) were seen to have an increased risk of death (relative risk 1.8 (95% CI[1.4, 2.4])).

I identified one study which looked specifically at the association between liver function and mortality in the elderly, which came from a small population of 70 year-olds in Jerusalem.<sup>77</sup> Categorising subjects as above or below the mean value of LFT, this study did not show a statistically significant association between elevated AST or ALP and all-cause mortality. However, they reported a higher mortality in patients with low ALT measurement in contrast to the above studies which considered transaminases together. No increased mortality was seen with elevated AST in a population of adults in the US.<sup>73</sup> The exclusion of subjects with excess alcohol consumption again introduces a significant selection bias into this population.

I did not identify any studies which specifically looked at the relationship between either AST, ALP or bilirubin with mortality from causes other than liver disease.

## 1.5. Thesis objectives

The overall objective of this thesis was to examine aspects regarding the epidemiology of cirrhosis and elevated liver function tests in the UK.

Specifically, six linked studies were conducted and are outlined below.

**Chapter 3** reports on the incidence and prevalence of cirrhosis in the UK.

**Chapter 4** describes the mortality of people with cirrhosis in the UK compared with the general population.

**Chapter 5** examines the progression of people with cirrhosis in the UK based on the identification of clinical symptoms.

**Chapter 7** reports the prevalence of elevated liver function tests in a population of people aged 75 and over in the UK.

**Chapter 8** describes the demographic, lifestyle and clinical factors associated with elevated liver function tests in this same population.

**Chapter 9** examines the association of elevated liver function tests with all-cause and cause-specific mortality in people aged 75 and over in the UK.

In addition, **Chapter 2** describes the General Practice Research Database (GPRD) – the database used for the studies described within Chapters 3, 4 and 5 – and **Chapter 6** describes the “MRC Elderly” database – the database used for the studies described within Chapters 7, 8 and 9.

Finally, **Chapter 10** provides a summary of the main findings of this work and suggests directions for future research that have arisen from this thesis.

## **2. The General Practice Research Database**

This chapter provides an overview of the General Practice Research Database (GPRD), its data format, its strengths and weaknesses particularly with reference to the studies in chapters 3 through 5 and details concerning the data extracted for use in the studies on cirrhosis contained within these three chapters. Additional study-specific information on the exact data used is detailed in the methods section of each individual chapter.

### **2.1. Introduction to the GPRD**

The GPRD is a longitudinal database consisting of anonymous, computerised primary care records for over 13 million patients in the UK, including over 40 million person-years of data. Data included within this database are recorded through direct entry during face-to-face general practice appointments and also following information received from hospital care, including hospital letters and discharge summaries.

The GPRD was established in June 1987 as the VAMP (Value Added Medical Products) Research Databank as a commercial venture. In 1993 VAMP Ltd. was subsumed by Reuters, who donated the database to the Department of Health and renamed it as the GPRD. The GPRD is currently administered through the Medicines & Healthcare products Regulatory Agency (MHRA).

As part of the GPRD recording guidelines General Practitioners (GPs) are required to record certain data onto their desktop computers using Vision software which enables the database to be subsequently used for research purposes.<sup>78</sup> For all active patients in the practice the following data are required to be completed:

- Registration details, including date of birth, sex, date of registration with the individual practice and current registration status.
- Morbidity events, including events resulting in a hospitalisation or referral; events resulting in the prescription of a drug; and events requiring more than one consultation.
- Diagnoses, symptoms, procedures and investigations.
- Death details, including date of death and cause, if known.
- Pregnancy outcomes.
- Prescribing information.

Following entry into the GPRD a practice is required to submit at least 95% of this 'Research Information' to be considered "up-to-standard" (UTS).

## **2.2. Data format of the GPRD**

The GPRD is a relational database which, at the time of data extraction for the work contained within this thesis (April 2002), was provided as four data files linked by a unique patient identifier (see Figure 2-1). The unique patient identifier in all files is a string variable combining the encrypted practice identification number and the encrypted patient identification number.

The four files comprise a patient data file, a medical data file, a therapy data file and a prevention data file.

The patient data file contains one line of data per patient per practice including the patient's date of birth, family identification number, sex, registration date with the practice, registration status, date of transfer out of the practice (if applicable) and the start and end dates pertaining to UTS data.

The medical data file contains information recorded each time the patient has an 'episode' including the event date, a code for the medical diagnosis, symptom or intervention utilising a modification of the Oxford Medical

Information System (OXMIS) classification and Read codes and the location of the consultation.

The therapy data file contains information recorded on any prescriptions that the patient might have received including the prescription date, the drug prescribed (coded using the Multilex drug code), and the quantity, dosage and duration of the prescription.

The prevention data file contains information recorded each time a patient has a test e.g. blood tests, and information recorded on other aspects of medical care including weight and height, vaccinations, smoking status and alcohol intake. The event date and the location are again recorded.

There can be several lines of data per patient in each of the medical, therapy and prevention files.

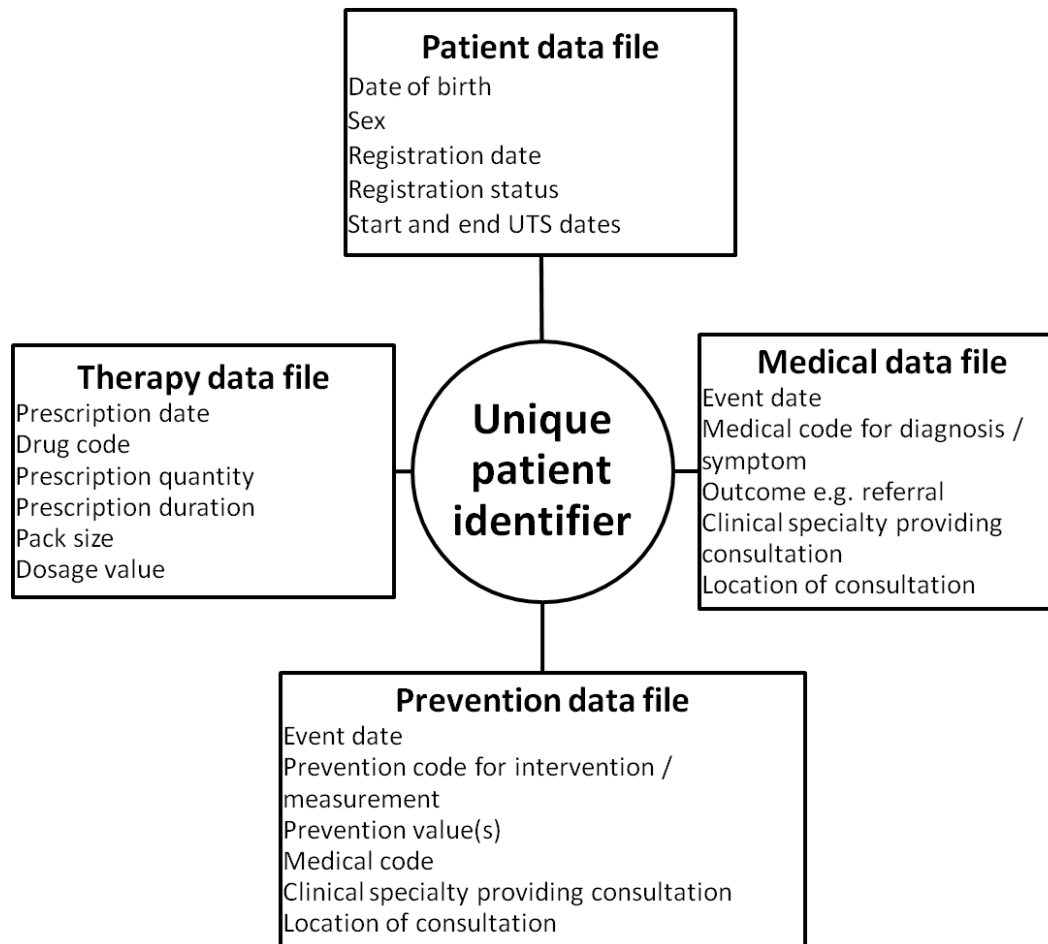


Figure 2-1 Structure of GPRD at time of data extraction

### **2.3. Strengths and weaknesses of the GPRD**

The GPRD is an excellent resource for descriptive epidemiology and has been well utilised as such. However, as with any database there are limitations to its usefulness which should be considered. The relative merits and limitations of the GPRD, particularly with reference to studies of cirrhosis, are discussed below.

#### **2.3.1. Size**

The GPRD is a very large longitudinal primary care database making it a particularly attractive database for research into relatively uncommon conditions, including cirrhosis. Utilising such a large database as the GPRD will allow more precise estimates of the prevalence of cirrhosis and outcomes associated with this chronic disease than would previously have been afforded using smaller, clinically driven databases.

#### **2.3.2. Representative**

The practices included within the GPRD were initially self-selected but have subsequently been shown to be broadly representative of the general population of the UK in respect to estimates of levels of morbidity and mortality.<sup>42 79</sup> It would therefore seem reasonable to generalise results from the GPRD to the population of the UK as a whole with respect to the burden of a disease.



### **2.3.3. Prospectively collected**

The majority of data within the GPRD are prospectively collected as part of the general course of medical care for each individual patient. Using the dates of the patient's entry into the practice and event dates it is possible to ascertain which data are prospectively collected and which are retrospectively collected. Hence there is much less opportunity for bias in the recording of individual diagnoses, symptoms or particularly exposures than might be present in smaller studies designed to answer a specific research question. Indeed there is no opportunity for bias in the reporting of primary care prescriptions as the prescription information contained within the database is generated electronically at the exact same time as the prescription itself is generated. However, as some of the data included in the GPRD are based on correspondence from secondary care it is possible that there is some misclassification in the recording of exact dates of events.

### **2.3.4. Contemporaneous**

The data used in this thesis were extracted based on code lists for all patients with a record of one or more liver diseases between June 1987 and April 2002. For the assessment of the incidence of cirrhosis and subsequent mortality of those patients with cirrhosis, this represents a fairly contemporaneous data source for both those patients with cirrhosis and also the general population control cohort.

### **2.3.5. Validity**

As well as ensuring that practices are contributing data that are considered "up-to-standard" the MHRA enables the independent validation of data by

researchers. Following the request for paper records, based on the unique patient identifier, GPs provide anonymised copies of the notes which can then be examined. Alternatively some GPs will be willing to complete questionnaires to validate particular points of interest on cases within the database. This cost of this service (at £100 upwards per validated subject) prohibits the validation of a large number of cases unless specific funding is obtained but does allow for the validation of a sample of cases. A recent systematic review identified 212 publications which included 357 validations of 183 different diagnoses and reported a median validation of 89% (range 24-100%).<sup>80</sup> A description of a validation for the diagnosis of cirrhosis is provided in Chapter 3.

### **2.3.6. Incomplete recording**

As data in the GPRD are collected routinely as part of the normal course of care certain information that may be desirable for research purposes, particularly those regarding past exposures, may be missing. In addition, as the data collection is based on what is important in the opinion of the GP for the ongoing care of the individual patient it is likely that there is a bias to which information is collected. Looking at information regarding any chronic liver disease a particular example of this is in the recording of alcohol intake. It is highly likely that a GP will record the knowledge of a patient drinking heavily as this may affect health but conversely a patient may not be recorded as being teetotal unless they actually suffered from a condition that may be considered to be associated with alcohol use.

Another potential gap in the information recorded within the GPRD is that of medications that are either prescribed in secondary care or taken as over the counter medication without the need for a prescription.

### **2.3.7. Duration of follow-up**

Although the GPRD is the largest longitudinal database of primary care data its size is limited in terms of the length of follow-up time that is contained on any individual patient with the maximum length of follow-up from index date in these data being 15 years. Indeed, as patients are free to change general practice whenever they wish, and there has been substantial turnover in participating practices during the lifetime of the GPRD, most subjects have considerably less follow-up than this. Though the power for the estimation of incidence within this database will be strong, the power for the follow-up of these incident cohorts is reduced due to the short length of individual person time.

### **2.3.8. Reproducibility**

The GPRD is an ongoing database allowing for the application of the same methods again in order to assess trends over time.

## **2.4. Data used for chapters 3-5**

### **2.4.1. Original data extracted for liver disease grant**

Data were requested from the MHRA for all patients with a record of one or more liver diseases recorded between June 1987 and April 2002 based on several code lists. (See Appendix III-a Codes for liver disease)

For each case up to ten controls were requested, to be matched by gender, age (within 5 years) and practice. Each control had to be alive and contributing data to the GPRD on the date of the first occurrence of any liver disease (between June 1987 and April 2002) in their matched case's records. The control was not allowed to have a diagnosis of that same first recorded liver disease as their matched case throughout their GPRD record.

All data contained within the GPRD on both cases and controls (patient data files, medical data files, therapy data files, prevention data files and a linkage file to determine which controls were linked to which case) were provided in ASCII format. I subsequently imported these data into Stata version 9.2SE for all further manipulation and analyses.

### **2.4.2. Data manipulation for date variables**

To ensure successful anonymisation of patients within the GPRD only the year of birth is included within the database. To enable suitable manipulation of these data the assumption of a date of birth of July 1 was imputed for all subjects. Though this will change the exact true length of follow-up for an individual patient the overall aggregated estimates of follow-up should not be biased unduly.

In addition the GPRD uses a redundant date of 1/1/1900. Any episodes with this date assigned were dropped from the data used for these studies.

### **2.4.3. Extraction of data on patients with cirrhosis**

From this large dataset of all patients with any recorded liver disease and their matched controls I then extracted data for all patients with cirrhosis. Cirrhosis was defined using code lists for diagnostic and therapeutic codes for cirrhosis, portal hypertension and oesophageal varices (Table 2-1, Table 2-2, Table 2-3 respectively).

Codes for the specific disease of primary biliary cirrhosis were not included as this disease, although often a precursor to cirrhosis, is a distinct and different disease to cirrhosis itself.

**Table 2-1 Medical codes for cirrhosis of the liver**

| Description  | medcode |
|--|---------|
| [X]OTHER AND UNSPECIFIED CIRRHOSIS OF LIVER              | Jyu7100 |
| ALCOHOLIC CIRRHOSIS OF LIVER                             | J612.00 |
| BACTERIAL PORTAL CIRRHOSIS                               | J615D00 |
| BILIARY CIRRHOSIS  | J616.00 |
| BILIARY CIRRHOSIS NOS                                    | J616z00 |
| BILIARY CIRRHOSIS OF CHILDREN                            | J616200 |
| CAPSULAR PORTAL CIRRHOSIS                                | J615600 |
| CARDIAC PORTAL CIRRHOSIS                                 | J615700 |
| CARDITUBERCULOUS CIRRHOSIS                               | J615E00 |
| CIRRHOSIS  | 5719CL  |
| CIRRHOSIS - NON ALCOHOLIC                                | J615.00 |
| CIRRHOSIS ALCOHOLIC                                      | 5710CA  |
| CIRRHOSIS AND CHRONIC LIVER DISEASE                      | J61..00 |
| CIRRHOSIS CARDIAC  | 5719CC  |
| CIRRHOSIS OF LIVER NOS                                   | J615z13 |
| CIRRHOSIS PORTAL   | 5719CP  |
| CONGESTIVE CIRRHOSIS                                     | J615711 |
| CRYPTOGENIC CIRRHOSIS OF LIVER                           | J615z12 |
| DIFFUSE NODULAR CIRRHOSIS                                | J615300 |
| FATTY PORTAL CIRRHOSIS                                   | J615400 |
| FLORID CIRRHOSIS   | J612.11 |
| GLYCOGENOSIS WITH HEPATIC CIRRHOSIS                      | C310400 |
| HYPERTROPHIC PORTAL CIRRHOSIS                            | J615500 |
| INFECTIOUS CIRRHOSIS NOS                                 | J615H00 |
| LAENNEC'S CIRRHOSIS                                      | J612.12 |
| LAENNEC'S CIRRHOSIS, NON-ALCOHOLIC                       | J615z14 |
| LIVER CIRRHOSIS  | 5719HP  |
| MACRONODULAR CIRRHOSIS                                   | 5719MA  |
| MACRONODULAR CIRRHOSIS OF LIVER                          | J615z11 |
| MICRONODULAR CIRRHOSIS                                   | 5710MC  |
| MIXED PORTAL CIRRHOSIS                                   | J615200 |
| MULTILOBULAR PORTAL CIRRHOSIS                            | J615100 |
| NON-ALCOHOLIC CIRRHOSIS NOS                              | J615z00 |
| OESOPHAGEAL VARICES IN ALCOHOLIC CIRRHOSIS OF THE LIVER  | G852300 |
| OESOPHAGEAL VARICES IN CIRRHOSIS OF THE LIVER            | G852200 |
| PIGMENTARY CIRRHOSIS OF LIVER                            | C350012 |
| PIGMENTARY PORTAL CIRRHOSIS                              | J615900 |
| PIPE-STEM PORTAL CIRRHOSIS                               | J615A00 |
| PORTAL CIRRHOSIS   | J615.11 |
| PORTAL CIRRHOSIS UNSPECIFIED                             | J615y00 |
| POSTNECROTIC CIRRHOSIS OF LIVER                          | J615111 |
| SECONDARY BILIARY CIRRHOSIS                              | J616100 |
| SECONDARY BILIARY CIRRHOSIS (LIVER)                      | 5719CB  |
| SYPHILITIC PORTAL CIRRHOSIS                              | J615F00 |
| TOXIC LIVER DISEASE WITH FIBROSIS AND CIRRHOSIS OF LIVER | J635600 |
| TOXIC PORTAL CIRRHOSIS                                   | J615B00 |
| UNILOBULAR PORTAL CIRRHOSIS                              | J615000 |
| XANTHOMATOUS PORTAL CIRRHOSIS                            | J615C00 |
| ZOOPARASITIC PORTAL CIRRHOSIS                            | J615G00 |

**Table 2-2 Medical codes for oesophageal varices**

| Description   | medcode |
|---|---------|
| [X]OESOPHAGEAL VARICES IN DISEASES CLASSIFIED ELSEWHERE         | Gyu9400 |
| FIBROPTIC ENDOSCOPIC BANDING OF OESOPHAGEAL VARICES             | 760C500 |
| FIBROPTIC ENDOSCOPIC INJECTION SCLEROTHERAPY OESOPH<br>VARICES  | 760C300 |
| FUND HOLDING OP OESOPHAGEAL VARICES                             | K298 FH |
| GASTRIC VARICES   | G857.00 |
| INJECTION OESOPHAGEAL VARICES                                   | K2982   |
| LIGATION OESOPHAGEAL VARICES                                    | K2981   |
| LOCAL LIGATION OF OESOPHAGEAL VARICES                           | 7609300 |
| OESOPHAGEAL VARICES   | G85..11 |
| OESOPHAGEAL VARICES IN DISEASES EC                              | G852.00 |
| OESOPHAGEAL VARICES IN DISEASES EC NOS                          | G852z00 |
| OESOPHAGEAL VARICES NOS   | G858.00 |
| OESOPHAGEAL VARICES WITH BLEEDING                               | G850.00 |
| OESOPHAGEAL VARICES WITH BLEEDING IN DISEASES EC                | G852000 |
| OESOPHAGEAL VARICES WITHOUT BLEEDING                            | G851.00 |
| OESOPHAGEAL VARICES WITHOUT BLEEDING IN DISEASES EC             | G852100 |
| OPEN INJECTION SCLEROTHERAPY TO OESOPHAGEAL VARICES             | 7609400 |
| OPEN OPERATION ON OESOPHAGEAL VARICES NOS                       | 7609z00 |
| OPEN OPERATIONS ON OESOPHAGEAL VARICES                          | 7609    |
| OTHER SPECIFIED OPEN OPERATION ON OESOPHAGEAL VARICES           | 7609y00 |
| RIGID OESOPHAGOSCOPIC BANDING OF OESOPHAGEAL VARICES            | 760F400 |
| RIGID OESOPHAGOSCOPIC INJECTION SCLEROTHERAPY OESOPH<br>VARICES | 760F300 |
| TANNER DEVASCULARISATION FOR BLEEDING VARICES                   | 7609y11 |
| VARIX OESOPHAGUS  | 4560    |

**Table 2-3 Medical codes for portal hypertension**

| Description         | medcode |
|---------------------|---------|
| PORTAL HYPERTENSION | 5719PH  |
| PORTAL HYPERTENSION | J623.00 |



## **2.4.4. Definitions used throughout**

### **2.4.4.1. Death**

Death was defined through a combination of medical codes denoting death within the medical data file (see Appendix III-b Codes for death), a recording of death in the prevention data file (code 16000000 denoting death) and the registration status of case within the patient data file (code 13 representing that the patient had died). As it is possible that recording of information on the registration status of a person could lag behind the recording of fact of death the earliest date of first recording of any of these codes was taken as the date of death of the patient.

### **2.4.4.2. Age**

Age was defined both at index date and at date of diagnosis. Age was then categorised as necessary for individual studies (as described in the methods section for each chapter).

The studies in this thesis are concerned with adult liver disease. In order to examine only adult onset cirrhosis I excluded all cases with an age at diagnosis of less than 25 years to rule out the potential for including childhood diagnosed cirrhosis.

### **2.4.4.3. Alcohol**

Within the GPRD it is possible to examine the alcohol consumption of an individual patient using information contained within the prevention data file on reported units of alcohol consumed in a week.

First of all I attempted to define alcohol consumption based on units of alcohol consumed as recorded in the prevention file. This had a high proportion of missing data rendering these data unusable in isolation for the purposes of identifying problem alcohol use. I then adopted a pragmatic approach of

classifying patients as non-drinkers, drinkers, alcoholics (including patients referred to alcohol cessation services) and patients with other problems associated with drinking based on combination of recorded medical codes relating to alcohol use and also unit consumption.(see Appendix III-c Codes for alcohol use)

## **3 Incidence and prevalence of cirrhosis in the UK**

### **3.1 Introduction**

This study aims to quantify the occurrence and prevalence of cirrhosis in the general population of the UK and describes the trends in liver cirrhosis incidence with respect to age, sex and presumed aetiology for the period 1992-2001.

### **3.2 Methods**

#### **3.2.1 Dataset used**

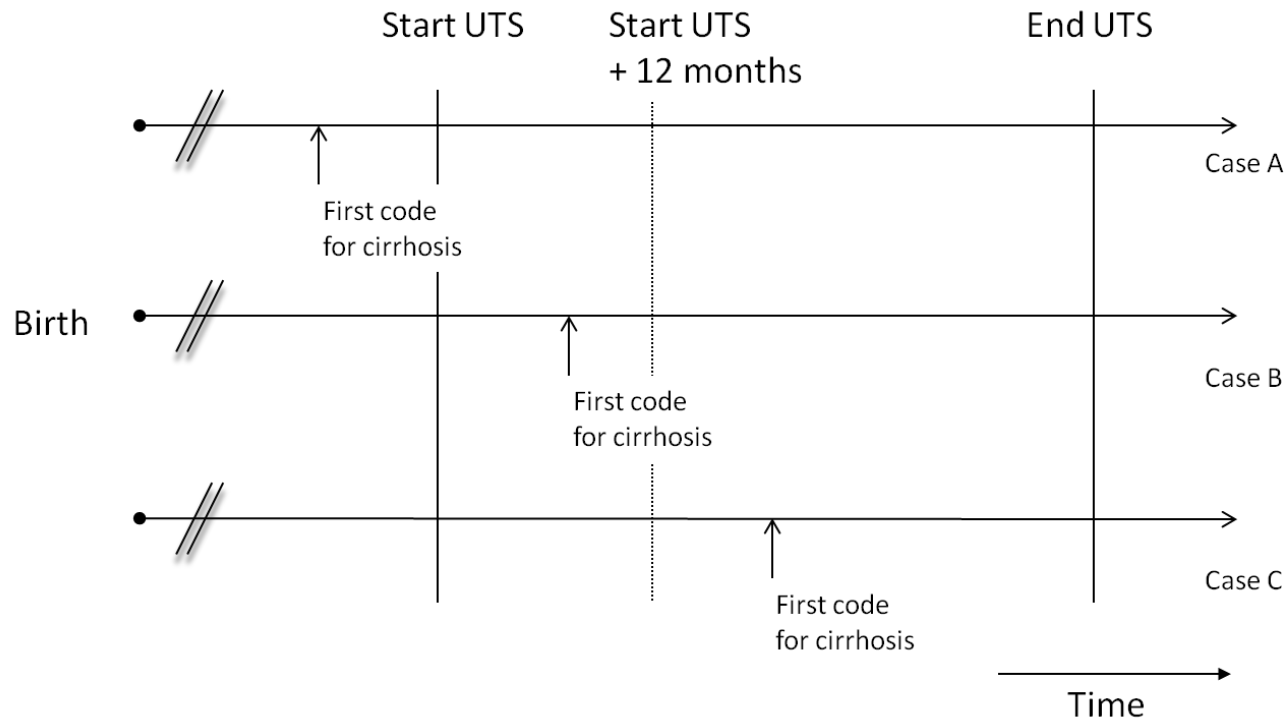
Data on all cases with cirrhosis (as described in section 2.4.3) were used in this analysis. Patients were assigned an UTS date as either the same UTS date as their general practice (for patients registered before the practice was considered “up-to-standard”) or their date of registration (for patients registering after their general practice was considered “up-to-standard”).

#### **3.2.2 Additional definitions**

##### **3.2.2.1 Incident and prevalent cases**

Patients were considered incident if the first recording of a diagnostic or therapeutic code for cirrhosis, oesophageal varices or portal hypertension occurred at least 12 months after the beginning of their UTS GPRD record. This method corrects for the potential for a prevalent case to be misclassified as an incident case following registration with a new practice and has previously been shown to more accurately reflect incidence rather than prevalence of other chronic diseases.<sup>81</sup> All patients with a first diagnosis of

cirrhosis before the beginning of their UTS GPRD record, or within the first 12 months following the start of their UTS record, were considered to be prevalent (see Figure 3-1).



Case A. First code for cirrhosis before Start UTS = prevalent

Case B. First code for cirrhosis within 12 months following Start UTS = prevalent

Case C. First code for cirrhosis after 12 months following Start UTS = incident

**Figure 3-1 Timeline to represent selection of cases as prevalent or incident**

### **3.2.2.2 Aetiology of cirrhosis**

I examined 4 specific presumed aetiologies: alcoholic, viral hepatitis, autoimmune liver disease and metabolic liver disease. All aetiologies were ascribed using data from the whole GPRD record, not just before the diagnosis of cirrhosis to capture investigations into the aetiology that may have been instigated subsequent to the diagnosis.

For the purposes of aetiology analysis alcoholic cirrhosis was defined as any mention of alcoholism, alcohol abuse, addiction or dependence i.e. all those patients classified as 'alcoholic' in their medical files (see section 2.4.4.3). Viral hepatitis included all forms of known viral hepatitis (see Appendix III-d Codes for viral hepatitis). Autoimmune liver disease consisted of primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune hepatitis (see Appendix III-e Codes for autoimmune liver disease). Metabolic liver disease consisted of haemochromatosis, Wilson's disease and alpha-1 antitrypsin deficiency (see Appendix III-f Codes for metabolic liver disease). All other patients were subsequently labelled as 'other unspecified causes of cirrhosis'. For the purposes of trend analysis, all cases not fulfilling the definition of alcoholic cirrhosis were grouped together as non-alcohol-related cirrhosis.

### **3.2.2.3 Age**

Age at diagnosis was subsequently categorised into 10-year age bands from 25-34 to 85+ years.

### **3.2.3 Validation**

In order to assess the accuracy of the recording of the diagnosis of cirrhosis paper records from the GPs were requested from a stratified, random sample of patients with a diagnostic or therapeutic code for cirrhosis. The patients' paper records were then examined by a consultant hepatologist (Guruprasad P Aithal). Information was gathered on whether there was any record of cirrhosis, whether the diagnosis had been made in primary or secondary care, whether this had been confirmed by biopsy and whether there was any record of the presumed aetiology of the cirrhosis.

### **3.2.4 Statistical analysis**

#### **3.2.4.1 Incidence**

To calculate overall incidence I used the total number of new cases of cirrhosis i.e. those cases whose first record of cirrhosis was recorded 12 months after the start of the 'up-to-standard' period (see section 3.2.2.1) as the numerator and the total population of the GPRD aged 25 years and over as the denominator, by summing the mid-year population numbers for each valid year. I excluded data previous to 1992 owing to the small number of practices contributing data in these years. Data from 2002 were also excluded as there was not a full calendar year of data available. I initially calculated crude incidence rates and then stratified by year of diagnosis, age group and sex. I also examined the trend in incidence of alcoholic and non-alcohol-related cirrhosis. Poisson regression was used to model fully adjusted incidence rate ratios and estimate confidence intervals.

#### **3.2.4.1.1 Alternative case definitions**

To account for potential over- and under-ascertainment bias I performed two additional analyses. To minimise the potential over-ascertainment bias introduced by including cases with oesophageal varices and portal hypertension who may not actually have cirrhosis I calculated incidence based purely on those cases with a medical code for cirrhosis (see Table 2-1). This provided a minimal estimate of incidence.

To minimise the potential of missing cases with underlying cirrhosis but lacking a formal diagnosis I searched the GPRD for patients with recorded liver disease and a further recording of non-malignant ascites (see Table 5-1) and/or encephalopathy (see Appendix III-g Codes for encephalopathy). I examined the trend in incidence with and without these cases. This provided a maximal estimate of incidence.

#### **3.2.4.2 Prevalence**

I calculated three separate point estimates of prevalence using all cases who were still contributing data to GPRD at 1 July 1993, 1 July 1997 and 1 July 2001. The total GPRD population aged 25 years or older at each time point was used as the denominator.

#### **3.2.4.3 Application of results to 2008 population**

I applied the age- and sex-specific incidence and prevalence figures to the 2008 age- and sex-stratified population of the United Kingdom to estimate the number of people being newly diagnosed with cirrhosis in the UK and the number of people living with cirrhosis in the UK.<sup>82</sup>



### **3.3 Results**

#### **3.3.1 Study population**

A total of 3,360 incident cases of cirrhosis aged 25 or over were identified between 1992 and 2001, 58% of whom were male. The median age at diagnosis was 56.3 years in men and 61.3 years in women ( $p < 0.001$ ).

Thirteen per cent of cases had their first recording of cirrhosis concurrent with the recording of time of death following correspondence from secondary care services. Over half of patients ( $n=1690$ , 50.3%) had a recording of alcoholism at any point within their GP records (see Table 3-1). For 1591 cases (47.4%) alcohol was the only specified associated factor. Overall, just under two-fifths of cases had no specified aetiologies within their GP record ( $n=1328$ , 39.5%), a proportion which remained roughly constant across the study period.

**Table 3-1 Presumed aetiology of incident cirrhosis cases**

| <b>Presumed aetiology*</b>                             | <b>n (%)</b><br><b>N=3360</b> |
|--|-------------------------------|
| <b>Alcohol-related</b>                                 | <b>1690 (50.3)</b>            |
| Alcohol-related only                                   | 1591 (47.4)                   |
| Alcohol-related and viral hepatitis                    | 77 (1.7)                      |
| Alcohol-related and autoimmune disease                 | 11 (0.3)                      |
| Alcohol-related and metabolic disease                  | 10 (0.3)                      |
| Alcohol-related, viral hepatitis and metabolic disease | 1 (<0.1)                      |
| <b>Viral hepatitis</b>                                 | <b>181 (5.4)</b>              |
| Viral hepatitis only                                   | 111 (3.3)                     |
| Viral hepatitis and alcohol-related                    | 77 (1.7)                      |
| Viral hepatitis and autoimmune disease                 | 5 (0.1)                       |
| Viral hepatitis, alcohol-related and metabolic disease | 1 (<0.1)                      |
| <b>Autoimmune disease</b>                              | <b>237 (7.1)</b>              |
| Autoimmune disease only                                | 225 (6.7)                     |
| Autoimmune disease and alcohol-related                 | 11 (0.3)                      |
| Autoimmune disease and viral hepatitis                 | 5 (0.1)                       |
| <b>Metabolic disease</b>                               | <b>29 (0.9)</b>               |
| Metabolic disease only                                 | 19 (0.6)                      |
| Metabolic disease and alcohol-related                  | 10 (0.3)                      |
| Metabolic disease, alcohol-related and viral hepatitis | 1 (<0.1)                      |
| <b>Other, unspecified</b>                              | <b>1328 (39.5)</b>            |

\*NB As some combinations of presumed aetiologies are included more than once, numbers in the table do not add up to 3360

### 3.3.2 Incidence

Over the 10-year period crude incidence was 14.5 cases per 100 000 person years, increasing from 12.0 in 1992 to 17.0 cases per 100 000 person years in 2001 (see Table 3-2).

This increase fitted a continuous model with an average yearly incidence rate ratio of 1.04 (95%CI [1.03, 1.06]) adjusted for age and sex, corresponding to a 45% increase in incidence over the decade studied. Incidence was about 50% higher in men than women, 17.5 cases per 100 000 person years and 11.8 cases per 100 000 person years respectively (incidence rate ratio 1.52; 95% CI [1.42-1.63] adjusted for age and year of diagnosis) (see Figure 3-2). Figure 3-3 shows that the incidence of cirrhosis was higher in men than women for all age groups. The highest incidence for women occurred at age 65-74 years (22.7 per 100 000 person years). Incidence at all age groups from 45-84 years for men was higher than this maximum for women.

**Table 3-2 Incidence of cirrhosis, 1992-2001**

|                    | <b>Cases</b> | <b>P-years</b>    | <b>Crude incidence rates [95% CI]<br/>per 100 000 p-years</b> |
|--------------------|--------------|-------------------|---|
| <b>Total</b>       | <b>3360</b>  | <b>23 093 805</b> | <b>14.5 [14.1, 15.0]</b>                                      |
| <b>Sex</b>         |              |                   |   |
| Female             | 1406         | 11 934 462        | 11.8 [11.2, 12.4]   |
| Male               | 1954         | 11 159 343        | 17.5 [16.8, 18.3]   |
| <b>Age (years)</b> |              |                   |   |
| 25-34              | 122          | 5 194 894         | 2.3 [2.0, 2.8]  |
| 35-44              | 461          | 4 776 754         | 9.7 [8.8, 10.6]   |
| 45-54              | 816          | 4 419 818         | 18.5 [17.2, 19.8]   |
| 55-64              | 790          | 3 362 078         | 23.5 [21.9, 25.2]   |
| 65-74              | 727          | 2 854 265         | 25.5 [23.7, 27.4]   |
| 75-84              | 386          | 1 828 533         | 21.1 [19.1, 23.3]   |
| 85+                | 58           | 657 463           | 8.8 [6.8, 11.4]   |
| <b>Year</b>        |              |                   |   |
| 1992               | 339          | 2 813 552         | 12.0 [10.8, 13.4]   |
| 1993               | 337          | 2 771 663         | 12.2 [10.9, 13.5]   |
| 1994               | 378          | 2 674 596         | 14.1 [12.8, 15.6]   |
| 1995               | 339          | 2 655 872         | 12.8 [11.5, 14.2]   |
| 1996               | 352          | 2 411 170         | 14.6 [13.2, 16.2]   |
| 1997               | 357          | 2 253 388         | 15.8 [14.3, 17.6]   |
| 1998               | 355          | 2 157 349         | 16.5 [14.8, 18.3]   |
| 1999               | 340          | 2 036 987         | 16.7 [15.0, 18.6]   |
| 2000               | 319          | 1 883 106         | 16.9 [15.2, 18.9]   |
| 2001               | 244          | 1 436 120         | 17.0 [15.0, 19.3]   |

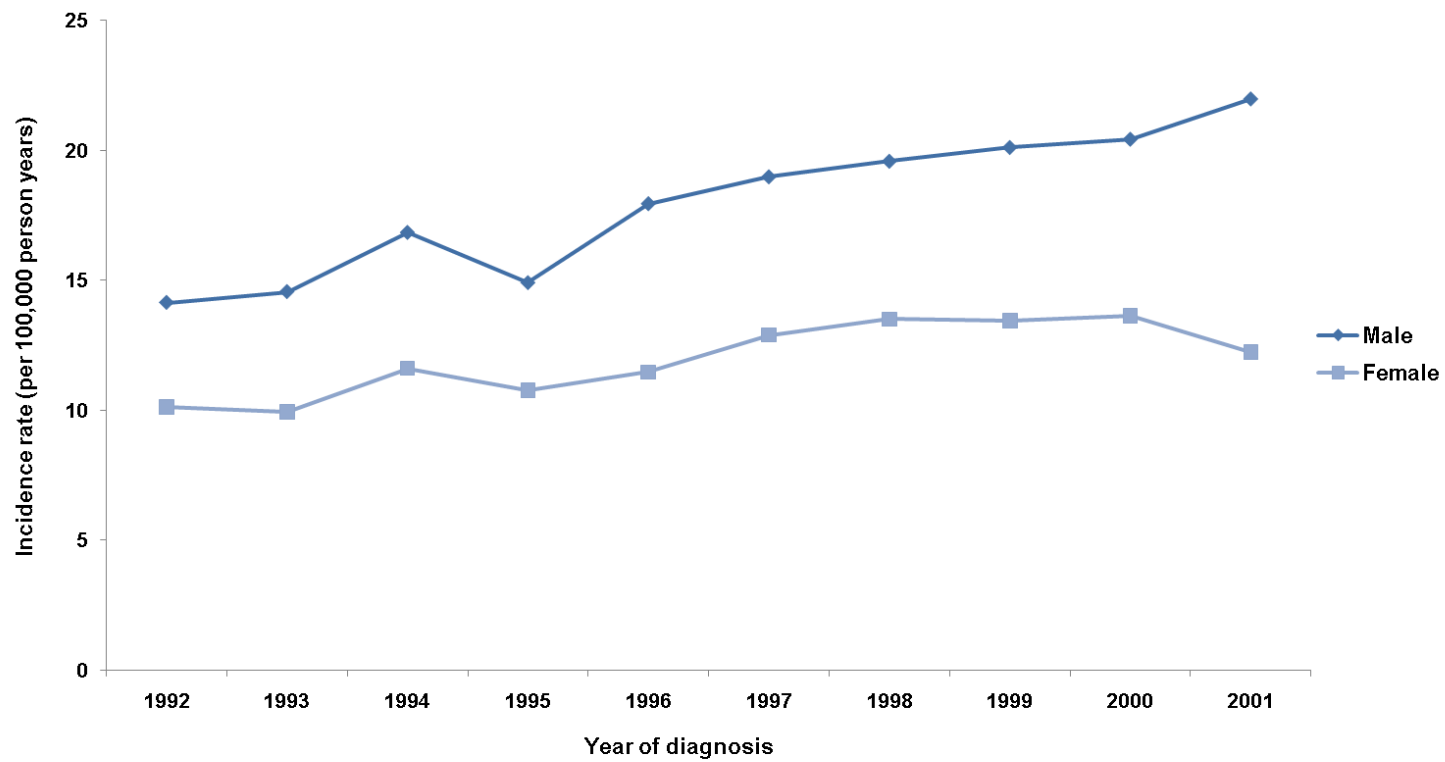


Figure 3-2 Incidence of cirrhosis (per 100,000 person years) by year and sex, UK, 1992-2001

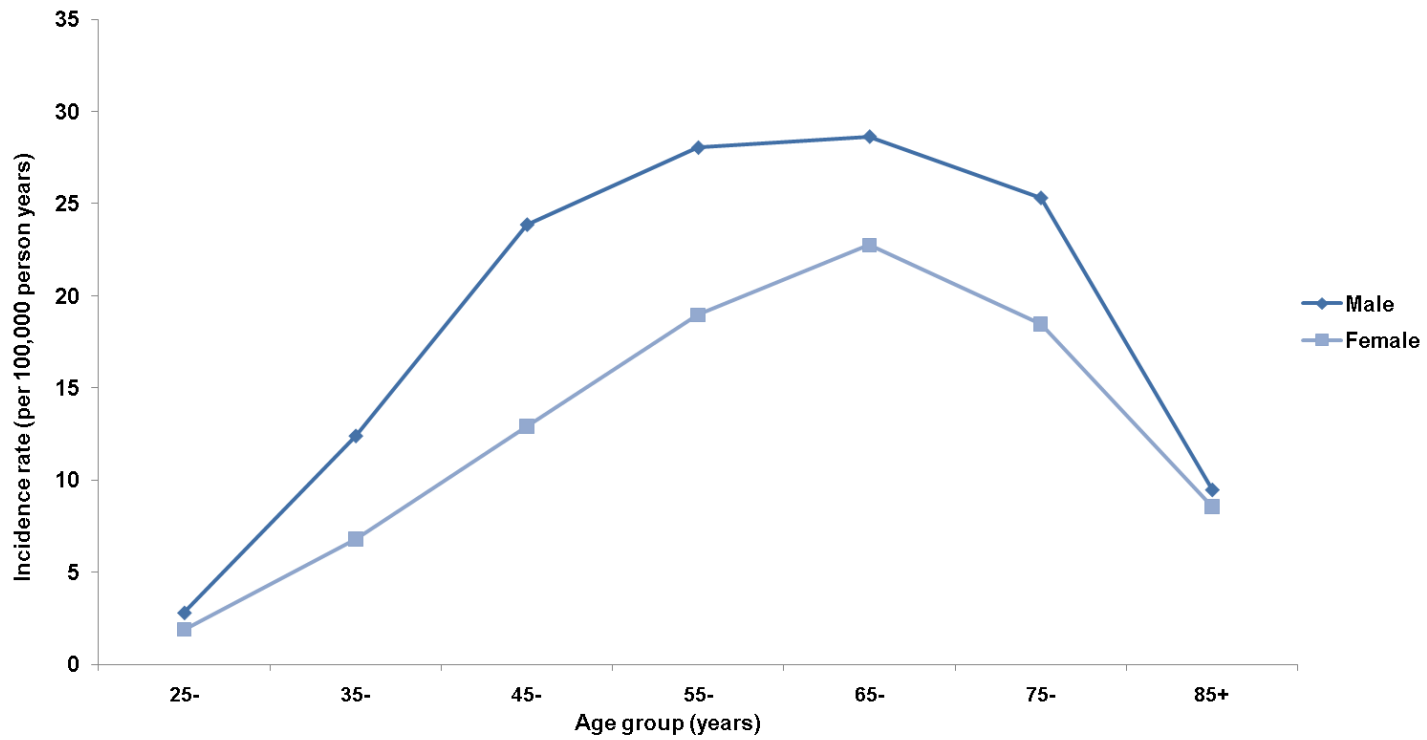


Figure 3-3 Incidence of cirrhosis by age group and sex, UK, 1992-2001

### **3.3.2.1 Alcoholic and non-alcohol-related cirrhosis**

Within the study population just over half (50.3%) of people with a record of cirrhosis were defined as alcoholic cirrhosis, according to the criteria described above (see Table 3-1). An increase in the incidence of both alcoholic cirrhosis and non-alcohol-related cirrhosis was seen in men, 70% ( $p < 0.001$ ) and 30% ( $p = 0.017$ ) increase respectively across the 10-year period, and also in women, 28% ( $p = 0.068$ ) and 36% ( $p = 0.004$ ) increase respectively over the 10-year period (see Figure 3-4 and Figure 3-5).

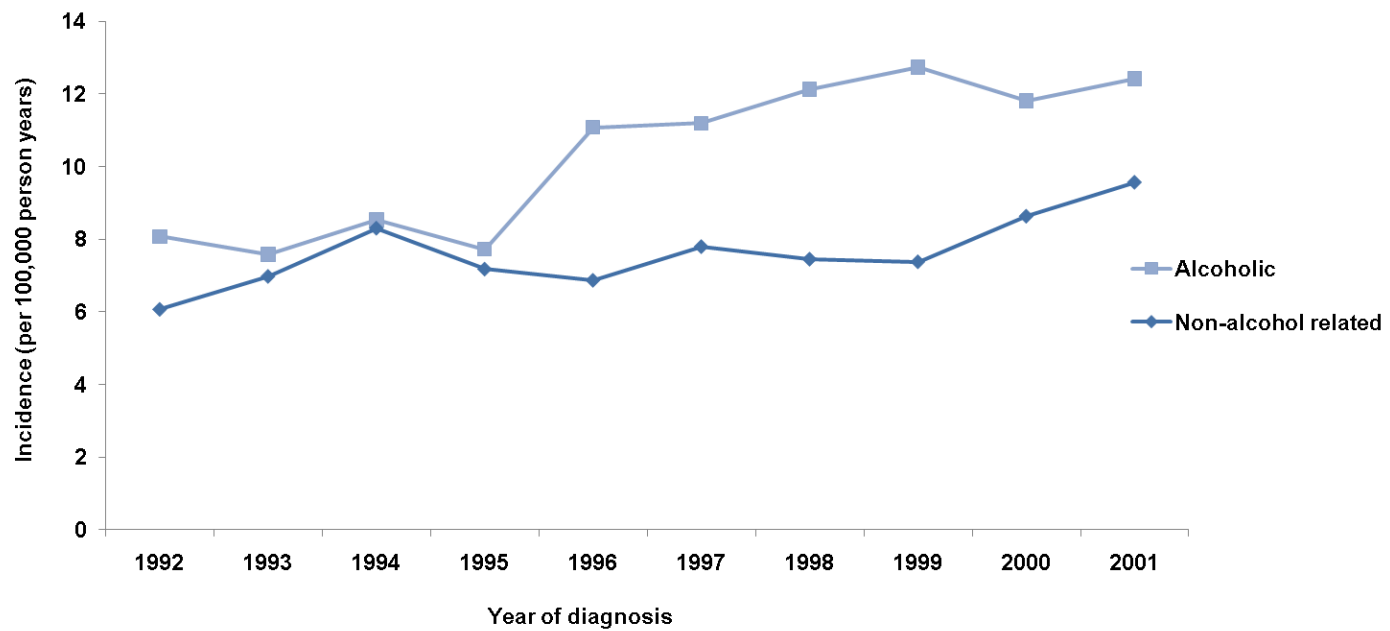


Figure 3-4 Incidence of alcoholic and non-alcohol-related cirrhosis in males, UK, 1992-2001



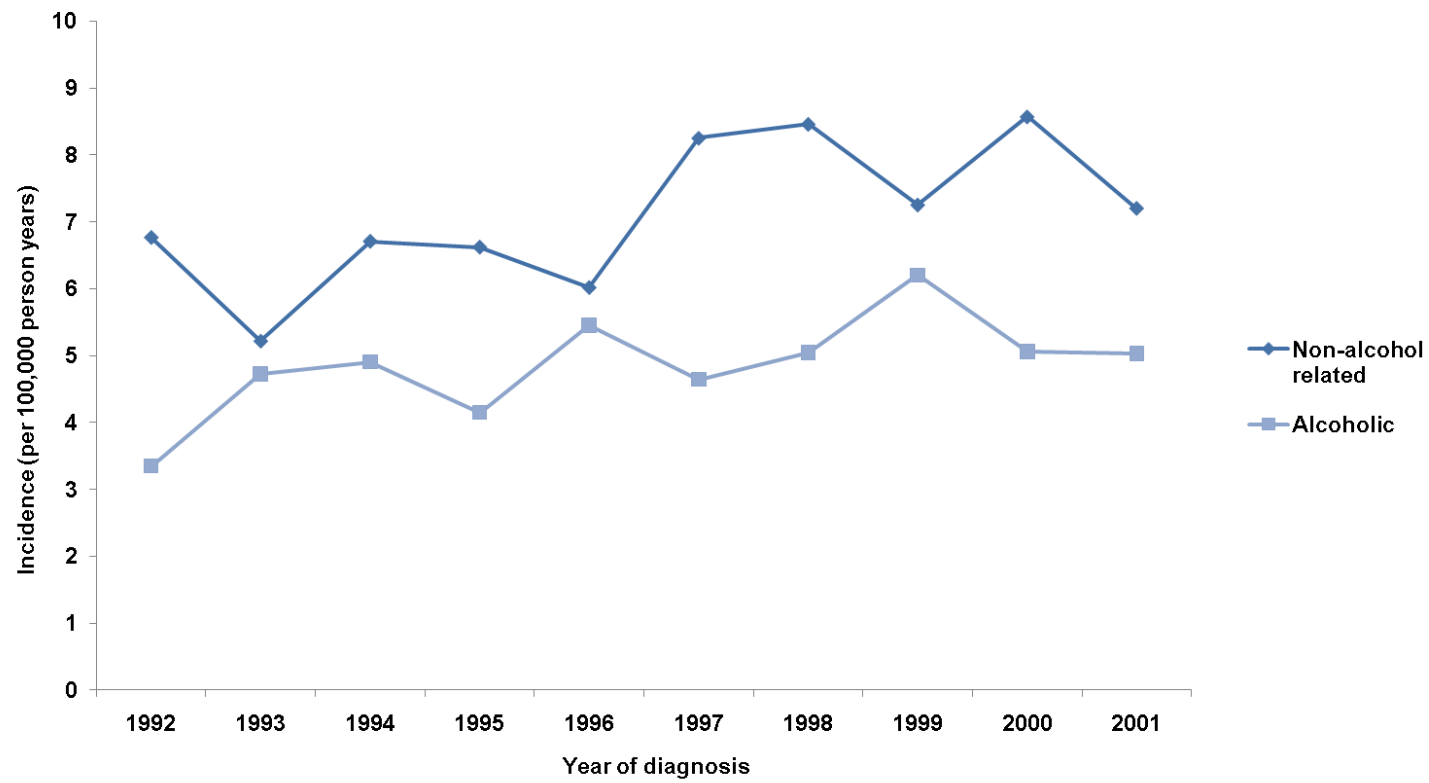


Figure 3-5 Incidence of alcoholic and non-alcohol related-cirrhosis in females, UK, 1992-2001

### **3.3.2.2 Incidence using alternative case definitions**

Including only patients with a diagnosis of cirrhosis itself i.e. excluding those patients with a diagnosis of oesophageal varices and portal hypertension the overall crude incidence, 1992-2001, decreased by 15% from 14.5 to 12.4 per 100,000 person years (see Figure 3-6).

Using the extended definition of cirrhosis an additional 505 incident cases were included. The overall crude incidence, 1992-2001, when the additional patients with liver disease and non-malignant ascites or encephalopathy were included, increased by 15% from 14.55 to 16.74 per 100,000 person years (see Figure 3-6).

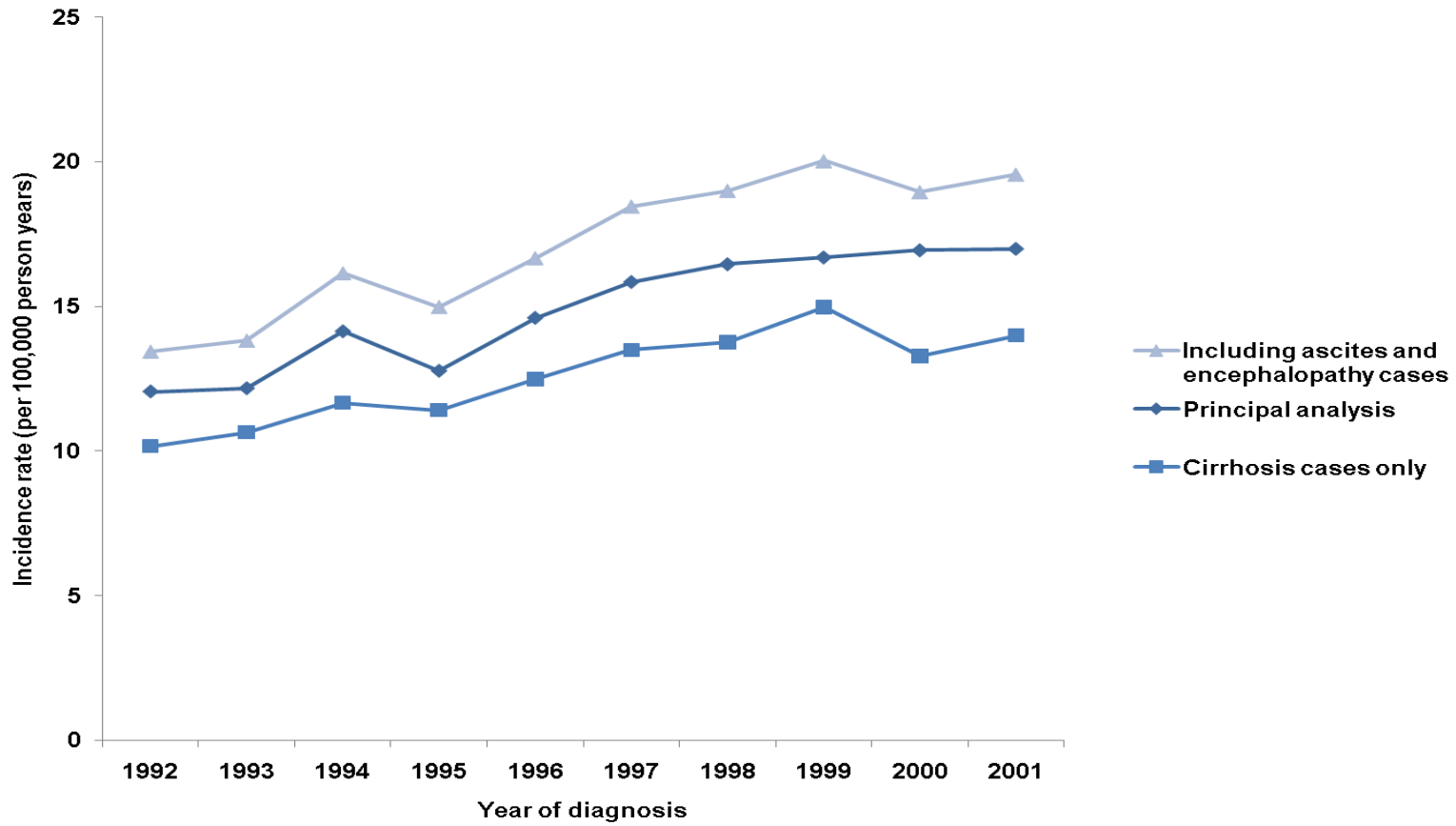


Figure 3-6 Incidence of cirrhosis using alternative case definitions

### **3.3.3 Prevalence**

Using all cases contributing to the GPRD at three separate time points I observed an increase in the prevalence of cirrhosis between 1 July 1993 and 1 July 2001 from 45.4 to 76.3 per 100,000 population aged 25 years or over (see Table 3-3) representing a 68% increase in the prevalence of this disease over the period studied. Prevalence was higher in men than women at all three time points.

**Table 3-3 Prevalence of cirrhosis**

|             | Prevalence (per 100,000 population) |       |       | Prevalence<br>rate ratio * |
|-------------|-------------------------------------|-------|-------|----------------------------|
|             | Females                             | Males | Total |                            |
| 1 July 1993 | 38.6                                | 52.8  | 45.4  | 1                          |
| 1 July 1997 | 58.2                                | 74.8  | 66.2  | 1.46                       |
| 1 July 2001 | 65.9                                | 87.2  | 76.3  | 1.68                       |

\*compared with 1 July 1993

### **3.3.4 Validation**

Responses were received for 49/59 patients whose notes were requested, a response rate of 83%. Of the responses received 13 sets of case notes were not available because either the patient had subsequently moved from the GP surgery (6), the patient had died (2) or the GP was unable to help (5). Of the 36 sets of case notes that could therefore be examined, 35 cases had chronic liver disease (97%, 95% confidence interval [85%, 99.9%]). A total of 27 patients (75%, 95% confidence interval [58%, 88%]) had evidence confirming cirrhosis, either biopsy proven cirrhosis, evidence of portal hypertension (with supportive evidence of liver disease as the cause of the portal hypertension) or clinical decompensation in the presence or absence of advanced changes seen at biopsy. Of the nine cases where cirrhosis could not be confirmed, all but one had evidence of chronic liver disease - three cases of primary biliary cirrhosis, three cases of alcoholic liver disease and one each of Budd-Chiari and autoimmune hepatitis. The one case which could not be considered as chronic liver disease was a patient with alcoholic pancreatitis. All of these diagnoses occurred in secondary care.

## **3.4 Discussion**

### **3.4.1 Key findings**

This study has described a 45% increase in the incidence of cirrhosis in the UK in the decade between 1992 and 2001 and a 68% rise in the prevalence. Cirrhosis occurred more commonly and at younger ages in men than women. Nonetheless, a significant increase in incidence was seen for all age groups and for both sexes across the period under study. Incidence of both alcoholic and non-alcohol-related cirrhosis increased in males and in females during the period.

Applying the 2001 prevalence and incidence figures to the 2008 age- and sex-stratified population of the UK, I estimate that, over the age of 25, at least 31,000 people in the UK are currently living with cirrhosis and approximately 7100 people are being newly diagnosed with this disease each year. If I use the estimate from the wider definition of cirrhosis this figure increases to an estimated 8000 people being newly diagnosed with cirrhosis each year.

These figures are still likely to be an underestimate of the burden of cirrhosis since they are based on diagnosed disease and do not take into account the possibility of a continuing increasing trend. This clearly represents a challenge for health care services and will have substantial implications for the future trends in mortality from this disease.

### **3.4.2 Strengths and limitations**

This is the first UK-wide population-based study of the occurrence of cirrhosis. I have examined contemporary data from general practices representative of the UK collected over a period of 10 years. The collection of data within the GPRD is not driven by a specific research question and is hence not subject to

the same ascertainment biases as may be present in smaller, hospital-based series.

The biggest potential limitation of this study lies with the case definition, having included as cases all patients with any mention of cirrhosis, oesophageal varices or portal hypertension within the primary care records. Although it is possible that portal hypertension and oesophageal varices are manifestations of diseases other than cirrhosis it was decided to include these codes within the list for cirrhosis as these symptom are widely regarded as being representative of cirrhosis in developed countries. The validation exercise, which took the form of a case note review, showed that the majority (75%) of the sampled cases had an assertion of cirrhosis within the medical records. Of the remaining 25% of patients, 8/9 had a confirmed chronic liver disease with the potential to develop cirrhosis, although cirrhosis itself was not recorded in the notes available to us. All of the confirmed diagnoses examined in the case note review had been communicated to the GP directly from secondary care. It is reasonable to suppose that this is a sufficiently robust definition to accurately capture cases of cirrhosis recorded in the GPRD and in such a way which is easily replicated allowing valid examination of trends over time. Although I may have inadvertently included as cases a few patients who did not have cirrhosis it is more likely that I am missing cases of cirrhosis where diagnosis was unconfirmed and/or not fed back from secondary care into the primary care records. This finding of an increase in incidence is unlikely to be due to increased ascertainment through diagnostic procedures as UK Hospital Episode Statistics report a decrease in the number of diagnostic fibre optic examinations of the upper gastrointestinal tract (-4%) in the period 1995/6 to 2004/5.<sup>83</sup>



While it was not possible to assign a presumed aetiology to 39% of cases from the available data this is similar to the largest previous study of cirrhosis with 35% being labelled as cryptogenic cirrhosis.<sup>37</sup> I have considered all patients with specific recording of alcoholism as having alcoholic cirrhosis. Owing to the known limitations of recording and referral for alcohol-related problems by GPs within this dataset,<sup>84</sup> it is likely that I have underestimated the number of patients with alcoholic cirrhosis. Although it is possible in a patient with recorded alcohol problems that alcohol intake itself was not the underlying cause of the cirrhosis, it is more likely that the true proportion of alcoholic cirrhosis is greater than the 50% seen in these data.

### **3.4.3 Comparison with previously published work**

The largest study, prior to this study, looking at the incidence of cirrhosis in the UK was a summary of data collected over 18 years in the 1960s and 1970s.<sup>37</sup> This previous study, which comprised 512 people identified to have cirrhosis, reported an incidence of cirrhosis of 10.3 per 100,000 population aged 15 years and over from patients diagnosed in a single district general hospital in west Birmingham and from Coroner's post-mortem reports. Though representative of the population served by this hospital, these figures are not generalisable to the rest of the UK as the West Midlands region has a higher than average mortality from liver disease compared with the general population of the UK.<sup>39</sup> With any hospital-based series there is the potential for an ascertainment bias with active case finding being employed, leading to a further over-estimate of incidence. In addition, in the study by Saunders et al, 11.3% of the subjects included as incident cases were as a result of incidental findings at post-mortem examination. The same factors are unlikely to have operated in my study.

The results displayed in this study show a higher or similar incidence of cirrhosis compared with the previous studies of cirrhosis in the UK<sup>37 38 40</sup> but owing to the small, non-representative nature of these studies, and a lack of clarity as to exact methods used, direct comparisons should be avoided. This study is the only study based on a contemporary, representative sample of the entire UK population and has utilised data collected for general medical purposes over a period of 10 years.

My data contrast with recent data from a hospital-based study in Denmark where no discernible trend in incidence of alcoholic cirrhosis was seen from 1994-2005.<sup>45</sup> The figures reported in this study similarly showed a higher incidence and prevalence of cirrhosis for men than women, and for those aged between 45 and 64 years of age, although the crude incidence figures for alcoholic cirrhosis were higher than I saw in my study. Other data from Scandinavia report similar figures to those reported in this chapter for Gothenburg, Sweden (incidence of 15.3 per 100,000 person years)<sup>85</sup> and Oslo, Norway (incidence of 13.3 per 100,000 person years)<sup>86</sup> but a much lower incidence for Iceland (incidence of 3.3 per 100,000 person years).<sup>85</sup>

I have presented the first data quantifying the current burden of alcoholic cirrhosis in the UK but it is important to note that the incidence of non-alcohol related cirrhosis also increased over this period. Though it is possible that some of these cases were indeed misclassified alcoholic cirrhosis, it is also possible that other causes of cirrhosis are also on the increase. From a public health perspective a particularly important and potentially modifiable set of risk factors are those of obesity and its relationship with type 2 diabetes. Where fatty liver leads to steatohepatitis, fibrosis can occur in roughly one third of patients.<sup>20</sup> In one study, a history of obesity and/or type 2 diabetes was found

in 73% of patients with 'cryptogenic' cirrhosis.<sup>87</sup> Although cirrhosis is far from recognised as an end-point for diabetes or obesity the sustained increase in these two potential risk factors may lead to further increases in the incidence of cirrhosis in the UK in the years to come.

#### **3.4.4 Conclusions**

Liver disease is one of very few chronic diseases where mortality in the UK has increased over the past three decades.<sup>88</sup> In contrast, mortality from ischaemic heart disease, cerebrovascular diseases and respiratory diseases have all decreased. With a minimum estimate of 31,000 people over the age of 25 living with cirrhosis, a figure which is likely to increase, and with no good treatment options other than liver transplant, mortality from this disease will continue to rise.

Although the accuracy of defining true incidence is somewhat difficult with a chronic condition with heterogeneous presentation such as cirrhosis the figures reported in this study represent the most up-to-date estimates of the absolute rates and trends in incidence and prevalence of cirrhosis in the UK having used population-based data over a period of 10 years.

Cirrhosis represents a serious and growing burden of morbidity in the general population of the UK. The continued rise in cirrhosis has significant implications for the provision of specialist services and the health of the nation.

## **4 All-cause mortality in people with cirrhosis compared with the general population**

### **4.1 Introduction**

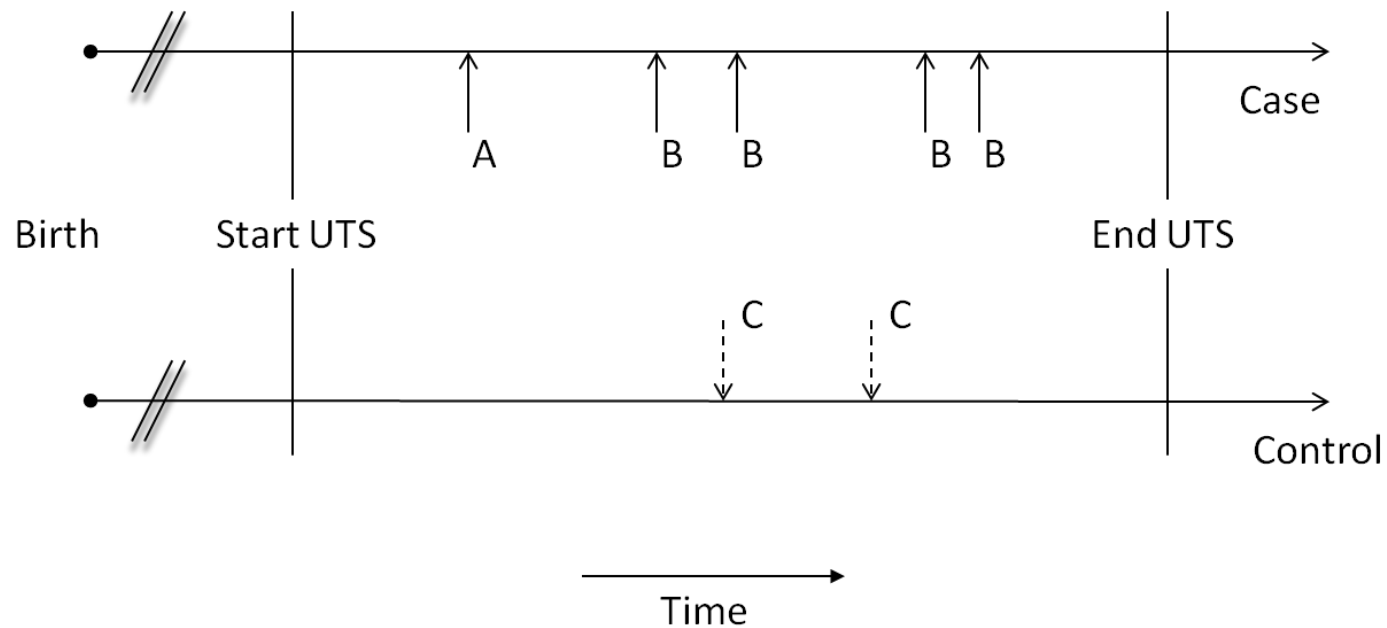
This study aims to describe the mortality experience of people with cirrhosis with reference to a general population cohort without cirrhosis.

### **4.2 Methods**

#### **4.2.1 Dataset used**

The data used in this chapter were from all subjects with a diagnosis of cirrhosis (as described in section 2.4.3) and their matched controls. By definition these controls were initially selected based on the exclusion of the first recorded liver disease within their matched case (see section 2.4.1). It was therefore possible that a control subsequently had a diagnosis of a liver disease other than the liver disease that first identified their matched case's record (see Figure 4-1). As cirrhosis was potentially not the first liver disease that a case was diagnosed with I excluded controls who

- a) had cirrhosis as a diagnosis at any point in their GPRD record, or
- b) were not alive at the time of diagnosis of cirrhosis in their matched case.



- A. Identification of case's first liver disease within UTS period. Control is free of this disease for whole UTS period.
- B. Further codes for liver disease within case's record. At least one of these must represent cirrhosis.
- C. Codes for liver disease within control's record

**Figure 4-1 Time-line showing potential diagnosis of cirrhosis in control subjects.**

## **4.2.2 Additional definitions**

### **4.2.2.1 Date of diagnosis / pseudo-diagnosis**

Cases were assigned a date of diagnosis as the first recorded date of any of the codes for cirrhosis in their general practice record (see section 2.4.3).

Matched controls were then given this date as their date of 'pseudo-diagnosis'.

### **4.2.2.2 Age**

Age at diagnosis, or pseudo-diagnosis for controls, was categorised into 25-44 years, 45-64 years and 65 years and above for the purposes of analysis.

### **4.2.2.3 Body Mass Index**

Body Mass Index (BMI in  $\text{kg/m}^2$ ) was defined using data on height, weight and/or BMI contained within the prevention data file. Data on height and weight contained several outliers of implausibly low or high values, mostly of an order of magnitude of 100 or 1000 times normal plausible values suggesting transcription errors in the number of zeroes recorded.

Consequently weights of greater than 300kg or less than 30kg, heights of greater than 2.5m or less than 1m, and BMI values of greater than 100 were excluded. Values of height and weight recorded at least one year before the date of diagnosis of cirrhosis for cases or date of pseudo-diagnosis for controls were then examined and the median value of each used to calculate the BMI of the patient. Where there was a value for a patient's BMI, again recorded at least one year before the date of diagnosis of cirrhosis or pseudo-diagnosis, this was used in preference to a calculated value using height and weight measurements. The 1-year cut off was used to try to ensure weight loss due to undiagnosed disease did not change the initial BMI categorisation of subjects.

BMI was then categorised according to recognised clinically meaningful limits: <18.5 (underweight), 18.5-24.9 (ideal weight), 25.0-29.9 (overweight), 30.0-34.9 (obese) and 35.0+ (severely obese).

#### **4.2.2.4 Smoking**

Smoking status was ascribed using a combination of medical codes for smoking contained within the medical data file and information recorded within the prevention file on the number of cigarettes smoked before the date of diagnosis or pseudo-diagnosis. Smoking codes in a subject's medical file were categorised as 'Non-smoker', 'Ex-smoker' or 'Smoker' (see

) If there was more than one category coded in a subject's record, subjects were assigned the category that indicated greatest smoking experience during their record.

#### **4.2.2.5 Alcohol use**

Alcohol use was observed in two ways. Firstly, looking at the alcohol consumption data from the prevention data file the number of units of alcohol consumption in a week was extracted. Secondly, information on recorded alcohol status, prior to diagnosis, was extracted from the medical file using the codes for alcohol use (see Appendix III-c Codes for alcohol use).

#### **4.2.2.6 Comorbidity**

Comorbidity was described using a composite measure of illnesses diagnosed in each patient, based on the Charlson score.<sup>89</sup> The original Charlson score includes a category for mild liver disease as a weighted score of 1 and a category for moderate or severe liver disease as a weighted score of 3 (see Table 4-1). For this study I excluded liver disease from the comorbidity score. For the purposes of this study diseases had to be identified prior to the date of

diagnosis or pseudo-diagnosis. Particular diseases were identified from data contained within the medical file, weighted and a comorbidity score derived (see Appendix III-j Codes for comorbidity). Scores were then categorised as 0, 1, or 2+ for the purposes of analysis. This has subsequently been validated by others as a good predictor of mortality in the GPRD.<sup>90</sup>

**Table 4-1 Charlson score – weighted index of comorbidity**

| <b>Assigned weights for diseases</b> | <b>Conditions</b>  |
|--------------------------------------|--|
| 1                                    | Myocardial infarction<br>Congestive heart failure<br>Peripheral vascular disease<br>Cerebrovascular disease<br>Dementia<br>Chronic pulmonary disease<br>Connective tissue disease<br>Ulcer disease<br><i>Mild liver disease (Not included in this study)</i><br>Diabetes |
| 2                                    | Hemiplegia<br>Moderate or severe renal disease<br>Diabetes with end organ damage<br>Any tumour<br>Leukaemia<br>Lymphoma  |
| 3                                    | <i>Moderate or severe liver disease (Not included in this study)</i>   |
| 6                                    | Metastatic solid tumour<br>AIDS  |



#### **4.2.2.7 Liver transplant**

For the end-point of some of the analyses I included liver transplant as well as death. Liver transplant was defined using medical codes from the medical file (see Appendix III-k Codes for liver transplant).

#### **4.2.2.8 Compensated and decompensated disease**

Cases were classified as being in a compensated or decompensated disease state at the date of diagnosis. Cases with a code for ascites or gastrointestinal bleed at or before the date of diagnosis were classified as being in a decompensated disease state (see Table 4-2).

#### **4.2.2.9 Aetiology of cirrhosis**

Aetiology was ascribed as per the methods in section 3.2.2.2.

**Table 4-2 Medical codes for ascites and GI bleed (decompensated disease)**

| Description  | medcode |
|--|---------|
| [D]ASCITES   | R095.00 |
| [D]ASCITES NOS   | R095z00 |
| [D]FLUID IN PERITONEAL CAVITY                              | R095000 |
| ACUTE GASTRIC ULCER WITH HAEMORRHAGE                       | J110100 |
| ACUTE GASTRIC ULCER WITH HAEMORRHAGE AND<br>PERFORATION    | J110300 |
| BLEEDING ACUTE GASTRIC ULCER                               | J110111 |
| BLEEDING CHRONIC DUODENAL ULCER                            | J121111 |
| BLEEDING CHRONIC GASTRIC ULCER                             | J111111 |
| CHRONIC DUODENAL ULCER WITH HAEMORRHAGE                    | J121100 |
| CHRONIC DUODENAL ULCER WITH HAEMORRHAGE AND<br>PERFORATION | J121300 |
| CHRONIC GASTRIC ULCER WITH HAEMORRHAGE                     | J111100 |
| CHRONIC GASTRIC ULCER WITH HAEMORRHAGE AND<br>PERFORATION  | J111300 |
| CHYLOUS ASCITES  | 457 CA  |
| CHYLOUS ASCITES  | G86y100 |
| DRAINAGE OF ASCITES NEC                                    | 7H2B200 |
| GASTROINTESTINAL HAEMORRHAGE UNSPECIFIED                   | J68z.00 |
| GASTROTOMY AND LIGATION OF BLEEDING POINT OF<br>STOMACH    | 7619100 |
| GI BLEEDING  | 569 M   |
| GIB - GASTROINTESTINAL BLEEDING                            | J68z.11 |
| HAEMATEMESIS   | J680.00 |
| HAEMORRHAGE GASTROINTESTINAL                               | 569 MI  |
| HEPATIC ASCITES  | 5719AH  |
| INSERTION OF DENVER PERITONEOVENOUS SHUNT                  | 7H2B111 |
| INSERTION OF LE VEEN PERITONEOVENOUS SHUNT                 | 7H2B112 |
| INSERTION OF PERITONEAL TO VENOUS SHUNT FOR<br>ASCITES     | 7H2B113 |
| INTESTINAL HAEMORRHAGE                                     | 569 MH  |
| MELAENA  | J681.00 |
| OESOPHAGEAL VARICES WITH BLEEDING                          | G850.00 |
| OESOPHAGEAL VARICES WITH BLEEDING IN DISEASES EC           | G852000 |
| OESOPHAGUS BLEEDING  | 5309H   |
| OESOPHAGUS HAEMORRHAGE                                     | 5309HA  |
| O/E - ASCITES  | 250..00 |
| O/E - ASCITES - DIPPING SHOWN                              | 2502.00 |
| O/E - ASCITES NOS  | 250Z.00 |
| O/E -ASCITES-SHIFTING DULLNESS                             | 2504.00 |
| O/E-ASCITES-FLUID THRILL SHOWN                             | 2503.00 |
| PARACENTESIS ABDOMINIS FOR ASCITES                         | 7H2B000 |
| PERITONEAL TO VENOUS DRAINAGE FOR ASCITES                  | 7H2B100 |
| TANNER DEVASCULARISATION FOR BLEEDING VARICES              | 7609y11 |
| UPPER GASTROINTESTINAL HAEMORRHAGE                         | 569 ME  |
| VOMITING OF BLOOD  | J680.11 |

### **4.2.3 Statistical analysis**

Using Cox proportional hazards regression I modelled the hazard of death in the cirrhosis cohort (classifying subjects with cirrhosis as either compensated or decompensated at entry (as described in section 4.2.2.8)) compared with the control cohort employing an historical matched cohort study design.

Subjects with cirrhosis and controls entered the analysis period at the date of diagnosis or pseudo-diagnosis respectively and exited at the earliest of either date of death, deregistration with their general practice or 30 April 2002 which was the last date of available data in this dataset. This principal analysis was adjusted, a priori, for age and sex. Additional potential confounders (BMI, smoking, alcohol intake and comorbidity group) were modelled as categorical variables (with a separate category for missing data) and included in the final Cox model if they conferred a 10% or greater adjustment in the hazard ratios seen.

Owing to the probable high influence of comorbidity on mortality, particularly at early stages, I split follow up time at 1 year and modelled hazard ratios during the first year following diagnosis and after 1 year stratified by comorbidity.

I then split the population of cases into those with alcoholic cirrhosis and those with non-alcohol related cirrhosis (as described in section 3.2.2.2) and examined the mortality rates and adjusted hazard ratios compared with their matched controls for these two aetiologic groups.

To minimise the potential for survival bias I ran the principal analysis again comparing mortality between compensated and decompensated cases and controls using all incident cases (as described in section 3.2.2.1) and their matched controls. To try to account for potential attrition bias I also ran the principal analysis using the earliest of date of death, deregistration or last

recorded appointment in the GPRD as the exit-point for the analysis. Finally, the principal analysis was repeated using death and liver transplant as the end-point for the Cox model.

Proportional hazards assumptions were checked using Schoenfeld residuals and log-log plots.

### **4.3 Results**

A total of 4537 subjects with cirrhosis and 44,403 appropriately matched controls contributing a total of 226,412 person years of follow-up were included within this analysis, with a median follow-up time of 3.5 years per patient.

#### **4.3.1 Population characteristics**

As would be expected due to the method of control selection the cirrhosis cohort and the control cohort had very similar age distributions and sex profile (see Table 4-3). Most of the subjects in both the cirrhosis and control cohorts had no recorded comorbidity prior to diagnosis. Subjects with cirrhosis were slightly more likely to have some recorded comorbidity than controls. Notably there was a high proportion of missing data in both cohorts for BMI, smoking status and alcohol consumption (as measured by unit intake). Subjects with cirrhosis were much more likely to have a recorded alcohol status (as per codes within the medical file) than controls prior to the date of diagnosis (or pseudo-diagnosis).

There were few liver transplants recorded with only 2.3% of all cirrhosis subjects having a liver transplant subsequent to diagnosis with cirrhosis. Just over four-fifths of the cirrhosis cohort entered the analysis in a compensated state of disease. Just over half of the cirrhosis subjects (50.9%) had alcohol as their presumed aetiology (when taking into account recording of alcohol problems at any point in the record).

**Table 4-3 Demographic, lifestyle and clinical characteristics of cirrhosis cohort and general population cohort**

|  | Cirrhosis Cohort<br>(N=4537)      | Control Cohort<br>(N=44 403)       |
|--|-----------------------------------|------------------------------------|
| <b>Demographics / lifestyle factors</b>      |                                   |                                    |
| <b>Age at diagnosis (years)</b>              |                                   |                                    |
| Median age [IQR]<br>(range)                  | 56.5 [46.9, 67.0]<br>(25.2, 99.6) | 56.2 [46.8, 66.8]<br>(25.2, 102.9) |
| 25-44  | 943 (20.8)                        | 9403 (21.2)                        |
| 45-64  | 2256 (49.7)                       | 22 219 (50.0)                      |
| 65+  | 1338 (29.5)                       | 12 781 (28.8)                      |
| <b>Sex</b>                                   |                                   |                                    |
| Male   | 2612 (57.6)                       | 25 599 (57.7)                      |
| Female                                       | 1925 (42.4)                       | 18 804 (42.3)                      |
| <b>BMI</b>                                   |                                   |                                    |
| Median BMI [IQR]                             | 25.5 [22.5, 28.7]                 | 25.3 [23, 28.2]                    |
| No recorded BMI                              | 3624 (80.0)                       | 33 294 (75.0)                      |
| <b>Smoking status (prior to diagnosis)</b>   |                                   |                                    |
| No smoker                                    | 10 (0.2)                          | 92 (0.2)                           |
| Ex-smoker                                    | 15 (0.3)                          | 113 (0.3)                          |
| Smoker                                       | 387 (8.5)                         | 2461 (5.5)                         |
| Missing                                      | 4125 (90.9)                       | 41 737 (94.0)                      |
| <b>Alcohol consumption (units)</b>           |                                   |                                    |
| Median consumption per week<br>[IQR] (range) | 7 [0, 29]<br>(0, 400)             | 2 [0, 10]<br>(0, 700)              |
| Mean unit intake (sd)                        | 20.8 (33.7)                       | 7.2 (14.5)                         |
| No recorded unit intake                      | 2577 (56.8)                       | 22 792 (51.3)                      |
| <b>Alcohol status (prior to diagnosis)</b>   |                                   |                                    |
| Non-drinker                                  | 2 (<0.1)                          | 10 (<0.1)                          |
| Drinker                                      | 170 (3.8)                         | 1007 (2.3)                         |
| Alcoholic                                    | 1377 (30.4)                       | 740 (1.7)                          |
| Not recorded                                 | 2988 (65.9)                       | 42 646 (96.0)                      |
| <b>Comorbidity score</b>                     |                                   |                                    |
| 0  | 3525 (77.7)                       | 37 085 (83.5)                      |
| 1  | 534 (11.8)                        | 3704 (8.3)                         |
| 2+   | 478 (10.5)                        | 3614 (8.1)                         |
| <b>Clinical characteristics</b>              |                                   |                                    |
| <b>Liver transplants</b>                     | 105 (2.3)                         | 2 (<0.1)                           |
| <b>Disease state at entry</b>                |                                   |                                    |
| Compensated                                  | 3660 (80.6)                       |                                    |
| Decompensated                                | 877 (19.4)                        | -                                  |
| <b>Presumed Aetiology†</b>                   |                                   |                                    |
| Alcoholic                                    | 2307 (50.9)                       |                                    |
| Viral hepatitis                              | 238 (5.3)                         |                                    |
| Metabolic liver disease                      | 48 (1.1)                          | -                                  |
| Autoimmune liver disease                     | 354 (7.8)                         |                                    |
| No specified aetiology                       | 1730 (38.1)                       |                                    |

†as a case could have more than one presumed aetiology numbers in the table do not necessarily add up to 4537.

## **4.3.2 Cox regression modelling**

### **4.3.2.1 Overall survival**

When building the Cox regression model only the a priori confounders of age and sex remained in the model.

Overall, patients with cirrhosis had a hazard ratio for death (adjusted for age and sex) of 5.8 (95%CI[5.5, 6.1]) compared with the general population cohort (see Table 4-4). A still higher hazard ratio for death was seen in patients with decompensated disease compared with the general population with an adjusted hazard ratio of 9.6 (95%CI[8.7, 10.7]) but a significantly higher hazard of death was still seen for patients with compensated disease with an adjusted hazard ratio of 5.2 (95%CI[4.9, 5.5] (see Figure 4-2).

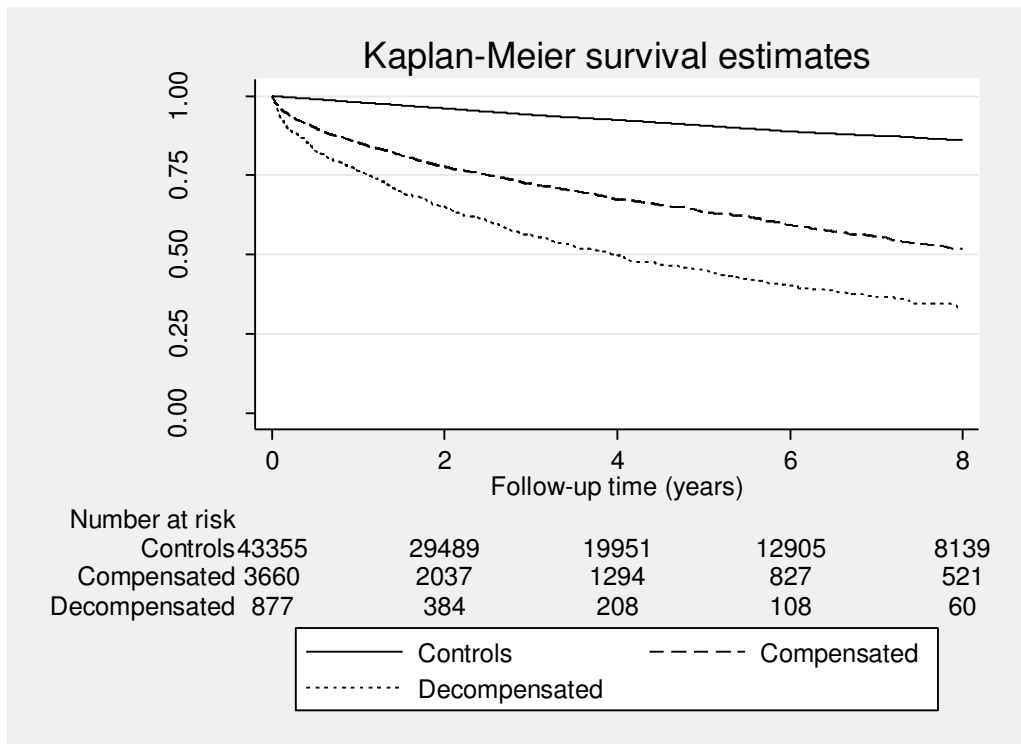
Crude survival at 1 and 5 years was correspondingly lower for patients with decompensated disease (76.4% (95%CI[73.3%, 79.2%]) and 45.2% (95%CI[40.9%, 49.3%]) respectively) than for patients with compensated disease (85.2% (95%CI[84.0%, 86.3%]) and 63.5% (61.5%(95%CI[61.5%, 65.3%]) respectively). For all patients with cirrhosis survival was 83.5% (95%CI [82.4, 84.6]) at 1 year and 60.1% (95%CI [58.3, 61.8]) at 5 years compared with 98.0% (95%CI [97.9, 98.1]) and 90.7% (95%CI [90.3, 91.0]) respectively for the control population.

**Table 4-4 Cox proportional hazards model for overall mortality**

|  | <b>Events</b> | <b>Person-years</b> | <b>Mortality rate<br/>(per 1000 person years)</b> | <b>Hazard ratio<br/>[95%CI]</b> | <b>Adjusted Hazard<br/>ratio* [95%CI]</b> |
|--|---------------|---------------------|---|---------------------------------|---|
| <b>Controls</b>                        | 4033          | 209 554             | 19.2 [18.7, 19.8]                                 | -                               | -   |
| <b>All cirrhosis</b>                   | 1769          | 16 858              | 104.9 [100.1, 109.9]                              | 5.4 [5.1, 5.7]                  | 5.8 [5.5, 6.1]                            |
| <b>Compensated<br/>    cirrhosis</b>   | 1360          | 14 560              | 93.4 [88.6, 98.5]                                 | 4.8 [4.5, 5.1]                  | 5.2 [4.9, 5.5]                            |
| <b>Decompensated<br/>    cirrhosis</b> | 409           | 2298                | 178.0 [161.5, 196.1]                              | 8.8 [8.0, 9.8]                  | 9.6 [8.7, 10.7]                           |

\*adjusted for age and sex





**Figure 4-2 Survival estimates for controls, subjects with compensated cirrhosis and subjects with decompensated cirrhosis.**

### **4.3.2.2 Testing the proportional hazards assumptions**

Examination of the log-log plot and the plot of Schoenfeld residuals against time showed that there was a significant decrease in the hazard of death in the first year or so of follow-up (see Figure 4-3, Figure 4-4). As I had already planned to split follow-up time at one year I present all the remaining results as mortality during the first year and mortality subsequent to the first year.

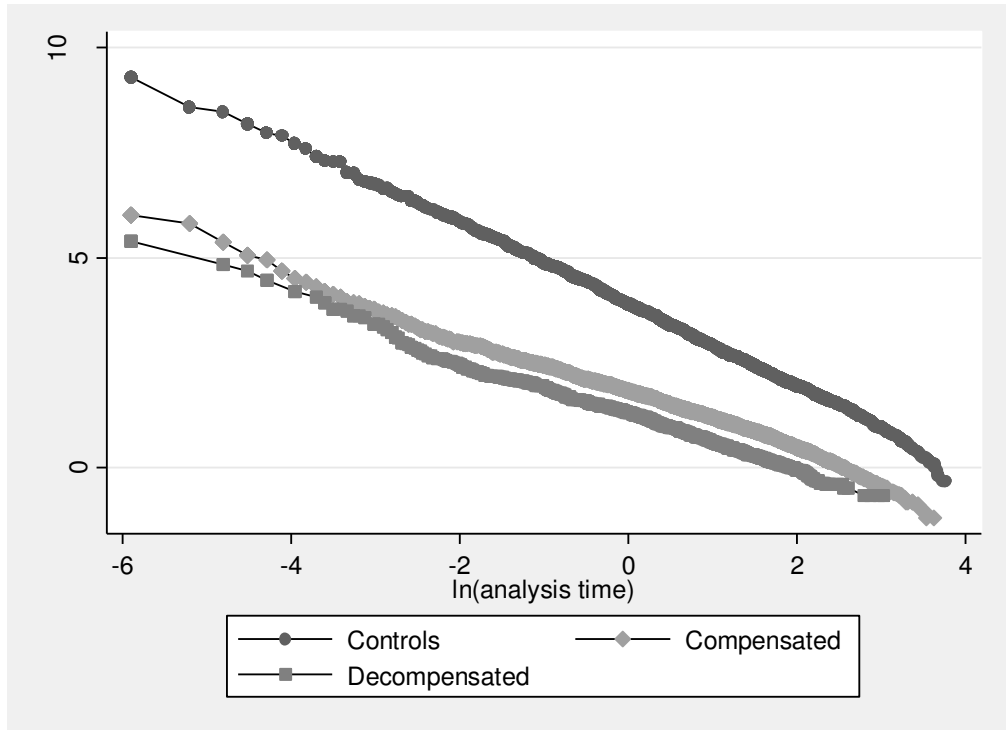
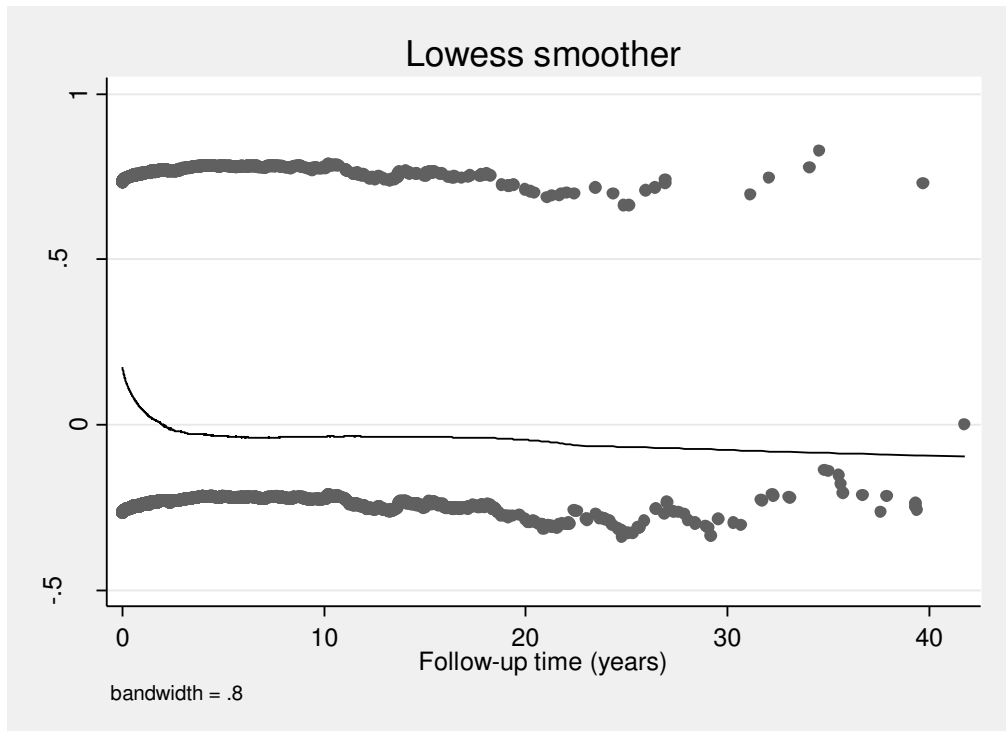


Figure 4-3 Log-log plot for overall mortality analysis



**Figure 4-4** Schoenfeld residuals against time for overall mortality

#### **4.3.2.3 Survival by follow-up and comorbidity score**

Mortality for subjects with cirrhosis was higher during the first year following diagnosis than subsequently but also remained substantial beyond one year (see Table 4-5). Stratification by comorbidity showed that although the absolute mortality rates were lowest in those with no recorded comorbidity the adjusted hazard ratios for death were highest in this group. This high relative risk of death was most noticeable in the first year following diagnosis with hazard ratios of 8.5 for the compensated cohort compared with the general population and 14.2 for the decompensated cohort, approximately double those seen in the years following the first year after diagnosis.

Comorbidity appeared to have more of an influence on the mortality of the subjects with compensated disease than those with decompensated disease.

Table 4-5 Overall mortality analysis split by follow-up time and stratified by Charlson index

|                             | Mortality rate (per 1000) |                    |                      | Adjusted hazard ratio * |                      |
|-----------------------------|---------------------------|--------------------|----------------------|-------------------------|----------------------|
|                             | Control cohort            | Compensated cohort | Decompensated cohort | Compensated cohort      | Decompensated cohort |
| <b>During first year</b>    |                           |                    |                      |                         |                      |
| <b>Overall</b>              | 20.1                      | 167.1              | 288.1                | 8.5 [7.6, 9.5]          | 14.2 [12.1, 16.6]    |
| <b>Charlson score</b>       |                           |                    |                      |                         |                      |
| 0                           | 16.5                      | 159.1              | 266.3                | 9.9 [8.7, 11.2]         | 16.6 [13.7, 20.3]    |
| 1                           | 28.6                      | 174.8              | 249.0                | 6.8 [4.9, 9.4]          | 9.3 [6.0, 14.3]      |
| 2+                          | 49.5                      | 233.9              | 424.5                | 4.8 [3.5, 6.4]          | 8.9 [6.4, 12.5]      |
| <b>Following first year</b> |                           |                    |                      |                         |                      |
| <b>Overall</b>              | 19.0                      | 73.8               | 133.0                | 4.3 [3.9, 4.6]          | 7.9 [6.9, 9.1]       |
| <b>Charlson score</b>       |                           |                    |                      |                         |                      |
| 0                           | 16.4                      | 70.6               | 118.9                | 4.7 [4.3, 5.1]          | 8.3 [7.0, 9.8]       |
| 1                           | 32.8                      | 90.3               | 126.0                | 3.2 [2.6, 4.1]          | 5.2 [3.6, 7.4]       |
| 2+                          | 43.0                      | 94.6               | 246.1                | 2.4 [1.8, 3.1]          | 7.2 [5.2, 10.0]      |

\*adjusted for age and sex

#### **4.3.2.4 Survival by presumed aetiology**

As might be expected following the previous analysis mortality during the first year for both alcoholic cirrhosis and non-alcohol related cirrhosis was higher than in subsequent years (see Table 4-6).

The absolute mortality rate of subjects with non-alcohol related cirrhosis was higher than that of subjects with alcoholic cirrhosis in the first year following diagnosis. Subsequent to the first year mortality was similar in both groups. However, the adjusted hazard ratios for mortality were much higher in the subjects with alcoholic cirrhosis compared to those with non-alcohol-related cirrhosis. This is a result of the absolute mortality rates seen in the control population. The matched controls of subjects with alcoholic cirrhosis had a considerably lower mortality than the matched controls of subjects with non-alcohol related cirrhosis. Examining the age and sex distribution of the patients with cirrhosis showed a significantly higher age at diagnosis for subjects with non-alcohol related cirrhosis compared to those with alcoholic cirrhosis (see Table 4-7).

The age- and sex-adjusted hazards ratios for subjects with alcoholic cirrhosis following the first year after diagnosis were similar to those of non-alcohol related cirrhosis during the first year following diagnosis.

**Table 4-6 Mortality split by follow-up time and stratified by alcoholic aetiology**

|                                      | Events | Person-years | Mortality rate<br>(per 1000 person years) | Adjusted hazard<br>ratio* [95%CI] |
|--------------------------------------|--------|--------------|---|-----------------------------------|
| <b>During first year</b>             |        |              |   |                                   |
| <b>Alcoholic cirrhosis</b>           |        |              |   |                                   |
| Controls                             | 271    | 20 344       | 13.3 [11.8, 15.0]                         | -                                 |
| Compensated cirrhosis                | 234    | 1519         | 154.1 [135.5, 175.1]                      | 11.8 [9.9, 14.1]                  |
| Decompensated cirrhosis              | 94     | 393          | 239.0 [195.2, 292.5]                      | 17.6 [13.9, 22.2]                 |
| <b>Non-Alcohol-related cirrhosis</b> |        |              |   |                                   |
| Controls                             | 525    | 19 257       | 27.3 [25.0, 29.7]                         | -                                 |
| Compensated cirrhosis                | 278    | 1544         | 180.0 [160.0, 202.4]                      | 6.9 [5.9, 7.9]                    |
| Decompensated cirrhosis              | 98     | 273          | 358.9 [294.4, 437.4]                      | 12.3 [9.9, 15.3]                  |
| <b>Following first year</b>          |        |              |   |                                   |
| <b>Alcoholic cirrhosis</b>           |        |              |   |                                   |
| Controls                             | 1181   | 90 469       | 13.1 [12.3, 13.8]                         | -                                 |
| Compensated cirrhosis                | 465    | 5825         | 79.8 [72.9, 87.4]                         | 6.4 [5.7, 7.1]                    |
| Decompensated cirrhosis              | 128    | 960          | 133.3 [112.1, 158.5]                      | 12.4 [10.3, 14.9]                 |
| <b>Non-Alcohol-related cirrhosis</b> |        |              |   |                                   |
| Controls                             | 2056   | 79 485       | 25.9 [24.8, 27.0]                         | -                                 |
| Compensated cirrhosis                | 383    | 5671         | 67.5 [61.1, 74.6]                         | 3.1 [2.7, 3.4]                    |
| Decompensated cirrhosis              | 89     | 671          | 132.6 [107.7, 163.2]                      | 5.2 [4.2, 6.4]                    |

\*adjusted for age and sex



**Table 4-7 Sex and age distribution of subjects with alcoholic and non-alcohol-related cirrhosis**

|                       | <b>All cirrhosis</b> | <b>Alcoholic cirrhosis</b> | <b>Non-alcohol-related cirrhosis</b> |
|-----------------------|----------------------|----------------------------|--------------------------------------|
|                       | <b>N=4537</b>        | <b>N=2307</b>              | <b>N=2230</b>                        |
|                       | <b>n(%)</b>          | <b>n(%)</b>                | <b>n(%)</b>                          |
| <b>Sex</b>            |                      |                            |                                      |
| Male                  | 2612 (57.6)          | 1528 (66.2)                | 1084 (48.6)                          |
| Female                | 1925 (42.4)          | 779 (33.8)                 | 1146 (51.4)                          |
| <b>Age (in years)</b> |                      |                            |                                      |
| Median [IQR]          | 56.5 [46.9, 67.0]    | 51.7 [44.1, 60.5]          | 62.6 [52.0, 71.9]                    |
| 25-44                 | 943 (20.8)           | 643 (27.9)                 | 300 (13.5)                           |
| 45-64                 | 2256 (49.7)          | 1311 (56.8)                | 945 (42.4)                           |
| 65+                   | 1338 (29.5)          | 353 (15.3)                 | 985 (44.2)                           |

#### **4.3.2.5 Cox proportional hazards model using different cohort definitions**

Running the analyses using an incident cohort, censoring subjects at the date of their last appointment within the GPRD, or using death or liver transplant as the end-point led to no substantial differences in the adjusted hazard ratios for mortality either during the first year following diagnosis or subsequently (see Table 4-8).

Analysis using an incident cohort restricted the number of cases to 2787 and 26,176 appropriately matched controls. I showed a slightly higher hazard of death for subjects with compensated cirrhosis both during the first year following diagnosis and subsequently compared to the initial analysis including both prevalent and incident cases. Patients with decompensated disease showed a slightly lower hazard of death in the first year following diagnosis but a greater hazard of death subsequently compared to the initial analysis.

When censoring subjects at either death, de-registration or date of last appointment within the GPRD (as opposed to the end of the UTS period) there was a slightly lower hazard of death for both subjects with compensated and decompensated disease at both time periods studied compared to the initial analysis.

For the analysis using death and liver transplant as the outcome there was a slight increase in the adjusted hazard ratios for death in all subjects at both time periods studied compared with the initial analysis.

None of the hazard ratios observed in any of these three variations on analysis led to any significant differences to those calculated from the initial analysis.

Table 4-8 Cox proportional hazards model using different cohort definitions

|                                      | Mortality rate (per 1000) |                    |                      | Adjusted hazard ratio * |                          |
|--------------------------------------|---------------------------|--------------------|----------------------|-------------------------|--------------------------|
|                                      | Control cohort            | Compensated cohort | Decompensated cohort | Compensated cohort      | Decompensated cohort     |
| <b>During first year</b>             |                           |                    |                      |                         |                          |
| <b>Principal analysis</b>            | <b>20.1</b>               | <b>167.1</b>       | <b>288.1</b>         | <b>8.5 [7.6, 9.5]</b>   | <b>14.2 [12.1, 16.6]</b> |
| Incident cohort                      | 24.1                      | 212.3              | 309.7                | 9.0 [7.9, 10.2]         | 13.1 [11.0, 15.8]        |
| Censoring at last GPRD appointment   | 22.5                      | 171.1              | 293.8                | 7.9 [7.1, 8.9]          | 13.2 [11.3, 15.5]        |
| Death and liver transplant end point | 20.1                      | 172.8              | 300.1                | 8.8 [7.8, 9.8]          | 14.7 [12.6, 17.2]        |
| <b>Following first year</b>          |                           |                    |                      |                         |                          |
| <b>Principal analysis</b>            | <b>19.0</b>               | <b>73.8</b>        | <b>133.0</b>         | <b>4.3 [3.9, 4.6]</b>   | <b>7.9 [6.9, 9.1]</b>    |
| Incident cohort                      | 22.7                      | 96.1               | 158.1                | 4.6 [1.4, 5.1]          | 8.8 [7.4, 10.5]          |
| Censoring at last GPRD appointment   | 21.3                      | 75.8               | 137.2                | 4.0 [3.7, 4.3]          | 7.4 [6.5, 8.5]           |
| Death and liver transplant end point | 19.1                      | 80.6               | 142.0                | 4.6 [4.3, 5.0]          | 8.3 [7.2, 9.5]           |

\*adjusted for age and sex

## **4.4 Discussion**

### **4.4.1 Key findings**

Patients with a diagnosis of cirrhosis are at an increased risk of death than their age- and sex-matched general population controls with an adjusted hazard ratio for death of 5.8 (95%CI[5.5, 6.1]). Those with decompensated disease have an even worse prognosis with 5- year survival only 45.2% compared with 63.5% for those with compensated disease. The increased risk of death was particularly high during the first year following diagnosis but remained high subsequently, even following adjustment for some measure of comorbidity. The hazard ratio for death was highest in those with no reported comorbidity although absolute mortality rates were highest in those with reported comorbidities. Patients with a presumed aetiology of alcoholic cirrhosis had a worse survival at all stages than those with non-alcohol related cirrhosis.

### **4.4.2 Strengths and limitations**

This study has been performed using a large, representative, population-based cohort of patients with cirrhosis alongside an appropriately matched general population based control cohort. These cohorts were identified relatively recently (1987 – 2002) and the results observed reflect the natural history of cirrhosis during this time period.

The size of the dataset used for this analysis has allowed the estimation of mortality rates and adjusted hazard ratios for death stratifying by severity of disease, follow-up time and comorbidity.

Perhaps the most significant potential limitation of this analysis is related to the coding of the diagnosis of cirrhosis. As discussed in section 3.4.2 the inclusion of all patients with any mention of cirrhosis, oesophageal varices or portal hypertension within the medical records may have led to the inclusion of some patients who did not have cirrhosis. However, the same counter-argument is applicable in this situation that it is more likely that there are cases with cirrhosis that are missing from the data source where the diagnosis of cirrhosis was unconfirmed and / or not fed back from secondary care to primary care records. This will potentially have led to an underestimate of the hazard ratio for death as cases with undiagnosed cirrhosis may be included within the control population.

In addition to the potential for misclassification of the diagnosis of cirrhosis it is possible that there exists further misclassification in the accuracy of the severity of cirrhosis as compensated or decompensated. Whilst the results of the validation described in section 3.3.4 lend credence to the diagnosis of cirrhosis itself, with evidence that most diagnoses occurred in secondary care, the prohibitive cost of validation within the GPRD system did not allow for the validation of the additional signs and symptoms of ascites and gastrointestinal bleeding used to define decompensated disease. Indeed, these clinical symptoms may only be recorded if they are of obvious clinical relevance to the GP. Ascites and gastrointestinal bleeding are however serious complications of cirrhosis and as such one might expect that these events would be considered important and therefore recorded within the primary care record, either following hospital correspondence or from an individual patient consultation. It is possible that the recording of ascites, if it occurred in the absence of further information from hospital, would only be large-volume, clinically significant ascites visible at the general practice appointment rather than that only identified by ultrasound. Assuming that the misclassification is

most likely to act through misclassifying patients with decompensated cirrhosis as having compensated disease this will have led to an overestimate of the hazard ratios for death for people with compensated disease and a corresponding underestimate of the hazard ratios for death for people with decompensated disease.

The size of the database used has allowed the description of the mortality experience of patients with both alcoholic and non-alcohol related cirrhosis alongside their matched controls. The small numbers of cases with other presumed aetiologies meant that it was not possible to model the hazard of death for other causes of cirrhosis with any precision.

It could be argued that the inclusion of both incident and prevalent cases in the cirrhosis cohort might lead to the introduction of survival bias as those cases who are prevalent have, by definition, already survived a particular length of time to still be included in the analysis. As such, I ran the principal analysis using only those subjects who were considered incident as defined in section 3.2.2.1. The estimates of the mortality rates and therefore the hazard ratios for death were slightly higher than those seen when including all incident and prevalent cases, apart from subjects with decompensated disease in the first year following diagnosis who showed a slightly lower hazard ratio for death. However, all estimates remained within the 95% confidence interval of the principal analysis. The results I have reported including all incident and prevalent cases probably more accurately reflects the real world of clinical practice within the general population and allows for the communication of results that are directly valid to the patients an individual GP may see in their practice.

Though the data available have allowed for an appropriate individually-matched adjustment for some confounders (age and sex) it was not possible to examine the potential associations or modifying effects of other variables either because they are not available in the GPRD at all e.g. any measure of socio-economic status which is known to be associated with mortality, or because there was such a high proportion of missing data. Recent studies have suggested an interaction between raised BMI and alcohol consumption leading to an increased risk of death from liver disease.<sup>91</sup> Additionally it was not possible within this dataset to examine the cause of death of these patients as this information was not systematically available.

Of note is the discrepancy in the proportion of patients who were recorded to be alcoholics before the diagnosis of cirrhosis (30.4%) and the proportion of patients assigned a presumed aetiology of alcoholism (50.9%). Aetiologies were ascribed using information contained in the whole medical record (including after the diagnosis of cirrhosis). This would therefore suggest that roughly two-fifths of those patients with alcoholic cirrhosis were not known to be (or at least not recorded as) alcoholics before the onset of their disease. However, when taken in context to the 96.0% of controls who did not have their alcohol status recorded before the date of pseudo diagnosis, it is perhaps encouraging that so many patients with cirrhosis had already been identified as alcoholics.



#### **4.4.3 Comparison with previously published work**

In the UK the most recent published study on cirrhosis mortality observed the mortality of patients with all chronic liver disease who had been admitted to hospital in a small geographically distinct region of the UK between 1968 and 1999.<sup>41</sup> This study reported an SMR for one year follow-up of 16.3. This figure is higher than the 1-year adjusted hazard ratios that I have reported for either patients with compensated or decompensated disease.

Other large cohort studies from European centres have similarly shown worse survival than I have reported in this chapter. In Denmark between 1995 and 2006 a hospital cohort of 14,976 patients with cirrhosis described a 1-year survival of only 65.5% and 5-year survival of 37.5%, notably lower than that I have reported.<sup>92</sup> This study was not able to categorise patients into compensated or decompensated disease and additionally did not report the hazard ratios for mortality compared with their matched control cohort.

Previously the same authors had reported SMRs for patients hospitalized with cirrhosis compared with the general population of 32.3 for the first year following diagnosis and 5.7 thereafter.<sup>46</sup>

These poorer survival estimates are perhaps unsurprising as these previous studies used cohorts of patients admitted to hospital. Whilst the diagnosis of cirrhosis in my study population is likely to have come from a hospital diagnosis it does not necessarily follow that these patients were hospitalized for this diagnosis to occur. As my study is a population-based cohort the results seen are also unlikely to have been affected by the variation in referrals and follow-ups seen in cohorts selected from secondary care. As such it is probable that my results can be more widely generalised to patients diagnosed with cirrhosis including those ambulatory patients who have not been admitted to hospital.

Perhaps the most commonly referenced figures in the literature looking at the mortality experience of patients with cirrhosis based on the severity of disease are those based on 1155 consecutive patients admitted to a single hospital in Sicily during the 1970s and 1980s which reported 6-year survival of 54% and 21% in patients with compensated and decompensated cirrhosis respectively.<sup>44</sup> It is possible that the survival figures I report are better than those reported in this smaller study, particularly for those patients with decompensated disease, because there have been significant improvements in the management and outcomes of the complications of cirrhosis in the intervening decades. This has been shown for oesophageal varices in studies in both the USA and more recently Sweden.<sup>58 60</sup> Additionally, the proportion of cases ascribed as alcoholic cirrhosis is lower in the Sicilian population than in my study population with a correspondingly higher proportion of patients with hepatitis B virus. It is therefore possible that the survival figures reflect a different spectrum of aetiology of cirrhosis in the two populations.

Other estimates of mortality in patients with cirrhosis in the UK come from much older studies. Saunders et al report the 5-year survival of patients with alcoholic cirrhosis, 36%, and non-alcohol related cirrhosis, 14%.<sup>37</sup> An earlier study, also from Birmingham, covering patients with cirrhosis in a single hospital between 1959-64 reports similarly low 5-year survival figures of 14.4% after first admission to hospital, again with patients with alcoholic cirrhosis having a better prognosis (5-year survival of 20% compared with 5.1% for patients with cryptogenic cirrhosis).<sup>43</sup>

The survival figures I have reported are better than these two previous studies but conversely show that survival with non-alcohol related cirrhosis confers a lower risk of mortality than that seen with an alcoholic aetiology.

#### 4.4.4 Conclusions

In this study I have shown that the survival of patients with a diagnosis of cirrhosis, whilst better than previously reported studies,<sup>37 41 43 44 45 46 47 48 57 93</sup> is still poor with 1-year survival of 83% and 5-year survival of 60%. This study represents the most contemporary estimate of the mortality experience of patients with cirrhosis and also allows comparison with the general population. Even in those patients with no comorbidity the adjusted hazard ratio for death is significantly higher than that of the general population.

I have been able to describe the mortality experience of patients with compensated and decompensated disease, showing a substantial increase in mortality for those with decompensated disease at diagnosis.

Defining decompensated cirrhosis as the presence of ascites or GI bleeding appears to accurately reflect an increased probability of death compared to compensated cirrhosis. Although there is the possibility of misclassification of patients with decompensated disease as compensated as differences in follow-up at individual sites may exist, these general population based data provide an 'average' estimate of the mortality experienced by patients with cirrhosis. These figures will be of particular importance for service providers and for individual clinicians and general practitioners to communicate to their patients.

For the purposes of service provision and planning it is important to note that even patients with compensated disease had an increased hazard of death compared to the general population. This is in contrast to the assumptions made for the purposes of the cost-effectiveness analysis carried out in a recent HTA systematic review where it was claimed that existing data suggest

that there is no excess mortality in those patients with compensated disease compared with the general population.<sup>49</sup>

An aetiology of alcoholic cirrhosis remains a particularly bad prognostic indicator with mortality in patients with alcoholic cirrhosis nearly double that of patients with non-alcohol related cirrhosis. With roughly 60% of all patients with alcoholic cirrhosis being known to their GPs as alcoholics before the date of diagnosis of cirrhosis this may provide an opportunity for intervention(s) leading to behaviour and risk modification.

## **5 Progression of disease in people with cirrhosis**

### **5.1 Introduction**

This study aims to describe the progression of people with a diagnosis of cirrhosis based on clinical symptoms.

### **5.2 Methods**

#### **5.2.1 Dataset used**

Data on all cases with cirrhosis (as described in section 2.4.3) were used in this analysis. Both subjects with incident and prevalent cirrhosis (as described in section 3.2.2.1), were included in this analysis. Subjects with no follow-up time were subsequently excluded from this analysis.

#### **5.2.2 Additional definitions**

##### **5.2.2.1 Stages of disease**

Within the population of cases with cirrhosis it was necessary for this study to define different stages or status of disease. I utilised the stages of cirrhosis as agreed at the Baveno IV consensus conference.<sup>94</sup> Each of these four stages is defined by the presence or absence of certain clinical symptoms:

**Stage 1** – cirrhosis, no oesophageal varices, no ascites

**Stage 2** – cirrhosis with oesophageal varices, no ascites, no bleeding

**Stage 3** – cirrhosis with ascites with or without oesophageal varices

**Stage 4** – cirrhosis with GI bleeding with or without ascites

Code lists were therefore constructed to represent ascites (Table 5-1) and any GI bleeding (see Table 5-2). The original code list for oesophageal varices

(see Table 2-2) was split into 2 separate lists – one representing non-bleeding oesophageal varices to represent stage 2 (see Table 5-3) and the second for bleeding oesophageal varices (see Table 5-4). These codes for bleeding oesophageal varices are also found in the code list for any GI bleeding.

**Table 5-1 Medical codes for ascites (stage 3)**

| Description  | medcode |
|--|---------|
| [D]ASCITES   | R095.00 |
| [D]ASCITES NOS   | R095z00 |
| [D]FLUID IN PERITONEAL CAVITY                          | R095000 |
| ASCITES (ABDOMINAL)                                    | 7853    |
| CHYLOUS ASCITES  | 457 CA  |
| CHYLOUS ASCITES  | G86y100 |
| DRAINAGE OF ASCITES NEC                                | 7H2B200 |
| HEPATIC ASCITES  | 5719AH  |
| INSERTION OF DENVER PERITONEOVENOUS SHUNT              | 7H2B111 |
| INSERTION OF LE VEEN PERITONEOVENOUS SHUNT             | 7H2B112 |
| INSERTION OF PERITONEAL TO VENOUS SHUNT FOR<br>ASCITES | 7H2B113 |
| O/E - ASCITES  | 250..00 |
| O/E - ASCITES - DIPPING SHOWN                          | 2502.00 |
| O/E - ASCITES NOS                                      | 250Z.00 |
| O/E -ASCITES-SHIFTING DULLNESS                         | 2504.00 |
| O/E-ASCITES-FLUID THRILL SHOWN                         | 2503.00 |
| PARACENTESIS ABDOMINIS FOR ASCITES                     | 7H2B000 |
| PERITONEAL TO VENOUS DRAINAGE FOR ASCITES              | 7H2B100 |

**Table 5-2 Medical codes for GI bleed (stage 4)**

| Description  | medcode |
|--|---------|
| ACUTE GASTRIC ULCER WITH HAEMORRHAGE                       | J110100 |
| ACUTE GASTRIC ULCER WITH HAEMORRHAGE AND<br>PERFORATION    | J110300 |
| BLEEDING ACUTE GASTRIC ULCER                               | J110111 |
| BLEEDING CHRONIC DUODENAL ULCER                            | J121111 |
| BLEEDING CHRONIC GASTRIC ULCER                             | J111111 |
| CHRONIC DUODENAL ULCER WITH HAEMORRHAGE                    | J121100 |
| CHRONIC DUODENAL ULCER WITH HAEMORRHAGE AND<br>PERFORATION | J121300 |
| CHRONIC GASTRIC ULCER WITH HAEMORRHAGE                     | J111100 |
| CHRONIC GASTRIC ULCER WITH HAEMORRHAGE AND<br>PERFORATION  | J111300 |
| GASTROINTESTINAL HAEMORRHAGE UNSPECIFIED                   | J68z.00 |
| GASTROTOMY AND LIGATION OF BLEEDING POINT OF<br>STOMACH    | 7619100 |
| GI BLEEDING  | 569 M   |
| GIB - GASTROINTESTINAL BLEEDING                            | J68z.11 |
| HAEMATEMESIS   | J680.00 |
| HAEMORRHAGE GASTROINTESTINAL                               | 569 MI  |
| INTESTINAL HAEMORRHAGE                                     | 569 MH  |
| MELAENA  | J681.00 |
| OESOPHAGEAL VARICES WITH BLEEDING                          | G850.00 |
| OESOPHAGEAL VARICES WITH BLEEDING IN DISEASES EC           | G852000 |
| OESOPHAGUS BLEEDING  | 5309H   |
| OESOPHAGUS HAEMORRHAGE                                     | 5309HA  |
| TANNER DEVASCULARISATION FOR BLEEDING VARICES              | 7609y11 |
| UPPER GASTROINTESTINAL HAEMORRHAGE                         | 569 ME  |
| VOMITING OF BLOOD  | J680.11 |



**Table 5-3 Code list for non-bleeding oesophageal varices (stage 2)**

| Description  | medcode |
|--|---------|
| [X]OESOPHAGEAL VARICES IN DISEASES CLASSIFIED ELSEWHERE      | Gyu9400 |
| FIBROPTIC ENDOSCOPIC BANDING OF OESOPHAGEAL VARICES          | 760C500 |
| FIBROPTIC ENDOSCOPIC INJECTION SCLEROTHERAPY OESOPH VARICES  | 760C300 |
| FUND HOLDING OP OESOPHAGEAL VARICES                          | K298 FH |
| GASTRIC VARICES  | G857.00 |
| INJECTION OESOPHAGEAL VARICES                                | K2982   |
| LIGATION OESOPHAGEAL VARICES                                 | K2981   |
| LOCAL LIGATION OF OESOPHAGEAL VARICES                        | 7609300 |
| OESOPHAGEAL VARICES  | G85..11 |
| OESOPHAGEAL VARICES IN DISEASES EC                           | G852.00 |
| OESOPHAGEAL VARICES IN DISEASES EC NOS                       | G852z00 |
| OESOPHAGEAL VARICES NOS                                      | G858.00 |
| OESOPHAGEAL VARICES WITHOUT BLEEDING                         | G851.00 |
| OESOPHAGEAL VARICES WITHOUT BLEEDING IN DISEASES EC          | G852100 |
| OPEN INJECTION SCLEROTHERAPY TO OESOPHAGEAL VARICES          | 7609400 |
| OPEN OPERATION ON OESOPHAGEAL VARICES NOS                    | 7609z00 |
| OPEN OPERATIONS ON OESOPHAGEAL VARICES                       | 7609    |
| OTHER SPECIFIED OPEN OPERATION ON OESOPHAGEAL VARICES        | 7609y00 |
| RIGID OESOPHAGOSCOPIC BANDING OF OESOPHAGEAL VARICES         | 760F400 |
| RIGID OESOPHAGOSCOPIC INJECTION SCLEROTHERAPY OESOPH VARICES | 760F300 |
| VARIX OESOPHAGUS   | 4560    |

**Table 5-4 Code list for bleeding oesophageal varices**

| Description   | medcode |
|---|---------|
| OESOPHAGEAL VARICES WITH BLEEDING                   | G850.00 |
| OESOPHAGEAL VARICES WITH BLEEDING IN DISEASES<br>EC | G852000 |
| TANNER DEVASCULARISATION FOR BLEEDING<br>VARICES    | 7609y11 |

I assigned a date of entry to each stage as the earliest date of any recorded code contained within each stage including data collected in the pre-UTS period. Cases were then assigned a stage of entry into the study as the earliest of these 4 stages. Due to the nature of the original extraction of cases with cirrhosis (including therapeutic or diagnostic codes for oesophageal varices and codes for portal hypertension) it was possible for a case to enter this study at a stage later than stage 1. It was also possible for a case to have a code for an early stage subsequent to a code for a later stage. For example, if a case had a code for stage 1 subsequent to a code for stage 3 the case would be assigned an entry stage as stage 3 and would not be included in stage 1 or 2 at any point in the analysis.

Compensated cirrhosis was then defined as patients when in either of stages 1 and 2 with decompensated cirrhosis as stages 3 and 4.

To minimise the potential for misclassification of patients with decompensated cirrhosis as patients with compensated disease I additionally looked for recording of one or more prescriptions for spironolactone as evidence for decompensation.

### **5.2.3 Statistical analysis**

I examined the probabilities of patients with cirrhosis progressing from an individual stage to a subsequent stage or death within one year and state progressions across the whole time period of their records. 95% CIs were calculated using the binomial distribution. I calculated the proportion of GI bleed that was coded as oesophageal bleeding.

As mortality was seen to vary substantially by presumed aetiology (see section 4.3.2.4) I also then stratified the cohort into those with alcoholic cirrhosis and those with non-alcohol related cirrhosis.

Using Cox proportional hazards I modelled the rate of decompensation in the group of patients with compensated disease. Subjects entered the analysis period at the date of earliest recorded code for stage 1 or 2 and exited at the earliest of either date of earliest recorded code for stage 3 or 4, date of death, date of deregistration with their general practice or 30 April 2002 which was the last date of available data in this dataset. Again, I examined progression for subjects with alcoholic cirrhosis and those with non-alcohol related cirrhosis. Follow-up time was split at 1 year and I modelled the rate of decompensation during the first year after diagnosis and subsequent to that first year again stratifying by presumed aetiology.

### 5.3 Results

Of the 4,537 patients identified with cirrhosis, 66.0% entered the study cohort at stage 1, 14.6% at stage 2, 10.5% at stage 3 and 8.8% at stage 4.

Of the 877 patients considered decompensated at entry 71% had evidence of spironolactone use at any point in their record compared with 43% of subjects considered compensated (at entry). Of the 3660 patients considered compensated at entry, 505 (13.8%) had evidence of a prescription of spironolactone occurring before a recording of decompensation within their GPRD record. Of the patients with a record of GI bleed at any point in their record, for only 7.4% of these patients was this specified as oesophageal bleeding.

Outcome probabilities in the first year are shown in Figure 5-1. Patients in stage 1 and 2, i.e. compensated cirrhosis, had a one-year probability of proceeding directly to death of just over 10%. The mortality in patients in stage 3 and 4, i.e. decompensated cirrhosis, was much higher with 25.9% and 18.2% respectively of patients proceeding directly to death.

State progressions across the whole study period are shown in Figure 5-2. Of note is the high proportion of people in the early stages of disease i.e. patients with compensated cirrhosis, who progressed directly to death without the recording of other clinical symptoms of decompensation.

The probability of progressing both during the first year and state progressions subsequently for those with alcoholic cirrhosis and non alcohol-related cirrhosis are shown in Table 5-5 and Table 5-6 respectively. Reading across the table shows the stage at which patients began their follow-up. The rows in the column represent the stage to which the patients directly progressed. For

example looking at the first column we can see that alcoholics who began follow-up in stage 1 had a 74.4% chance of remaining in stage 1 during the first year, with 4.0% progressing directly to stage 2 (oesophageal varices), and so on. In the first year following diagnosis patients with alcoholic cirrhosis had a slightly higher probability of progressing to another stage of cirrhosis than those with non-alcohol related cirrhosis but a lower probability of progressing directly to death. Across the whole study period patients with a presumed aetiology of alcoholic cirrhosis were again more likely to progress to another later stage of cirrhosis than those with non-alcohol related cirrhosis. The differences in progression directly to death were not so marked across the whole time period, rather less patients with alcoholic cirrhosis remained in their entry stage with the exception of patients in stage 3.

Overall, the rate of decompensation for those patients with compensated disease was 5.5% per year (95%CI[5.1%, 5.9%]). As might be expected (following the results in Chapter 4 and those reported above) this figure varied considerably both by length of follow-up and by presumed aetiology.

During the first year after diagnosis the rate of decompensation for those patients with a presumed aetiology of alcoholic cirrhosis was 16% (95%CI [14.1%, 18.3%]) compared with only 9.7% (95%CI [8.2%, 11.4%]) for those with non-alcohol related cirrhosis.

Following the first year the rate of decompensation did not vary much by presumed aetiology with a rate of 3.8% per year (95%CI [3.3%, 4.4%]) for those with alcoholic cirrhosis compared with a rate of decompensation of 3.0% per year (95%CI [2.6%, 3.6%]) for those with non-alcohol related cirrhosis.

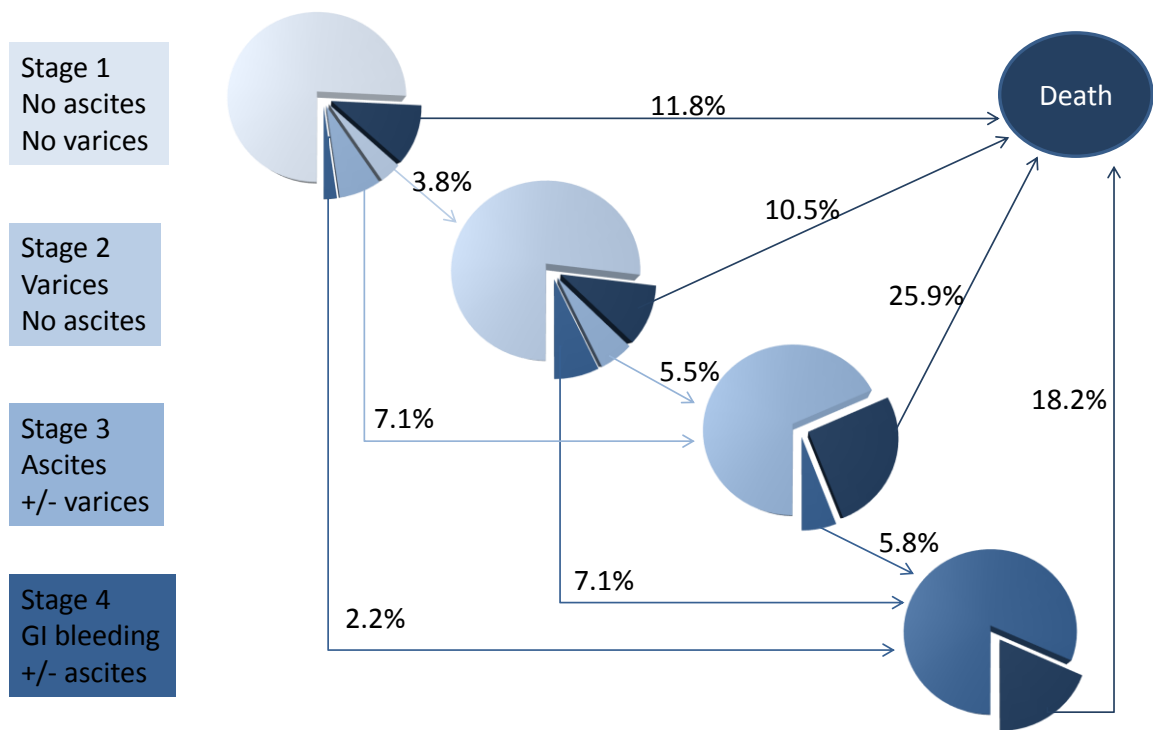


Figure 5-1 Probabilities for progression within one year, all patients

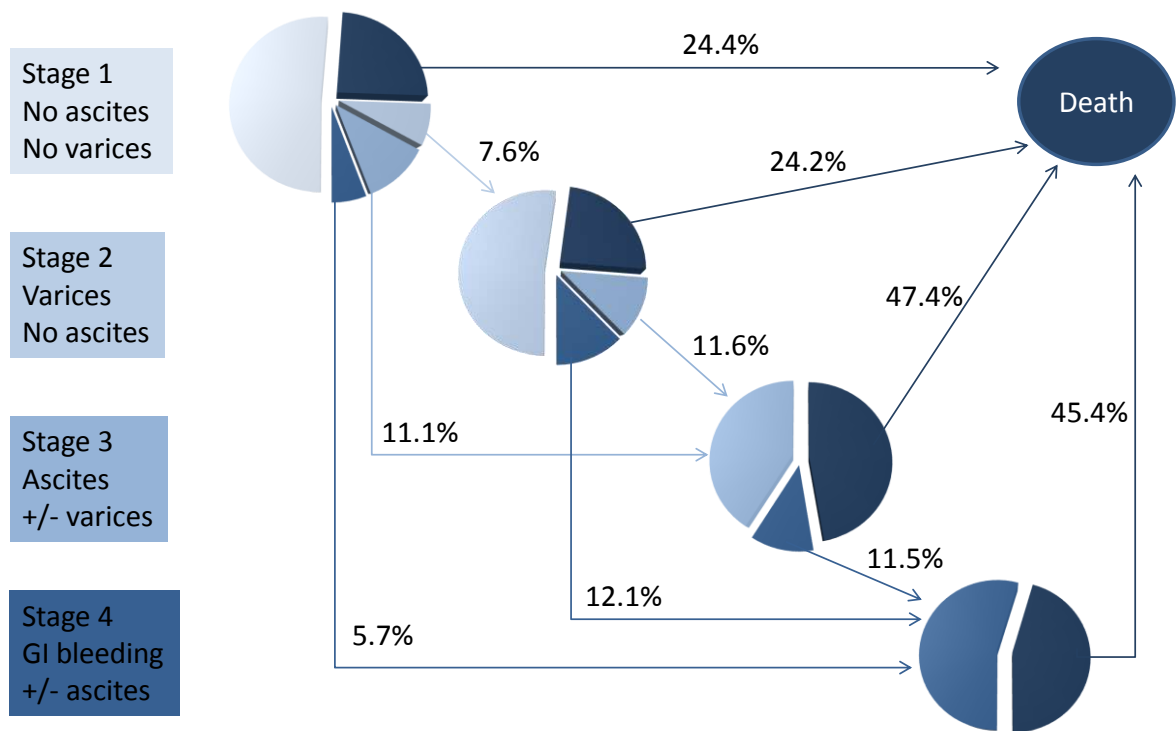


Figure 5-2 State progression across whole record, all patients



Table 5-5 Probability of progression in first year, patients with alcoholic and non-alcohol related cirrhosis

|                                       |         | Stage from           |                      |                      |                      |                      |                      |                      |                      |
|---------------------------------------|---------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|                                       |         | Stage 1              |                      | Stage 2              |                      | Stage 3              |                      | Stage 4              |                      |
|                                       |         | Alcoholic            | Non-alcohol related  | Alcoholic            | Non-alcohol related  | Alcoholic            | Non-alcohol related  | Alcoholic            | Non-alcohol related  |
| Progression directly to / remained in | Stage 1 | 74.4<br>[72.2, 76.5] | 77.4<br>[75.1, 79.5] | -                    | -                    | -                    | -                    | -                    | -                    |
|                                       | Stage 2 | 4.0 [3.1, 5.1]       | 3.6 [2.7, 4.7]       | 74.0<br>[69.0, 78.6] | 78.8<br>[75.1, 82.2] | -                    | -                    | -                    | -                    |
|                                       | Stage 3 | 8.6 [7.2, 10.1]      | 5.5 [4.4, 6.9]       | 6.2 [3.9, 9.3]       | 5.0 [3.3, 7.2]       | 72.7<br>[68.8, 76.4] | 61.7<br>[56.5, 66.7] | -                    | -                    |
|                                       | Stage 4 | 3.2 [2.3, 4.1]       | 1.1 [0.7, 1.8]       | 9.4 [6.5, 13.1]      | 5.6 [3.8, 7.9]       | 7.0 [5.0, 9.4]       | 4.1 [2.3, 6.6]       | 83.5<br>[79.5, 86.9] | 79.6<br>[74.8, 83.8] |
|                                       | Death   | 9.9 [8.5, 11.5]      | 12.3<br>[10.7, 14.2] | 10.3 [7.3, 14.1]     | 10.6 [8.1, 13.5]     | 20.3<br>[17.0, 24.0] | 34.2<br>[29.4, 39.3] | 16.5<br>[13.1, 20.5] | 20.4<br>[16.2, 25.2] |

Table 5-6 State progression across whole record, patients with alcoholic and non-alcohol related cirrhosis

|                                       |         | Stage from           |                      |                       |                      |                      |                      |                      |                      |
|---------------------------------------|---------|----------------------|----------------------|-----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|                                       |         | Stage 1              |                      | Stage 2               |                      | Stage 3              |                      | Stage 4              |                      |
|                                       |         | Alcoholic            | Non-alcohol related  | Alcoholic             | Non-alcohol related  | Alcoholic            | Non-alcohol related  | Alcoholic            | Non-alcohol related  |
| Progression directly to / remained in | Stage 1 | 47.4<br>[44.9, 49.9] | 55.4<br>[52.8, 58.0] | -                     | -                    | -                    | -                    | -                    | -                    |
|                                       | Stage 2 | 8.1 [6.8, 9.5]       | 7.1 [5.8, 8.6]       | 47.2<br>[41.8, 52.7]  | 55.2<br>[50.9, 59.5] | -                    | -                    | -                    | -                    |
|                                       | Stage 3 | 13.2<br>[11.6, 15.0] | 8.8 [7.4, 10.4]      | 13.6 [10.1, 17.7]     | 10.4 [8.0, 13.3]     | 45.2<br>[41.0, 49.5] | 35.1<br>[30.2, 40.2] | -                    | -                    |
|                                       | Stage 4 | 6.8 [5.6, 8.2]       | 4.4 [3.4, 5.6]       | 15.3<br>[11.7, 19.6]  | 10.0 [7.6, 12.9]     | 13.2<br>[10.5, 16.3] | 9.0 [6.3, 12.4]      | 54.7<br>[49.8, 59.5] | 54.5<br>[48.9, 60.0] |
|                                       | Death   | 24.5<br>[22.4, 26.7] | 24.3<br>[22.1, 26.6] | 23.9<br>[19.35, 28.8] | 24.3<br>[20.8, 28.2] | 41.6<br>[37.4, 45.8] | 56.0<br>[50.7, 61.1] | 45.3<br>[40.5, 50.2] | 45.5<br>[40.0, 51.1] |

## **5.4 Discussion**

### **5.4.1 Key findings**

Using the clinical observations recorded in the primary care records of people with cirrhosis I have described the progression of disease as experienced by patients and as recorded by primary care physicians in the UK. The presence of ascites rather than GI bleed appears to represent a more serious marker of mortality within the first year following diagnosis.

Overall the rate of decompensation was 5.5% per year (95%CI[5.1%, 5.9%]).

The rate of decompensation varied considerably by presumed aetiology of cirrhosis with alcoholic cirrhosis conferring a worse prognosis in the first year following diagnosis (16% versus 10%). These differences were largely removed following this first year and the rate of decompensation was approximately 3-4% per year for all patients.

### **5.4.2 Strengths and limitations**

This study has tried to utilise a recognised staging system of cirrhosis and apply its definitions to a cohort of patients whose data are recorded in primary care. The usefulness of a staging system such as this, particularly one with no reliance on laboratory measurements, allows for a simpler identification of patients at a higher risk of progression and/or mortality and the easier communication of this risk to patients and their families.

This study is three times the size of that of the previous study upon which the Baveno IV consensus stages were derived and on which I have based my methodology. The inclusion of patients who did not necessarily have to be hospitalised in this study means that the results are perhaps more relevant to

those ambulatory patients, as would be being seen in primary care and outpatients clinics, than previously available figures. By virtue of the size of this study it was possible to stratify the probabilities of progression by presumed aetiology.

The principal limitation with this study, similar to that with the previous two studies, is that of the diagnosis and recording of the symptoms of cirrhosis that define the staging. The cost of requesting records of patients within each stage means that I was unable to validate the specific stages of cirrhosis in this cohort. Within the GPRD itself there is insufficient data to assess what level of follow-up was being performed for an individual patient. It is probable that many patients in stage 1 were not undergoing regular screening endoscopies for the presence of oesophageal varices and so the probability of progressing from stage 1 to stage 2 is therefore underestimated with oesophageal varices perhaps only being recorded if they had led to a bleed. Similarly it is possible that only more severe bleeds are being recorded if a patient was not undergoing regular screening endoscopies. It is additionally possible that those patients who died in hospital following bleeding oesophageal varices (or indeed any other sort of GI bleed) had the fact of death communicated to the GP but not the circumstances leading up to it. For this reason it is possible that the progression to stage 4, and the probability of proceeding from stage 4 to death is underestimated within these data. These limitations in the validity of the staging system could also lead to an overestimate in the progression directly to death for earlier stages. However, I would argue that the figures I have reported represent the 'real-life' situation of what is identified and communicated regardless of the variation in the follow-up of patients that may exist in different regions or indeed individual hospitals. These figures are therefore a useful adjunct to other available data for the

communication of risk to patients in both the primary care and outpatient settings.

I was not able to calculate other more commonly used measures of severity of disease such as the Child-Pugh score or MELD score as the blood indices required for the calculation of these scores were not available in the data. There are however limitations in these scores, particularly the speed with which it is possible to calculate a Child-Pugh or MELD score and the day-to-day clinically observed variations in blood measurements that may cause a significant change in the scores (particularly with respect to creatinine and prothrombin time). These scores are also more difficult to communicate in a meaningful way to most patients where the presence or absence of clinical symptoms is likely to be more readily understood. Indeed a considerable wealth of literature exists suggesting that rather than a measure of individual risk patients are more likely to comprehend figures which are described in terms of the proportions of patients likely to experience an outcome.<sup>95</sup> These sorts of figures can easily be extracted from the results reported above e.g. if a patient has been diagnosed with alcoholic cirrhosis in stage 1 it would be possible to communicate to that patient 'In the first year following diagnosis with alcoholic cirrhosis, such as yourself, 3 in 4 patients will remain in this disease stage and not experience any further sequelae. The other 1 in 4 patients will experience some further symptoms including varices, ascites, bleeding and 1 in 10 may even die within a year' or similar.

With respect to the presumed aetiology of cirrhosis there are potential limitations in the methods I have employed to assign the cause of cirrhosis as described in section 3.4.2. The likelihood of misclassifying patients with alcoholic cirrhosis as non-alcohol related cirrhosis could lead to an

underestimate of the true progression associated with an aetiology of alcoholic cirrhosis and a corresponding overestimate of the progression associated with non-alcohol related cirrhosis. Again, owing to the relatively small number of patients with other known aetiologies (viral hepatitis, autoimmune liver disease or metabolic liver disease) it was not possible to describe the progression of these patients with precision.

### **5.4.3 Comparison with previously published work**

In this study I have attempted to replicate a staging system for cirrhosis adopted at the Baveno IV consensus conference.<sup>94</sup> These stages are based on data from a single hospital in Sicily in the 1970s and 1980s, published as one paper and one abstract.<sup>44 96</sup> The two studies were aggregated and the 1-year outcome probabilities were published in a systematic review looking at prognostic indicators of survival in cirrhosis.<sup>55</sup> The methods for calculating the 1-year outcome probabilities are uncertain as there are no methods included in this latter paper. Going back to the original paper and the abstract, 1-year outcome probabilities for the occurrence of oesophageal varices were calculated as cumulative 10-year progression divided by 10 to get the annual progression, with the methods for progression to other states not clarified. Progression is not necessarily uniform across time, particularly not within the first year as I have demonstrated with my data, and as such the validity of these widely referenced figures is somewhat questionable. Bearing in mind the limitations of the description of the methods employed to calculate data, the 1-year progression probabilities described by D'Amico and colleagues are the most logical comparison for my results and are displayed in Table 5-7.

**Table 5-7 Probability of progression in cirrhosis**

as reported in D'Amico G, Garcia-Tsao G, Pagliaro L. 'Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies' J Hepatol (2006)44(1):217-231

|                |         | Progression from |         |         |         |
|----------------|---------|------------------|---------|---------|---------|
|                |         | Stage1           | Stage 2 | Stage 3 | Stage 4 |
| Progression to | Stage 1 | 88.6%            | -       | -       | -       |
|                | Stage 2 | 7%               | 86%     | -       | -       |
|                | Stage 3 | 4.4%             | 6.6%    | 72.4%   | -       |
|                | Stage 4 | 0%               | 4%      | 7.6%    | 43%     |
|                | Death   | 1%               | 3.4%    | 20%     | 57%     |

In terms of mortality my results show a much higher progression to death from both stage 1 and stage 2 but a very much lower progression to death from stage 4. Aside from the possible methodological considerations there are probably two principal reasons for these observed differences. Firstly, as described above it is possible that without regular follow-up there is misclassification of patients as stage 1 when in fact they have already reached a later stage, but that this has not been diagnosed or has not been reported back to primary care and therefore is not recorded in the GPRD. However, as we do not know the exact methods of follow-up in the Sicilian population (the abstract references patients undergoing 'endoscopy at 1-3 year intervals or at bleeding')<sup>96</sup> it is not conclusive that it is difference in follow-up that would have led to these differences in reported survival. Secondly, it is possible that the composition of the cirrhosis cohorts in this earlier study and in my study have significant differences in aetiology. Indeed the population of Sicily has a much higher prevalence of hepatitis than I have reported in my data. Given that patients with alcoholic cirrhosis appear to have a worse prognosis (as seen from my data) it is possible that this discrepancy in survival for compensated patients is a reflection of the large proportion of alcoholic cirrhosis within the UK population who fare worse than those with an aetiology of non-alcohol related cirrhosis.

The observation that the presence of ascites rather than GI bleed seems to confer a greater risk of mortality within the first year is in contrast to those data from Sicily. However, given that the main period of data collection is some 20 years later, it is probable that the patients included in my study have had available to them many of the clinical improvements in the management of variceal bleeding that were not likewise available for those people in the earlier study. These improvements include endoscopic sclerotherapy, endoscopic ligation, medications such as vasopressin, somatostatin and octreotide, all of which are likely to have been available during the period of my study but not for the patients in the study in Sicily.<sup>97</sup> Indeed, three relatively recent papers from the USA, France and Sweden report improved survival after oesophageal variceal bleeding.<sup>58 59 60</sup> However, the overall mortality from GI bleeding in my data is still lower than the 579 days median survival reported in the US for patients hospitalized with an oesophageal bleed in 1988-91,<sup>58</sup> or the 1-year mortality of over 50% reported in Sweden for patients discharged between 1990-2002 after a diagnosis of oesophageal varices.<sup>60</sup> Gastrointestinal bleeding is multi-factorial and it is possible that the bleeding I have identified and included in my study is not as severe as the bleeding reported in these previous studies. Indeed only 7.4% of the bleeding identified was recorded as variceal in origin.

The 1-year probability of progression from stage 1 to stage 2 of 3.8% though similar to that seen in some studies describing the yearly 'incidence' of varices<sup>98 99</sup> is lower than that reported in most studies looking at the natural history of cirrhosis including the study from Sicily.<sup>55 100 101 102</sup> This is quite likely to be due to the fact that we do not know what, if any, level of endoscopic surveillance was being undertaken on these patients. There was



no definitive screening guideline in place in the UK at the time of data collection and as such I will likely have an underestimate of the progression from stage 1 to stage 2 (as discussed in section 5.4.2). However, if I include the 2.2% of patients who progressed directly from stage 1 to stage 4 i.e. identification of bleeding without prior identification of varices, assuming all these bleeds were of variceal origin, the progression to varices becomes quite similar, at 6%. Inevitably, in the absence of routine screening endoscopies, some varices will be identified only if they bleed.

The 1-year progression to stage 3 from either stage 1 or stage 2 (cumulative progression 12.6%) was similar to the 11% observed by D'Amico and colleagues.<sup>55</sup> Studies looking at populations with a high proportion of viral cirrhosis report variable rates of progression to ascites with 5-year incidence of only 11%<sup>103</sup> and 24.8%.<sup>101</sup> The study by Benvegnu et al. showed that alcohol abuse was associated with a higher incidence of ascites compared with those with no history of alcohol abuse.<sup>103</sup> Overall progression to ascites in my study with over half of the study population having a presumed aetiology of alcoholic cirrhosis was 22.7%. Progression to ascites was higher in those with alcoholic cirrhosis than those with non-alcohol related cirrhosis both within the first year and throughout the study period.

Progression to stage 4 (GI bleeding) within the first year following diagnosis is slightly higher in my study than that reported by D'Amico and colleagues<sup>55</sup> but is consistent with the 24% bleeding rate at 2 years from two earlier studies.<sup>104</sup>

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It is possible to compare the prognosis figures for patients with alcoholic cirrhosis directly to a study conducted in Denmark and reported in 2009.<sup>56</sup>

The authors report on 449 patients with alcoholic cirrhosis diagnosed and followed up between 1993 and 2005 in a single hospital centre. The 1-year progression directly to death in this hospital was 10% for those with no reported complications, almost identical to the 9.9% I saw in my study. The 1-year progression directly to death for patients with clinical symptoms of ascites and variceal bleeding was 15% and 11% respectively, slightly lower than the figures I reported for stage 3 and stage 4 (20.3% and 16.5%) although the confidence intervals around these point estimates do overlap. Perhaps unsurprisingly, this study reported that the complications of cirrhosis do not develop in such a well-determined order as put forward by the staging system I have tried to replicate with ascites reported as the most frequent first complication (in 12% of patients) but nearly as many (10% in total) developing variceal bleeding (6%) or hepatic encephalopathy (4%) as their first complication. There are no such comparable figures for patients with non-alcohol related cirrhosis although the work from D'Amico and colleagues is probably more likely to reflect non-alcohol related cirrhosis given the high proportion of hepatitis in that population.<sup>55</sup>

#### **5.4.4 Conclusions**

This study has described the clinical progression following a diagnosis of cirrhosis as recorded in contemporary clinical practice in primary care.

The figures based on this relatively simplistic staging system are potentially more relevant and readily understood by those living with cirrhosis and those communicating risk to these patients.

This study is the first (to my knowledge) to describe the rate of decompensation in patients with compensated disease stratified by aetiology and shows a significantly higher rate of decompensation for those with alcoholic cirrhosis in the first year compared to those with non-alcohol related cirrhosis. These figures will be of use to service providers to factor in the aetiology of cirrhosis in the planning of therapies, interventions and follow-up as well as to individual clinicians and their patients to enable a clearer understanding of the likely clinical course of this disease.

## **6 The “MRC Elderly” Database**

This chapter provides an overview of the “MRC Elderly” database, its data format, its strengths and weaknesses particularly with reference to the studies in chapters 7 through 9 and details regarding the data used for studies contained within these three chapters. Additional study-specific information on the exact data used is detailed in the methods section of each individual chapter.

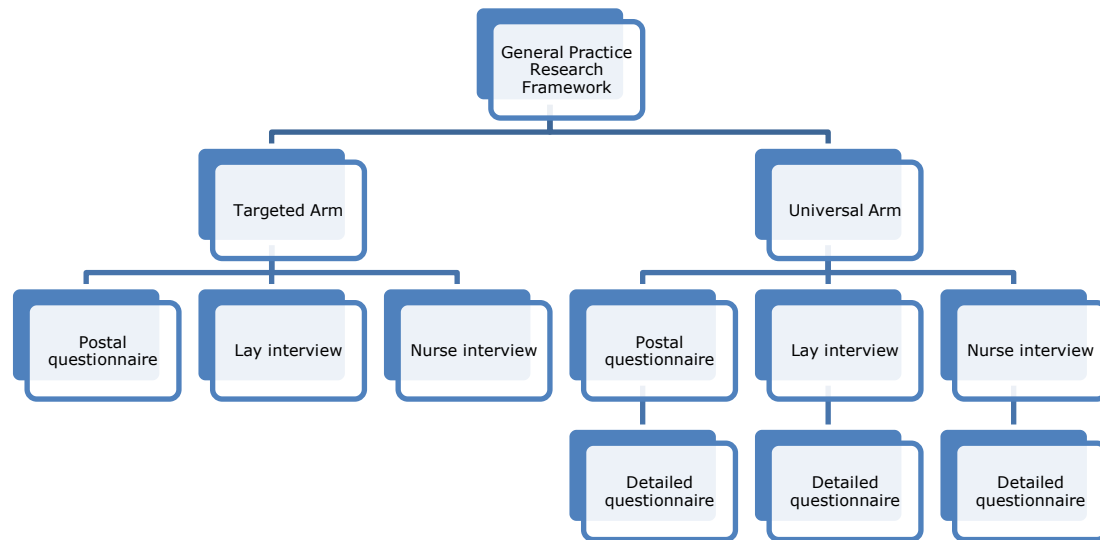
### **6.1 Original data collection**

These studies utilise data collected as part of the Medical Research Council (MRC) Trial of Assessment and Management of Older People in the Community which has been reported on previously.<sup>106 107 108</sup> Briefly, practices within the MRC General Practice Research Framework with list sizes of between 200 and 700 patients aged 75 and over, selected to represent the population of the UK based on mortality (SMRs) and deprivation (Jarman score), were eligible to be randomised into the trial. In total, 109 practices were invited to participate in the trial and a final total of 106 practices provided data.

All people aged 75 or over registered with the selected general practices, non-resident in nursing homes, and who were not known to be terminally ill, were eligible for inclusion in the data collection which comprised two arms comparing multi-dimensional assessment of the elderly. The first arm (universal arm) invited all patients to an in-depth health assessment whilst the second arm (targeted arm) invited only selected patients.

Recruitment and data collection took place between 1995 and 1999. Local Research Ethics Committee approvals were obtained for each participating practice.

All participants in the original trial received a brief assessment of health covering all areas included within the GP contract<sup>109</sup> with data collected either at interview with a lay person, at interview by a study nurse or by postal questionnaire (see Figure 6-1). Following this brief assessment subjects in the universal arm of the trial had a detailed nurse assessment covering these same areas but in more detail. Additional biological measurements were made, including blood pressure and heart rate, and participants had a blood sample taken for a biochemical screen including measurements of serum aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin. The studies described in chapters 7-9 utilise data collected from participants within the universal arm of the trial only.



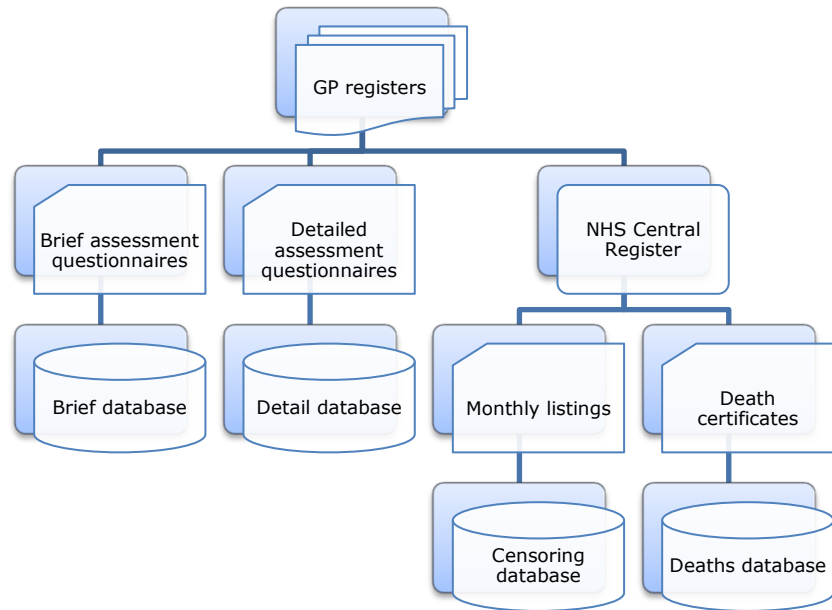
**Figure 6-1 Design of the MRC trial of assessment and management of older people in the community**

## **6.2 Data flow**

Data flow was initiated following the recruitment of participants from general practices registered as part of the MRC General Practice Research Framework. All participants then had information recorded from the brief assessment questionnaires stored in the 'brief' database. All data collected during the detailed assessment were stored in the 'detail' database.

All participants in the trial were registered with the NHS central register (NHSCR) and listings of events including death, embarkation, registration with the armed services, 'cancellations' (when a patient can no longer be contacted at a particular general practice the NHSCR will mark the record as 'cancelled' until such time as the patient transfers to another GP or a death occurs and can be traced to that individual) and re-entries were received on a monthly basis. All 'non-death' events were stored in the 'censoring' database. Death certificates were also received on a monthly basis with coded cause of death and date of death recorded in the 'deaths' database.

A schematic diagram of the data flows is shown in Figure 6-2.



**Figure 6-2 Data repositories and information flow in the MRC elderly study**



### **6.3 Strength and weaknesses**

The “MRC Elderly” is a useful resource for descriptive epidemiology and has recently been utilised to describe kidney disease in older people.<sup>110</sup> However, as with any database there are limitations to its usefulness which should be considered. The relative merits and limitations of the “MRC Elderly” database, particularly with reference to studies of liver function, are discussed below.

#### **6.3.1 Representative**

The cluster randomised nature of the initial study means that participants included in the universal arm of the trial (and therefore the subjects in my following studies) were chosen in a way which is representative of the population of the UK with respect to mortality and deprivation. The subsequent exclusion of patients who were in long-term care or those with terminal illness should mean that the results of these subsequent studies can be generalised to the ambulatory, non-terminally ill population of the UK aged 75 and over.

#### **6.3.2 Availability of data on liver function tests**

All participants in the universal arm had a blood sample taken with several biochemical markers examined including three markers commonly used in the assessment of liver function, namely serum aspartate transaminase (AST), alkaline phosphatase (ALP) and bilirubin. As these data are being used as a secondary source and there was no opportunity for further data collection from the participants there are certain data items that are not available that would have been desirable if setting up this study specifically to look at liver function

tests. These include particular biochemistry markers e.g. alanine aminotransferase, INR or pro-thrombin time, and also potential confounders such as the diagnosis of recognised liver disease.

### **6.3.3 Follow-up**

Follow-up of the “MRC Elderly” cohort for the principal event of interest of death was well executed through the flagging with the NHSCR and continues to be updated. At the time of data extraction for these studies death data were available up until 5 November 2005. With death being a common event in a population of people aged 75 and over this gives the study good power to examine the association between elevated liver function tests with mortality.

## **6.4 Data used for chapters 7-9**

For the purposes of the following studies I obtained data on those subjects from 53/106 general practices which comprised the universal arm. This included all of the information from the detailed nurse interview, including blood test results, and separate data files from the NHSCR giving information on the subjects within the study who had subsequently died or migrated. Details on the exact data used for each study are described in the appropriate chapter.

## **7 Prevalence of elevated liver function tests in the elderly**

### **7.1 Introduction**

This study aims to estimate the prevalence of elevated liver function tests in a sample of people aged 75 and over resident in the UK.

### **7.2 Methods**

#### **7.2.1 Data set used**

The data used in this study are those from the detailed nurse assessment contained within the 'detail' database (see Figure 6-2). A total of 15,308 participants aged 75 and over are included in the subsequent analyses.

#### **7.2.2 Imputation of laboratory reference ranges**

In order to assess the prevalence of elevated liver function it is necessary to have an agreed cut off limit or definition for abnormality. However, there was no standard definition of abnormality in use at the time of data collection for any of the three tests that I was interested in. Different laboratories used different assays and these were calibrated individually and hence had different designated limits of normality. In addition, reference ranges were frequently set at different levels for males and for females.

Reference ranges for the upper and lower limits of normal tests were not collected at the time of the study and, following requests after the completion of the study, only half of the practices involved had any recorded reference

ranges for the three liver function tests I was interested in. For those practices where I did not have a provided reference range it was therefore necessary to impute a sensible value to use as a cut off for limits of normality.

To do this I examined the distribution of the values of the upper and lower limits of normal for the laboratories which had provided reference ranges. Where the distribution of tests appeared to be unimodal I inferred that there was broadly one standard test in operation for the particular test. Where the distribution of tests appeared to be bimodal I inferred that there were two standard tests operating in parallel. This assumption was discussed with clinical colleagues using these tests throughout the time period of the data collection and was agreed to be representative of laboratory practices at that time. Practices were assigned to either the lower or upper test limit depending on the median value of test results from participants within that practice.

For those practices where information on reference ranges was provided these values were used. For practices without reference ranges I derived three sets of upper limits:

1. Upper limit based on the median values given for those practices for which information was already available.
2. Upper limit based on the minimum upper limit for those practices for which information was already available – this provides an estimate of the maximum number of abnormal test results.
3. Upper limit based on the maximum upper limit for those practices for which information was already available – this provides an estimate of the minimum number of abnormal test results.

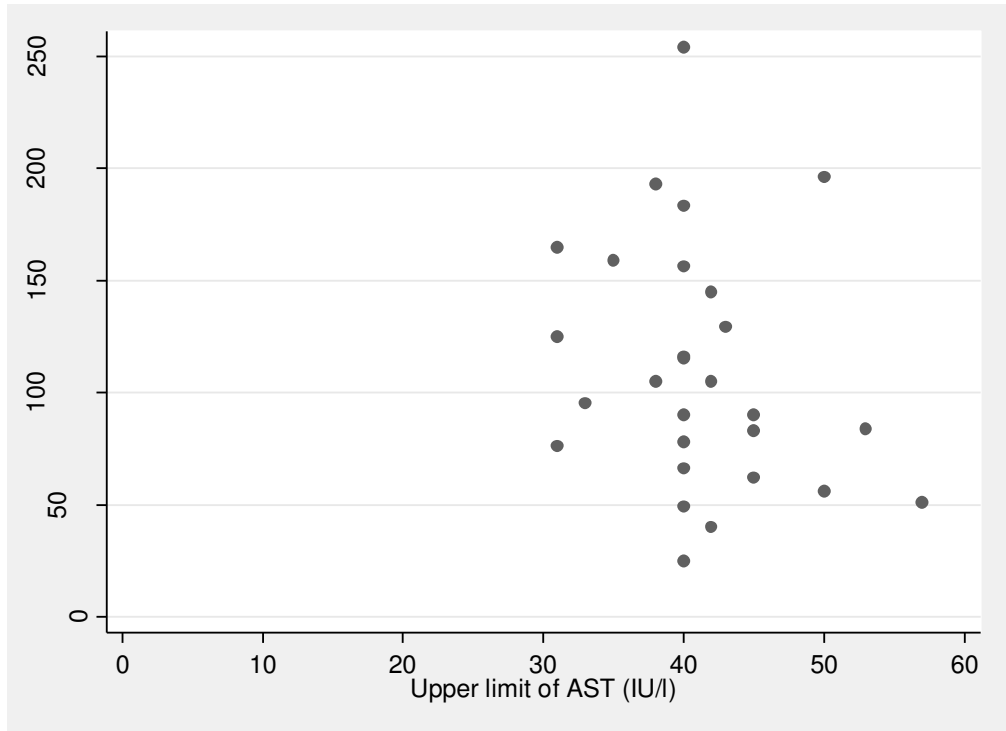
### 7.2.2.1 AST

A total of 28/53 (53%) practices had some information recorded on AST reference ranges. All reference ranges provided were for adults of all ages. Some practices provided different reference ranges dependent on the sex of the patient. It was therefore necessary to impute value for upper limits for men and women for 25 practices without a given reference range. Graphical representation of the upper limits showed the distributions of the upper limits to be largely unimodal around 40IU/l for both males and females (see Figure 7-1 for males; same distribution seen for females (not shown)). Interrogation of the actual test results showed a similar unimodal distribution of the median values by practice (see Figure 7-2).

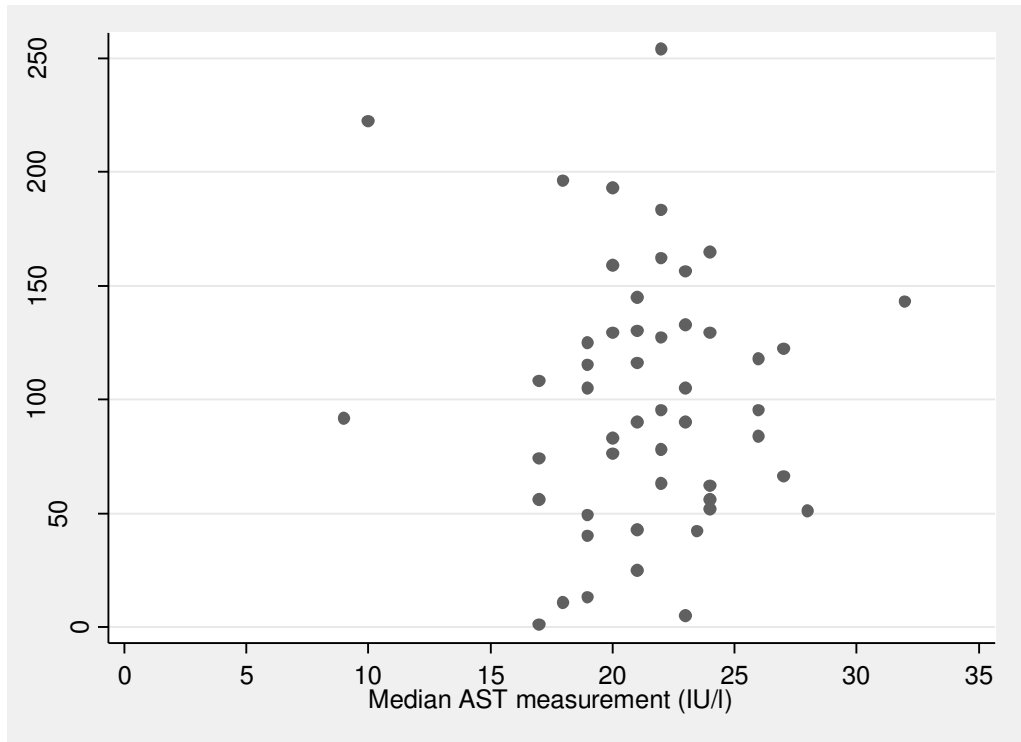
I therefore inferred that there was only one primary test in operation for AST among the practices included in the trial at the time these data were collected. Summary statistics on the distribution of given reference ranges can be seen in Table 7-1.

For practices without reference ranges the three sets of upper limits imputed were:

1. Based on the median values – 40IU/l for both males and females.
2. Based on the minimum upper limit – 31IU/l for males, 30IU/l for females.
3. Based on the maximum upper limit – 57IU/l for males, 53IU/l for females.



**Figure 7-1 Graphical representation of upper limits of reference range for AST test by size of practice (males only)**



**Figure 7-2 Graphical representation of median AST test measurements by size of practice (males only)**

**Table 7-1 Lower and upper limits of normal range of AST**

|         |             | <b>Number of<br/>practices</b> | <b>Median<br/>[IQR] (IU/l)</b> | <b>Range<br/>(IU/l)</b> |
|---------|-------------|--------------------------------|--------------------------------|-------------------------|
| Males   | Lower limit | 20                             | 10 [0.5, 11]                   | 0-20                    |
|         | Upper limit | 28                             | 40 [39, 44]                    | 31-57                   |
| Females | Lower limit | 20                             | 5 [0.5, 10]                    | 0-15                    |
|         | Upper limit | 28                             | 40 [35, 42]                    | 30-53                   |



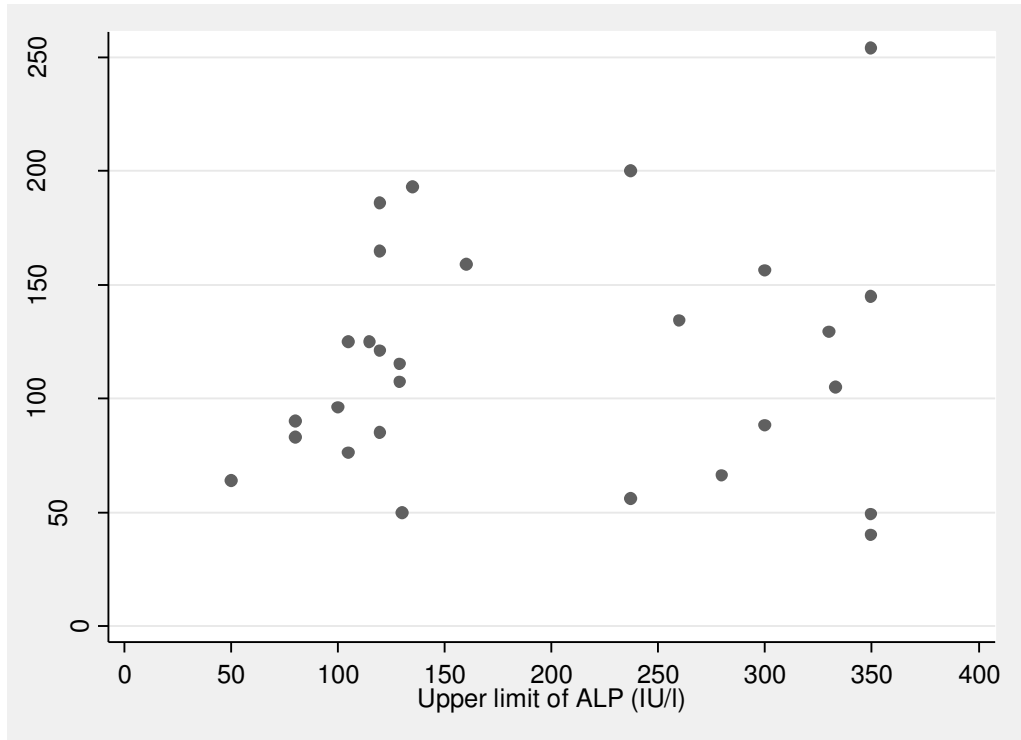
### 7.2.2.2 ALP

A total of 28/53 (53%) practices had some information recorded on ALP reference ranges. Reference ranges provided were for adults of all ages or for adults aged 60 and over. Some practices provided different reference ranges dependent on the sex of the patient. It was therefore necessary to impute upper limits for 25 practices without a given reference range. Graphical representation of the upper limits showed the distributions to be bimodal with one peak at around 110IU/l and another at around 300IU/l for both males and females (see Figure 7-3 for males; same distribution for females (not shown)). Interrogation of actual test results showed a similar bimodal distribution of the median values by practice (see Figure 7-4). I therefore inferred that there were two primary tests in operation for ALP among the practices included in the trial at the time these data were collected. Practices without reference ranges were assigned to the lower or higher test based on the median of actual test results of the participants within the practice. Summary statistics on the distribution of given reference ranges for the lower and higher test can be seen in Table 7-2 and Table 7-3 respectively.

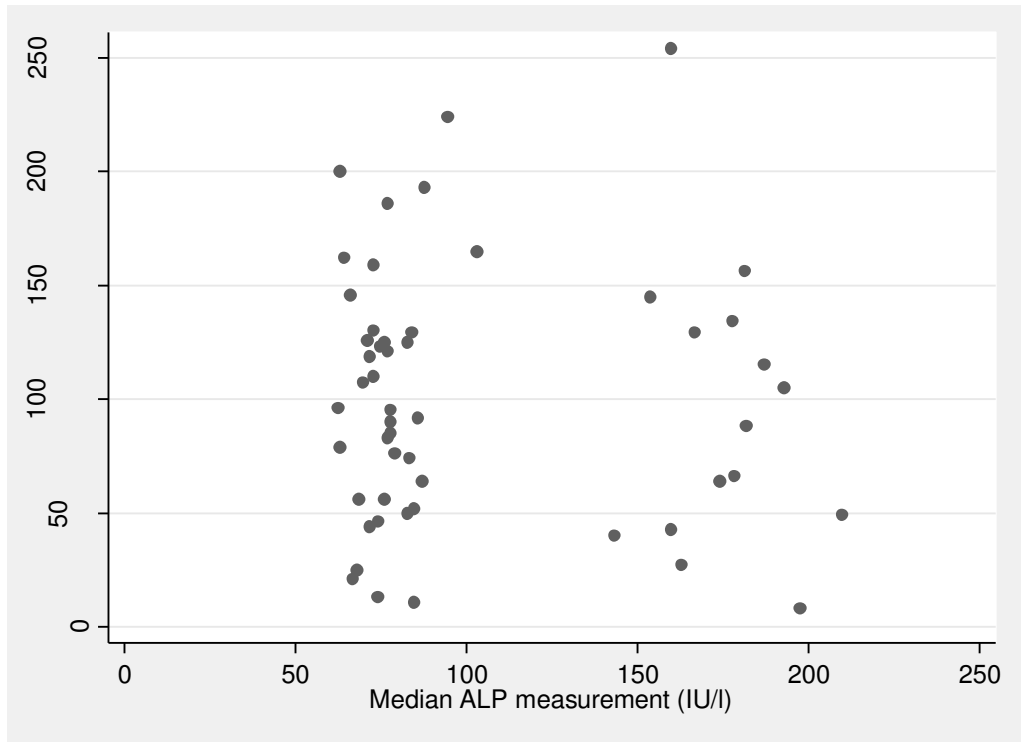
For practices without reference ranges the three sets of upper limits imputed were:

1. Based on the median values – 120IU/l for both males and females in lower test group; 330IU/l for both males and females in higher test group.
2. Based on the minimum upper limit – 50IU/l for both males and females in lower test group; 129IU/l for males and 104IU/l for females in higher test group.

3. Based on the maximum upper limit – 237IU/l for both males and females in lower test group; 350IU/l for both males and females in higher test group.



**Figure 7-3 Graphical representation of upper limits of reference range for ALP test by size of practice (males only)**



**Figure 7-4 Graphical representation of median ALP test measurements by size of practice (males only)**

**Table 7-2 ALP Lower test – known reference ranges**

|         |             | <b>Number of<br/>practices</b> | <b>Median<br/>[IQR] (IU/l)</b> | <b>Range<br/>(IU/l)</b> |
|---------|-------------|--------------------------------|--------------------------------|-------------------------|
| Males   | Lower limit | 17                             | 30 [25, 35]                    | 0-40                    |
|         | Upper limit | 17                             | 120 [105, 130]                 | 50-237                  |
| Females | Lower limit | 17                             | 30 [25, 35]                    | 0-40                    |
|         | Upper limit | 17                             | 120 [105, 135]                 | 50-237                  |

**Table 7-3 ALP Higher test – known reference ranges**

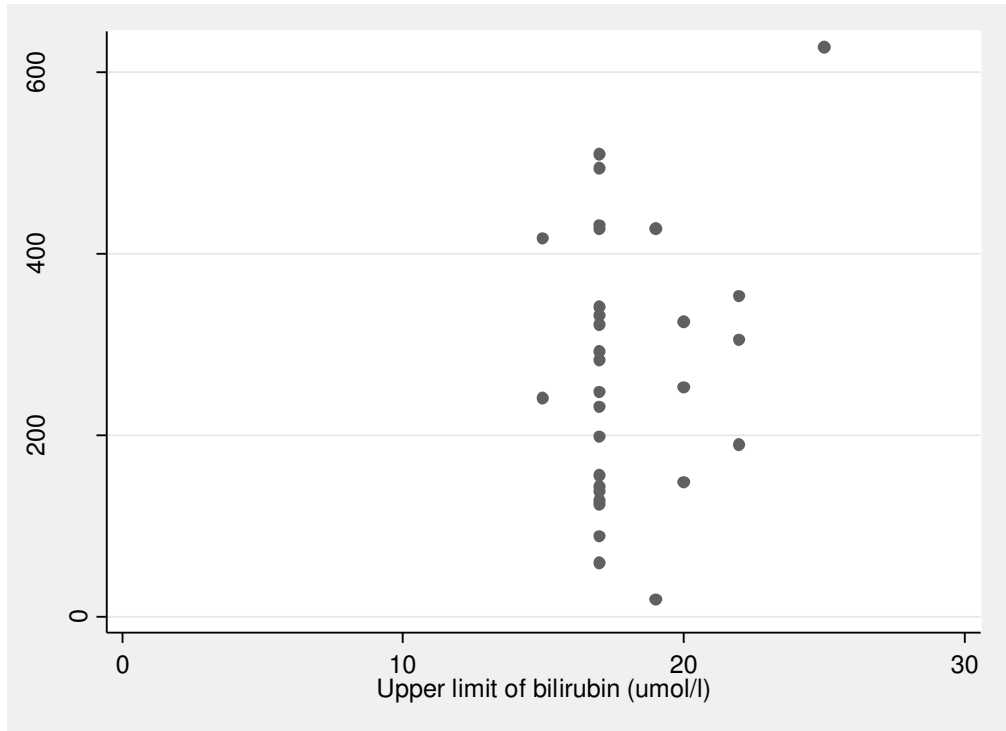
|         |             | <b>Number of<br/>practices</b> | <b>Median [IQR]<br/>(IU/l)</b> | <b>Range<br/>(IU/l)</b> |
|---------|-------------|--------------------------------|--------------------------------|-------------------------|
| Males   | Lower limit | 11                             | 70 [0, 100]                    | 0-100                   |
|         | Upper limit | 11                             | 330 [280, 350]                 | 129-350                 |
| Females | Lower limit | 11                             | 70 [0, 100]                    | 0-100                   |
|         | Upper limit | 11                             | 330 [280, 350]                 | 104-350                 |

### 7.2.2.3 Bilirubin

A total of 30/53 (57%) of practices had some information recorded on bilirubin reference ranges. Reference ranges provided were for adults of all ages. No practices provided different reference ranges dependent on the sex of the patient. It was therefore necessary to impute upper limits for 23 practices without a given reference range. Graphical representation of the upper limits showed the distribution to be unimodal around 17 $\mu$ mol/l (see Figure 7-5). Interrogation of actual test results showed a similar unimodal distribution of the median values by practice (see Figure 7-6). I therefore inferred that there was only one primary test in operation for bilirubin among the practices included in the trial at the time these data were collected. Summary statistics on the distribution of given reference ranges can be seen in Table 7-4.

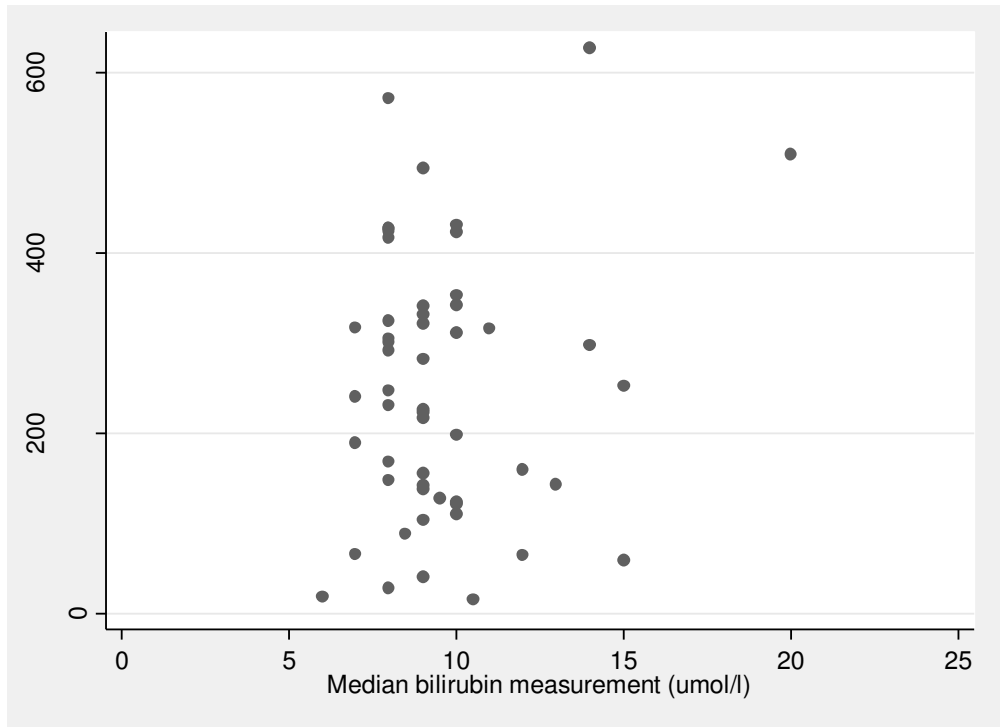
For practices without reference ranges the three upper limits imputed were:

1. Based on the median values – 17 $\mu$ mol/l for both males and females.
2. Based on the minimum upper limit – 15 $\mu$ mol/l for both males and females.
3. Based on the maximum upper limit – 25 $\mu$ mol/l for both males and females.



**Figure 7-5 Graphical representation of upper limits of reference range for bilirubin test by size of practice**





**Figure 7-6 Graphical representation of median bilirubin test measurements by size of practice**

**Table 7-4 Bilirubin tests – known reference ranges**

|             | <b>Number of practices</b> | <b>Median [IQR] (<math>\mu\text{mol/l}</math>)</b> | <b>Range (<math>\mu\text{mol/l}</math>)</b> |
|-------------|----------------------------|--|---|
| Lower limit | 30                         | 0 [0, 3]   | 0-5   |
| Upper limit | 30                         | 17 [17, 19]  | 15-25                                       |

### **7.2.3 Additional definitions**

#### **7.2.3.1 Elevated liver function**

Elevated liver function tests were defined as the result being above the upper limit of normal (ULN) relative to the reported or imputed laboratory reference range. Elevated results were then categorised as being between 1 and 2x the ULN or above 2x the ULN.

### **7.2.4 Statistical analysis**

Prevalence of elevated liver function tests were calculated as the number of people with an elevated result (or multiple elevated test results) divided by the number of participants with a valid test (or combination of tests). 95% CIs were calculated using the binomial distribution.

I examined the association between median age, sex and comorbidity and not having a valid liver function test result.

## **7.3 Results**

### **7.3.1 Prevalence of elevated liver function**

#### **7.3.1.1 AST**

I examined the proportion of patients who had an elevated AST test result based on the reference ranges given by their individual laboratory. Between 2.3% and 6.7% of the patients with a valid AST measurement had an elevated AST according to the reference ranges given (or imputed) by the laboratory (see Table 7-5). Using the median imputed reference ranges, 3.3% of participants had an elevated AST.

#### **7.3.1.2 ALP**

I examined the proportion of patients who had an elevated ALP test result based on the reference ranges given by their individual laboratory. Between 5.8% and 41.3% of the patients with a valid ALP measurement had an elevated ALP according to the reference ranges given (or imputed) by the laboratory (see Table 7-6). Using the median imputed reference ranges, 9.2% of participants had an elevated ALP.

#### **7.3.1.3 Bilirubin**

I examined the proportion of patients who had an elevated bilirubin test result based on the reference ranges given by their individual laboratory. Between 3.6% and 7.2% of the patients with a valid bilirubin measurement had an elevated bilirubin according to the reference ranges given (or imputed) by the laboratory (see Table 7-7). Using the median imputed reference ranges, 5.4% of participants had an elevated bilirubin.

**Table 7-5 Prevalence of elevated AST**

|                         | <b>Above upper limit of<br/>reference<br/>n (% of those with valid test<br/>result)</b> | <b>Within<br/>reference<br/>range</b> | <b>Below lower<br/>limit of reference</b> | <b>No value<br/>for test</b> | <b>Total</b> |
|-------------------------|---|---------------------------------------|---|------------------------------|--------------|
| Using median reference  | 429 (3.3)   | 12,287                                | 110                                       | 2,482                        | 15,308       |
| Using minimum reference | 865 (6.7)   | 11,851                                | 110                                       | 2,482                        | 15,308       |
| Using maximum reference | 301 (2.3)   | 12,415                                | 110                                       | 2,482                        | 15,308       |

**Table 7-6 Prevalence of elevated ALP**

|                         | <b>Above upper limit of<br/>reference<br/>n (% of those with valid test<br/>result)</b> | <b>Within<br/>reference<br/>range</b> | <b>Below lower<br/>limit of reference</b> | <b>No value<br/>for test</b> | <b>Total</b> |
|-------------------------|---|---------------------------------------|---|------------------------------|--------------|
| Using median reference  | 1,246 (9.2)   | 12,207                                | 46  | 1,809                        | 15,308       |
| Using minimum reference | 5,572 (41.3)  | 7,881                                 | 46  | 1,809                        | 15,308       |
| Using maximum reference | 783 (5.8)   | 12,670                                | 46  | 1,809                        | 15,308       |

**Table 7-7 Prevalence of elevated bilirubin**

|                         | <b>Above upper limit of<br/>reference<br/>n (% of those with valid test<br/>result)</b> | <b>Within<br/>reference<br/>range</b> | <b>Below lower<br/>limit of reference</b> | <b>No value<br/>for test</b> | <b>Total</b> |
|-------------------------|---|---------------------------------------|---|------------------------------|--------------|
| Using median reference  | 690 (5.4)   | 11,980                                | 20  | 2,618                        | 15,308       |
| Using minimum reference | 918 (7.2)   | 11,752                                | 20  | 2,618                        | 15,308       |
| Using maximum reference | 452 (3.6)   | 12,218                                | 20  | 2,618                        | 15,308       |

#### **7.3.1.4 Any elevated liver function**

For the rest of the analyses imputation according to the median reference ranges is used.

Of 15 308 participants in the universal arm of the trial, 13 276 (86.7%) had at least one valid measurement of liver function. Participants who did not have a valid test result were more likely to be female (OR 1.33 [1.19, 1.49]), were slightly older (median age 81.5 years for those without a valid test result compared with 80.2 years for those with a test) and had more missing data with respect to comorbidity compared with those people who had at least one valid test result.

Overall, 16.1% of those with one or more valid measurement had at least one elevated liver function test. The most common elevated liver function test within this population was ALP with 9.2% (95%CI [8.7%, 9.7%]) of people having a result above the ULN (see Table 7-8). Only 5.4% (95%CI [5.0%, 5.8%]) of people had an elevated bilirubin test, whilst an even smaller proportion had an elevated AST result, 3.3% (95%CI [3.0%, 3.7%]) of those with a valid measurement. The majority of subjects with an elevated measurement had a test result less than or equal to 2x the ULN: 86.2% AST; 90.0% ALP, 93.8% bilirubin.



**Table 7-8 Prevalence of elevated liver function tests**

| <b>Elevated test(s)<br/>(Number with valid test)</b> | <b>Number<br/>elevated (% of<br/>elevated)</b> | <b>% of valid tests<br/>elevated [95% CI]</b> |
|--|--|---|
| <b>Any elevated (N=13546)</b>                        | 2175   | 16.1 [15.4, 16.7]                             |
| <b>AST (N=12826)</b>                                 | 429 (100)                                      | 3.34 [3.04, 3.67]                             |
| ≤ 2x ULN   | 370 (86.2)                                     | 2.88 [2.60, 3.19]                             |
| Above 2x ULN   | 59 (13.8)                                      | 0.46 [0.35, 0.59]                             |
| <b>ALP (N=13499)</b>                                 | 1246 (100)                                     | 9.23 [8.75, 9.73]                             |
| ≤ 2x ULN   | 1122 (90.0)                                    | 8.31 [7.85, 8.79]                             |
| Above 2x ULN   | 124 (10.0)                                     | 0.92 [0.76, 1.09]                             |
| <b>Bilirubin (N=12690)</b>                           | 690 (100)                                      | 5.44 [5.05, 5.85]                             |
| ≤ 2x ULN   | 647 (93.8)                                     | 5.10 [4.72, 5.50]                             |
| Above 2x ULN   | 43 (6.2)                                       | 0.34 [0.25, 0.46]                             |
| AST and ALP (N=12794)                                | 90   | 0.70 [0.57, 0.86]                             |
| AST and bilirubin (N=12021)                          | 42   | 0.35 [0.25, 0.47]                             |
| ALP and bilirubin (N=12648)                          | 67   | 0.52 [0.41, 0.67]                             |
| AST, ALP and bilirubin<br>(N=11994)                  | 9  | 0.07 [0.03, 0.14]                             |
| <b>All 3 within reference range<br/>(N=11994)</b>    | 10025  | 83.6 [82.9, 84.2]                             |

## **7.4 Discussion**

### **7.4.1 Key findings**

I found that nearly 1 in 6 of the general population aged 75 and over had at least one elevated liver function test. Over half of these abnormalities can be accounted for by an elevated measurement of ALP (9.2% of all subjects) and the vast majority were within 1x the upper limit of normal for the test measured. Very few participants had more than one recorded elevated liver function test (<1% for any combinations of one or more elevated liver function tests) with only 9 participants having all 3 liver function tests recorded as elevated.

### **7.4.2 Strengths and limitations**

In this study I was able to assess, for the first time, the liver function of a representative randomly selected community-based sample of people aged 75 and over. That blood samples were available for most of the people in the MRC elderly gives this study a distinct advantage over many other studies looking at liver function insofar as the study population was not selected on the basis of known or suspected liver disease.

Arguably, abnormalities of AST, ALP and bilirubin are of secondary importance when looking at liver function compared with a measurement of alanine aminotransferase (ALT) which is specific to the liver. I was unable to investigate this as a blood test for this enzyme was not a part of the original study design.

As a result of the multi-site nature of this large study I was reliant on data collection from several laboratories across the UK. Not all laboratories were able to provide reference ranges for the liver function tests so I relied on imputation for nearly half of the reference ranges. Basing the upper limit of normal on the median reference range for those practices where imputation was necessary may under- or over-estimate the true level of elevated liver function in this population. This could make a significant difference to the proportion of older people who would be considered to have elevated liver function as seen particularly in the measurement of ALP. Using the minimum reference ranges for elevated upper limits an estimated 41.3% of participants had an elevated ALP test result compared with only 9.2% when using the median reference range.

Data having been collected from multiple laboratories also meant that I was unable to describe absolute values of enzymatic activity as there was not one uniform test in operation at all of the different sites.

In some laboratories there were different normal reference ranges provided for ALP for people aged 60 and above, those aged less than 60 and in some cases for children. It may be that reference ranges for the LFTs measured should be provided in even finer categories than this. I examine the association between abnormal measurements and age in the next chapter.

### **7.4.3 Comparison with previously published work**

Information on the prevalence of elevated liver function in the UK is surprisingly lacking. These results show a lower prevalence of elevated transaminase (3.3% elevated AST vs. 7.0% elevated AST or alanine transaminase), ALP (9.2% vs. 10.4%) and bilirubin (5.4% vs. 7.1%) than those

reported in a recent study of adults of all ages from Scotland.<sup>66</sup> This is perhaps expected as the population within this study was selected on the basis that subjects already had a measurement of liver function contained within their primary care records. The authors acknowledge that they do not know why liver function tests were requested and this is likely to include the investigation of suspected liver disease leading to a non-representative sample of the general population.

In a study in America,<sup>76</sup> again only a selected group of participants had a blood test, and it is likely that the true population prevalence of elevated liver function tests may have been over estimated. Indeed, 12.8% of those with a measurement of AST had an elevated test, nearly four times that seen in my study. Another study from the USA also showed a slightly higher prevalence of elevated AST to that which I have described in this study, with 3.7% and 4.9% of the population aged 20 or over having an elevated AST in 1988-1994 and 1999-2002 respectively.<sup>71</sup> However, given that my study looks only at people aged 75 and over, it may be that the prevalence of elevated liver function tests in a population of older people is indeed lower than that found in the general adult population of all ages. This is supported by data from America where the prevalence of elevated ALT or AST in the population aged 70 or older was reported as 4.9%, statistically significantly lower than the prevalence of elevated transaminases in younger age groups.<sup>70</sup>

#### **7.4.4 Conclusions**

Current guidelines recommend that liver function tests should be carried out before and within 1-3 months of starting treatment on statins to monitor for signs of altered liver function.<sup>111</sup> With an estimated 40% of all 75-79 year olds have at least one prescription for statins annually,<sup>112</sup> incidental findings of

elevated LFTs in this age group of the population in the absence of symptoms are likely to occur regularly. The study reported in this chapter has shown that abnormalities in liver function are fairly common in people aged 75 and over. Using population estimates for 2008 if every person aged 75 and over was to undergo these three blood tests elevated levels in one or more of the LFTs would be found in 770,000 patients. It will be important to determine the correct course of action for the follow-up and assessment of older people with elevated liver function tests to avoid unnecessary follow-up and investigation and potential anxiety for an individual.

## **8 Demographic, lifestyle and medical characteristics associated with an elevated liver function test**

### **8.1 Introduction**

This study aims to examine the association between elevated liver function tests and selected demographic, lifestyle and clinical characteristics in people aged 75 and over.

### **8.2 Methods**

#### **8.2.1 Dataset used**

The data used in this study are those from the detailed nurse assessment contained within the 'detail' database (see Figure 6-2). A total of 15,308 participants aged 75 and over are included in the subsequent analyses. The definition of elevated liver function is as described in section 7.2.3.1 following imputation of missing upper limits using the median reference ranges.

#### **8.2.2 Additional definitions**

##### **8.2.2.1 Alcohol consumption**

Alcohol consumption was calculated as the total number of self-reported units of alcohol consumed as beer (assuming one unit per half pint), wine (assuming one unit per glass of wine, sherry or port) and spirits (assuming one unit in a single measure) in the past week. Intake was then categorised as none and in seven-unit increments.

### **8.2.2.2 Smoking**

Smoking status was recorded at the time of interview as either current smoker, ex-smoker or never a smoker.

### **8.2.2.3 Body Mass Index**

Body Mass Index (BMI) was defined as weight (in kg) divided by height (in m) squared, each of which were measured once only. I subsequently categorised BMI into clinically recognised categories: <18.5 (underweight), 18.5-24.9 (normal weight), 25.0-29.9 (overweight) and 30+ (obese).

### **8.2.2.4 Waist:hip ratio**

Waist circumference was measured to the nearest 0.1cm midway between the iliac crest and the lower rib margin by using an insertion tape. Hip circumference was measured as the widest circumference over the buttocks and below the iliac crest. Hip and waist were both measured twice (having asked patients to roll down their undergarments) and an average of the two values used in the calculation of waist:hip ratio (WHR).

### **8.2.2.5 Comorbidities**

Diabetes was classified as present following either a self-reported medical diagnosis, prescription of anti-diabetic medication or a single high random blood glucose measurement.<sup>113</sup> Heart attack, hypertension, stroke, cancer and ulcer were defined as a positive self-reported medical diagnosis. Angina was defined as full angina as per the Rose score.<sup>114</sup> Dementia was defined as a score of <9 on the mini-mental state examination.<sup>115</sup>

In order to assess the potential for correlation between multiple co-morbid illnesses I derived a co-morbidity score. A patient was given a score of zero (not present) or one (present ever before the date of interview) for each of the following self-reported medical conditions: asthma, stomach / digestive ulcer,

hypertension, heart attack, stroke, fractured hip or spine (within last year only), Parkinson's disease, cancer, and for each of the following: angina, dementia and diabetes (as per definitions above). Scores were added together to give an overall score and then categorised into 0, 1, 2 and 3 or more comorbidities.

### **8.2.3 Statistical analysis**

To examine the association between elevated liver function tests and demographic, lifestyle and medical characteristics I used logistic regression to calculate odds ratios and 95% CIs. Analysis was performed treating an individual practice as a clustered unit with a random effects model employed. After univariable analyses, a priori confounders of age, sex and comorbidity plus additional statistically significant associations were built into a multivariable logistic regression model to account for potential confounding. Multivariable models were constructed in 2 ways. Firstly, missing values for covariables were modelled as a separate category to ensure all subjects remained within the analysis. Secondly, multivariable models were fitted using only participants with complete data and modelling continuous variables as linear trends.



## **8.3 Results**

### **8.3.1 AST**

Of the 12,836 participants with a valid measurement of AST, 429 (3.3%) had an elevated serum level of AST (as reported in section 7.3.1.1).

#### **8.3.1.1 Univariable associations**

##### Sex

Of those with an elevated AST 60% were female which was not statistically different to the 61% of those with a normal measurement of AST, OR 0.96 (95%CI [0.79, 1.18]) (see Table 8-1).

##### Age

Participants with an elevated AST were more likely to be younger than those with a normal AST measurement. For example, those over 90 years of age were 50% less likely to have an abnormal AST measurement than those aged 75. The odds ratio for a yearly increase in age fitted a linear trend and was 0.97 (95% CI[0.94, 0.99]).

##### Alcohol consumption

Data on total number of units of alcohol consumed in the previous week were missing for 18.5% of those with a normal AST and for 16.1% of those with an elevated AST. A further 35.9% of both groups recorded no consumption of alcohol within the previous week. There was a statistically significant association between alcohol consumption and an elevated AST with an odds ratio of 1.22 (95% CI[1.08, 1.37]) for each 7-unit increase in weekly consumption. Patients reported as consuming 22 or more units of alcohol in a

week were over twice as likely to have an elevated AST measurement than those who did not drink any alcohol.

### Smoking

A much smaller percentage of participants had missing data on smoking compared with alcohol consumption, only 2.7% compared with 18.4% respectively. There was no statistically significant association between elevated AST and either being an ex- or current smoker compared with being classified as a never smoker.

### Body size (BMI and WHR)

The majority of participants (52.8%) were recorded as being overweight or obese i.e. having a BMI of 25 or above with a further 8.5% having missing data on BMI. Having an elevated AST was not associated with either a low or high BMI. Having a higher waist-to-hip ratio was associated with elevated AST. For example, the odds of having an elevated AST if you had a WHR of between 1.05 and 1.15 were over 3 times that compared to if you had a WHR of between 0.75 and 0.84. Although no other individual category of WHR conferred a statistically significant association with elevated AST when examined a continuous categorical variable there was an association with higher WHR group and elevated AST (OR 1.17 (95% CI[1.03, 1.32])).

### Comorbidities

Of the comorbidities examined only diabetes and dementia were seen to be associated with an elevated AST. Having had a heart attack, hypertension, a stroke, cancer, ulcer or angina were not statistically significantly associated with an elevated AST. When examining comorbidity as a composite score

there was no statistically significant association seen between the derived comorbidity index and elevation of AST.

### **8.3.1.2 Multivariable associations**

To build the multivariable model a priori confounders of age, sex and comorbidity as well as alcohol consumption and WHR were included. Upon adjustment there remained a statistically significant association between elevated AST and age, alcohol consumption and high WHR (see Table 8-1). There was no evidence of substantial confounding with the exception of the estimates for the association with sex which increased following adjustment for age, alcohol consumption, WHR and comorbidity. The change in association between sex and elevated AST suggested some form of interaction. Fitting a third multivariable model including an interaction term for age and sex led to a further slight increase in the association between being female and having an elevated measurement of AST.

**Table 8-1 Associations between elevated AST test and demographic, lifestyle and clinical characteristics**

|                                | Normal AST<br>(N=12397)        |      | Elevated AST (N=429)        |      | OR [95% CI]       | OR [95% CI]       | OR [95% CI]       | OR [95% CI]       |
|--------------------------------|--------------------------------|------|-----------------------------|------|-------------------|-------------------|-------------------|-------------------|
|                                | N                              | %    | N                           | %    | Univariable       | Model 1*          | Model 2*          | Model 3*          |
| <b>Sex</b>                     |                                |      |                             |      |                   |                   |                   |                   |
| Male                           | 4838                           | 39.0 | 173                         | 40.0 | -                 | -                 |                   |                   |
| Female                         | 7559                           | 61.0 | 256                         | 60.0 | 0.96 [0.79, 1.18] | 1.27 [0.98, 1.64] | 1.34 [1.01, 1.78] | 1.47 [0.99, 2.18] |
| <b>Age (years)</b>             |                                |      |                             |      |                   |                   |                   |                   |
| Median age<br>[IQR]<br>(range) | 80.2 [77.2, 84.2]<br>(75, 108) |      | 79.2 [77, 83.2]<br>(75, 99) |      |                   |                   |                   |                   |
| 75-                            | 1099                           | 8.9  | 56                          | 13.1 | -                 | -                 |                   |                   |
| 76-                            | 1569                           | 12.7 | 52                          | 12.1 | 0.70 [0.47, 1.05] | 0.70 [0.47, 1.04] |                   |                   |
| 77-                            | 1300                           | 10.5 | 55                          | 12.8 | 0.90 [0.60, 1.33] | 0.89 [0.60, 1.33] |                   |                   |
| 78-                            | 936                            | 7.6  | 41                          | 9.6  | 0.95 [0.62, 1.45] | 0.94 [0.61, 1.45] |                   |                   |
| 79-                            | 943                            | 7.6  | 29                          | 6.8  | 0.66 [0.41, 1.06] | 0.67 [0.41, 1.07] |                   |                   |
| 80-                            | 878                            | 7.1  | 25                          | 5.8  | 0.59 [0.36, 0.96] | 0.59 [0.36, 0.97] |                   |                   |
| 81-                            | 874                            | 7.1  | 35                          | 8.2  | 0.85 [0.54, 1.32] | 0.87 [0.55, 1.36] |                   |                   |
| 82-                            | 774                            | 6.2  | 25                          | 5.8  | 0.67 [0.41, 1.11] | 0.70 [0.43, 1.16] |                   |                   |
| 83-                            | 706                            | 5.7  | 17                          | 4.0  | 0.46 [0.26, 0.80] | 0.47 [0.27, 0.84] |                   |                   |
| 84-                            | 624                            | 5.0  | 18                          | 4.2  | 0.63 [0.36, 1.10] | 0.65 [0.37, 1.13] |                   |                   |
| 85-                            | 527                            | 4.3  | 15                          | 3.5  | 0.61 [0.34, 1.10] | 0.62 [0.34, 1.13] |                   |                   |
| 86-                            | 449                            | 3.6  | 13                          | 3.0  | 0.65 [0.35, 1.22] | 0.68 [0.36, 1.28] |                   |                   |
| 87-                            | 404                            | 3.3  | 10                          | 2.3  | 0.52 [0.26, 1.04] | 0.54 [0.27, 1.09] |                   |                   |
| 88-                            | 323                            | 2.6  | 13                          | 3.0  | 0.89 [0.47, 1.69] | 0.93 [0.49, 1.76] |                   |                   |
| 89-                            | 264                            | 2.1  | 9                           | 2.1  | 0.69 [0.33, 1.43] | 0.71 [0.34, 1.49] |                   |                   |
| 90+                            | 665                            | 5.4  | 16                          | 3.7  | 0.49 [0.28, 0.88] | 0.52 [0.29, 0.94] |                   |                   |
| Missing                        | 62                             | 0.5  | 0                           | 0    | -                 | -                 |                   |                   |

|   |                           |      |                         |      |                   |                   |                   |
|---|---------------------------|------|-------------------------|------|-------------------|-------------------|-------------------|
| Odds ratio for yearly increase in age                     |                           |      |                         |      | 0.97 [0.94, 0.99] | 0.97 [0.94, 1.00] | 1.00 [0.91, 1.10] |
| <b>Alcohol</b>  |                           |      |                         |      |                   |                   |                   |
| Median units of alcohol intake in past week [IQR] (range) | 1 [0,4] (0,90)<br>N=10106 |      | 1 [0,7] (0,87)<br>N=360 |      |                   |                   |                   |
| Alcohol units   |                           |      |                         |      |                   |                   |                   |
| 0   | 4453                      | 35.9 | 154                     | 35.9 | -                 |                   |                   |
| 1-  | 4341                      | 35.0 | 133                     | 31.0 | 0.86 [0.68, 1.10] | 0.86 [0.67, 1.10] |                   |
| 8-  | 856                       | 6.9  | 43                      | 10.0 | 1.54 [1.07, 2.21] | 1.51 [1.04, 2.20] |                   |
| 15-   | 250                       | 2.0  | 15                      | 3.5  | 1.85 [1.04, 3.29] | 1.83 [1.02, 3.28] |                   |
| 22+   | 206                       | 1.7  | 15                      | 3.5  | 2.36 [1.33, 4.22] | 2.37 [1.31, 4.30] |                   |
| Missing   | 2291                      | 18.5 | 69                      | 16.1 | 0.85 [0.63, 1.15] | 0.86 [0.64, 1.17] |                   |
| Odds ratio for step increase in alcohol                   |                           |      |                         |      | 1.22 [1.08, 1.37] | 1.16 [1.02, 1.32] | 1.16 [1.02, 1.32] |
| <b>Smoking</b>  |                           |      |                         |      |                   |                   |                   |
| Never   | 4774                      | 38.5 | 177                     | 41.3 |                   |                   |                   |
| Ex  | 6081                      | 49.1 | 200                     | 46.6 | 0.86 [0.70, 1.07] |                   |                   |
| Current   | 1200                      | 9.7  | 47                      | 11.0 | 0.97 [0.69, 1.35] |                   |                   |
| Missing   | 342                       | 2.8  | 5                       | 1.2  | 0.48 [0.19, 1.19] |                   |                   |
| <b>BMI group</b>  |                           |      |                         |      |                   |                   |                   |
| <18.5   | 253                       | 2.0  | 6                       | 1.4  | 0.73 [0.32, 1.69] |                   |                   |
| 18.5-   | 4541                      | 36.6 | 152                     | 35.4 | -                 |                   |                   |
| 25-   | 4719                      | 38.1 | 167                     | 38.9 | 1.08 [0.86, 1.36] |                   |                   |
| 30-   | 1495                      | 12.1 | 61                      | 14.2 | 1.26 [0.92, 1.72] |                   |                   |
| 35+   | 328                       | 2.7  | 14                      | 3.3  | 1.28 [0.72, 2.27] |                   |                   |
| Missing   | 1061                      | 8.6  | 29                      | 6.8  | 0.95 [0.62, 1.43] |                   |                   |
| Increase in BMI group                                     |                           |      |                         |      | 1.11 [0.98, 1.26] |                   |                   |

|   |      |      |     |      |                   |                   |                   |                   |
|---|------|------|-----|------|-------------------|-------------------|-------------------|-------------------|
| <b>Waist:hip</b>                              |      |      |     |      |                   |                   |                   |                   |
| 0.65-0.74                                     | 421  | 3.4  | 10  | 2.3  | 0.81 [0.42, 1.56] | 0.80 [0.41, 1.56] |                   |                   |
| 0.75-0.84                                     | 3908 | 31.5 | 127 | 29.6 |                   |                   |                   |                   |
| 0.85-0.94                                     | 4775 | 38.5 | 175 | 40.8 | 1.10 [0.86, 1.39] | 1.13 [0.87, 1.47] |                   |                   |
| 0.95-1.04                                     | 2161 | 17.4 | 74  | 17.3 | 1.12 [0.83, 1.51] | 1.14 [0.80, 1.63] |                   |                   |
| 1.05-1.15                                     | 197  | 1.6  | 17  | 4.0  | 3.26 [1.88, 5.65] | 3.22 [1.79, 5.80] |                   |                   |
| Missing                                       | 935  | 7.5  | 26  | 6.1  | 1.00 [0.65, 1.56] | 1.10 [0.70, 1.73] |                   |                   |
| Increase in waist:hip ratio group             |      |      |     |      | 1.17 [1.03, 1.32] |                   | 1.27 [1.07, 1.50] | 1.27 [1.08, 1.50] |
| <b>Presence of Co-morbidity</b>               |      |      |     |      |                   |                   |                   |                   |
| Diabetes                                      | 977  | 7.9  | 48  | 11.2 | 1.53 [1.12, 2.10] |                   |                   |                   |
| Heart attack                                  | 1319 | 10.6 | 39  | 9.1  | 0.87 [0.62, 1.22] |                   |                   |                   |
| Hypertension                                  | 4121 | 33.2 | 152 | 35.4 | 1.13 [0.92, 1.39] |                   |                   |                   |
| Stroke  | 1070 | 8.6  | 36  | 8.4  | 1.04 [0.73, 1.49] |                   |                   |                   |
| Cancer  | 1272 | 10.3 | 45  | 10.5 | 1.09 [0.79, 1.50] |                   |                   |                   |
| Ulcer   | 1476 | 11.9 | 57  | 13.3 | 1.15 [0.86, 1.54] |                   |                   |                   |
| Angina  | 778  | 6.3  | 23  | 5.4  | 0.88 [0.57, 1.36] |                   |                   |                   |
| Dementia                                      | 80   | 0.7  | 6   | 1.4  | 2.71 [1.15, 6.37] |                   |                   |                   |
| <b>Co-morbidity score</b>                     |      |      |     |      |                   |                   |                   |                   |
| 0   | 4427 | 34.5 | 852 | 34.3 |                   |                   |                   |                   |
| 1   | 4809 | 37.5 | 850 | 34.3 | 1.14 [0.90, 1.44] | 1.11 [0.88, 1.41] |                   |                   |
| 2   | 2353 | 18.4 | 442 | 17.8 | 1.21 [0.91, 1.61] | 1.18 [0.88, 1.57] |                   |                   |
| 3+  | 1036 | 8.1  | 189 | 7.6  | 1.27 [0.87, 1.84] | 1.23 [0.84, 1.80] |                   |                   |
| Missing                                       | 201  | 1.6  | 149 | 6.0  | 0.80 [0.34, 1.87] | 0.81 [0.34, 1.94] |                   |                   |
| Odds ratio for increase in co-morbidity score |      |      |     |      | 1.09 [0.98, 1.21] |                   | 1.08 [0.96, 1.22] | 1.08 [0.96, 1.22] |

\*Multivariable model 1 adjusted for sex, age, alcohol consumption, WHR and comorbidity as categorical variables; model 2 using only subjects with complete data adjusted for sex plus age, alcohol consumption, WHR and comorbidity fitted as linear trend variables; model 3 as model 2 with an interaction term for age and sex.

### **8.3.2 ALP**

Of the 13,499 participants with a valid measurement of ALP, 1246 (9.2%) had an elevated serum level of ALP (as reported in section 7.3.1.2).

#### **8.3.2.1 Univariable associations**

##### Sex

Of those with an elevated ALP 62.9% were female which was not statistically different to the 60.9% of those with a normal measurement of ALP, OR 1.05 (95%CI [0.93, 1.19]) (see Table 8-2).

##### Age

In direct contrast to that seen with elevations of AST (section 8.3.1 above) participants with an elevated ALP were more likely to be older than those with a normal ALP measurement, the odds ratio for a yearly increase in age being 1.05 (95% CI[1.04, 1.07]). Those aged 90 and over were twice as likely to have an elevated measurement of ALP than those aged 75.

##### Alcohol consumption

There was a statistically significant association between lower alcohol consumption and an elevated ALP with an odds ratio of 0.81 (95% CI[0.74, 0.88]) for each 7-unit increase in weekly consumption meaning that for each additional 7 units consumed in a week participants were 20% less likely to have a measurement of elevated ALP. Those participants reported as consuming 22 or more units of alcohol per week were 50% less likely to have an elevated measurement of ALP than those who did not report consuming any alcohol.

### Smoking

There was no statistically significant association between elevated ALP and being a current smoker but there was a small 'protective' effect conferred in those recorded as ex-smokers with an odds ratio of 0.82 (95% CI[0.72, 0.94]) of having an elevated ALP compared with never smokers.

### Body size (BMI and WHR)

There was no trend in association seen with increasing BMI category and elevated ALP. However, those participants in the highest BMI category – severely obese (BMI 35 or more) – had a 50% greater chance of having an elevated ALP (OR 1.52 (95% CI[1.10, 2.10])). There were no statistically significant associations seen between WHR and elevated ALP measurement.

### Comorbidities

Reported history of diabetes and heart attack were associated with an elevated ALP (OR 1.64 (95% CI[1.35, 1.99]) and 1.24 (95% CI[1.03, 1.49]) respectively). Additionally an assessment of dementia was significantly associated with an elevated measurement of ALP (OR 2.64 (95% CI[1.58, 4.42])).

### **8.3.2.2 Multivariable associations**

To build the multivariable model a priori confounders of age, sex and comorbidity as well as alcohol consumption were included. Upon adjustment there remained a statistically significant association between elevated ALP and age, alcohol consumption and comorbidity score (see Table 8-2).



**Table 8-2 Associations between demographic, lifestyle and medical characteristics and elevated ALP test**

|                             | Normal ALP<br>(N=12253)        |      | Elevated ALP (N=1246)         |      | OR [95% CI]       | OR [95% CI]       |                   |
|-----------------------------|--------------------------------|------|-------------------------------|------|-------------------|-------------------|-------------------|
|                             | N                              | %    | N                             | %    | Univariable       | Model 1*          | Model 2*          |
| <b>Sex</b>                  |                                |      |                               |      |                   |                   |                   |
| Female                      | 7456                           | 60.9 | 784                           | 62.9 | 1.05 [0.93, 1.19] | 0.90 [0.79, 1.03] | 0.94 [0.80, 1.09] |
| Male                        | 4797                           | 39.1 | 462                           | 37.1 |                   |                   |                   |
| <b>Age (years)</b>          |                                |      |                               |      |                   |                   |                   |
| Median age [IQR]<br>(range) | 80.2 [77.2, 84.0]<br>(75, 108) |      | 81.4 [77.6, 85.8]<br>(75, 98) |      |                   |                   |                   |
| 75-                         | 1127                           | 9.2  | 87                            | 7.0  | -                 | -                 | -                 |
| 76-                         | 1581                           | 12.9 | 139                           | 11.2 | 1.01 [0.76, 1.34] | 1.02 [0.76, 1.35] |                   |
| 77-                         | 1319                           | 10.8 | 106                           | 8.5  | 0.95 [0.71, 1.29] | 0.96 [0.71, 1.30] |                   |
| 78-                         | 939                            | 7.7  | 81                            | 6.5  | 1.01 [0.73, 1.40] | 1.01 [0.73, 1.39] |                   |
| 79-                         | 927                            | 7.6  | 89                            | 7.1  | 1.14 [0.83, 1.56] | 1.12 [0.82, 1.54] |                   |
| 80-                         | 893                            | 7.3  | 67                            | 5.4  | 0.85 [0.61, 1.19] | 0.83 [0.59, 1.16] |                   |
| 81-                         | 861                            | 7.0  | 77                            | 6.2  | 1.07 [0.77, 1.49] | 1.06 [0.76, 1.47] |                   |
| 82-                         | 767                            | 6.3  | 83                            | 6.7  | 1.28 [0.93, 1.77] | 1.24 [0.90, 1.72] |                   |
| 83-                         | 689                            | 5.6  | 77                            | 6.2  | 1.29 [0.92, 1.79] | 1.25 [0.90, 1.74] |                   |
| 84-                         | 609                            | 5.0  | 71                            | 5.7  | 1.42 [1.01, 1.99] | 1.37 [0.97, 1.92] |                   |
| 85-                         | 515                            | 4.2  | 61                            | 4.9  | 1.35 [0.95, 1.92] | 1.30 [0.91, 1.85] |                   |
| 86-                         | 428                            | 3.5  | 51                            | 4.1  | 1.40 [0.96, 2.04] | 1.34 [0.92, 1.95] |                   |
| 87-                         | 385                            | 3.1  | 49                            | 3.9  | 1.56 [1.07, 2.28] | 1.47 [1.00, 2.15] |                   |
| 88-                         | 319                            | 2.6  | 34                            | 2.7  | 1.22 [0.80, 1.88] | 1.16 [0.76, 1.79] |                   |
| 89-                         | 240                            | 2.0  | 46                            | 3.7  | 2.39 [1.60, 3.56] | 2.29 [1.53, 3.42] |                   |
| 90+                         | 600                            | 4.9  | 117                           | 9.4  | 2.40 [1.77, 3.25] | 2.33 [1.71, 3.17] |                   |
| Missing                     | 54                             | 0.4  | 11                            | 0.9  | 2.54 [1.24, 5.21] | 2.38 [1.16, 4.90] |                   |

|   |                           |      |                         |       |                   |                   |                   |
|---|---------------------------|------|-------------------------|-------|-------------------|-------------------|-------------------|
| Odds ratio for yearly increase in age       |                           |      |                         |       | 1.05 [1.04, 1.07] | 1.05 [1.03, 1.06] |                   |
| <b>Alcohol</b>                              |                           |      |                         |       |                   |                   |                   |
| Median units of alcohol intake in past week | 1 [0,4] (0,90)<br>N=10008 |      | 1 [0,4] (0,87)<br>N=960 |       |                   |                   |                   |
| Alcohol units                               |                           |      |                         |       |                   |                   |                   |
| 0   | 4369                      | 35.7 | 493                     | 39.6  | -                 |                   |                   |
| 1-  | 4305                      | 35.1 | 356                     | 28.6  | 0.70 [0.61, 0.82] | 0.72 [0.62, 0.83] |                   |
| 8-  | 866                       | 7.1  | 77                      | 6.2   | 0.71 [0.55, 0.92] | 0.71 [0.54, 0.93] |                   |
| 15-   | 251                       | 2.1  | 20                      | 1.6   | 0.54 [0.34, 0.88] | 0.57 [0.35, 0.93] |                   |
| 22+   | 217                       | 1.8  | 14                      | 1.1   | 0.49 [0.28, 0.86] | 0.49 [0.28, 0.87] |                   |
| Missing                                     | 2245                      | 18.3 | 286                     | 23.0  | 1.09 [0.93, 1.29] | 1.04 [0.89, 1.23] |                   |
| Odds ratio for increase in alcohol group    |                           |      |                         |       | 0.81 [0.74, 0.88] | 0.83 [0.76, 0.91] |                   |
| <b>Smoking</b>                              |                           |      |                         |       |                   |                   |                   |
| Never                                       | 4696                      | 38.3 | 519                     | 41.7  |                   |                   |                   |
| Ex  | 6028                      | 49.2 | 557                     | 44.7  | 0.82 [0.72, 0.94] | 0.92 [0.80, 1.06] | 0.91 [0.77, 1.06] |
| Current                                     | 1189                      | 9.7  | 142                     | 11.4  | 1.06 [0.86, 1.29] | 1.22 [0.99, 1.51] | 1.25 [0.98, 1.58] |
| Missing                                     | 340                       | 2.8  | 28                      | 2.3   | 0.79 [0.52, 1.18] | 0.76 [0.50, 1.15] |                   |
| <b>BMI group</b>                            |                           |      |                         |       |                   |                   |                   |
| <18.5                                       | 239                       | 2.0  | 34                      | 2.7   | 1.36 [0.93, 1.99] |                   |                   |
| 18.5-                                       | 4470                      | 36.5 | 475                     | 38.1  | -                 |                   |                   |
| 25-   | 4709                      | 38.4 | 414                     | 33.2  | 0.85 [0.74, 0.98] |                   |                   |
| 30-   | 1521                      | 12.4 | 125                     | 10.0  | 0.79 [0.64, 0.98] |                   |                   |
| 35+   | 317                       | 2.6  | 51                      | 4.1   | 1.52 [1.10, 2.10] |                   |                   |
| Missing                                     | 997                       | 8.1  | 147                     | 11.8  | 1.57 [1.28, 1.94] |                   |                   |
|   |                           |      |                         | Trend | 0.95 [0.88, 1.03] |                   |                   |

| <b>Waist:hip</b>                              |      |      |     |       |                   |                   |
|---|------|------|-----|-------|-------------------|-------------------|
| 0.65-0.74                                     | 411  | 3.4  | 40  | 3.2   | 1.02 [0.72, 1.45] |                   |
| 0.75-0.84                                     | 3886 | 31.7 | 367 | 29.5  | -                 |                   |
| 0.85-0.94                                     | 4721 | 38.5 | 499 | 40.1  | 1.09 [0.94, 1.26] |                   |
| 0.95-1.04                                     | 2130 | 17.4 | 196 | 15.7  | 0.99 [0.83, 1.21] |                   |
| 1.05-1.15                                     | 204  | 1.7  | 16  | 1.3   | 0.90 [0.53, 1.54] |                   |
| Missing                                       | 901  | 7.4  | 128 | 10.3  | 1.75 [1.40, 2.19] |                   |
|   |      |      |     | Trend | 1.00 [0.93, 1.08] |                   |
| <b>Presence of Co-morbidity</b>               |      |      |     |       |                   |                   |
| Diabetes                                      | 925  | 7.6  | 144 | 11.6  | 1.64 [1.35, 1.99] |                   |
| Heart attack                                  | 1277 | 10.4 | 159 | 12.8  | 1.24 [1.03, 1.49] |                   |
| Hypertension                                  | 4114 | 33.6 | 388 | 31.1  | 0.89 [0.78, 1.01] |                   |
| Stroke  | 1045 | 8.5  | 111 | 8.9   | 1.05 [0.85, 1.29] |                   |
| Cancer  | 1242 | 10.1 | 126 | 10.1  | 0.97 [0.80, 1.19] |                   |
| Ulcer   | 1461 | 11.9 | 159 | 12.8  | 1.11 [0.92, 1.32] |                   |
| Angina  | 753  | 6.2  | 82  | 6.6   | 1.02 [0.80, 1.30] |                   |
| Dementia                                      | 77   | 0.6  | 20  | 1.6   | 2.64 [1.58, 4.42] |                   |
| Co-morbidity score                            |      |      |     |       |                   |                   |
| 0   | 4262 | 34.8 | 413 | 33.2  | -                 | -                 |
| 1   | 4593 | 37.5 | 468 | 37.6  | 1.06 [0.92, 1.22] | 1.08 [0.94, 1.25] |
| 2   | 2238 | 18.3 | 228 | 18.3  | 1.04 [0.87, 1.24] | 1.08 [0.91, 1.29] |
| 3+  | 972  | 7.9  | 115 | 9.2   | 1.25 [1.00, 1.57] | 1.29 [1.03, 1.62] |
| Missing                                       | 188  | 1.5  | 22  | 1.8   | 1.45 [0.91, 2.31] | 1.22 [0.76, 1.96] |
| Odds ratio for increase in co-morbidity score |      |      |     |       | 1.05 [0.99, 1.12] | 1.12 [1.04, 1.21] |

\*Multivariable model 1 adjusted for sex, age, alcohol consumption, smoking status and comorbidity as categorical variables; model 2 using only subjects with complete data adjusted for sex, smoking status plus age, alcohol consumption and comorbidity fitted as linear trend variables

### **8.3.3 Bilirubin**

Of the 12,690 participants with a valid measurement of bilirubin, 690 (5.4 %) had an elevated serum level of bilirubin (as reported in section 7.3.1.3).

#### **8.3.3.1 Univariable associations**

##### Sex

Of those with an elevated bilirubin only 38.3% were female which was significantly different to the 62.4% of those with a normal measurement of bilirubin (OR 0.37 (95%CI [0.32, 0.44])) (see Table 8-3).

##### Age

Unlike with AST and ALP there was no association seen between elevated bilirubin and age (OR 0.99 (95% CI[0.97, 1.01])).

##### Alcohol consumption

There was a statistically significant association between higher alcohol consumption and an elevated bilirubin with an odds ratio of 1.20 (95% CI[1.09, 1.31]) for each 7-unit increase in weekly consumption meaning that for each additional 7 units consumed in a week a participants were 20% more likely to have a measurement of elevated bilirubin. Those participants who reported consuming 22 or more units of alcohol in a week were over twice as likely to have an measurement of elevated bilirubin compared to those who did not consume any alcohol.

### Smoking

There was a statistically significant association between elevated bilirubin and being an ex-smoker (OR 1.22 (95% CI[1.03, 1.44])) but there was no association for those recorded as current smokers compared with never smokers (OR 0.76 (95% CI[0.56, 1.05])).

### Body Size (BMI and WHR)

There was no trend in association seen with increasing BMI category and elevated bilirubin. However, those participants in the highest BMI category – severely obese (BMI 35 or more) – had a greater than 50% reduction in the chance of having an elevated bilirubin measurement (OR 0.44 (95% CI[0.22, 0.86])). There was a statistically significant association seen in increasing WHR and elevated bilirubin with each increase in WHR category conferring a 27% increase in odds of having an elevated bilirubin (OR 1.27 (95% CI[1.15, 1.40])).

### Comorbidities

None of the individual comorbidities examined showed any association with elevated bilirubin. Unsurprisingly, when examining comorbidity as a composite score there was no statistically significant association seen between increasing score in the derived comorbidity index and elevation of bilirubin.

### **8.3.3.2 Multivariable associations**

To build the multivariable model a priori confounders of age, sex and comorbidity as well as alcohol consumption, smoking and WHR were included. Upon adjustment there remained a statistically significant

association between elevated bilirubin and sex but the associations between alcohol consumption and WHR with elevated bilirubin were removed (see Table 8-3)

**Table 8-3 Associations between demographic, lifestyle and medical characteristics and an elevated bilirubin test**

|                             | Normal bilirubin<br>(N=12000)  |      | Elevated bilirubin<br>(N=690) |      | OR [95% CI]       | Adjusted OR<br>[95% CI] | Adjusted OR<br>[95% CI] |
|-----------------------------|--------------------------------|------|-------------------------------|------|-------------------|-------------------------|-------------------------|
|                             | N                              | %    | N                             | %    | Univariable       | Model 1*                | Model 2*                |
| <b>Sex</b>                  |                                |      |                               |      |                   |                         |                         |
| Male                        | 4518                           | 37.6 | 426                           | 61.7 | -                 |                         |                         |
| Female                      | 7482                           | 62.4 | 264                           | 38.3 | 0.37 [0.32, 0.44] | 0.33 [0.27, 0.41]       | 0.33 [0.26, 0.42]       |
| <b>Age (years)</b>          |                                |      |                               |      |                   |                         |                         |
| Median age [IQR]<br>(range) | 80.2 [77.2, 84.1]<br>(75, 108) |      | 80.0 [77.0, 83.4]<br>(75, 98) |      |                   |                         |                         |
| 75-                         | 1056                           | 8.8  | 66                            | 9.6  | -                 | -                       |                         |
| 76-                         | 1536                           | 12.8 | 98                            | 14.2 | 0.99 [0.71, 1.37] | 0.99 [0.71, 1.37]       |                         |
| 77-                         | 1261                           | 10.5 | 66                            | 9.6  | 0.83 [0.58, 1.18] | 0.83 [0.58, 1.19]       |                         |
| 78-                         | 934                            | 7.8  | 50                            | 7.3  | 0.82 [0.56, 1.20] | 0.83 [0.57, 1.23]       |                         |
| 79-                         | 899                            | 7.5  | 59                            | 8.6  | 1.03 [0.71, 1.48] | 1.04 [0.72, 1.51]       |                         |
| 80-                         | 865                            | 7.2  | 42                            | 6.1  | 0.75 [0.50, 1.12] | 0.79 [0.52, 1.18]       |                         |
| 81-                         | 831                            | 6.9  | 55                            | 8.0  | 1.00 [0.69, 1.46] | 1.05 [0.71, 1.53]       |                         |
| 82-                         | 748                            | 6.2  | 53                            | 7.7  | 1.11 [0.76, 1.62] | 1.21 [0.83, 1.78]       |                         |
| 83-                         | 681                            | 5.7  | 40                            | 5.8  | 0.94 [0.62, 1.41] | 0.99 [0.65, 1.50]       |                         |
| 84-                         | 604                            | 5.0  | 27                            | 3.9  | 0.69 [0.43, 1.10] | 0.72 [0.45, 1.16]       |                         |
| 85-                         | 515                            | 4.3  | 26                            | 3.8  | 0.79 [0.49, 1.26] | 0.80 [0.50, 1.30]       |                         |
| 86-                         | 436                            | 3.6  | 15                            | 2.2  | 0.53 [0.30, 0.94] | 0.56 [0.31, 1.01]       |                         |
| 87-                         | 380                            | 3.2  | 30                            | 4.4  | 1.22 [0.77, 1.92] | 1.36 [0.86, 2.16]       |                         |
| 88-                         | 318                            | 2.7  | 15                            | 2.2  | 0.75 [0.42, 1.34] | 0.86 [0.48, 1.55]       |                         |
| 89-                         | 257                            | 2.1  | 12                            | 1.7  | 0.70 [0.37, 1.33] | 0.79 [0.41, 1.50]       |                         |
| 90+                         | 623                            | 5.2  | 29                            | 4.2  | 0.73 [0.46, 1.15] | 0.87 [0.55, 1.39]       |                         |
| Missing                     | 56                             | 0.5  | 7                             | 1.0  | 1.71 [0.74, 3.98] | 1.75 [0.74, 4.14]       |                         |

|   |                                  |      |                                 |      |                   |                   |                   |
|---|----------------------------------|------|---------------------------------|------|-------------------|-------------------|-------------------|
| Odds ratio for yearly increase in age       |                                  |      |                                 |      | 0.99 [0.97, 1.01] | 0.99 [0.97, 1.01] |                   |
| <b>Alcohol</b>                              |                                  |      |                                 |      |                   |                   |                   |
| Median units of alcohol intake in past week | 1<br>[0, 4]<br>(0, 90)<br>N=9746 |      | 1<br>[0, 6]<br>(0, 44)<br>N=585 |      |                   |                   |                   |
| Alcohol units                               |                                  |      |                                 |      |                   |                   |                   |
| 0   | 4361                             | 36.3 | 234                             | 33.9 | -                 |                   |                   |
| 1-  | 4117                             | 34.3 | 251                             | 36.4 | 1.15 [0.96, 1.39] | 1.02 [0.85, 1.24] |                   |
| 8-  | 830                              | 6.9  | 61                              | 8.8  | 1.42 [1.05, 1.91] | 1.04 [0.76, 1.41] |                   |
| 15-   | 243                              | 2.0  | 19                              | 2.8  | 1.60 [0.98, 2.63] | 1.10 [0.66, 1.81] |                   |
| 22+   | 195                              | 1.6  | 20                              | 2.9  | 2.24 [1.37, 3.66] | 1.45 [0.88, 2.40] |                   |
| Missing                                     | 2254                             | 18.8 | 105                             | 15.2 | 0.90 [0.71, 1.15] | 0.94 [0.73, 1.20] |                   |
| Odds ratio for increase in alcohol group    |                                  |      |                                 |      | 1.20 [1.09, 1.31] | 1.06 [0.96, 1.18] |                   |
| <b>Smoking</b>                              |                                  |      |                                 |      |                   |                   |                   |
| Never                                       | 4617                             | 38.5 | 244                             | 35.4 |                   |                   |                   |
| Ex  | 5823                             | 48.5 | 381                             | 55.2 | 1.22 [1.03, 1.44] | 0.83 [0.69, 1.00] | 0.79 [0.65, 0.97] |
| Current                                     | 1212                             | 10.1 | 50                              | 7.3  | 0.76 [0.56, 1.05] | 0.53 [0.38, 0.73] | 0.47 [0.32, 0.68] |
| Missing                                     | 348                              | 2.9  | 15                              | 2.2  | 0.86 [0.50, 1.48] | 0.63 [0.36, 1.10] |                   |
| <b>BMI group</b>                            |                                  |      |                                 |      |                   |                   |                   |
| <18.5                                       | 247                              | 2.1  | 14                              | 2.0  | 0.95 [0.54, 1.66] |                   |                   |
| 18.5-                                       | 4402                             | 36.7 | 256                             | 37.1 | -                 |                   |                   |
| 25-   | 4504                             | 37.5 | 292                             | 42.3 | 1.10 [0.92, 1.31] |                   |                   |
| 30-   | 1452                             | 12.1 | 79                              | 11.5 | 0.91 [0.70, 1.19] |                   |                   |
| 35+   | 333                              | 2.8  | 9                               | 1.3  | 0.44 [0.22, 0.86] |                   |                   |
| Missing                                     | 1062                             | 8.9  | 40                              | 5.8  | 0.67 [0.47, 0.94] |                   |                   |
| Odds ratio for increase in BMI group        |                                  |      |                                 |      | 0.94 [0.85, 1.04] |                   |                   |



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**Waist:hip**

|           |      |      |     |       |                   |                   |                   |
|-----------|------|------|-----|-------|-------------------|-------------------|-------------------|
| 0.65-0.74 | 391  | 3.3  | 20  | 2.9   | 1.36 [0.84, 2.20] | 1.51 [0.93, 2.45] |                   |
| 0.75-0.84 | 3827 | 31.9 | 149 | 21.6  |                   |                   |                   |
| 0.85-0.94 | 4608 | 38.4 | 314 | 45.5  | 1.73 [1.41, 2.12] | 1.07 [0.85, 1.34] |                   |
| 0.95-1.04 | 2008 | 16.7 | 154 | 22.3  | 1.88 [1.48, 2.38] | 0.86 [0.65, 1.13] |                   |
| 1.05-1.15 | 195  | 1.6  | 15  | 2.2   | 1.65 [0.94, 2.90] | 0.75 [0.41, 1.35] |                   |
| Missing   | 971  | 8.1  | 38  | 5.5   | 1.00 [0.69, 1.45] | 0.72 [0.49, 1.06] |                   |
|           |      |      |     | Trend | 1.27 [1.15, 1.40] |                   | 0.90 [0.79, 1.03] |

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**Presence of Co-morbidity**

|              |      |      |     |      |                   |  |  |
|--------------|------|------|-----|------|-------------------|--|--|
| Diabetes     | 941  | 7.8  | 61  | 8.8  | 1.12 [0.85, 1.48] |  |  |
| Heart attack | 1283 | 10.7 | 71  | 10.3 | 0.97 [0.75, 1.25] |  |  |
| Hypertension | 3987 | 33.2 | 231 | 33.5 | 1.00 [0.85, 1.18] |  |  |
| Stroke       | 1041 | 8.7  | 48  | 7.0  | 0.77 [0.57, 1.04] |  |  |
| Cancer       | 1219 | 10.2 | 62  | 9.0  | 0.90 [0.68, 1.17] |  |  |
| Ulcer        | 1446 | 12.1 | 91  | 13.2 | 1.14 [0.90, 1.43] |  |  |
| Angina       | 746  | 6.2  | 47  | 6.8  | 1.14 [0.84, 1.56] |  |  |
| Dementia     | 92   | 0.8  | 2   | 0.3  | 0.38 [0.09, 1.54] |  |  |

**Co-morbidity score**

|   |      |      |     |      |                   |                   |                   |
|---|------|------|-----|------|-------------------|-------------------|-------------------|
| 0   | 4152 | 34.6 | 238 | 34.5 | -                 |                   |                   |
| 1   | 4502 | 37.5 | 254 | 36.8 | 0.99 [0.82, 1.19] | 0.98 [0.81, 1.18] |                   |
| 2   | 2174 | 18.1 | 137 | 19.9 | 1.10 [0.88, 1.37] | 1.07 [0.85, 1.34] |                   |
| 3+  | 980  | 8.2  | 48  | 7.0  | 0.87 [0.63, 1.21] | 0.86 [0.65, 1.13] |                   |
| Missing                                       | 192  | 1.6  | 13  | 1.9  | 1.30 [0.72, 2.34] | 0.75 [0.41, 1.35] |                   |
| Odds ratio for increase in co-morbidity score |      |      |     |      | 0.99 [0.91, 1.07] |                   | 0.98 [0.89, 1.08] |

\*Multivariable model 1 adjusted for sex, age, alcohol consumption, smoking status, WHR and comorbidity as categorical variables; model 2 using only subjects with complete data adjusted for sex, smoking status plus age, alcohol consumption, WHR and comorbidity fitted as linear trend variables

## **8.4 Discussion**

### **8.4.1 Key findings**

This study has determined the associations between elevated LFTs and various demographic, lifestyle and clinical characteristics in a population of people aged 75 and over.

Of note were the observed associations between age and alcohol consumption with elevated AST and ALP. The odds ratios for the associations between AST and these variables were almost exactly the inverse of the associations seen between ALP and these variables. Increasing age was associated with a decreased risk of an elevated measurement of AST (adjusted OR for 1-year increase in age 0.97 (95% CI[0.94, 0.99])) but an increased risk of an elevated measurement of ALP (adjusted OR for 1-year increase in age 1.04 (95% CI[1.03, 1.06])). Increasing alcohol consumption was associated with an increased risk of an elevated measurement of AST (adjusted OR for seven unit increase in alcohol consumption 1.16 (95% CI[1.02, 1.32])) but a decreased risk of an elevated measurement of ALP (adjusted OR for seven unit increase in alcohol consumption 0.83 (95% CI[0.76, 0.91])).

Both elevated AST and ALP were shown to be associated with the diagnosis of diabetes and dementia. Additionally elevated ALP was associated with heart attack.

Being male was very highly associated with having a abnormal measurement of bilirubin (adjusted OR for elevated bilirubin for females 0.45 (95% CI[0.35, 0.58])). Upon multivariable adjustment both being an ex-smoker or a current smoker appeared to confer some protection against having an elevated bilirubin measurement.

### **8.4.2 Strengths and limitations**

This study relied on a single measurement of each of AST, ALP and bilirubin. Naturally it would be desirable to have multiple measurements of these liver function tests in order to assess whether an abnormality was persistent and therefore that there was a consistent association with any given characteristic of interest.

Although I have been able to examine the associations of several characteristics with elevated LFTs in this large population there are limitations in the interpretation of these findings resulting from the absence of particular data items from the initial data collection. Particularly the absence of data on diagnosed or recognised liver disease means that I am not able to exclude the presence of liver disease as a potential confounder of any of the associations seen. The examination of so many associations will also potentially have led to some statistically significant findings occurring just through chance alone.

I was able to examine the associations between several individual diseases and elevated LFTs as well as a derived comorbidity index. The derivation of a comorbidity index was a pragmatic approach to try and account for the potential for multiple diseases to be present in one individual. As I was analysing these data as a secondary source it was not possible to derive a more recognised comorbidity index, such as the Charlson score (described in section 4.2.2) as several of the data items needed to create such a score were not available from the original questionnaires.

As well as not being able to adjust for some relevant comorbidity it was also not possible to adjust for any medications that the participants may have been

taking (as this information was not available to me) which may have affected the levels of serum enzymes recorded. However, the adjusted odds ratios include a measure of comorbidity which may have partially taken this into account.

As with any cross-sectional study it is not possible to infer anything regarding causality from these results. For example, it is equally possible that having had a heart attack led to an elevation in ALP or that the underlying reason for the elevation in ALP was also the mechanism that led to the heart attack. Either pathway would result in a positive association as seen in these data.

### **8.4.3 Comparison with previous studies**

As discussed in section 1.4.2.2 there have been a number of studies reporting associations between various characteristics and elevated LFTs but with little consistency in the definition of abnormality and some disagreement in the direction and magnitude of the associations. Many of these studies have also focussed on abnormalities in transaminases, considering elevations of AST and ALT together, with a lack of data on individual elevations of AST, ALP or bilirubin.

The recent study of residents in Tayside, Scotland with a measurement of liver function showed a very different pattern of association with comorbidity to that which I have described in this study.<sup>66</sup> An elevated measurement of ALP was associated with a statistically significant lower risk of several comorbidities (ischaemic heart disease, diabetes, respiratory disease and cancer) but with a slightly higher risk of biliary disease probably reflecting the selection bias inherent in this study. My analysis has shown an increased risk of diabetes,

heart attack and dementia with elevated ALP. In the study in Tayside, an elevated measurement of bilirubin was associated with a statistically significant lower risk of all of these comorbidities with the exception of diabetes in contrast with my analysis where there was no association between bilirubin and any of the diagnosed or self-reported diseases recorded. However, the proportion of patients within this study with these diagnosed comorbidities is much lower than that seen in my study, perhaps reflecting the older age group of my study.

Similar to the results shown in section 8.3.1 the authors of the study in Scotland showed a higher proportion of patients with elevated transaminases to have a record of alcohol abuse.<sup>66</sup> However, they did not present any data on actual alcohol consumption. In contrast to my results in section 8.3.2 they also report a higher proportion of patients with an elevated ALP to have a record of alcohol abuse.

One study from America showed a lower prevalence of elevated aminotransferases in older ages (70+), which would be consistent with my findings of lower risk of elevated AST with increasing age, but there were no details presented at the fine level as in my study.<sup>70</sup>

Several studies report an association between an elevated measurement of AST and the presence or development of diabetes similar to that seen in my study.<sup>68 70 73 74</sup>

Many studies also report an association between increasing BMI and elevated liver function tests, particularly transaminases.<sup>69 70 71 75</sup> I did not see a relationship between increasing BMI and elevated liver function but did observe a relationship between increasing WHR category and elevated AST and also elevated bilirubin. This is possibly due to the fact that WHR is

considered a more accurate assessment of body fatness in older people owing to the increase in BMI that will occur as a result of shortening height.<sup>116</sup> A similar relationship as I have described between increasing alcohol consumption and elevated transaminases has previously been shown in studies in both the USA and South Korea.<sup>68 71 75</sup> Another study has not shown this relationship though it is hard to directly compare my data with this study as they classify drinkers as simply more or less than 3 units per day as opposed to examining a trend in increasing consumption.<sup>69</sup>

#### **8.4.4 Conclusions**

This study has shown a number of potentially interesting associations between demographic, lifestyle and clinical factors and elevated liver function tests. That the results for measurement of elevated AST and ALP with respect to age and alcohol are almost the exact opposite of each other is particularly worthy of note. That an elevated measurement of AST is associated with an increasing alcohol consumption even at older ages may suggest continued damage or sustained damage following earlier damage caused by consistently high levels of alcohol consumption.

The finding of elevated bilirubin to be so strongly associated with being male is also worth consideration. It is possible that there is a much higher prevalence of Gilbert's syndrome among men although I could not examine this within these data.

The LFTs that I have studied may not actually be markers of liver function (as discussed in section 1.4.2). Indeed the observed associations with other comorbid conditions, particularly diabetes, might suggest that these enzymes are produced in more significant amounts in the presence of other diseases.

It is possible that diabetes is a marker of undiagnosed (or non-recorded) non-alcoholic fatty liver disease or other underlying syndromes that may be the precursor of liver disease.

## **9 Mortality associated with elevated liver function tests**

### **9.1 Introduction**

This study aims to determine the health consequences in people aged over 75 with elevated liver function tests, in terms of the risk of all cause and cause-specific mortality.

### **9.2 Methods**

#### **9.2.1 Dataset used**

The data used in this study are those from the detailed nurse assessment contained within the 'detail' database as well as information taken from the 'deaths' and 'censoring' databases (See Figure 6-2). A total of 15,308 participants aged 75 and over are included in the subsequent analyses. The definition of elevated liver function is as described in section 7.2.3.1 following imputation of missing upper limits using the median reference ranges.

#### **9.2.2 Additional definitions**

##### **9.2.2.1 Cause of death**

Deaths were coded according to the International Classification for Diseases, 9<sup>th</sup> revision (ICD9) until September 2002, and according to the 10<sup>th</sup> revision (ICD10) afterwards. I specifically examined causes of death that are most common in patients of this age group,<sup>117</sup> namely from cardiovascular disease (ICD9 401-405, 410-414, 425-447; ICD10 I10-I15, I20-I25, I42-I52, I6-I77, I79), cancer (all cancers excluding liver cancer (ICD9 140-154, 156-239;



ICD10 C0-C21, C23-D4)), respiratory disease (ICD9 46-51; ICD10 J). I was additionally interested in mortality from liver disease (viral hepatitis, liver cancer and liver disease (ICD9 070, 155, 570-573; ICD10 B15-B19, C22, K7)). Participants were assigned cause of death based on the underlying cause of death as given by the NHSCR.

### **9.2.3 Statistical analysis**

Subjects were considered as contributing time to the analysis from the date of interview until death, censoring (migration) or 5 November 2005 (the last date of available data from the ONS) whichever came earliest. Associations between death and demographic, lifestyle and medical characteristics were examined in a control population consisting of all those people without any LFT abnormality in order to identify appropriate confounding variables. All cause and cause-specific mortality were examined for each elevated LFT in turn. Cox proportional hazards regression analysis was used to compare the survival of cohorts with normal and elevated LFTs. Analysis was performed treating an individual practice as a clustered unit. A priori confounders of age, sex and co-morbidity as well as other confounders identified in Section 8.3 for individual LFTs were included within multivariate cox proportional hazards models to provide adjusted hazard ratios. Proportional hazards assumptions were checked using Schoenfeld residuals and log-log plots.

## **9.3 Results**

### **9.3.1 Mortality of whole population**

Of the 15,308 participants in this study, 9268(60.5%) had died by 5 November 2005 (see Table 9-1). Deaths from cardiovascular disease, cancer and respiratory disease accounted for 7200 (77.7%) of all deaths in this population. Only 52 (0.6%) participants were recorded as having died from liver disease.

**Table 9-1 Selected causes of death**

| <b>Cause of death</b> | <b>N</b>    | <b>%<br/>(of total<br/>deaths)</b> |
|-----------------------|-------------|------------------------------------|
| <b>Total deaths</b>   | <b>9268</b> | <b>100</b>                         |
| Cancer                | 1715        | 18.5                               |
| CVD                   | 3912        | 42.2                               |
| Respiratory           | 1573        | 17.0                               |
| Liver                 | 52          | 0.6                                |
| All other             | 1999        | 21.6                               |
| Missing               | 17          | 0.2                                |
| <b>Alive</b>          | <b>6040</b> |                                    |

### **9.3.2 Associations between death and demographic, lifestyle and clinical characteristics**

Examining the population of participants with no elevated LFTs revealed significant associations between sex, age, smoking status, BMI, WHR and comorbidity and risk of death on univariable analysis (see Table 9-2). There was a decreased risk of death associated with being female and increasing BMI for increase in BMI category) but an increased risk of death associated with increasing age, being a smoker (current or ex-), increasing WHR and increasing comorbidity score. All individual comorbidities examined showed an increased risk of death, bar cancer and hypertension. There was no statistically significant association between increasing alcohol consumption and death.

Multivariable analysis included sex, age, smoking status, WHR and comorbidity score with all variables remaining statistically significantly associated with death upon mutual adjustment.

**Table 9-2 Association between demographic, lifestyle and clinical factors and death in population with no elevated liver function test**

|  | Alive<br>(N=4227) |      | Dead<br>(N=5798) |      | OR [95% CI]       |                   |
|--|-------------------|------|------------------|------|-------------------|-------------------|
|  | N                 | %    | N                | %    | Univariable       | Multivariable     |
| <b>Sex</b>   |                   |      |                  |      |                   |                   |
| Female   | 2841              | 67.2 | 3381             | 58.3 | 0.67 [0.61, 0.72] | 0.62 [0.55, 0.70] |
| Male   | 1386              | 32.8 | 2417             | 41.7 |                   |                   |
| <b>Age</b>   |                   |      |                  |      |                   |                   |
| Median age   |                   |      |                  |      |                   |                   |
| [IQR] (range)  |                   |      |                  |      |                   |                   |
| Age group<br>(fine)                                  |                   |      |                  |      |                   |                   |
| 75-  | 539               | 12.7 | 352              | 6.1  |                   |                   |
| 76-  | 766               | 18.1 | 517              | 8.9  |                   |                   |
| 77-  | 629               | 14.9 | 450              | 7.7  |                   |                   |
| 78-  | 408               | 9.7  | 376              | 6.5  |                   |                   |
| 79-  | 350               | 8.3  | 400              | 6.9  |                   |                   |
| 80-  | 326               | 7.7  | 406              | 7.0  |                   |                   |
| 81-  | 306               | 7.2  | 406              | 7.0  |                   |                   |
| 82-  | 234               | 5.5  | 382              | 6.6  |                   |                   |
| 83-  | 166               | 3.9  | 403              | 7.0  |                   |                   |
| 84-  | 148               | 3.5  | 350              | 6.0  |                   |                   |
| 85-  | 97                | 2.3  | 323              | 5.6  |                   |                   |
| 86-  | 78                | 1.9  | 292              | 5.0  |                   |                   |
| 87-  | 61                | 1.4  | 255              | 4.4  |                   |                   |
| 88-  | 44                | 1.0  | 224              | 3.9  |                   |                   |
| 89-  | 23                | 0.5  | 175              | 3.0  |                   |                   |
| 90+  | 31                | 0.7  | 463              | 8.0  |                   |                   |
| Missing  | 21                | 0.5  | 24               | 0.4  |                   |                   |
| Odds ratio for yearly increase in age                |                   |      |                  |      | 1.20 [1.18, 1.21] | 1.22 [1.20, 1.23] |
| <b>Alcohol</b>                                       |                   |      |                  |      |                   |                   |
| Median units<br>of alcohol<br>intake in past<br>week |                   |      |                  |      |                   |                   |
| Alcohol units  |                   |      |                  |      |                   |                   |
| 0  | 1490              | 35.3 | 2104             | 36.3 |                   |                   |
| 1-   | 1640              | 38.8 | 1919             | 33.1 |                   |                   |
| 8-   | 309               | 7.3  | 383              | 6.6  |                   |                   |
| 15-  | 92                | 2.2  | 114              | 2.0  |                   |                   |
| 22+  | 58                | 1.4  | 104              | 1.8  |                   |                   |
| Missing  | 638               | 15.0 | 1174             | 20.2 |                   |                   |
| Odds ratio for increase in alcohol group             |                   |      |                  |      | 0.95 [0.91, 1.01] | -                 |
| <b>Smoking</b>                                       |                   |      |                  |      |                   |                   |
| Never  | 1743              | 41.2 | 2074             | 35.8 |                   |                   |
| Ex   | 2070              | 49.0 | 2854             | 49.2 | 1.16 [1.06, 1.26] | 1.18 [1.06, 1.31] |
| Current  | 301               | 7.1  | 685              | 11.8 | 1.88 [1.61, 2.18] | 2.42 [2.04, 2.87] |
| Missing  | 113               | 2.7  | 185              | 3.2  |                   |                   |
| <b>BMI group</b>                                     |                   |      |                  |      |                   |                   |

|   |      |      |      |      |                   |                   |
|---|------|------|------|------|-------------------|-------------------|
| <18.5   | 49   | 1.2  | 156  | 2.7  | 2.16 [1.56, 3.01] |                   |
| 18.5-   | 1505 | 35.6 | 2152 | 37.1 | -                 |                   |
| 25-   | 1837 | 14.5 | 1998 | 34.5 | 0.76 [0.69, 0.83] |                   |
| 30-   | 543  | 12.9 | 679  | 11.7 | 0.87 [0.76, 0.99] |                   |
| 35+   | 124  | 2.9  | 132  | 2.3  | 0.72 [0.56, 0.93] |                   |
| Missing                                       | 169  | 4.0  | 681  | 11.8 |                   |                   |
| Odds ratio for increase in BMI group          |      |      |      |      | 0.86 [0.82, 0.91] |                   |
| <b>Waist:hip</b>                              |      |      |      |      |                   |                   |
| 0.65-0.74                                     | 174  | 4.1  | 157  | 2.7  | 0.87 [0.69, 1.10] |                   |
| 0.75-0.84                                     | 1580 | 37.4 | 1638 | 28.3 | -                 |                   |
| 0.85-0.94                                     | 1573 | 37.2 | 2253 | 38.9 | 1.42 [1.29, 1.56] |                   |
| 0.95-1.04                                     | 665  | 15.7 | 1047 | 18.1 | 1.59 [1.41, 1.80] |                   |
| 1.05-1.15                                     | 52   | 1.2  | 110  | 1.9  | 2.20 [1.56, 3.09] |                   |
| Missing                                       | 183  | 4.3  | 593  | 10.2 |                   |                   |
| Trend   |      |      |      |      | 1.28 [1.21, 1.34] | 1.08 [1.01, 1.16] |
| <b>Presence of Co-morbidity</b>               |      |      |      |      |                   |                   |
| Diabetes                                      | 219  | 5.2  | 530  | 9.1  | 1.85 [1.57, 2.19] |                   |
| Heart attack                                  | 303  | 7.2  | 741  | 12.8 | 1.89 [1.64, 2.18] |                   |
| Hypertension                                  | 1406 | 33.3 | 1925 | 33.2 | 1.02 [0.93, 1.11] |                   |
| Stroke  | 196  | 4.6  | 684  | 11.8 | 2.74 [2.32, 3.23] |                   |
| Cancer  | 419  | 9.9  | 616  | 10.6 | 1.09 [0.95, 1.24] |                   |
| Ulcer   | 468  | 11.1 | 734  | 12.7 | 1.14 [1.01, 1.29] |                   |
| Angina  | 236  | 5.6  | 393  | 6.8  | 1.21 [1.02, 1.44] |                   |
| Dementia                                      | 5    | 0.1  | 56   | 1.0  | 7.86 [3.14, 19.7] |                   |
| <b>Co-morbidity score</b>                     |      |      |      |      |                   |                   |
| 0   | 1677 | 39.7 | 1813 | 32.3 |                   |                   |
| 1   | 1635 | 38.7 | 2114 | 36.5 | 1.20 [1.09, 1.31] |                   |
| 2   | 648  | 15.3 | 1171 | 20.2 | 1.68 [1.49, 1.89] |                   |
| 3+  | 224  | 5.3  | 583  | 10.0 | 2.43 [2.05, 2.88] |                   |
| Odds ratio for increase in co-morbidity score |      |      |      |      | 1.32 [1.26, 1.38] | 1.39 [1.32, 1.46] |

\*adjusted for age, sex, smoking, WHR and comorbidity score.

### **9.3.3 Mortality associated with elevated AST**

Mortality in subjects with an elevated AST was 104.8 per 1000 person-years representing an increase of 10 deaths per 1000 person-years of follow-up compared to subjects with a normal AST (see Table 9-3). This corresponded to an adjusted hazard ratio of 1.27, i.e. an elevated AST was associated with a 27% (95% CI [9%, 47%]) increased hazard for all-cause mortality. This is displayed visually in the Kaplan-Meier plot (see Figure 9-1). There was an increased hazard of death observed with increasing levels of abnormality with patients, with an elevated AST over 2 times the ULN having a 62% increased hazard of death.

An elevated AST was associated with an increase in mortality from cancer (56% increased hazard) and mortality from liver disease (7-fold increased hazard) (see Table 9-3). It should be noted that only 8 out of 429 subjects (1.8%) with an elevated AST died from liver disease.

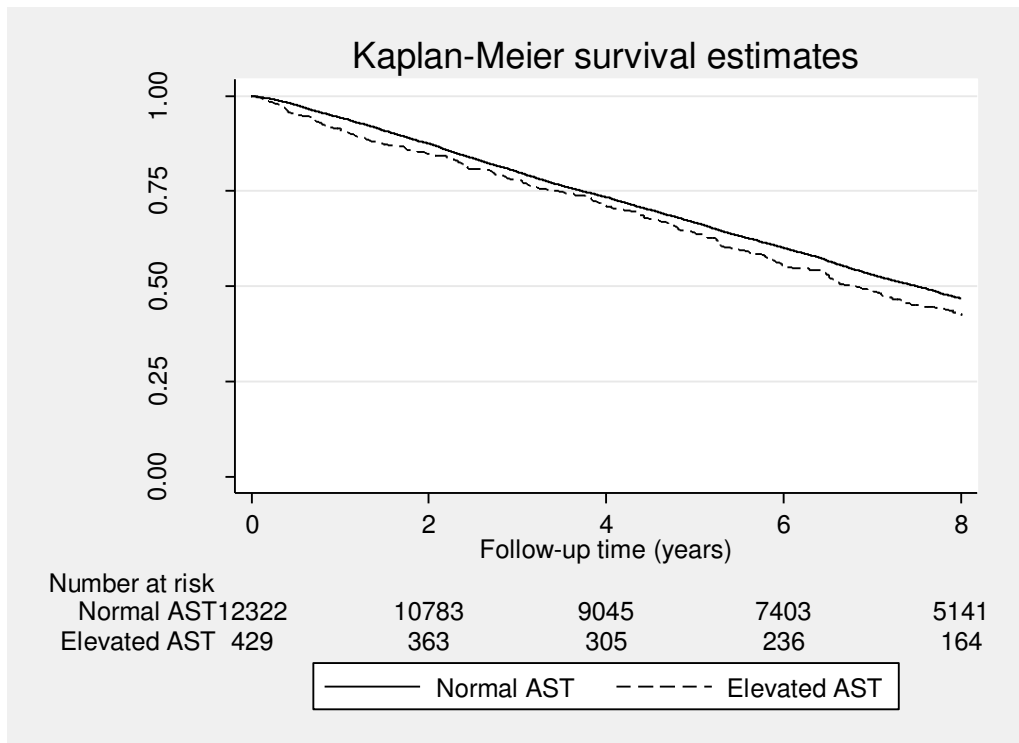
Examining the Schoenfeld residuals and log-log plots gave no evidence of invalidation of the proportional hazards assumption (see Figure 9-2 and Figure 9-3).

**Table 9-3 Cox proportional hazards model for death (all-cause and cause-specific mortality) by AST test**

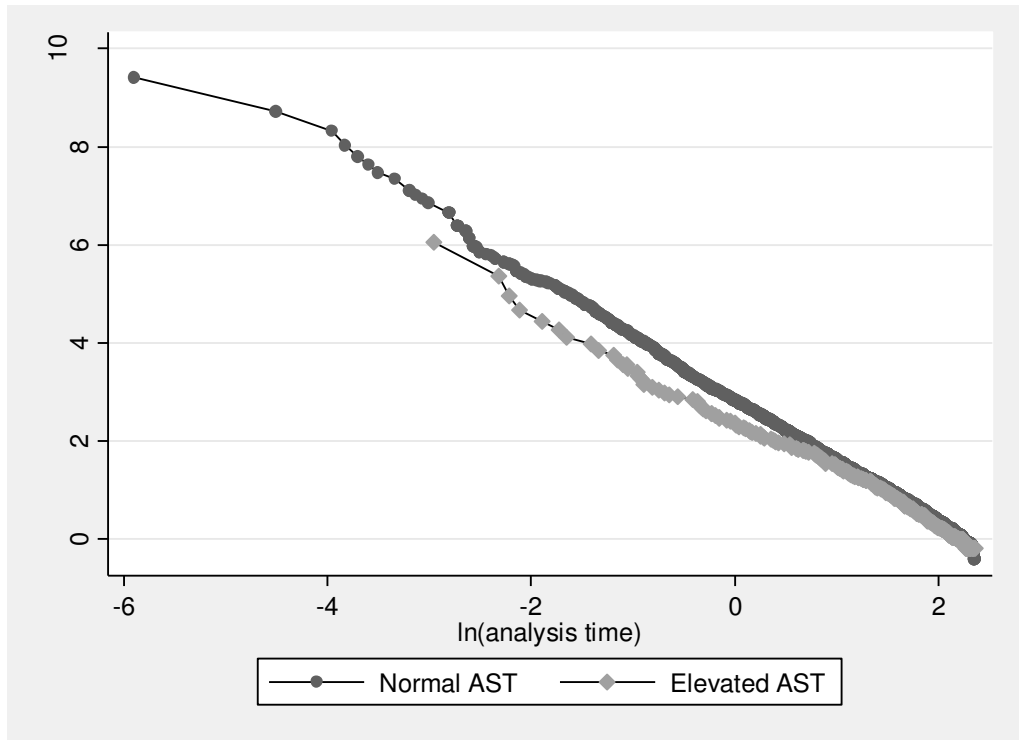
|  | Events | Person-years | Mortality rate<br>(per 1000<br>person years) | Hazard ratio<br>[95%CI] | Adjusted Hazard ratio* [95%CI] |
|--|--------|--------------|--|-------------------------|--------------------------------|
| <b>All-cause mortality</b>                         |        |              |  |                         |                                |
| Normal AST   | 7319   | 77485        | 94.5   | -                       |                                |
| Elevated AST                                       | 271    | 2586         | 104.8  | 1.11 [0.99, 1.26]       | 1.27 [1.09, 1.47]              |
| Elevated AST within 1x                             | 229    | 2267         | 101.0  | 1.07 [0.92, 1.24]       | 1.17 [1.02, 1.34]              |
| Elevated AST over 2x                               | 42     | 319          | 131.7  | 1.43 [1.04, 1.96]       | 1.62 [1.22, 2.16]              |
| Hazard ratio for increase in AST abnormality group |        |              |  | 1.12 [1.02, 1.24]       | 1.26 [1.12, 1.41]              |
| <b>Cause-specific mortality</b>                    |        |              |  |                         |                                |
| <b>CVD</b>   |        |              |  |                         |                                |
| Normal AST   | 3097   | 77485        | 40.0   | -                       |                                |
| Elevated AST                                       | 109    | 2586         | 42.1   | 1.06 [0.87, 1.28]       | 1.15 [0.92, 1.44]              |
| <b>Cancer (excluding liver cancer)</b>             |        |              |  |                         |                                |
| Normal AST   | 1359   | 77485        | 17.5   | -                       |                                |
| Elevated AST                                       | 63     | 2586         | 24.4   | 1.40 [1.09, 1.80]       | 1.56 [1.21, 2.01]              |
| <b>Respiratory disease</b>                         |        |              |  |                         |                                |
| Normal AST   | 1235   | 77485        | 15.9   | -                       |                                |
| Elevated AST                                       | 33     | 2586         | 12.7   | 0.80 [0.57, 1.13]       | 1.03 [0.70, 1.52]              |
| <b>Liver disease</b>                               |        |              |  |                         |                                |
| Normal AST   | 38     | 77485        | 0.49   | -                       |                                |
| Elevated AST                                       | 8      | 2586         | 3.09   | 6.28 [2.92, 13.5]       | 7.00 [2.88, 17.06]             |

\*adjusted for age, sex, comorbidity group, alcohol intake and WHR group.

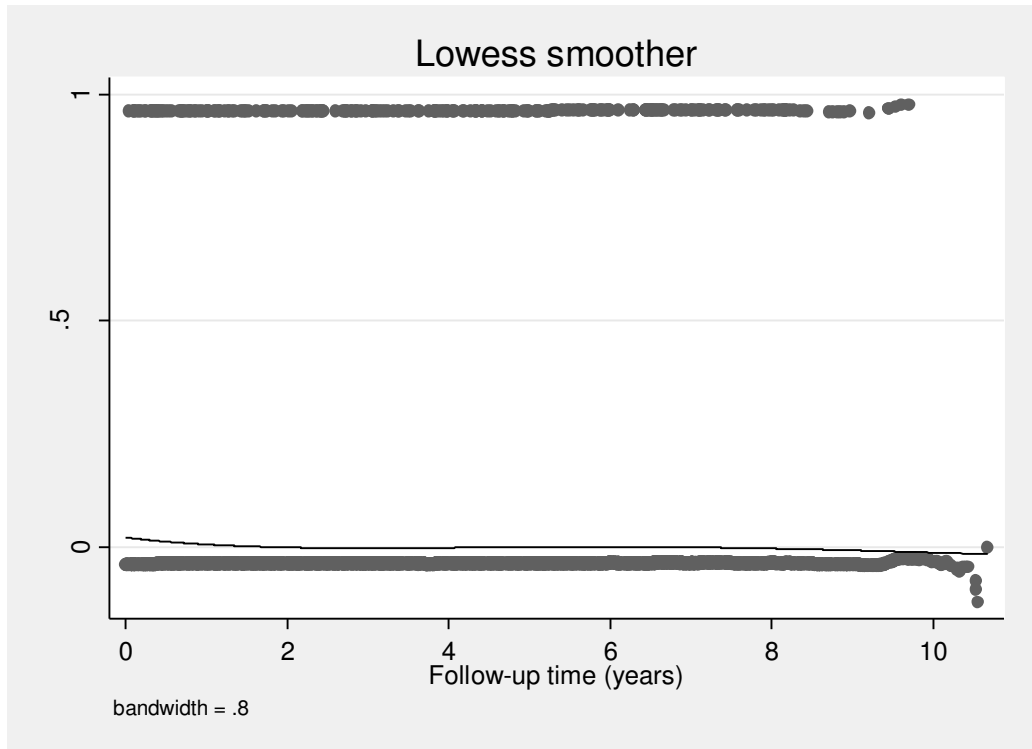




**Figure 9-1 Kaplan-Meier survival estimates for all-cause mortality for AST measurement**



**Figure 9-2 Log-log plot for all-cause mortality for AST measurement**



**Figure 9-3 Schoenfeld residuals against time for all-cause mortality for measurement of AST**

### **9.3.4 Mortality associated with elevated ALP**

Mortality in subjects with an elevated ALP was 138.8 per 1000 person-years of follow-up representing an increase of nearly 50 deaths per 1000 person years compared with subjects with a normal ALP measurement (see Table 9-4). An elevated ALP measurement was associated with a 47% increase in hazard of death, adjusted for age, sex, co-morbidity score and alcohol intake (hazard ratio 1.47; 95% CI [1.35, 1.61]). This higher hazard of death is shown graphically in the Kaplan-Meier plot (see Figure 9-4).

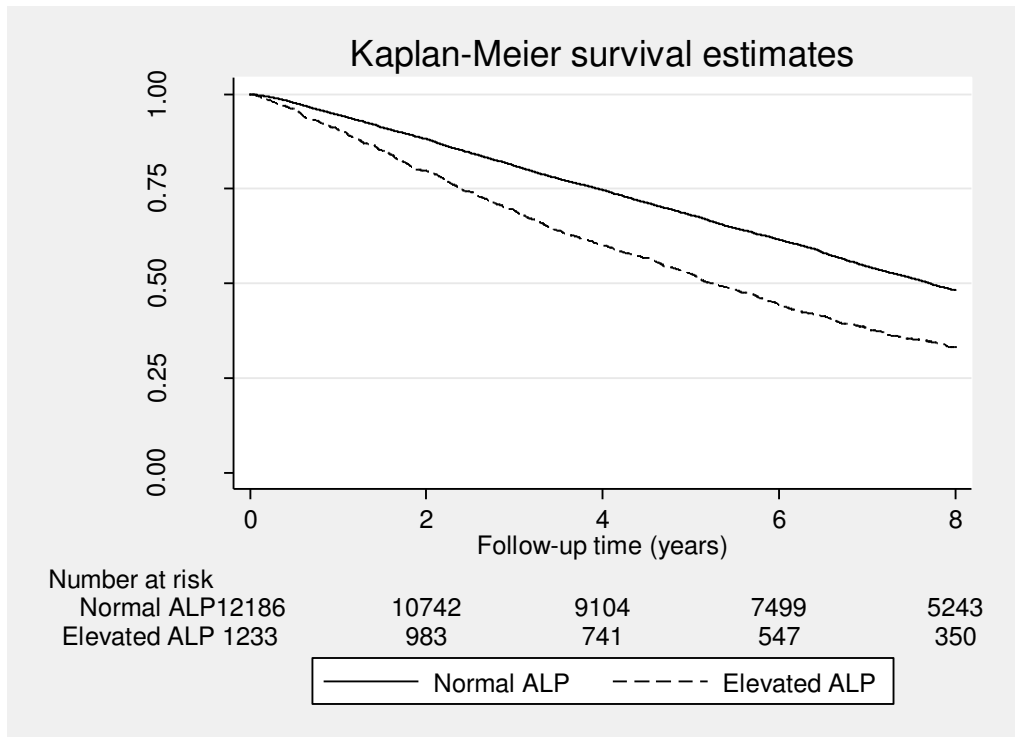
An elevated ALP was associated with an increased hazard for death from CVD (34% increase), death from cancer (61% increase), death from respiratory disease (58% increase) and death from liver disease (nearly 6-fold increase) (see Table 9-4). However, only 13 out of 1246 subjects (1.0%) with an elevated ALP died from liver disease.

Examining the Schoenfeld residuals and log-log plots gave no evidence of invalidation of the proportional hazards assumption (see Figure 9-5 and Figure 9-6).

**Table 9-4 Cox proportional hazards model for death (all-cause and cause-specific mortality) by ALP test**

|  | Events | Person-years | Mortality rate<br>(per 1000<br>person years) | Hazard ratio [95%CI] | Adjusted Hazard ratio*<br>[95%CI] |
|--|--------|--------------|--|----------------------|-----------------------------------|
| <b>All-cause mortality</b>                         |        |              |  |                      |                                   |
| Normal ALP   | 7068   | 77752        | 90.9   | -                    |                                   |
| Elevated ALP                                       | 903    | 6503.9       | 138.8  | 1.58 [1.47, 1.69]    | 1.47 [1.35, 1.61]                 |
| Elevated ALP within 1x                             | 809    | 5895.7       | 137.2  | 1.56 [1.44, 1.68]    | 1.42 [1.32, 1.52]                 |
| Elevated ALP over 2x                               | 94     | 608.3        | 154.5  | 1.76 [1.44, 1.68]    | 1.44 [1.13, 1.84]                 |
| Hazard ratio for increase in ALP abnormality group |        |              |  | 1.47 [1.39, 1.56]    | 1.37 [1.26, 1.48]                 |
| <b>Cause-specific mortality</b>                    |        |              |  |                      |                                   |
| <b>Cardiovascular disease</b>                      |        |              |  |                      |                                   |
| Normal ALP   | 3010   | 77752        | 38.7   | -                    |                                   |
| Elevated ALP                                       | 358    | 6504         | 55.0   | 1.46 [1.30, 1.62]    | 1.34 [1.17, 1.55]                 |
| <b>Cancer (excluding liver cancer)</b>             |        |              |  |                      |                                   |
| Normal ALP   | 1324   | 77752        | 17.0   | -                    |                                   |
| Elevated ALP                                       | 174    | 6504         | 26.8   | 1.61 [1.37, 1.89]    | 1.61 [1.39, 1.86]                 |
| <b>Respiratory disease</b>                         |        |              |  |                      |                                   |
| Normal ALP   | 1181   | 77752        | 15.2   | -                    |                                   |
| Elevated ALP                                       | 161    | 6504         | 24.8   | 1.68 [1.42, 1.98]    | 1.58 [1.32, 1.90]                 |
| <b>Liver disease</b>                               |        |              |  |                      |                                   |
| Normal ALP   | 35     | 77752        | 0.45   | -                    |                                   |
| Elevated ALP                                       | 13     | 6503.9       | 2.00   | 4.59 [2.43, 8.69]    | 5.95 [2.83, 12.51]                |

\*adjusted for age, sex, comorbidity group and alcohol intake



**Figure 9-4 Kaplan-Meier survival estimates for all-cause mortality for ALP measurement**

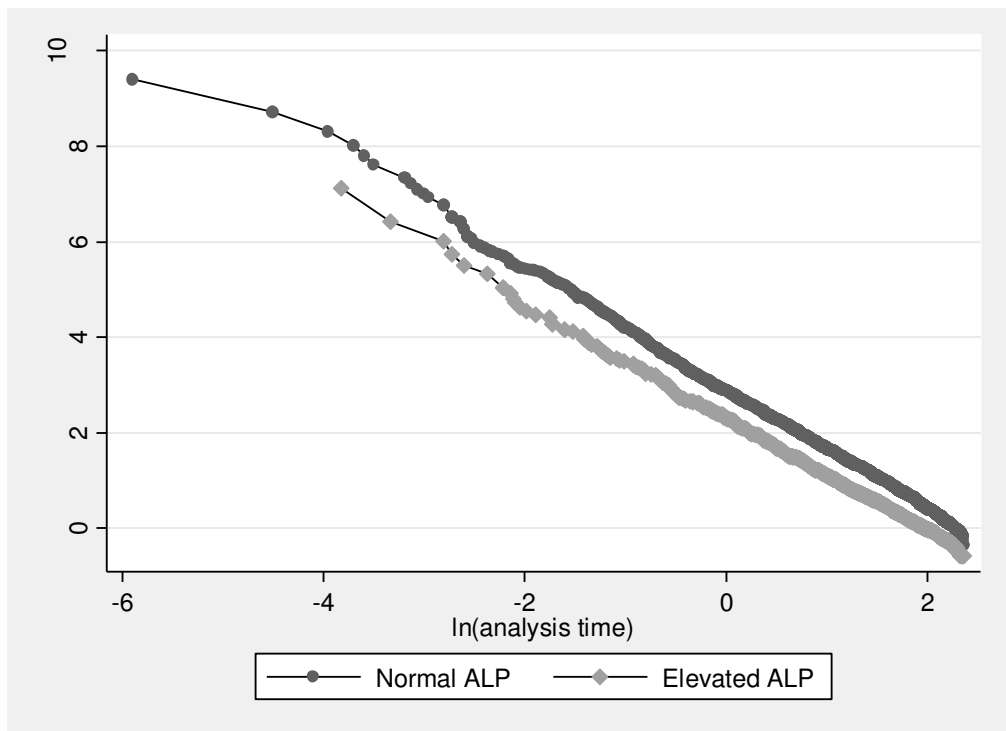
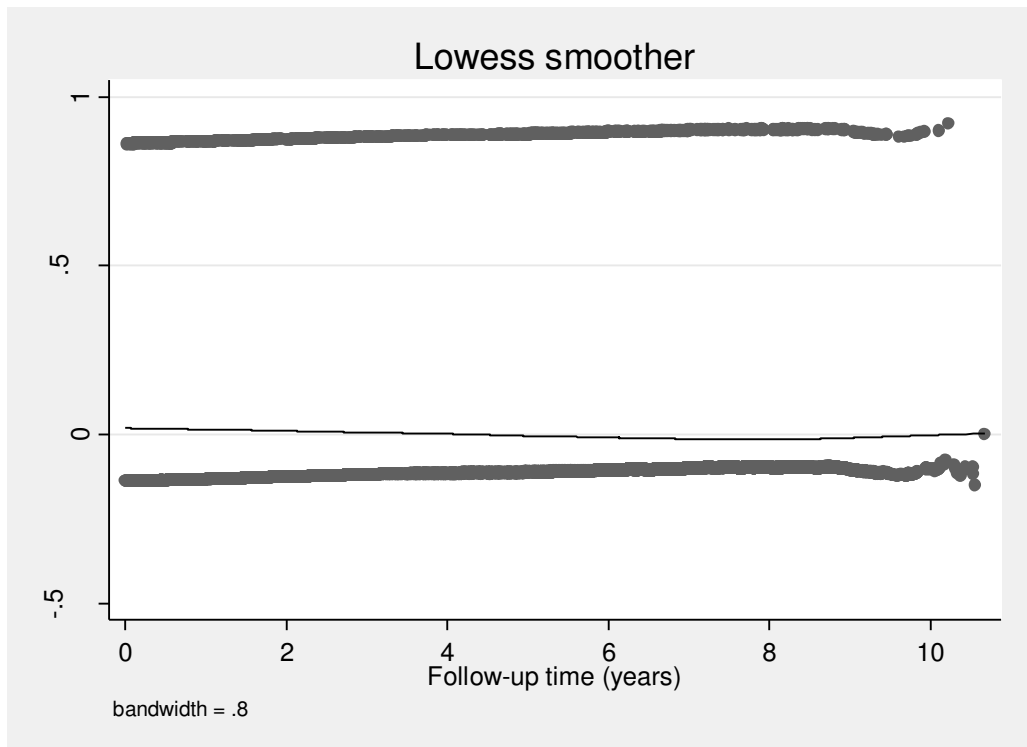


Figure 9-5 Log-log plot for all-cause mortality for ALP measurement



**Figure 9-6 Schoenfeld residuals against time for all-cause mortality for measurement of ALP**



### **9.3.5 Mortality associated with elevated bilirubin**

Elevated bilirubin was associated with a small increase in hazard of death (15%, 95%CI [2%, 30%]) following adjustment for the confounding factors of age, sex, comorbidity score, smoking status, alcohol consumption and WHR group (see Table 9-5). This slight increase in hazard of death is shown graphically in the Kaplan-Meier plot (see Figure 9-10).

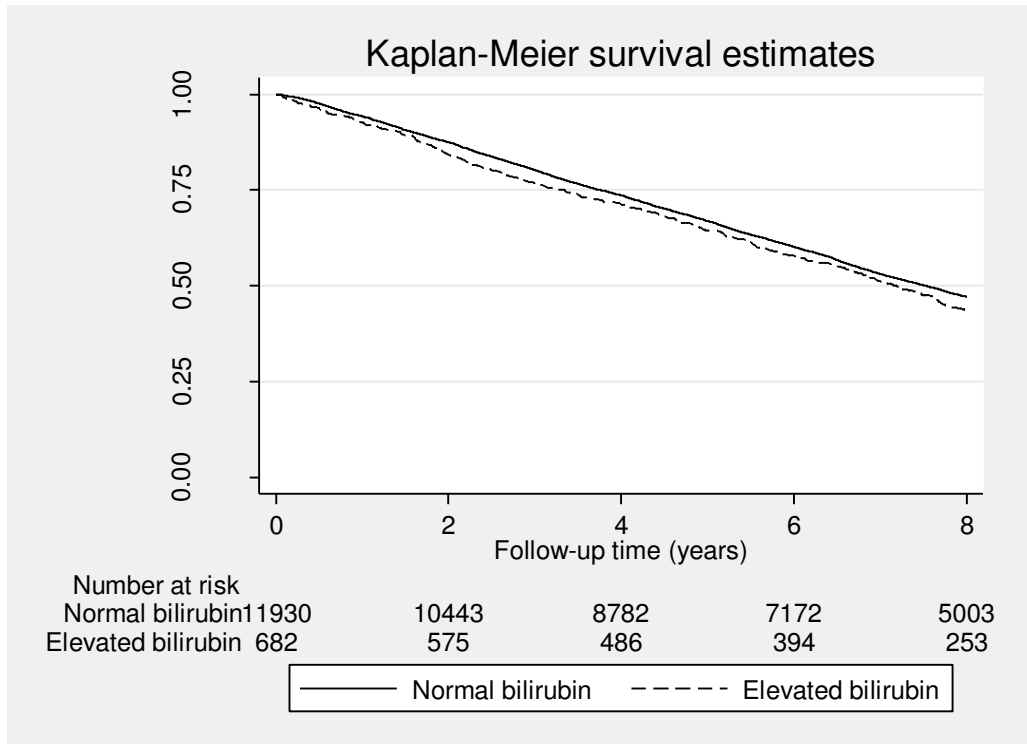
Elevated bilirubin was not associated with a change in hazard of any cause-specific mortality examined (see Table 9-5).

Examining the Schoenfeld residuals and log-log plots gave no evidence of invalidation of the proportional hazards assumption (see Figure 9-8 and Figure 9-9).

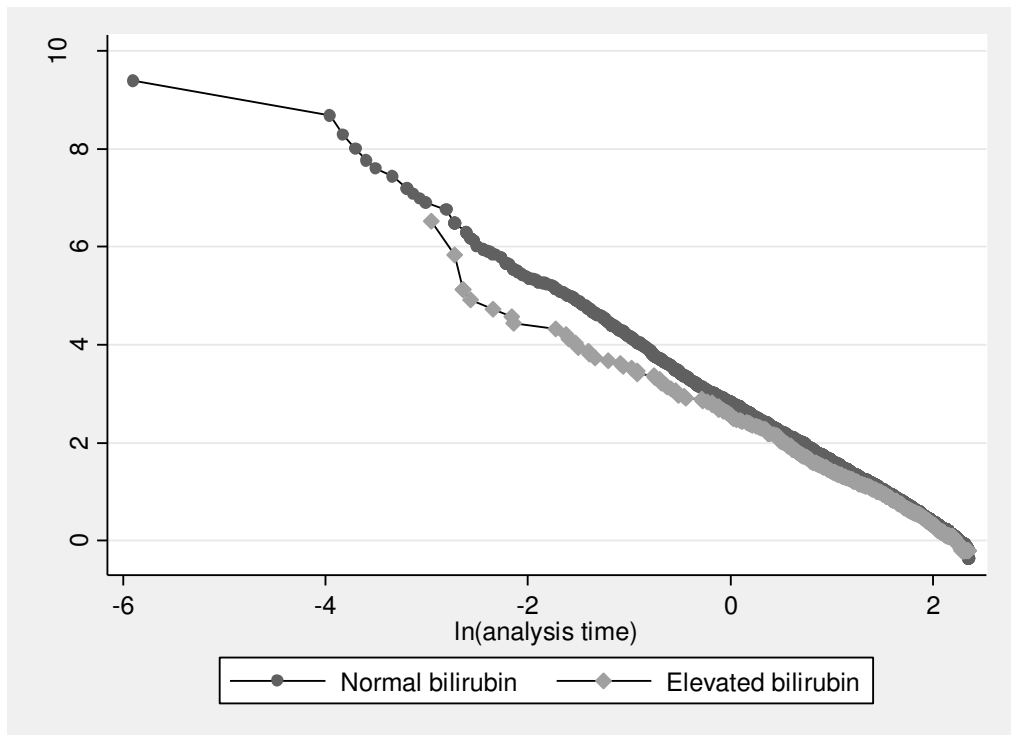
**Table 9-5 Cox proportional hazards model for death (all-cause and cause-specific mortality) by bilirubin test**

|  | Events | Person-<br>years | Mortality rate<br>(per 1000<br>person years) | Hazard ratio [95%CI] | Adjusted Hazard ratio*<br>[95%CI] |
|--|--------|------------------|--|----------------------|-----------------------------------|
| <b>All-cause mortality</b>                               |        |                  |  |                      |                                   |
| Normal Bilirubin   | 7063   | 75176            | 94.0   | -                    |                                   |
| Elevated Bilirubin                                       | 416    | 4109             | 101.2  | 1.09 [0.99, 1.20]    | 1.15 [1.02, 1.30]                 |
| Elevated bilirubin within 1x                             | 388    | 3866             | 100.4  | 1.08 [0.98, 1.19]    | 1.14 [0.99, 1.29]                 |
| Elevated bilirubin over 2x                               | 28     | 243              | 115.3  | 1.24 [0.86, 1.79]    | 1.35 [0.91, 2.00]                 |
| Hazard ratio for increase in bilirubin abnormality group |        |                  |  | 1.09 [1.00, 1.18]    | 1.07 [0.98, 1.17]                 |
| <b>Cause-specific mortality</b>                          |        |                  |  |                      |                                   |
| <b>Cardiovascular disease</b>                            |        |                  |  |                      |                                   |
| Normal Bilirubin   | 2981   | 75176            | 39.7   | -                    |                                   |
| Elevated Bilirubin                                       | 190    | 4109             | 46.2   | 1.18 [1.02, 1.36]    | 1.15 [0.98, 1.36]                 |
| <b>Cancer (excluding liver cancer)</b>                   |        |                  |  |                      |                                   |
| Normal Bilirubin   | 1331   | 75176            | 17.7   | -                    |                                   |
| Elevated Bilirubin                                       | 69     | 4109             | 16.8   | 0.96 [0.75, 1.22]    | 0.90 [0.68, 1.19]                 |
| <b>Respiratory disease</b>                               |        |                  |  |                      |                                   |
| Normal Bilirubin   | 1203   | 75176            | 16.0   | -                    |                                   |
| Elevated Bilirubin                                       | 58     | 4109             | 14.1   | 0.89 [0.68, 1.16]    | 0.97 [0.69, 1.35]                 |
| <b>Liver disease</b>                                     |        |                  |  |                      |                                   |
| Normal Bilirubin   | 44     | 75176            | 0.6  | -                    |                                   |
| Elevated Bilirubin                                       | 5      | 4109             | 1.22   | 2.11 [0.84, 5.32]    | 1.71 [0.63, 4.65]                 |

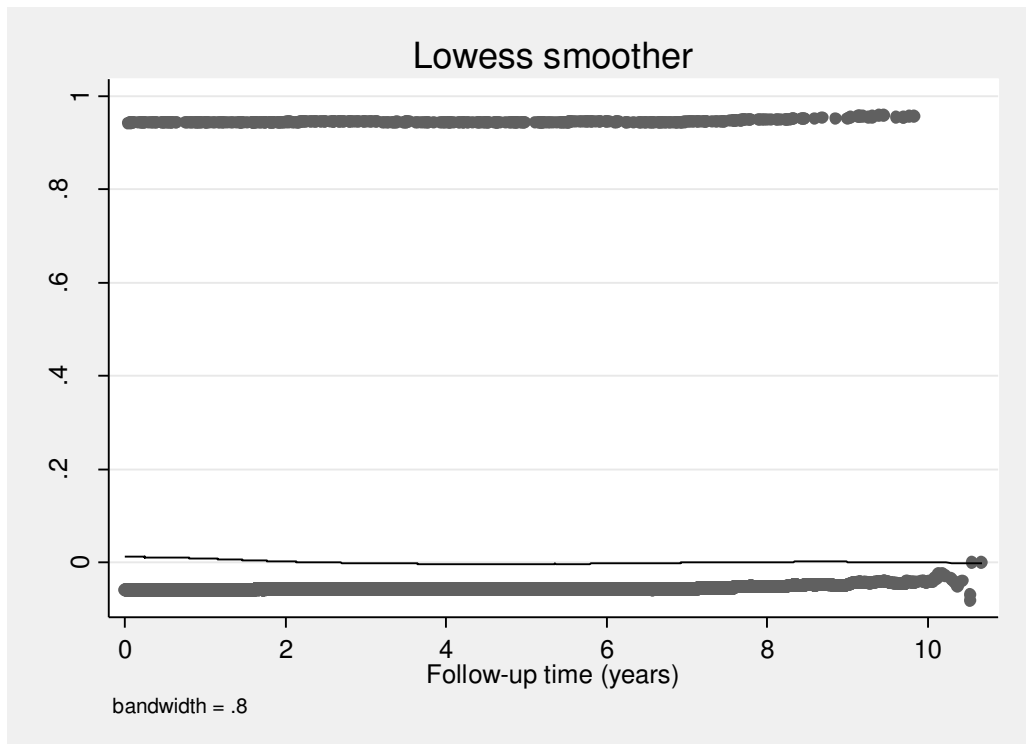
\*adjusted for age, sex, comorbidity group, alcohol intake, smoking status and WHR group.



**Figure 9-7 Kaplan-Meier survival estimates for all-cause mortality for bilirubin measurement**



**Figure 9-8 Log-log plot for all-cause mortality for bilirubin measurement**



**Figure 9-9 Schoenfeld residuals against time for all-cause mortality for measurement of bilirubin**

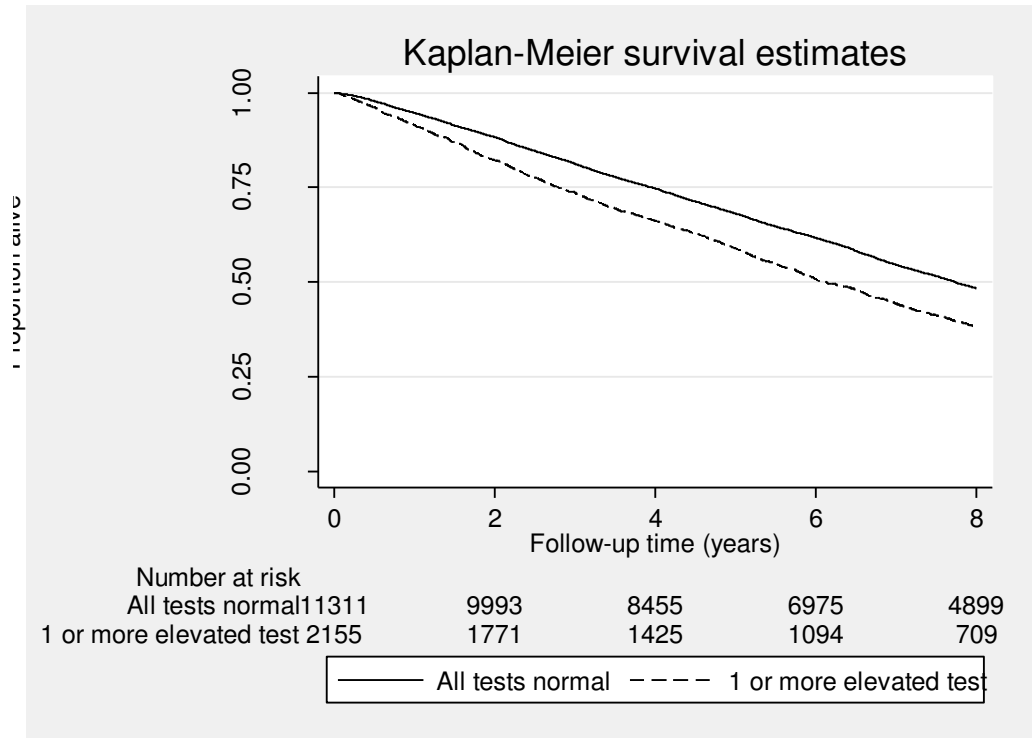
### **9.3.6 Mortality associated with any elevated LFT**

Mortality in subjects with any elevated LFT was 118.4 per 1000 person-years representing an increase of nearly 18 deaths per 1000 person-years of follow-up compared to subjects with all normal LFTs (see Table 9-6). This corresponded to an adjusted hazard ratio of 1.27, i.e. any elevated LFT was associated with a 27% (95% CI [19%, 36%]) increased hazard for all-cause mortality. This is displayed visually in the Kaplan-Meier plot (see Figure 9-10). Any elevated LFT was associated with an increase in mortality from all the specific causes that were examined. For deaths from cardiovascular disease a 27% increased hazard was seen, death from cancer a 23% increased hazard, death from respiratory disease a 21% increased hazard and a 3-fold hazard of death from liver disease (see Table 9-6). There was less than 1 excess death from liver disease per 1000 person years for persons with any abnormal LFT compared with those with all normal LFTs. Examining the Schoenfeld residuals and log-log plots gave no evidence of invalidation of the proportional hazards assumption (see Figure 9-11 and Figure 9-12).

**Table 9-6 Cox proportional hazards model for death (all-cause and cause-specific mortality) for any elevated LFT**

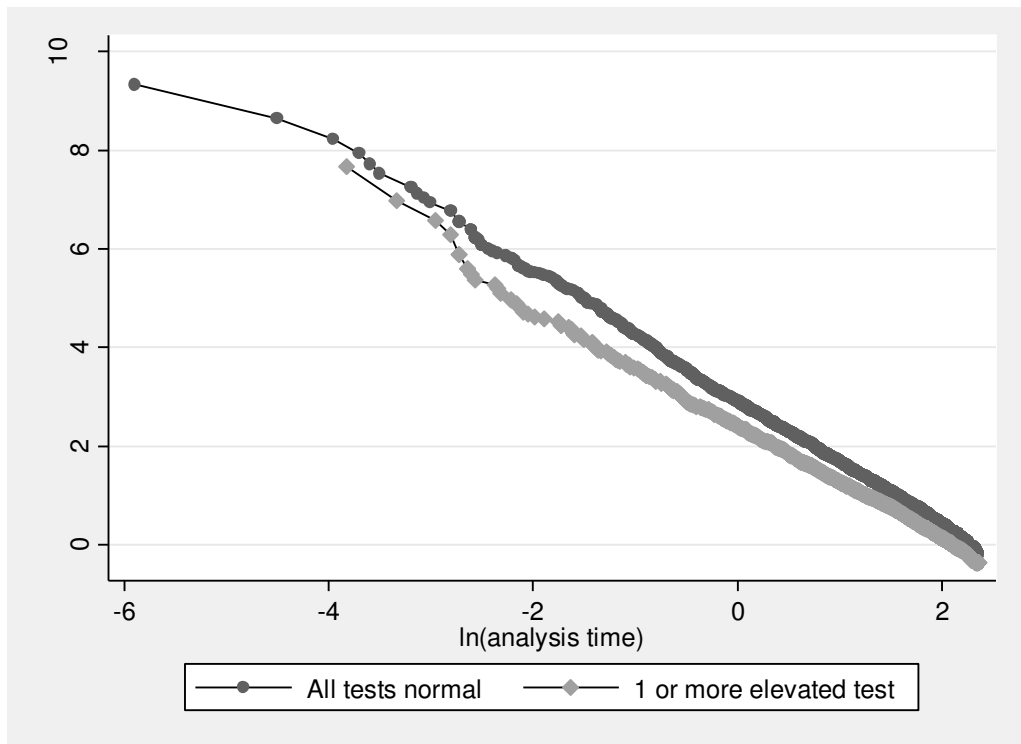
|  | Events | Person-years | Mortality rate<br>(per 1000<br>person years) | Hazard ratio [95%CI] | Adjusted Hazard ratio*<br>[95%CI] |
|--|--------|--------------|--|----------------------|-----------------------------------|
| <b>All-cause mortality</b>             |        |              |  |                      |                                   |
| Normal                                 | 6556   | 72,320       | 90.7   |                      |                                   |
| Elevated                               | 1447   | 12,217       | 118.4  | 1.33 [1.26, 1.41]    | 1.27 [1.19, 1.36]                 |
| <b>Cause-specific mortality</b>        |        |              |  |                      |                                   |
| <b>Cardiovascular disease</b>          |        |              |  |                      |                                   |
| Normal                                 | 2768   | 72,320       | 38.3   |                      |                                   |
| Elevated                               | 611    | 12,217       | 50.0   | 1.33 [1.22, 1.45]    | 1.27 [1.16, 1.39]                 |
| <b>Cancer (excluding liver cancer)</b> |        |              |  |                      |                                   |
| Normal                                 | 1240   | 72,30        | 17.1   |                      |                                   |
| Elevated                               | 266    | 12,217       | 21.8   | 1.29 [1.13, 1.47]    | 1.23 [1.10, 1.39]                 |
| <b>Respiratory disease</b>             |        |              |  |                      |                                   |
| Normal                                 | 1112   | 72,30        | 15.4   |                      |                                   |
| Elevated                               | 234    | 12,217       | 19.2   | 1.27 [1.10, 1.46]    | 1.21 [1.02, 1.42]                 |
| <b>Liver disease</b>                   |        |              |  |                      |                                   |
| Normal                                 | 32     | 72,30        | 0.44   |                      |                                   |
| Elevated                               | 17     | 12,217       | 1.39   | 3.22 [1.79, 5.79]    | 3.11 [1.74, 5.54]                 |

\*adjusted for sex, age and comorbidity group

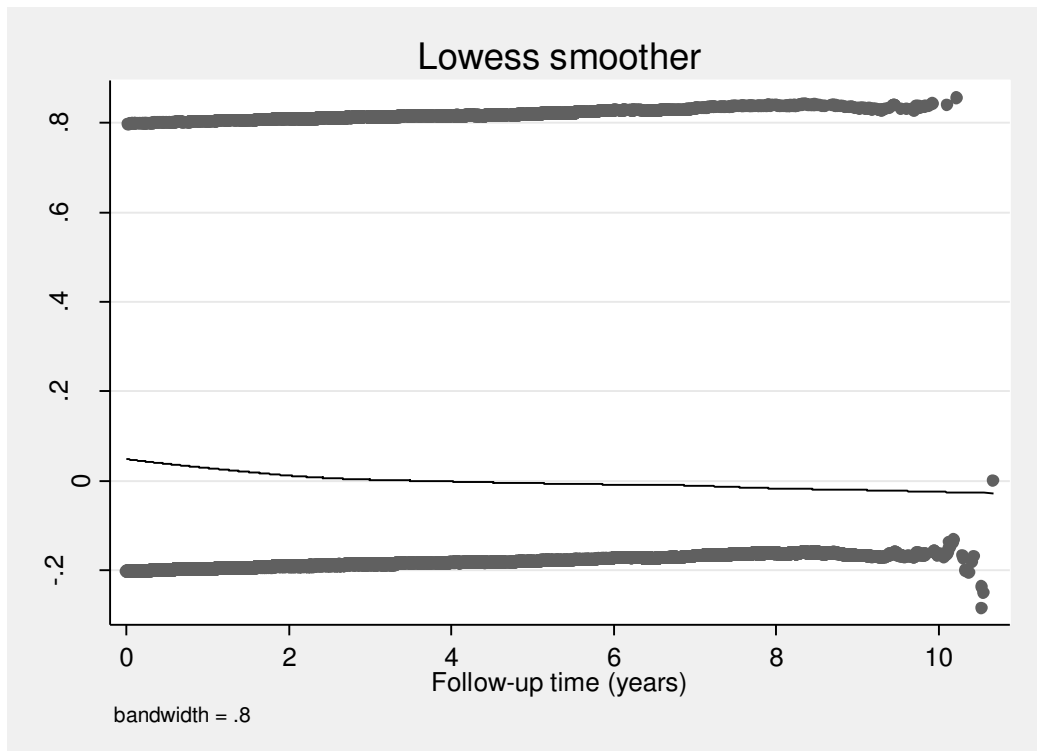


**Figure 9-10 Kaplan-Meier survival estimates for all normal LFTs vs. any elevated LFT**





**Figure 9-11 Log-log plot for all-cause mortality for any elevated LFT measurement**



**Figure 9-12 Schoenfeld residuals against time for all-cause mortality for any elevated LFT measurement**

## **9.4 Discussion**

### **9.4.1 Key findings**

A single elevated liver function test was associated with a higher risk of death overall, and for AST and ALP in particular a higher risk of death from liver disease, compared to those with normal liver function tests.

### **9.4.2 Strengths and limitations**

In this study I was able to assess the association of certain liver function tests with subsequent mortality in a representative sample of all people aged 75 and over. Given that people of this age have such a high mortality and therefore there were a large number of events (deaths) I was able to perform survival analysis looking at both all-cause mortality and specific causes of death. This has enabled me to provide estimates of the association of elevated liver function test and cause-specific mortality which has not been previously available. In addition to an unsurprising increased risk of death from liver disease (albeit mediated through very small absolute numbers of deaths) both elevated AST and ALP were seen to be associated with an increased risk of death from cancer (excluding liver cancer). Elevated ALP was also associated with an increased risk of the other two specific causes of death examined, cardiovascular disease and respiratory disease. Rather than being related to liver function per se, this may reflect the fact that these enzymes are also present in other body tissues, not just specific to the liver. As previously discussed it is arguable that abnormalities of AST, ALP and bilirubin are of secondary importance when looking at liver function compared with a measurement of alanine aminotransferase (ALT) which is specific to the

liver. I was unable to investigate this as a blood test for this enzyme was not a part of the original study design.

### **9.4.3 Comparison with previously published work**

Although I was unable to exclude people with previously diagnosed liver disease, the representative nature of this study enables me to provide a possibly more accurate estimate of the association of elevated liver function tests in the general population with mortality than has been previously available.<sup>66 76</sup> A higher risk of death was seen with increasingly abnormal results in both these studies as with my data. These previous studies, by virtue of the method of data collection, will have introduced an inherent selection bias to their study populations as to which people within the geographic area had a recorded measurement of liver function, most likely to lead to an overestimate of the association between elevated liver function and mortality. Indeed the estimates of mortality associated with transaminases and ALP in the population from Scotland are slightly higher than those reported in this chapter.<sup>66</sup> Further studies from working populations in Germany and South Korea also report greater increases in hazard of all-cause mortality than those shown in my data.<sup>68 75</sup>

I identified one study that specifically looked at the association between liver function and mortality in the elderly, which came from a small population of 70 year-olds in Jerusalem.<sup>77</sup> This study did not show any significant associations between either AST or ALP and all-cause mortality. However, the categorisation of liver function as above or below the mean value in the study population makes the interpretation of these results difficult to compare with

my study where I was specifically looking at abnormalities as defined by upper limits of normal reference ranges.

#### **9.4.4 Conclusions**

This study has shown that although abnormalities in liver function are fairly common they are associated with only a modest increased risk in all-cause mortality in the elderly population.

The findings of an association between elevated liver function tests and mortality from cardiovascular disease, cancer, respiratory disease as well as liver disease, independent of comorbidity, suggest that rather than simply a marker of liver function the investigation of people with elevated LFTs, particularly those greater than 2 x the ULN, may lead to the identification of potentially treatable conditions that underlie death. However, by comparison the simply derived comorbidity score exhibited a stronger relationship with death than any of the LFTs examined.

A recent report from Department of Health Quality Strategy Team on Liver Disease called for guidance to be made available to general practitioners on the use and interpretation of liver function tests.<sup>9</sup> I await the results of two HTA funded studies which may provide additional recommendations for the management of elevated liver function tests.<sup>118 119</sup>

It will be particularly important to evaluate the use of liver function tests and subsequent referrals in this growing sector of the population of the UK,<sup>120</sup> those aged 75 and over, where incidental findings, and therefore potentially costly and avoidable referral and follow-up, are even more likely owing to

prescribing practices (as discussed in section 7.4.4). What action needs to be taken on obtaining a single elevated liver function test in this group of older people remains open to debate and further study. Though two studies have shown that underlying liver disease was present in the majority of people who presented with elevated liver function tests but were otherwise asymptomatic for liver disease and did not have a history of drug or alcohol problems<sup>121 122</sup> it would seem that, in the absence of any evidence for any overwhelming increases in mortality following a single elevated measurement of liver function, current practise of referral and active investigation of patients only with persistent abnormalities should be continued.

## **10 Conclusions**

### **10.1 Overall findings**

In describing some aspects of the epidemiology of cirrhosis and liver function this thesis has addressed, in part, the burden of liver disease in the UK as highlighted in the four areas discussed in section 1.1.

1. I have considered the frequency of liver disease through examination of the incidence and prevalence of cirrhosis and the frequency of potentially undiagnosed liver disease through examination of the prevalence of abnormal liver function tests in a group of people aged 75 and over.
2. I have considered the mortality from liver disease through examination of mortality subsequent to a diagnosis of cirrhosis and subsequent to a single elevated LFT measurement.
3. I have considered the morbidity associated with liver disease through examination of the progression of cirrhosis using recognised clinical sequelae including an estimate of the rate of decompensation.
4. Although I have not attempted to consider the financial or service requirements associated with liver disease through any formal mechanisms the measures described above will of themselves be useful in the modelling and cost-effectiveness analyses that could be undertaken to look at the burden of liver disease in the UK. I have also applied my results to recent UK population figures to provide an estimate of the annual number of new cases of cirrhosis, the total number of people living with cirrhosis and the number of older people who might be expected to have one or more abnormal LFTs.

## **10.2 Suggestions for further research**

### Epidemiology of cirrhosis

The data used in chapters 3 through 5 were extracted from the GPRD in April 2002. Recently (2009) the GPRD has established formal data links with the HES data and with the ONS vital statistics database of death registrations.

Using a more recent extraction of data it should be possible

- a) to explore if the increasing trend in incidence of cirrhosis has continued throughout the last decade,
- b) to examine the cause of death of patients with cirrhosis compared with the general population (available in new GPRD data extractions), and
- c) to describe the progression of cirrhosis using information contained within linked hospital data, including additional clinical sequelae and commonly used prognostic scores through the availability of laboratory data (again, available in new GPRD data extractions).

In addition, it is probable that a diagnosis of cirrhosis is associated with other sequelae that have not been addressed in this thesis. Of particular interest clinically is the occurrence of hepatocellular carcinoma. Further exploration of readily available data would inform the current practices for surveillance of hepatocellular carcinoma and potentially identify both high and low risk groups in which to either target or stop surveillance.



### Epidemiology of liver function

I have described the epidemiology of elevated liver function in a particular group of the population, those aged 75 and above. It would be interesting to obtain data from cohorts of people of younger age groups to observe

- a) the absolute proportion of people who had elevated liver function, and
- b) whether similar associations between clinical, demographic and lifestyle factors and mortality exist at other ages

As elevated AST and ALP were both associated with deaths from cancer it would be interesting to examine whether these elevated LFTs were also associated with the incidence of cancer. This should be possible using the same "MRC Elderly" dataset as this has been linked to the national cancer registry.

The utility of a single measurement of elevated liver function remains questionable and it would be worthwhile to try to obtain data on patients who had had repeated measures of liver function to see if persistently elevated LFTs were more strongly associated with mortality, as would probably be expected.

### **10.3 Overall conclusion**

This thesis has described the increasing incidence of cirrhosis in the UK over the period 1992-2001 and the considerable excess mortality and rapid progression associated with a diagnosis of cirrhosis.

As cirrhosis probably represents the end stage of many chronic liver diseases it is perhaps now of even greater importance to consider the aetiological factors that lead to the acquisition of cirrhosis and consider measures to reduce the occurrence of these liver diseases and eventually cirrhosis.

Elevated liver function tests appear to be associated with more than just liver disease. It will be important to consider how these tests should in future be used – more widely as a measure of general health or targeted more specifically. The necessity of accurate estimates of the prevalence of elevated LFTs and their associations will be paramount to any changes in the current practices of investigation and referral.

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## **Appendix I Papers published from the work in this thesis**

Fleming KM, Aithal GP, Solaymani-Dodaran M, Card T, West J. Incidence and prevalence of cirrhosis in the United Kingdom, 1992-2001: A general population-based study. *J Hepatol* 2008 49(5):732-8

## **Appendix II Abstracts presented at conferences based on work in this thesis**

### Oral presentations

- United European Gastroenterology Week. Oral presentation: Updated estimates of the 1-year progression of disease following diagnosis of cirrhosis.
- British Association for Studies of the Liver Annual meeting, September 2007. Plenary presentation: Incidence of cirrhosis in the UK, 1992-2001: a population-based study.

### Poster presentations

- Updated estimates of the 1-year progression of disease following diagnosis of cirrhosis. BASL, Sept 2008.
- Incidence of cirrhosis in the UK, 1992-2001: a population-based study. AASLD, Nov 2007; UEGW, Oct 2007 (prize for best poster awarded).

## **Appendix III Code lists**

Appendix III-a Codes for liver disease

Appendix III-b Codes for death

Appendix III-c Codes for alcohol use

Appendix III-d Codes for viral hepatitis

Appendix III-e Codes for autoimmune liver disease

Appendix III-f Codes for metabolic liver disease

Appendix III-g Codes for encephalopathy

Appendix III-h Codes for smoking

Appendix III-j Codes for comorbidity

Appendix III-k Codes for liver transplant

## Appendix III-a Codes for liver disease

| description                           | medcode |
|---------------------------------------|---------|
| TYPHOIDAL HEPATITIS                   | 001 C   |
| AMOEBIC ABSCESS LIVER                 | 0060B   |
| HEPATITIS AMOEBIC                     | 0060BH  |
| AMOEBIC ABSCESS BRAIN & LIVER         | 0060C   |
| AMOEBIC ABSCESS LUNG & LIVER          | 0060D   |
| AMOEBIC ABSCESS SPLEEN & LIVER        | 0060E   |
| TUBERCULOUS HEPATITIS                 | 014 H   |
| TULARAEMIA HEPATITIS                  | 021 H   |
| HEPATITIS BRUCELLOSIS                 | 0239H   |
| LEPROTIC HEPATITIS                    | 0309H   |
| PNEUMOCOCCAL HEPATITIS                | 0382H   |
| HEPATITIS GAS GANGRENE                | 0390H   |
| HERPES VIRUS HEPATITIS                | 054 H   |
| RUBELLA HEPATITIS                     | 056 H   |
| YELLOW FEVER HEPATITIS                | 0609H   |
| INFECTIOUS HEPATITIS                  | 70      |
| VIRUS HEPATITIS TYPE A                | 070 A   |
| HEPATITIS C                           | 070 AC  |
| HEPATITIS TYPE C                      | 070 AD  |
| VIRUS HEPATITIS TYPE B                | 070 B   |
| HEPATITIS CATARRHAL                   | 070 C   |
| HEPATITIS FULMINANT                   | 070 F   |
| HEPATITIS CHRONIC AGGRESSIVE          | 070 G   |
| JAUNDICE CATARRHAL                    | 070 JC  |
| JAUNDICE EPIDEMIC                     | 070 JE  |
| JAUNDICE FEBRILE                      | 070 JF  |
| JAUNDICE INFECTIOUS                   | 070 JN  |
| HEPATITIS TYPE NON- A NON- B          | 070 N   |
| HEPATITIS PERSISTENT CHRONIC          | 070 P   |
| VIRUS HEPATITIS                       | 070 RL  |
| HEPATITIS COXSACKIE VIRUS             | 0749H   |
| INFECTIOUS MONONUCLEOSIS HEPATITIS    | 075 H   |
| HEPATITIS ADENOVIRUS                  | 0788H   |
| HEPATITIS CYTOMEGALIC INCLUSION VIRUS | 0795H   |
| Q FEVER HEPATITIS                     | 0831H   |
| MALARIAL HEPATITIS                    | 0840H   |
| SYPHILIS LIVER CONGENITAL             | 0900L   |
| SYPHILIS LIVER ACQUIRED               | 095 L   |
| HEPATITIS GONOCOCCAL                  | 0988H   |
| PERIHEPATITIS GONOCOCCAL              | 0988PH  |
| SPIROCHAETAL HAEMORRHAGIC JAUNDICE    | 1000EJ  |
| LEPTOSPIRAL HEPATITIS                 | 1000H   |
| JAUNDICE EPIDEMIC LEPTOSPIRAL         | 1000WL  |

|  |         |
|--|---------|
| JAUNDICE EPIDEMIC SPIROCHAETAL           | 1000WR  |
| ACTINOMYCOSIS LIVER                      | 113 L   |
| COCCIDIOIDOMYCOSIS LIVER                 | 114 L   |
| HISTOPLASMOSIS LIVER                     | 115 L   |
| CRYPTOCOCCOSIS LIVER                     | 1160CL  |
| BLASTOMYCOSIS LIVER                      | 1169L   |
| SCHISTOSOMIASIS LIVER                    | 1208L   |
| CAT LIVER FLUKE INFECTION                | 1210C   |
| CHINESE LIVER FLUKE DISEASE              | 1211CH  |
| INFESTATION DISTOMA HEPATICUM            | 1213D   |
| SHEEP LIVER FLUKE INFECTION              | 1213HF  |
| HYDATID CYST LIVER                       | 1220C   |
| HYDATID CYST                             | 1229C   |
| FH: PORPHYRIA                            | 1265    |
| TOXOPLASMOSIS LIVER CONGENITAL           | 1302    |
| SARCOIDOSIS                              | 135     |
| SARCOID                                  | 135 AA  |
| SARCOID BOECK'S                          | 135 BK  |
| SARCOIDOSIS LIVER                        | 135 L   |
| SARCOIDOSIS PULMONARY                    | 135 P   |
| H/O: LIVER DISEASE                       | 14C5.00 |
| H/O: JAUNDICE                            | 14C6.00 |
| H/O: BILIARY DISEASE                     | 14C7.00 |
| H/O: GALLBLADDER DISEASE                 | 14C7.11 |
| H/O: LIVER RECIPIENT                     | 14S8.00 |
| MALIGNANT NEOPLASM LIVER                 | 1550A   |
| MALIGNANT NEOPLASM LIVER PRIMARY         | 1550AP  |
| HEPATOMA                                 | 1550B   |
| HAEMANGIOENDOTHELIAL SARCOMA LIVER       | 1550BH  |
| SARCOMA LIVER PRIMARY                    | 1550BP  |
| CARCINOMA LIVER                          | 1550C   |
| HEPATOBLASTOMA                           | 1550HB  |
| MALIGNANT NEOPLASM HEPATOCELLULAR        | 1550HC  |
| MALIGNANT CHOLANGIOMA                    | 1551A   |
| MALIGNANT NEOPLASM GALLBLADDER           | 1560A   |
| CARCINOMA GALLBLADDER                    | 1560C   |
| MALIGNANT NEOPLASM EXTRAHEPATIC BILE DUC | 1561A   |
| CARCINOMA EXTRAHEPATIC BILE DUCT         | 1561C   |
| MALIGNANT NEOPLASM AMPULLA OF VATER      | 1562A   |
| CARCINOMA AMPULLA VATER                  | 1562C   |
| MALIGNANT NEOPLASM BILE/BILIARY TRACT    | 1569A   |
| YELLOW/JAUNDICED COLOUR                  | 1675    |
| JAUNDICE - SYMPTOM                       | 1675.11 |
| BILIARY COLIC                            | 1965    |
| BILIARY COLIC SYMPTOM                    | 1965.11 |
| SECONDARY NEOPLASTIC DEPOSITS LIVER      | 1977    |

|  |         |
|--|---------|
| MALIGNANT NEOPLASM LIVER SECONDARY                                 | 1977A   |
| METASTASIS LIVER   | 1977M   |
| BENIGN ADENOMA LIVER   | 2115AD  |
| BENIGN ANGIOMA LIVER   | 2115AN  |
| BENIGN CHOLANGIOMA   | 2115CH  |
| NEUROMA CYSTIC DUCT  | 2115CN  |
| FIBROMA EXTRAHEPATIC BILE DUCTS                                    | 2115EF  |
| HYPERPLASIA FOCAL NODULAR LIVER                                    | 2115FH  |
| ADENOMA GALLBLADDER  | 2115GA  |
| PAPILLOMA GALLBLADDER  | 2115GP  |
| ADENOMA EXTRAHEPATIC BILE DUCTS                                    | 2115HA  |
| PAPILLOMA EXTRAHEPATIC BILE DUCTS                                  | 2115HP  |
| BENIGN TERATOMA LIVER  | 2115TE  |
| O/E - JAUNDICED COLOUR   | 2274    |
| O/E - JAUNDICED  | 2274.11 |
| CYSTINE STORAGE DISEASE  | 2703T   |
| ANDERSEN'S GLYCOGEN STORAGE DISEASE                                | 2711B   |
| GLYCOGEN STORAGE DISEASE SUBTYPE IIB                               | 2711D   |
| RENAL INVOLVEMENT FABRY'S DISEASE                                  | 2728    |
| ERYTHROPOIETIC PORPHYRIA   | 2731E   |
| PORPHYRIA  | 2731P   |
| PORPHYRIA CONGENITAL   | 2731PC  |
| HAEMOCHROMATOSIS   | 2732    |
| IRON STORAGE DISEASE   | 2732A   |
| DIABETES BRONZE (HAEMOCHROMATOSIS)                                 | 2732B   |
| HAEMOCHROMATOSIS IDIOPATHIC  | 2732HI  |
| HEPATOLENTICULAR DEGENERATION                                      | 2733    |
| WILSON'S DISEASE   | 2733W   |
| JAUNDICE IDIOPATHIC DYSERYTHROPOIETIC -<br>SYNDROME DUBIN- JOHNSON | 2735    |
| SYNDROME ROTOR'S   | 2735DJ  |
| AMYLOIDOSIS CARDIAC  | 2735R   |
| AMYLOIDOSIS FAMILIAL WITH FEBRILE URTICA                           | 276 CD  |
| AMYLOIDOSIS  | 276 FR  |
| AMYLOID NEPHROPATHY  | 276 N   |
| AMYLOID NEUROPATHY   | 276 NP  |
| PERIODIC FEVER (AMYLOIDOSIS)                                       | 276 NR  |
| AMYLOIDOSIS RENAL  | 276 PF  |
| PORPHYRIA SECONDARY/ACQUIRED                                       | 276 RN  |
| PORPHYRIA CUTANEA TARDA  | 279 AP  |
| ANTITRYPSIN DEFICIENCY   | 279 E   |
| JAUNDICE FAMILIAL/CONGENITAL ACHOLURIC                             | 2790AD  |
| JAUNDICE HAEMOLYTIC  | 2820    |
| JAUNDICE ACHOLURIC ACQUIRED  | 2839C   |
| HEPATITIS A - CURRENT INFECTION                                    | 2839CA  |
| PORPHYRIA ASSOCIATED WITH DRUG ADDICTION                           | 2J23.00 |
|  | 3048PA  |



|  |         |
|--|---------|
| HEPATITIS B SURFACE ANTIG +VE            | 43B4.00 |
| HEPATITIS E ANTIGEN PRESENT              | 43B5.00 |
| MITOCHONDRIAL ANTIBODIES POSITIVE        | 43GB100 |
| MITOCHONDRIAL ANTIBODIES WEAKLY POSITIVE | 43GB200 |
| HEPATITIS A TEST POSITIVE                | 43M2.00 |
| HEPATITIS C ANTIBODY TEST POSITIVE       | 43X3.00 |
| ARTERIOSCLEROSIS HEPATIC ARTERY          | 4403H   |
| ANEURYSM HEPATIC ARTERY                  | 442 H   |
| OCCLUSION HEPATIC ARTERY                 | 4449HC  |
| EMBOLISM HEPATIC ARTERY                  | 4449HE  |
| THROMBOSIS HEPATIC ARTERY                | 4449HT  |
| LIVER FUNCTION TESTS ABNORMAL            | 44D2.00 |
| LIVER ENZYMES ABNORMAL                   | 44G2.00 |
| THROMBOSIS PORTAL VEIN                   | 452     |
| SYNDROME BUDD- CHIARI                    | 453 BC  |
| OCCLUSION HEPATIC VEIN                   | 453 HP  |
| VARIX OESOPHAGUS                         | 4560    |
| PORPHYRINS IN URINE                      | 46R3.11 |
| ALPHA-1-ANTITRYPSIN PHENOTYPE            | 4L00.00 |
| BILIARY CONTR.RADIOG.ABNORMAL            | 54G3.00 |
| PER-ORAL CHOLECYSTOGRAPHY ABNORMAL       | 54GA100 |
| ACUTE HEPATITIS                          | 570     |
| HEPATITIS NEONATAL                       | 570 AC  |
| HEPATITIS IDIOPATHIC                     | 570 AG  |
| SUBACUTE MASSIVE HEPATIC NECROSIS        | 570 B   |
| NECROSIS MASSIVE HEPATIC ACUTE           | 570 M   |
| CIRRHOSIS ALCOHOLIC                      | 5710CA  |
| HEPATITIS ALCOHOLIC                      | 5710HA  |
| MICRONODULAR CIRRHOSIS                   | 5710MC  |
| HEPATIC ASCITES                          | 5719AH  |
| SECONDARY BILIARY CIRRHOSIS (LIVER)      | 5719CB  |
| CIRRHOSIS CARDIAC                        | 5719CC  |
| FIBROSIS CARDIAC (HEPATIC)               | 5719CF  |
| HEPATITIS CHRONIC                        | 5719CH  |
| CIRRHOSIS                                | 5719CL  |
| CIRRHOSIS PORTAL                         | 5719CP  |
| FATTY LIVER                              | 5719FL  |
| HEPATOLIENAL FIBROSIS                    | 5719HL  |
| HEPATOSPLENOMEGALY                       | 5719HM  |
| LIVER CIRRHOSIS                          | 5719HP  |
| MACRONODULAR CIRRHOSIS                   | 5719MA  |
| INDIAN CHILDHOOD CIRRHOSIS               | 5719NC  |
| PRIMARY BILIARY CIRRHOSIS (LIVER)        | 5719PB  |
| PORTAL HYPERTENSION                      | 5719PH  |
| ABSCESS LIVER                            | 572 A   |
| ABSCESS HEPATIC                          | 572 AH  |

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| HEPATITIS SUPPURATIVE                    | 572 PR |
| STREPTOCOCCAL HEPATITIS                  | 572 PT |
| THROMBOPHLEBITIS PORTAL VEIN             | 572 TP |
| HEPATIC COMA                             | 573 B  |
| LIVER DISEASE                            | 573 C  |
| INTRAHEPATIC CHOLESTASIS                 | 573 CH |
| CYST LIVER                               | 573 CL |
| PAIN LIVER                               | 573 E  |
| HEPATIC FAILURE                          | 573 FH |
| SYNDROME HEPATORENAL                     | 573 HR |
| HEPATITIS                                | 573 HT |
| LIVER INFECTION                          | 573 N  |
| PERIHEPATITIS ACUTE                      | 573 PA |
| PERIHEPATITIS                            | 573 PH |
| SYMPTOMS LIVER                           | 573 PT |
| TOXIC HEPATITIS                          | 573 T  |
| TOXIC HEPATITIS DUE ANAESTHETIC AGENT    | 573 TA |
| TOXIC HEPATITIS DUE ANTIBIOTICS          | 573 TB |
| TOXIC HEPATITIS DUE CARBON TETRACHLORIDE | 573 TC |
| TOXIC HEPATITIS DUE DRUG SENSITIVITY     | 573 TD |
| TOXIC HEPATITIS DUE CYTOTOXIC AGENTS     | 573 TE |
| HEPATITIS DUE FOOD POISONING             | 573 TF |
| TOXIC HEPATITIS DUE CHEMICALS            | 573 TH |
| HEPATITIS TOXIC DUE HORMONES             | 573 TM |
| TOXIC HEPATITIS DUE PLANT ALKALOIDS      | 573 TP |
| TOXIC HEPATITIS DUE ANTIARTHRITIC AGENT  | 573 TR |
| TRAUMATIC HAEMOBILIA                     | 573 TT |
| HEPATITIS CHRONIC ACTIVE                 | 5730CA |
| HEPATOCELLULAR DAMAGE                    | 5730D  |
| GALLSTONES                               | 574 A  |
| CHOLECYSTOLITHIASIS                      | 574 AC |
| CHOLEDOCHOLITHIASIS                      | 574 AD |
| CHOLELITHIASIS                           | 574 AL |
| CHOLANGITIS WITH STONE                   | 574 B  |
| COLIC BILIARY                            | 574 C  |
| GALLBLADDER COLIC                        | 574 CG |
| LITHIASIS BILIARY                        | 574 L  |
| STONE CYSTIC DUCT                        | 5740D  |
| CHOLECYSTITIS                            | 575    |
| CHOLANGITIS                              | 575 A  |
| SECONDARY SCLEROSING CHOLANGITIS         | 575 AD |
| PERICHOLANGITIS                          | 575 AE |
| SCLEROSING CHOLANGITIS PRIMARY           | 575 AL |
| SUPPURATIVE CHOLANGITIS                  | 575 AP |
| RECURRENT CHOLANGITIS                    | 575 AR |
| ABSCESS BILE/BILIARY DUCT                | 575 BB |

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| ABSCESS GALLBLADDER              | 575 BG  |
| ABSCESS HEPATIC DUCT             | 575 BH  |
| ABSCESS PERICHOLECYSTIC          | 575 BP  |
| CHOLECYSTITIS ACUTE              | 575 CA  |
| CHRONIC CHOLECYSTITIS            | 575 CC  |
| SYNDROME CAROLI'S                | 575 CR  |
| GALLBLADDER EMPYEMA              | 575 EM  |
| INFECTION GALLBLADDER            | 575 NF  |
| OBSTRUCTIVE JAUNDICE             | 576 A   |
| OBSTRUCTION BILE DUCT            | 576 AB  |
| BILIARY TRACT DISEASE            | 576 B   |
| BILIARY DYSKINESIA               | 576 BD  |
| GALLBLADDER DYSKINESIA           | 576 BG  |
| GALLBLADDER DISEASE              | 576 C   |
| DISEASE CAROLI'S                 | 576 CR  |
| PAIN GALLBLADDER                 | 576 D   |
| CHOLESTEROSIS                    | 576 E   |
| CHOLESTEROLOSIS                  | 576 EL  |
| SYMPTOMS BILIARY                 | 576 F   |
| FISTULA CHOLECYSTODUODENAL       | 576 FC  |
| PROBLEM GALLBLADDER              | 576 FP  |
| PERITONITIS BILE                 | 576 G   |
| HYDROPS GALLBLADDER              | 576 H   |
| MUCOCELE GALLBLADDER             | 576 MC  |
| ABSENCE GALLBLADDER ACQUIRED     | 576 NA  |
| NONFUNCTIONING GALLBLADDER       | 576 NF  |
| PSEUDODIVERTICULUM GALLBLADDER   | 576 PD  |
| CYST BILE DUCT                   | 576 RB  |
| CYST GALLBLADDER                 | 576 RG  |
| TORSION GALLBLADDER              | 576 TG  |
| STRICTURE BILE DUCTS ACQUIRED    | 576 TR  |
| INFECTIOUS HEPATITIS VACCINAT    | 65O1.12 |
| VIRAL HEPATITIS CARRIER          | 65Q7.00 |
| NOTIFICATION OF INF. JAUNDICE    | 65V3.00 |
| HEPATITIS NOTIFICATION           | 65V3.11 |
| ABSENCE VEIN PORTAL CONGENITAL   | 7474PT  |
| ANOMALY HEPATIC ARTERY           | 7476HA  |
| SOLITARY NONPARASITIC LIVER CYST | 7515LC  |
| CYSTIC LIVER DISEASE CONGENITAL  | 7515LD  |
| FIBROSIS HEPATIC CONGENITAL      | 7515LF  |
| ACCESSORY GALLBLADDER CONGENITAL | 7516AC  |
| DOUBLE GALLBLADDER               | 7516AD  |
| MULTISEPTATE GALLBLADDER         | 7516AE  |
| BILOBED GALLBLADDER              | 7516AF  |
| PHRYGIAN-CAP GALLBLADDER         | 7516AG  |
| INTRAHEPATIC GALLBLADDER         | 7516AH  |

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| DIVERTICULA GALLBLADDER CONGENITAL                           | 7516AK  |
| LEFT-SIDED GALLBLADDER                                       | 7516AL  |
| CONGENITAL ADHESIONS GALLBLADDER                             | 7516AM  |
| ABERRANT HEPATIC DUCT  | 7516B   |
| ACCESSORY HEPATIC DUCTS CONGENITAL                           | 7516BC  |
| ACCESSORY BILE DUCT CONGENITAL                               | 7516CA  |
| ABSENCE BILE BILIARY DUCT CONGENITAL                         | 7516CB  |
| ABERRANT BILE DUCTS  | 7516CD  |
| CONGENITAL BILIARY ATRESIA                                   | 7516CS  |
| CONGENITAL ATRESIA BILE DUCTS                                | 7516CT  |
| ABSENCE LIVER CONGENITAL                                     | 7516DA  |
| ACCESSORY LIVER CONGENITAL                                   | 7516DC  |
| ECTOPIIC LIVER   | 7516DE  |
| CORSET LIVER   | 7516DH  |
| ACCESSORY CYSTIC DUCT CONGENITAL                             | 7516E   |
| FIBROCYSTIC DISEASE LIVER                                    | 7516FD  |
| CONGENITAL ABSENCE GALLBLADDER                               | 7516GA  |
| PARTIAL ATROPHY LIVER CONGENITAL                             | 7516HA  |
| ATROPHY PARTIAL LIVER  | 7516HB  |
| FAMILIAL INTRAHEPATIC CHOLESTASIS                            | 7516JA  |
| DILATATION BILE DUCTS CONGENITAL                             | 7516JD  |
| ROKITANSKY- ASCHOFF SINUSES GALLBLADDER                      | 7516RA  |
| OPEN OPERATIONS ON OESOPHAGEAL VARICES                       | 7609    |
| LOCAL LIGATION OF OESOPHAGEAL VARICES                        | 7609300 |
| OPEN INJECTION SCLEROTHERAPY TO OESOPHAGEAL VARICES          | 7609400 |
| OTHER SPECIFIED OPEN OPERATION ON OESOPHAGEAL VARICES        | 7609y00 |
| TANNER DEVASCULARISATION FOR BLEEDING VARICES                | 7609y11 |
| OPEN OPERATION ON OESOPHAGEAL VARICES NOS                    | 7609z00 |
| FIBREOPTIC ENDOSCOPIC INJECTION SCLEROTHERAPY OESOPH VARICES | 760C300 |
| FIBREOPTIC ENDOSCOPIC BANDING OF OESOPHAGEAL VARICES         | 760C500 |
| RIGID OESOPHAGOSCOPIC INJECTION SCLEROTHERAPY OESOPH VARICES | 760F300 |
| RIGID OESOPHAGOSCOPIC BANDING OF OESOPHAGEAL VARICES         | 760F400 |
| ENTEROTOMY AND REMOVAL OF GALLSTONE                          | 7648700 |
| JAUNDICE BREAST MILK   | 7789AB  |
| NEONATAL JAUNDICE  | 7789NJ  |
| PHYSIOLOGICAL JAUNDICE NEWBORN                               | 7799AJ  |
| LIVER OPERATIONS   | 780..00 |
| TRANSPLANTATION OF LIVER                                     | 7800    |
| ORTHOTOPIC TRANSPLANTATION OF LIVER                          | 7800000 |
| HETEROTOPIC TRANSPLANTATION OF LIVER                         | 7800100 |
| AUXILLARY LIVER TRANSPLANT                                   | 7800111 |
| PIGGY BACK LIVER TRANSPLANT                                  | 7800112 |
| REPLACEMENT OF PREVIOUS LIVER TRANSPLANT                     | 7800200 |
| OTHER SPECIFIED TRANSPLANTATION OF LIVER                     | 7800y00 |
| TRANSPLANTATION OF LIVER NOS                                 | 7800z00 |
| PARTIAL EXCISION OF LIVER                                    | 7801    |

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| PARTIAL HEPATECTOMY  | 7801.11 |
| RIGHT HEMIHEPATECTOMY  | 7801000 |
| LEFT HEMIHEPATECTOMY   | 7801100 |
| RESECTION OF SEGMENT OF LIVER                                | 7801200 |
| WEDGE EXCISION OF LIVER                                      | 7801300 |
| MARSUPIALISATION OF LESION OF LIVER                          | 7801400 |
| LEFT HEPATIC TRISEGMENTECTOMY                                | 7801500 |
| OTHER SPECIFIED PARTIAL EXCISION OF LIVER                    | 7801y00 |
| PARTIAL EXCISION OF LIVER NOS                                | 7801z00 |
| EXTIRPATION OF LESION OF LIVER                               | 7802    |
| EXCISION OF LESION OF LIVER                                  | 7802000 |
| DESTRUCTION OF LESION OF LIVER                               | 7802100 |
| OTHER SPECIFIED EXTIRPATION OF LESION OF LIVER               | 7802y00 |
| EXTIRPATION OF LESION OF LIVER NOS                           | 7802z00 |
| REPAIR OF LIVER  | 7803    |
| REMOVAL OF LACERATED FRAGMENT OF LIVER                       | 7803000 |
| REPAIR OF LACERATION OF LIVER                                | 7803100 |
| PACKING OF LACERATION OF LIVER                               | 7803200 |
| OTHER SPECIFIED REPAIR OF LIVER                              | 7803y00 |
| REPAIR OF LIVER NOS  | 7803z00 |
| HEPATOTOMY   | 7804.11 |
| OPEN DRAINAGE OF LIVER                                       | 7804000 |
| OPEN REMOVAL OF CALCULUS FROM LIVER                          | 7804100 |
| OPEN WEDGE BIOPSY OF LESION OF LIVER                         | 7804200 |
| LITTLE HEPATOTOMY  | 7804y11 |
| STROMEYER HEPATOTOMY   | 7804y12 |
| OTHER OPEN OPERATIONS ON LIVER                               | 7805    |
| OPEN DEVASCULARISATION OF LIVER                              | 7805000 |
| OPEN INSERTION OF CANNULA FOR PERFUSION OF LIVER             | 7805100 |
| EXPLORATION OF LIVER TRANSPLANT                              | 7805211 |
| REMOVAL OF FOREIGN BODY FROM LIVER                           | 7805300 |
| HEPATOPEXY   | 7805400 |
| BINNIE HEPATOPEXY  | 7805411 |
| KEHR HEPATOPEXY  | 7805412 |
| OTHER SPECIFIED OTHER OPEN OPERATION ON LIVER                | 7805y00 |
| OTHER OPEN OPERATION ON LIVER NOS                            | 7805z00 |
| THERAPEUTIC ENDOSCOPIC OPERATIONS ON LIVER USING LAPAROSCOPE | 7806    |
| ENDOSCOPIC REMOVAL OF CALCULUS FROM LIVER USING LAPAROSCOPE  | 7806000 |
| THERAPEUTIC LAPAROSCOPIC OPERATION ON LIVER OS               | 7806y00 |
| THERAPEUTIC LAPAROSCOPIC OPERATION ON LIVER NOS              | 7806z00 |
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| PERCUTANEOUS TRANSLUMINAL OPERATIONS ON LIVER BLOOD VESSEL   | 7808.11 |
| PERCUTANEOUS TRANSLUMINAL EMBOLISATION OF HEPATIC ARTERY     | 7808000 |
| PERCUTANEOUS TRANSLUMINAL EMBOLISATION OF PORTAL VEIN        | 7808100 |
| PERCUTANEOUS TRANSLUMINAL INJECT THERAPEUT SUBST INTO LIVER  | 7808200 |

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| TRANSLUMINAL OPERATION ON BLOOD VESSEL OF LIVER OS          | 7808y00 |
| TRANSLUMINAL OPERATION ON BLOOD VESSEL OF LIVER NOS         | 7808z00 |
| OTHER THERAPEUTIC PERCUTANEOUS OPERATIONS ON LIVER          | 7809    |
| PERCUTANEOUS DRAINAGE OF LIVER                              | 7809000 |
| PERCUTANEOUS REMOVAL OF CALCULUS FROM LIVER                 | 7809100 |
| THERAPEUTIC ASPIRATION OF LIVER                             | 7809200 |
| OTHER THERAPEUTIC PERCUTANEOUS OPERATION ON LIVER OS        | 7809y00 |
| OTHER THERAPEUTIC PERCUTANEOUS OPERATION LIVER NOS          | 7809z00 |
| PERCUTANEOUS TRANSVASCULAR BIOPSY OF LESION OF LIVER        | 780A000 |
| PERCUTANEOUS BIOPSY OF LESION OF LIVER NEC                  | 780A100 |
| OTHER SPECIFIED DIAGNOSTIC PERCUTANEOUS OPERATION ON LIVER  | 780Ay00 |
| OTHER PUNCTURE OF LIVER                                     | 780B.00 |
| BIOPSY OF LESION OF LIVER NEC                               | 780B011 |
| ASPIRATION OF LIVER NEC                                     | 780B100 |
| ASPIRATION OF LESION OF LIVER NEC                           | 780B111 |
| OTHER SPECIFIED OTHER PUNCTURE OF LIVER                     | 780By00 |
| OTHER PUNCTURE OF LIVER NOS                                 | 780Bz00 |
| OTHER OPERATIONS ON LIVER                                   | 780C.00 |
| EXTRACORPOREAL ASSISTANCE TO LIVER                          | 780C100 |
| OTHER SPECIFIED OTHER OPERATION ON LIVER                    | 780Cy00 |
| OTHER OPERATION ON LIVER NOS                                | 780Cz00 |
| OTHER SPECIFIED OPERATIONS ON LIVER                         | 780y.00 |
| LIVER OPERATIONS NOS  | 780z.00 |
| CHOLECYST OPERATIONS  | 781..11 |
| CHOLECYSTECTOMY   | 7810.11 |
| TOTAL CHOLECYSTECTOMY AND EXCISION OF SURROUNDING TISSUE    | 7810000 |
| TOTAL CHOLECYSTECTOMY AND EXPLORATION OF COMMON BILE DUCT   | 7810100 |
| TOTAL CHOLECYSTECTOMY NEC                                   | 7810200 |
| CHOLECYSTECTOMY NEC   | 7810211 |
| PARTIAL CHOLECYSTECTOMY AND EXPLORATION OF COMMON BILE DUCT | 7810300 |
| PARTIAL CHOLECYSTECTOMY NEC                                 | 7810400 |
| THOREK PARTIAL CHOLECYSTECTOMY                              | 7810411 |
| ENDOSCOPIC CHOLECYSTECTOMY                                  | 7810500 |
| LAPAROSCOPIC CHOLECYSTECTOMY                                | 7810511 |
| CHOLECYSTOGASTROSTOMY                                       | 7811011 |
| CHOLECYSTODUODENOSTOMY                                      | 7811111 |
| CHOLECYSTOJEJUNOSTOMY                                       | 7811211 |
| ROUX-EN-Y CHOLECYSTOJEJUNOSTOMY                             | 7811212 |
| CHOLECYSTOENTEROSTOMY                                       | 7811311 |
| WINIWATER CHOLECYSTOENTEROSTOMY                             | 7811312 |
| CLOSURE OF CHOLECYSTOTOMY                                   | 7812100 |
| CHOLECYSTOTOMY  | 7813.11 |
| CHOLECYSTOSTOMY NEC   | 7813111 |
| BILE DUCT OPERATIONS  | 782..00 |
| EXCISION OF BILE DUCT                                       | 7820    |
| EXCIS AMPULLA OF VATER & REPLANT COM BILE DUCT IN DUODENUM  | 7820000 |

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| PARTIAL EXCISION AND ANASTOMOSIS OF BILE DUCT TO DUODENUM    | 7820100 |
| PARTIAL EXCISION AND ANASTOMOSIS OF BILE DUCT TO JEJUNUM     | 7820200 |
| PARTIAL EXCISION AND END TO END ANASTOMOSIS OF BILE DUCT     | 7820300 |
| OTHER SPECIFIED EXCISION OF BILE DUCT                        | 7820y00 |
| EXCISION OF BILE DUCT NOS                                    | 7820z00 |
| EXTIRPATION OF LESION OF BILE DUCT                           | 7821    |
| EXCISION OF LESION OF BILE DUCT                              | 7821000 |
| DESTRUCTION OF LESION OF BILE DUCT                           | 7821100 |
| OTHER SPECIFIED EXTIRPATION OF LESION OF BILE DUCT           | 7821y00 |
| EXTIRPATION OF LESION OF BILE DUCT NOS                       | 7821z00 |
| CONNECTION OF HEPATIC DUCT                                   | 7822    |
| ANASTOMOSIS OF HEPATIC DUCT                                  | 7822.11 |
| LONGMIRE ANASTOMOSIS OF HEPATIC DUCT                         | 7822.12 |
| KASAI HEPATOJEJUNOSTOMY + INSERTION TUBAL PROSTHESIS         | 7822011 |
| RODNEY - SMITH HEPATOJEJUNOSTOMY+INSERTION TUBAL PROSTHESIS  | 7822012 |
| REVISION OF ANASTOMOSIS OF HEPATIC DUCT                      | 7822200 |
| OPEN DILATION OF ANASTOMOSIS OF HEPATIC DUCT                 | 7822300 |
| OTHER SPECIFIED CONNECTION OF HEPATIC DUCT                   | 7822y00 |
| CONNECTION OF HEPATIC DUCT NOS                               | 7822z00 |
| CONNECTION OF COMMON BILE DUCT                               | 7823    |
| REVISION OF ANASTOMOSIS OF COMMON BILE DUCT                  | 7823300 |
| OPEN DILATION OF ANASTOMOSIS OF COMMON BILE DUCT             | 7823400 |
| OTHER SPECIFIED CONNECTION OF COMMON BILE DUCT               | 7823y00 |
| CONNECTION OF COMMON BILE DUCT NOS                           | 7823z00 |
| OPEN OPERATIONS ON PROSTHESIS IN BILE DUCT                   | 7824    |
| OPEN INTRODUCTION OF PROSTHESIS INTO BILE DUCT               | 7824.11 |
| OPEN INSERT TUBAL PROSTHES IN BOTH HEPATIC+COMMON BILE DUCTS | 7824000 |
| OPEN INSERT TUBAL PROSTHES IN ONE HEPATIC+COMMON BILE DUCTS  | 7824100 |
| OPEN RENEWAL OF TUBAL PROSTHESIS IN BILE DUCT                | 7824200 |
| OPEN REMOVAL OF TUBAL PROSTHESIS FROM BILE DUCT              | 7824300 |
| ROUX-EN-Y PROCEDURE FOR BILIARY ATRESIA                      | 7824400 |
| SAWAGUCHI ROUX-EN-Y PROCEDURE FOR BILIARY ATRESIA            | 7824411 |
| OTHER SPECIFIED OPEN OPERATION ON PROSTHESIS IN BILE DUCT    | 7824y00 |
| OPEN OPERATION ON PROSTHESIS IN BILE DUCT NOS                | 7824z00 |
| REPAIR OF BILE DUCT  | 7825    |
| OTHER SPECIFIED REPAIR OF BILE DUCT                          | 7825y00 |
| REPAIR OF BILE DUCT NOS                                      | 7825z00 |
| INCISION OF BILE DUCT  | 7826    |
| EXPLORATION OF BILE DUCT                                     | 7826.12 |
| OPEN REMOVAL OF CALCULUS AND DRAINAGE OF BILE DUCT           | 7826000 |
| OPEN REMOVAL OF CALCULUS FROM BILE DUCT NEC                  | 7826100 |
| DRAINAGE OF BILE DUCT NEC                                    | 7826200 |
| INCISION AND DRAINAGE OF BILE DUCT NEC                       | 7826211 |
| EXPLORATION OF BILE DUCT                                     | 7826300 |
| OTHER SPECIFIED INCISION OF BILE DUCT                        | 7826y00 |
| INCISION OF BILE DUCT NOS                                    | 7826z00 |

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| PLASTIC REPAIR OF SPHINCTER OF ODDI USING DUODENAL APPROACH  | 7827      |
| SPHINCTEROPLASTY BILE DUCT & PANCREATIC DUCT DUODENAL APPR   | 7827000   |
| SPHINCTEROPLASTY OF BILE DUCT USING DUODENAL APPROACH NEC    | 7827100   |
| PLASTIC REPAIR OF SPHINCTER OF ODDI DUODENAL APPROACH OS     | 7827y00   |
| PLASTIC REPAIR OF SPHINCTER OF ODDI DUODENAL APPROACH NOS    | 7827z00   |
| INCISION OF SPHINCTER OF ODDI USING DUODENAL APPROACH        | 7828      |
| SPHINCTEROTOMY OF BILE DUCT & PANCREATIC DUCT DUODENAL APPR  | 7828000   |
| SPHINCTEROTOMY OF BILE DUCT USING DUODENAL APPROACH NEC      | 7828100   |
| INCISION OF SPHINCTER OF ODDI USING DUODENAL APPROACH OS     | 7828y00   |
| INCISION OF SPHINCTER OF ODDI USING DUODENAL APPROACH NOS    | 7828z00   |
| OTHER OPEN OPERATIONS ON BILE DUCT                           | 782A.00   |
| OPEN BIOPSY OF LESION OF BILE DUCT                           | 782A000   |
| OPERATIVE CHOLANGIOGRAPHY THROUGH CYSTIC DUCT                | 782A100   |
| OTHER SPECIFIED OTHER OPEN OPERATION ON BILE DUCT            | 782Ay00   |
| OTHER OPEN OPERATION ON BILE DUCT NOS                        | 782Az00   |
| ENDOSCOPIC INCISION OF SPHINCTER OF ODDI                     | 782B.00   |
| ENDOSC SPHINCTEROTOMY SPHINCTER OF ODDI+CALCULUS REMOVAL     | 782B000   |
| ERCP SPHINCTEROTOMY SPHINCTER OF ODDI AND CALCULUS REMOVAL   | 782B011   |
| ENDOSC SPHINCTEROT SPHINCT ODDI+INSERT BILE DUCT TUBE PROSTH | 782B100   |
| OTHER SPECIFIED ENDOSCOPIC INCISION OF SPHINCTER OF ODDI     | 782By00   |
| ENDOSCOPIC INCISION OF SPHINCTER OF ODDI NOS                 | 782Bz00   |
| ENDOSCOPIC RETROGRADE PLACEMENT OF PROSTHESIS IN BILE DUCT   | 782D.00   |
| ENDOSC RETROGRADE INSERT TUBAL PROSTH IN BOTH HEPATIC DUCTS  | 782D000   |
| ENDOSCOPIC RETROGRADE INSERT TUBAL PROSTH IN BILE DUCT NEC   | 782D100   |
| ENDOSCOPIC RETROGRADE RENEWAL TUBAL PROSTHESIS IN BILE DUCT  | 782D200   |
| ENDOSCOP RETROGRADE REMOVAL TUBAL PROSTHESIS FROM BILE DUCT  | 782D300   |
| ENDOSCOPIC RETROGRADE PLACEMENT PROSTHESIS IN BILE DUCT OS   | 782Dy00   |
| ENDOSCOPIC RETROGRADE PLACEMENT PROSTHESIS IN BILE DUCT NOS  | 782Dz00   |
| OTHER THERAPEUTIC ENDOSCOPIC RETROGRADE BILE DUCT OPERATIONS | 782E.00   |
| ENDOSCOPIC RETROGRADE EXTRACTION OF CALCULUS FROM BILE DUCT  | 7.82E+02  |
| ENDOSCOPIC DILATATION OF BILE DUCT NEC                       | 7.82E+102 |
| OTHER THERAPEUTIC ENDOSCOPIC RETROGRADE OP ON BILE DUCT OS   | 782Ey00   |
| OTHER THERAPEUTIC ENDOSCOPIC RETROGRADE OP ON BILE DUCT NOS  | 782Ez00   |
| ENDOSC RETROGRADE CHOLANGIOGRAPHY + BIOPSY LESION BILE DUCT  | 782H000   |
| THERAPEUTIC PERCUTANEOUS ATTENTION TO BILE DUCT CONNECTION   | 782K.00   |
| THERAPEUTIC PERCUTANEOUS ATTENTION TO BILE DUCT ANASTOMOSIS  | 782K.11   |
| PERCUTANEOUS DILATION ANAST BILE DUCT+INSERT TUBE PROSTH HFQ | 782K000   |
| PERCUTANEOUS DILATION OF ANASTOMOSIS OF BILE DUCT NEC        | 782K100   |
| THERAPEUTIC PERCUTANEOUS ATTENTION TO BILE DUCT CONNECT OS   | 782Ky00   |
| THERAPEUTIC PERCUTANEOUS ATTENTION TO BILE DUCT CONNECT NOS  | 782Kz00   |
| THERAPEUTIC PERCUTANEOUS INSERTION PROSTHESIS INTO BILE DUCT | 782L.00   |
| THERAPEUTIC PERCUTANEOUS INSERTION OF TUBE INTO BILE DUCT    | 782L.11   |
| PERCUTANEOUS INSERT TUBAL PROSTHESIS INTO BOTH HEPATIC DUCTS | 782L000   |
| PERCUTAN INSERT TUBAL PROSTHESIS TO RIGHT HEPATIC DUCT NEC   | 782L100   |
| PERCUTAN INSERT TUBAL PROSTHESIS INTO LEFT HEPATIC DUCT NEC  | 782L200   |
| PERCUTANEOUS INSERT TUBAL PROSTHESIS INTO HEPATIC DUCT NEC   | 782L300   |



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| PERCUTANEOUS INSERTION TUBAL PROSTHESIS TO COMMON BILE DUCT  | 782L400 |
| THERAPEUTIC PERCUTANEOUS INSERT PROSTHESIS TO BILE DUCT OS   | 782Ly00 |
| THERAPEUTIC PERCUTANEOUS INSERT PROSTHESIS TO BILE DUCT NOS  | 782Lz00 |
| OTHER THERAPEUTIC PERCUTANEOUS OPERATIONS ON BILE DUCT       | 782M.00 |
| PERCUTANEOUS ATTENTION TO TUBE IN BILE DUCT                  | 782M.11 |
| PERCUTANEOUS ATTENTION TO PROSTHESIS IN BILE DUCT            | 782M.12 |
| RENEWAL PERCUTANEOUSLY INSERTED TUBAL PROSTH IN BILE DUCT    | 782M000 |
| REMOVAL PERCUTANEOUSLY INSERTED TUBAL PROSTH FROM BILE DUCT  | 782M100 |
| ATTENTION TO PERCUT INSERTED TUBAL PROSTH IN BILE DUCT NEC   | 782M200 |
| OTHER THERAPEUTIC PERCUTANEOUS OPERATION ON BILE DUCT OS     | 782My00 |
| OTHER THERAPEUTIC PERCUTANEOUS OPERATION ON BILE DUCT NOS    | 782Mz00 |
| THERAPEUTIC OPERATIONS ON BILE DUCT ALONG T TUBE TRACK       | 782N.00 |
| ENDOSC REMOVAL OF CALCULUS FROM BILE DUCT ALONG T TUBE TRACK | 782N000 |
| PERCUTAN REMOVAL CALCULUS FROM BILE DUCT ALONG T TUBE TRACK  | 782N100 |
| THERAPEUTIC OPERATION ON BILE DUCT ALONG T TUBE TRACK OS     | 782Ny00 |
| THERAPEUTIC OPERATION ON BILE DUCT ALONG T TUBE TRACK NOS    | 782Nz00 |
| PERCUTANEOUS EXAMINATION OF BILE DUCT                        | 782P.00 |
| PERCUTANEOUS EXAMINATION OF BILE DUCT NOS                    | 782Pz00 |
| OTHER OPERATIONS ON BILE DUCT                                | 782Q.00 |
| EXTRACORPOREAL LITHOTRIPSY OF CALCULUS IN BILE DUCT          | 782Q000 |
| OTHER SPECIFIED OTHER OPERATION ON BILE DUCT                 | 782Qy00 |
| OTHER OPERATION ON BILE DUCT NOS                             | 782Qz00 |
| OTHER SPECIFIED OPERATIONS ON BILE DUCT                      | 782y.00 |
| BILE DUCT OPERATIONS NOS                                     | 782z.00 |
| LIVER ENLARGED   | 7851E   |
| JAUNDICE   | 7852    |
| ICTERUS  | 7852C   |
| JAUNDICE INCREASING  | 7852CR  |
| JAUNDICE DECREASING  | 7852DC  |
| JAUNDICE FADING  | 7852FA  |
| JAUNDICE FLUCTUATING   | 7852FL  |
| JAUNDICE CHOLESTATIC   | 7852JC  |
| JAUNDICE PAINLESS  | 7852PL  |
| EXCISION OR BIOPSY OF PORTA HEPATIS LYMPH NODE               | 7H62500 |
| [SO]SPHINCTER OF ODDI  | 7N33400 |
| RUPTURE LIVER  | 8640R   |
| BILIARY STONE DISSOLVING DIET                                | 8B54.00 |
| CHOLECYSTECTOMY PLANNED                                      | 8L1..00 |
| JAUNDICE DRUG INDUCED  | 9779PN  |
| PORPHYRIA DUE MEDICINAL DRUG                                 | 9779PR  |
| RADIATION HEPATITIS  | 9904HP  |
| REJECTION LIVER TRANSPLANT                                   | 9977LT  |
| SYNDROME CYSTIC DUCT   | 9989CD  |
| SERUM HEPATITIS  | 9992H   |
| SERUM JAUNDICE   | 9992J   |
| JAUNDICE AFTER INJECTION/INOCULATION/TRA                     | 9992JA  |

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| AMOEBIC LIVER ABSCESS                                       | A053.00 |
| TUBERCULOSIS OF LIVER                                       | A17y400 |
| ACTINOMYCOSIS OF LIVER                                      | A392200 |
| VIRAL HEPATITIS   | A70..00 |
| VIRAL HEPATITIS A WITH COMA                                 | A700.00 |
| VIRAL (INFECTIOUS) HEPATITIS A                              | A701.00 |
| INFECTIVE HEPATITIS   | A701.11 |
| VIRAL HEPATITIS B WITH COMA                                 | A702.00 |
| VIRAL (SERUM) HEPATITIS B                                   | A703.00 |
| OTHER SPECIFIED VIRAL HEPATITIS WITH COMA                   | A704.00 |
| VIRAL HEPATITIS C WITH COMA                                 | A704000 |
| OTHER SPECIFIED VIRAL HEPATITIS WITH HEPATIC COMA NOS       | A704z00 |
| OTHER SPECIFIED VIRAL HEPATITIS WITHOUT COMA                | A705.00 |
| VIRAL HEPATITIS C WITHOUT MENTION OF HEPATIC COMA           | A705000 |
| ACUTE DELTA-(SUPER)INFECTION OF HEPATITIS B CARRIER         | A705100 |
| ACUTE HEPATITIS E   | A705200 |
| HEPATITIS NON A NON B                                       | A705400 |
| OTHER SPECIFIED VIRAL HEPATITIS WITHOUT MENTION OF COMA NOS | A705z00 |
| UNSPECIFIED VIRAL HEPATITIS WITH COMA                       | A706.00 |
| CHRONIC VIRAL HEPATITIS                                     | A707.00 |
| CHRONIC VIRAL HEPATITIS B WITH DELTA-AGENT                  | A707000 |
| CHRONIC VIRAL HEPATITIS B WITHOUT DELTA-AGENT               | A707100 |
| CHRONIC VIRAL HEPATITIS C                                   | A707200 |
| CHRONIC VIRAL HEPATITIS, UNSPECIFIED                        | A707X00 |
| UNSPECIFIED VIRAL HEPATITIS                                 | A70z.00 |
| HEPATITIS C   | A70z000 |
| MUMPS HEPATITIS   | A72x000 |
| CYTOMEGALOVIRAL HEPATITIS                                   | A785200 |
| CONGENITAL SYPHILITIC HEPATOMEGALY                          | A900.15 |
| SECONDARY SYPHILITIC HEPATITIS                              | A916100 |
| SYPHILIS OF LIVER   | A953.00 |
| GONOCOCCAL HEPATITIS  | A98yy11 |
| GONOCOCCAL PERIHEPATITIS                                    | A98yy13 |
| LEPTOSPIROSIS ICTERHAEMORRHAGICA                            | AA00.00 |
| SPIROCHAETAL JAUNDICE                                       | AA00.11 |
| COCCIDIOMYCOSIS LIVER                                       | AB31.11 |
| HISTOPLASMOSIS LIVER  | AB4z600 |
| BLASTOMYCOSIS LIVER   | AB50300 |
| CRYPTOCOCCOSIS LIVER  | AB65300 |
| CAT LIVER FLUKE INFECTION                                   | AC10.11 |
| CHINESE LIVER FLUKE DISEASE                                 | AC11.11 |
| LIVER FLUKES NOS  | AC13.11 |
| SHEEP LIVER FLUKE INFECTION                                 | AC13.12 |
| LIVER ECHINOCOCCUS GRANULOSUS                               | AC20.00 |
| LIVER ECHINOCOCCUS MULTILOCULARIS                           | AC25.00 |
| LIVER ECHINOCOCCUS UNSPECIFIED                              | AC2y.00 |

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| CAPILLARIA HEPATICA   | AC8y100 |
| TOXOPLASMA HEPATITIS  | AD05.00 |
| SARCOIDOSIS   | AD5..00 |
| SARCOIDOSIS OF LUNG   | AD50.00 |
| SARCOIDOSIS OF LYMPH NODES                                  | AD51.00 |
| SARCOIDOSIS OF LUNG WITH SARCOIDOSIS OF LYMPH NODES         | AD52.00 |
| SARCOIDOSIS OF SKIN   | AD53.00 |
| SARCOIDOSIS OF INFERIOR TURBINATES                          | AD54.00 |
| SARCOID ARTHROPATHY   | AD55.00 |
| SEQUELAE OF VIRAL HEPATITIS                                 | AE23.00 |
| [X]VIRAL HEPATITIS  | AyuB.00 |
| [X]OTHER SPECIFIED ACUTE VIRAL HEPATITIS                    | AyuB000 |
| [X]OTHER CHRONIC VIRAL HEPATITIS                            | AyuB100 |
| [X]CHRONIC VIRAL HEPATITIS, UNSPECIFIED                     | AyuB200 |
| [X]UNSPECIFIED VIRAL HEPATITIS WITH COMA                    | AyuB300 |
| [X]UNSPECIFIED VIRAL HEPATITIS WITHOUT COMA                 | AyuB400 |
| [X]ECHINOCOCCOSIS, UNSPECIFIED, OF LIVER                    | AyuG400 |
| [X]SEQUELAE OF VIRAL HEPATITIS                              | AyuJ900 |
| MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCTS     | B15..00 |
| PRIMARY MALIGNANT NEOPLASM OF LIVER                         | B150.00 |
| PRIMARY CARCINOMA OF LIVER                                  | B150000 |
| HEPATOBLASTOMA OF LIVER                                     | B150100 |
| PRIMARY ANGIOSARCOMA OF LIVER                               | B150200 |
| HEPATOCELLULAR CARCINOMA                                    | B150300 |
| PRIMARY MALIGNANT NEOPLASM OF LIVER NOS                     | B150z00 |
| MALIGNANT NEOPLASM OF INTRAHEPATIC BILE DUCTS               | B151.00 |
| MALIGNANT NEOPLASM OF INTERLOBULAR BILE DUCTS               | B151000 |
| MALIGNANT NEOPLASM OF INTERLOBULAR BILIARY CANALS           | B151100 |
| MALIGNANT NEOPLASM OF INTRAHEPATIC BILIARY PASSAGES         | B151200 |
| MALIGNANT NEOPLASM OF INTRAHEPATIC CANALICULI               | B151300 |
| MALIGNANT NEOPLASM OF INTRAHEPATIC GALL DUCT                | B151400 |
| MALIGNANT NEOPLASM OF INTRAHEPATIC BILE DUCTS NOS           | B151z00 |
| MALIGNANT NEOPLASM OF LIVER UNSPECIFIED                     | B152.00 |
| SECONDARY MALIGNANT NEOPLASM OF LIVER                       | B153.00 |
| MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCTS NOS | B15z.00 |
| MALIGNANT NEOPLASM GALLBLADDER AND EXTRAHEPATIC BILE DUCTS  | B16..00 |
| MALIGNANT NEOPLASM OF GALLBLADDER                           | B160.00 |
| CARCINOMA GALLBLADDER                                       | B160.11 |
| MALIGNANT NEOPLASM OF EXTRAHEPATIC BILE DUCTS               | B161.00 |
| MALIGNANT NEOPLASM OF CYSTIC DUCT                           | B161000 |
| MALIGNANT NEOPLASM OF HEPATIC DUCT                          | B161100 |
| MALIGNANT NEOPLASM OF COMMON BILE DUCT                      | B161200 |
| CARCINOMA COMMON BILE DUCT                                  | B161211 |
| MALIGNANT NEOPLASM OF SPHINCTER OF ODDI                     | B161300 |
| MALIGNANT NEOPLASM OF EXTRAHEPATIC BILE DUCTS NOS           | B161z00 |
| MALIGNANT NEOPLASM OF AMPULLA OF VATER                      | B162.00 |

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| MALIGNANT NEOPLASM, OVERLAPPING LESION OF BILIARY TRACT      | B163.00 |
| MALIGNANT NEOPLASM OTHER GALLBLADDER/EXTRAHEPATIC BILE DUCT  | B16y.00 |
| MALIGNANT NEOPLASM GALLBLADDER/EXTRAHEPATIC BILE DUCTS NOS   | B16z.00 |
| SECONDARY MALIGNANT NEOPLASM OF LIVER                        | B577.00 |
| LIVER METASTASES   | B577.11 |
| BENIGN NEOPLASM OF LIVER AND BILIARY DUCTS                   | B715.00 |
| BENIGN NEOPLASM OF BILIARY SYSTEM                            | B715.11 |
| BENIGN NEOPLASM OF LIVER                                     | B715000 |
| BENIGN NEOPLASM OF INTRAHEPATIC BILE DUCTS                   | B715100 |
| BENIGN NEOPLASM OF GALLBLADDER                               | B715200 |
| BENIGN NEOPLASM OF CYSTIC DUCT                               | B715300 |
| BENIGN NEOPLASM OF HEPATIC DUCT                              | B715400 |
| BENIGN NEOPLASM OF BILE DUCT                                 | B715500 |
| BENIGN NEOPLASM OF SPHINCTER OF ODDI                         | B715600 |
| BENIGN NEOPLASM OF AMPULLA OF VATER                          | B715700 |
| BENIGN NEOPLASM OF LIVER AND BILIARY DUCTS NOS               | B715z00 |
| CARCINOMA IN SITU OF LIVER AND BILIARY SYSTEM                | B808.00 |
| CARCINOMA IN SITU OF BILIARY SYSTEM                          | B808.11 |
| CARCINOMA IN SITU OF LIVER                                   | B808000 |
| CARCINOMA IN SITU OF INTRAHEPATIC BILE DUCTS                 | B808100 |
| CARCINOMA IN SITU OF HEPATIC DUCT                            | B808200 |
| CARCINOMA IN SITU OF GALL BLADDER                            | B808300 |
| CARCINOMA IN SITU OF CYSTIC DUCT                             | B808400 |
| CARCINOMA IN SITU OF COMMON BILE DUCT                        | B808500 |
| CARCINOMA IN SITU OF AMPULLA OF VATER                        | B808600 |
| CARCINOMA IN SITU OF SPHINCTER OF ODDI                       | B808700 |
| CARCINOMA IN SITU OF LIVER OR BILIARY SYSTEM NOS             | B808z00 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF LIVER AND BILIARY PASSAGE | B903.00 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF BILIARY SYSTEM            | B903.11 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF LIVER                     | B903000 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF INTRA-HEPATIC BILE DUCTS  | B903100 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF HEPATIC DUCT              | B903200 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF GALL BLADDER              | B903300 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF CYSTIC DUCT               | B903400 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF COMMON BILE DUCT          | B903500 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF AMPULLA OF VATER          | B903600 |
| NEOPLASM OF UNCERTAIN BEHAVIOUR OF SPHINCTER OF ODDI         | B903700 |
| NEOP OF UNCERTAIN BEHAVIOUR OF LIVER OR BILIARY PASSAGES NOS | B903z00 |
| [M]HEPATOBIILIARY TRACT ADENOMAS AND CARCINOMAS              | BB5D.00 |
| [M]BILIARY TRACT ADENOMAS AND ADENOCARCINOMAS                | BB5D.11 |
| [M]BILE DUCT ADENOMA   | BB5D000 |
| [M]CHOLANGIOMA   | BB5D011 |
| [M]BILE DUCT CARCINOMA                                       | BB5D111 |
| [M]BILE DUCT CYSTADENOMA                                     | BB5D200 |
| [M]BILE DUCT CYSTADENOCARCINOMA                              | BB5D300 |
| [M]LIVER CELL ADENOMA  | BB5D400 |

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| [M]HEPATOCELLULAR ADENOMA                                   | BB5D411 |
| [M]HEPATOMA, BENIGN   | BB5D412 |
| [M]HEPATOCELLULAR CARCINOMA NOS                             | BB5D500 |
| [M]HEPATOMA NOS   | BB5D511 |
| [M]HEPATOMA, MALIGNANT                                      | BB5D512 |
| [M]LIVER CELL CARCINOMA                                     | BB5D513 |
| [M]HEPATOCHOLANGIOMA, BENIGN                                | BB5D600 |
| [M]COMBINED HEPATOCELLULAR CARCINOMA AND CHOLANGIOCARCINOMA | BB5D700 |
| [M]HEPATOCHOLANGIOCARCINOMA                                 | BB5D711 |
| [M]HEPATOCELLULAR CARCINOMA, FIBROLAMELLAR                  | BB5D800 |
| [M]HEPATOBIILIARY ADENOMA OR CARCINOMA NOS                  | BB5Dz00 |
| [M]HEPATOBLASTOMA   | BBL8.00 |
| [M]EMBRYONAL HEPATOMA                                       | BBL8.11 |
| [X]OTHER SARCOMAS OF THE LIVER                              | Byu1000 |
| [X]OTHER SPECIFIED CARCINOMAS OF LIVER                      | Byu1100 |
| CYSTINE STORAGE DISEASE                                     | C300311 |
| GLYCOGENOSIS - GLYCOGEN STORAGE DISEASE                     | C310.00 |
| GLYCOGEN STORAGE DISEASE                                    | C310.13 |
| GLYCOGENOSIS, TYPE 5  | C310012 |
| GENERALISED GLYCOGENOSIS                                    | C310100 |
| GLYCOGENOSIS, TYPE 2  | C310113 |
| HEPATORENAL GLYCOGENOSIS                                    | C310200 |
| GLYCOGENOSIS, TYPE 1  | C310213 |
| GLYCOGENOSIS OF LIVER AND MUSCLE                            | C310300 |
| GLYCOGENOSIS OF LIVER AND MUSCLE                            | C310311 |
| GLYCOGENOSIS, TYPE 3  | C310313 |
| GLYCOGENOSIS WITH HEPATIC CIRRHOSIS                         | C310400 |
| GLYCOGENOSIS, TYPE 4  | C310411 |
| OTHER SPECIFIED GLYCOGENOSIS                                | C310y00 |
| GLYCOGENOSIS NOS  | C310z00 |
| ANDERSON'S DISEASE  | C327.11 |
| FABRY'S DISEASE   | C327.12 |
| GAUCHER'S DISEASE   | C327100 |
| FABRY'S DISEASE   | C327411 |
| ANDERSON'S DISEASE  | C327412 |
| ANDERSON-FABRY DISEASE                                      | C327413 |
| STEATOSIS   | C32y500 |
| HEPATIC FAMILIAL STEATOSIS                                  | C32y511 |
| HAEMOCHROMATOSIS  | C350000 |
| BRONZED DIABETES  | C350011 |
| PIGMENTARY CIRRHOSIS OF LIVER                               | C350012 |
| HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE)            | C351000 |
| WILSON'S DISEASE  | C351011 |
| HYPERCUPRAEMIA  | C351100 |
| DISORDERS OF PORPHYRIN METABOLISM                           | C371.00 |
| CONGENITAL PORPHYRIA  | C371000 |

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| ERYTHROPOIETIC PROTOPORPHYRIA                         | C371100 |
| ACUTE INTERMITTENT PORPHYRIA                          | C371200 |
| PROTOCOPROPORPHYRIA                                   | C371300 |
| PORPHYRIA CUTANEA TARDA                               | C371400 |
| COPROPORPHYRIA  | C371500 |
| PORPHYRIA NOS   | C371z00 |
| AMYLOIDOSIS   | C373.00 |
| SPORADIC PRIMARY AMYLOIDOSIS                          | C373000 |
| FAMILIAL NEUROPATHIC AMYLOID                          | C373200 |
| FAMILIAL CARDIAC AMYLOID                              | C373300 |
| SECONDARY AMYLOIDOSIS                                 | C373500 |
| NEPHROPATHIC AMYLOIDOSIS                              | C373600 |
| PRIMARY AMYLOIDOSIS NEC                               | C373700 |
| ORGAN LIMITED NON-HEREDITARY AMYLOIDOSIS              | C373900 |
| HEREDOFAMILIAL AMYLOIDOSIS, UNSPECIFIED               | C373X00 |
| OTHER SPECIFIED AMYLOIDOSIS                           | C373y00 |
| AMYLOIDOSIS NOS                                       | C373z00 |
| CRIGLER - NAJJAR SYNDROME                             | C374000 |
| DUBIN - JOHNSON SYNDROME                              | C374100 |
| ROTOR SYNDROME  | C374300 |
| ALPHA-1-ANTITRYPSIN HEPATITIS                         | C376100 |
| ALPHA-1-ANTITRYPSIN DEFICIENCY                        | C376200 |
| [X]SARCOIDOSIS OF OTHER AND COMBINED SITES            | Cyu0600 |
| [X]OTHER LIPID STORAGE DISORDERS                      | Cyu8900 |
| [X]OTHER PORPHYRIA                                    | Cyu8H00 |
| [X]OTHER AMYLOIDOSIS                                  | Cyu8L00 |
| [X]HEREDOFAMILIAL AMYLOIDOSIS, UNSPECIFIED            | Cyu8U00 |
| FOLATE-DEFICIENCY ANAEMIA DUE TO LIVER DISORDERS      | D012400 |
| ACHOLURIC FAMILIAL JAUNDICE                           | D100.11 |
| DEFICIENCY OF COAGULATION FACTOR DUE TO LIVER DISEASE | D307000 |
| MENINGITIS DUE TO SARCOIDOSIS                         | F013.00 |
| AUTONOMIC NEUROPATHY DUE TO AMYLOID                   | F171000 |
| MULTIPLE CRANIAL NERVE PALSIES IN SARCOIDOSIS         | F326300 |
| POLYNEUROPATHY IN AMYLOIDOSIS                         | F374000 |
| POLYNEUROPATHY IN PORPHYRIA                           | F374800 |
| POLYNEUROPATHY IN SARCOIDOSIS                         | F374900 |
| MYOPATHY DUE TO AMYLOID                               | F396000 |
| MYOPATHY DUE TO SARCOIDOSIS                           | F396500 |
| DIFFUSE CHOLESTEATOSIS                                | F553400 |
| AMYLOID HEART DISEASE                                 | G557000 |
| SARCOID HEART DISEASE                                 | G558300 |
| SARCOID MYOCARDITIS                                   | G5y7.00 |
| CEREBRAL AMYLOID ANGIOPATHY                           | G674000 |
| ANEURYSM OF HEPATIC ARTERY                            | G72yA00 |
| EMBOLISM AND THROMBOSIS OF THE HEPATIC ARTERY         | G74y900 |
| PORTAL VEIN THROMBOSIS                                | G81..00 |

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| BUDD - CHIARI SYNDROME (HEPATIC VEIN THROMBOSIS)        | G820.00 |
| HEPATIC VEIN THROMBOSIS                                 | G820.11 |
| OESOPHAGEAL VARICES                                     | G85..11 |
| OESOPHAGEAL VARICES WITH BLEEDING                       | G850.00 |
| OESOPHAGEAL VARICES WITHOUT BLEEDING                    | G851.00 |
| OESOPHAGEAL VARICES IN DISEASES EC                      | G852.00 |
| OESOPHAGEAL VARICES WITH BLEEDING IN DISEASES EC        | G852000 |
| OESOPHAGEAL VARICES WITHOUT BLEEDING IN DISEASES EC     | G852100 |
| OESOPHAGEAL VARICES IN CIRRHOSIS OF THE LIVER           | G852200 |
| OESOPHAGEAL VARICES IN ALCOHOLIC CIRRHOSIS OF THE LIVER | G852300 |
| OESOPHAGEAL VARICES IN DISEASES EC NOS                  | G852z00 |
| GASTRIC VARICES   | G857.00 |
| OESOPHAGEAL VARICES NOS                                 | G858.00 |
| [X]OESOPHAGEAL VARICES IN DISEASES CLASSIFIED ELSEWHERE | Gyu9400 |
| EMPYEMA WITH HEPATOPLEURAL FISTULA                      | H500200 |
| PULMONARY AMYLOIDOSIS                                   | H57y000 |
| PULMONARY SARCOIDOSIS                                   | H57y200 |
| GALLSTONE ILEUS   | J503000 |
| SUBHEPATIC ABSCESS                                      | J552000 |
| PERITONITIS DUE TO BILE                                 | J55y300 |
| ACUTE AND SUBACUTE LIVER NECROSIS                       | J60..00 |
| ACUTE NECROSIS OF LIVER                                 | J600.00 |
| ACUTE HEPATIC FAILURE                                   | J600000 |
| ACUTE LIVER FAILURE                                     | J600011 |
| ACUTE HEPATITIS - NONINFECTIVE                          | J600100 |
| ACUTE YELLOW ATROPHY                                    | J600200 |
| ACUTE NECROSIS OF LIVER NOS                             | J600z00 |
| SUBACUTE NECROSIS OF LIVER                              | J601.00 |
| SUBACUTE HEPATIC FAILURE                                | J601000 |
| SUBACUTE HEPATITIS - NONINFECTIVE                       | J601100 |
| SUBACUTE YELLOW ATROPHY                                 | J601200 |
| SUBACUTE NECROSIS OF LIVER NOS                          | J601z00 |
| ACUTE AND SUBACUTE LIVER NECROSIS NOS                   | J60z.00 |
| CIRRHOSIS AND CHRONIC LIVER DISEASE                     | J61..00 |
| ALCOHOLIC FATTY LIVER                                   | J610.00 |
| ACUTE ALCOHOLIC HEPATITIS                               | J611.00 |
| ALCOHOLIC CIRRHOSIS OF LIVER                            | J612.00 |
| FLORID CIRRHOSIS  | J612.11 |
| LAENNEC'S CIRRHOSIS                                     | J612.12 |
| ALCOHOLIC FIBROSIS AND SCLEROSIS OF LIVER               | J612000 |
| ALCOHOLIC LIVER DAMAGE UNSPECIFIED                      | J613.00 |
| ALCOHOLIC HEPATIC FAILURE                               | J613000 |
| CHRONIC HEPATITIS                                       | J614.00 |
| CHRONIC PERSISTENT HEPATITIS                            | J614000 |
| CHRONIC ACTIVE HEPATITIS                                | J614100 |
| AUTOIMMUNE CHRONIC ACTIVE HEPATITIS                     | J614111 |

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| CHRONIC AGGRESSIVE HEPATITIS              | J614200 |
| RECURRENT HEPATITIS                       | J614300 |
| CHRONIC LOBULAR HEPATITIS                 | J614400 |
| CHRONIC HEPATITIS UNSPECIFIED             | J614y00 |
| CHRONIC HEPATITIS NOS                     | J614z00 |
| CIRRHOSIS - NON ALCOHOLIC                 | J615.00 |
| PORTAL CIRRHOSIS                          | J615.11 |
| UNILOBULAR PORTAL CIRRHOSIS               | J615000 |
| MULTILOBULAR PORTAL CIRRHOSIS             | J615100 |
| POSTNECROTIC CIRRHOSIS OF LIVER           | J615111 |
| MIXED PORTAL CIRRHOSIS                    | J615200 |
| DIFFUSE NODULAR CIRRHOSIS                 | J615300 |
| FATTY PORTAL CIRRHOSIS                    | J615400 |
| HYPERTROPHIC PORTAL CIRRHOSIS             | J615500 |
| CAPSULAR PORTAL CIRRHOSIS                 | J615600 |
| CARDIAC PORTAL CIRRHOSIS                  | J615700 |
| CONGESTIVE CIRRHOSIS                      | J615711 |
| JUVENILE PORTAL CIRRHOSIS                 | J615800 |
| CHILDHOOD FUNCTION CIRRHOSIS              | J615811 |
| INDIAN CHILDHOOD CIRRHOSIS                | J615812 |
| PIGMENTARY PORTAL CIRRHOSIS               | J615900 |
| PIPE-STEM PORTAL CIRRHOSIS                | J615A00 |
| TOXIC PORTAL CIRRHOSIS                    | J615B00 |
| XANTHOMATOUS PORTAL CIRRHOSIS             | J615C00 |
| BACTERIAL PORTAL CIRRHOSIS                | J615D00 |
| CARDITUBERCULOUS CIRRHOSIS                | J615E00 |
| SYPHILITIC PORTAL CIRRHOSIS               | J615F00 |
| ZOOPARASITIC PORTAL CIRRHOSIS             | J615G00 |
| INFECTIOUS CIRRHOSIS NOS                  | J615H00 |
| PORTAL CIRRHOSIS UNSPECIFIED              | J615y00 |
| NON-ALCOHOLIC CIRRHOSIS NOS               | J615z00 |
| MACRONODULAR CIRRHOSIS OF LIVER           | J615z11 |
| CRYPTOGENIC CIRRHOSIS OF LIVER            | J615z12 |
| CIRRHOSIS OF LIVER NOS                    | J615z13 |
| LAENNEC'S CIRRHOSIS, NON-ALCOHOLIC        | J615z14 |
| HEPATIC FIBROSIS                          | J615z15 |
| BILIARY CIRRHOSIS                         | J616.00 |
| PRIMARY BILIARY CIRRHOSIS                 | J616000 |
| SECONDARY BILIARY CIRRHOSIS               | J616100 |
| BILIARY CIRRHOSIS OF CHILDREN             | J616200 |
| BILIARY CIRRHOSIS NOS                     | J616z00 |
| ALCOHOLIC HEPATITIS                       | J617.00 |
| CHRONIC ALCOHOLIC HEPATITIS               | J617000 |
| OTHER NON-ALCOHOLIC CHRONIC LIVER DISEASE | J61y.00 |
| CHRONIC YELLOW LIVER ATROPHY              | J61y000 |
| NON-ALCOHOLIC FATTY LIVER                 | J61y100 |



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| HEPATOSPLENOMEGALY   | J61y200 |
| PORTAL FIBROSIS WITHOUT CIRRHOSIS                            | J61y300 |
| HEPATIC FIBROSIS   | J61y400 |
| HEPATIC SCLEROSIS  | J61y500 |
| HEPATIC FIBROSIS WITH HEPATIC SCLEROSIS                      | J61y600 |
| STEATOSIS OF LIVER   | J61y700 |
| OTHER NON-ALCOHOLIC CHRONIC LIVER DISEASE NOS                | J61yz00 |
| CHRONIC LIVER DISEASE NOS                                    | J61z.00 |
| LIVER ABSCESS AND SEQUELAE OF CHRONIC LIVER DISEASE          | J62..00 |
| LIVER ABSCESS - EXCLUDING AMOEBIC LIVER ABSCESS              | J620.00 |
| LIVER ABSCESS DUE TO PORTAL PYAEMIA                          | J620000 |
| LIVER ABSCESS DUE TO CHOLANGITIS                             | J620100 |
| LIVER ABSCESS VIA HEPATIC ARTERY                             | J620200 |
| LIVER ABSCESS VIA UMBILICUS                                  | J620300 |
| LIVER ABSCESS DUE TO DIRECT EXTENSION                        | J620400 |
| LIVER ABSCESS NOS  | J620z00 |
| PORTAL PYAEMIA   | J621.00 |
| PHLEBITIS OF PORTAL VEIN                                     | J621.11 |
| HEPATIC COMA   | J622.00 |
| ENCEPHALOPATHY - HEPATIC                                     | J622.11 |
| PORTAL HYPERTENSION  | J623.00 |
| HEPATORENAL SYNDROME   | J624.00 |
| [X] HEPATIC FAILURE  | J625.00 |
| [X] LIVER FAILURE  | J625.11 |
| OTHER SEQUELAE OF CHRONIC LIVER DISEASE                      | J62y.00 |
| HEPATIC FAILURE NOS  | J62y.11 |
| LIVER FAILURE NOS  | J62y.12 |
| HEPATIC FAILURE  | J62y.13 |
| LIVER ABSCESS AND CHRONIC LIVER DISEASE CAUSING SEQUELAE NOS | J62z.00 |
| OTHER LIVER DISORDERS  | J63..00 |
| CHRONIC PASSIVE LIVER CONGESTION                             | J630.00 |
| HEPATITIS IN VIRAL DISEASES EC                               | J631.00 |
| HEPATITIS IN COXSACKIE VIRUS                                 | J631000 |
| HEPATITIS IN CYTOMEGALIC INCLUSION VIRUS                     | J631100 |
| HEPATITIS IN INFECTIOUS MONONUCLEOSIS                        | J631200 |
| HEPATITIS IN MUMPS   | J631300 |
| HEPATITIS IN YELLOW FEVER                                    | J631400 |
| HEPATITIS IN OTHER VIRAL DISEASE                             | J631500 |
| HEPATITIS + ADENOVIRUS                                       | J631600 |
| HEPATITIS IN VIRAL DISEASES EC NOS                           | J631z00 |
| HEPATITIS IN OTHER INFECTIOUS DISEASES EC                    | J632.00 |
| HEPATITIS IN MALARIA   | J632000 |
| HEPATITIS IN LATE SYPHILIS                                   | J632100 |
| HEPATITIS IN SECONDARY SYPHILIS                              | J632200 |
| HEPATITIS IN TOXOPLASMOSIS                                   | J632300 |
| HEPATITIS IN INFECTIOUS DISEASES EC NOS                      | J632z00 |

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| HEPATITIS UNSPECIFIED  | J633.00 |
| TOXIC HEPATITIS  | J633000 |
| HEPATITIS UNSPECIFIED NOS                                    | J633z00 |
| HEPATIC INFARCTION   | J634.00 |
| TOXIC LIVER DISEASE  | J635.00 |
| TOXIC LIVER DISEASE WITH CHOLESTASIS                         | J635000 |
| TOXIC LIVER DISEASE WITH HEPATIC NECROSIS                    | J635100 |
| TOXIC LIVER DISEASE WITH ACUTE HEPATITIS                     | J635200 |
| TOXIC LIVER DISEASE WITH CHRONIC PERSISTENT HEPATITIS        | J635300 |
| TOXIC LIVER DISEASE WITH CHRONIC LOBULAR HEPATITIS           | J635400 |
| TOXIC LIVER DISEASE WITH CHRONIC ACTIVE HEPATITIS            | J635500 |
| TOXIC LIVER DISEASE WITH FIBROSIS AND CIRRHOSIS OF LIVER     | J635600 |
| TOXIC LIVER DISEASE, UNSPECIFIED                             | J635X00 |
| CENTRAL HAEMORRHAGIC NECROSIS OF LIVER                       | J636.00 |
| HEPATIC VENO-OCCLUSIVE DISEASE                               | J637.00 |
| PELIOSIS HEPATIS   | J638.00 |
| HEPATIC GRANULOMAS IN BERYLLIOSIS                            | J639.00 |
| HEPATIC GRANULOMAS IN SARCOIDOSIS                            | J63A.00 |
| GRANULOMATOUS HEPATITIS, NOT ELSEWHERE CLASSIFIED            | J63X.00 |
| OTHER SPECIFIED LIVER DISORDER                               | J63y.00 |
| HEPATOPTOSIS   | J63y000 |
| NONSPECIFIC REACTIVE HEPATITIS                               | J63y100 |
| LIVER CYST   | J63y200 |
| OTHER SPECIFIED LIVER DISORDER NOS                           | J63yz00 |
| LIVER DISORDER NOS   | J63z.00 |
| CHOLELITHIASIS   | J64..00 |
| BILE DUCT CALCULUS   | J64..11 |
| CALCULUS - BILIARY   | J64..12 |
| CYSTIC DUCT CALCULUS   | J64..13 |
| GALLBLADDER CALCULUS   | J64..14 |
| GALLSTONES   | J64..15 |
| STONE - BILIARY  | J64..16 |
| GALLBLADDER CALCULUS WITH ACUTE CHOLECYSTITIS                | J640.00 |
| GALLBLADDER CALCULUS WITH ACUTE CHOLECYSTITIS +NO OBSTRUCT   | J640000 |
| GALLBLADDER CALCULUS WITH ACUTE CHOLECYSTITIS + OBSTRUCTION  | J640100 |
| GALLBLADDER CALCULUS WITH ACUTE CHOLECYSTITIS - OBST NOS     | J640z00 |
| GALLBLADDER CALCULUS WITH OTHER CHOLECYSTITIS                | J641.00 |
| GALLBLADDER CALCULUS WITH OTHER CHOLECYSTITIS +NO OBSTRUCT   | J641000 |
| GALLBLADDER CALCULUS WITH OTHER CHOLECYSTITIS + OBSTRUCT     | J641100 |
| GALLBLADDER CALCULUS WITH OTHER CHOLECYSTITIS - OBSTRUCT NOS | J641z00 |
| GALLBLADDER CALCULUS WITHOUT MENTION OF CHOLECYSTITIS        | J642.00 |
| GALLBLADDER CALCULUS WITHOUT MENTION OF CHOLECYSTITIS        | J642.11 |
| GALLBLADDER CALCULUS WITHOUT MENTION CHOLECYSTITIS +NO OBSTR | J642000 |
| GALLBLADDER CALCULUS WITHOUT MENTION CHOLECYSTITIS + OBSTRUC | J642100 |
| BILIARY COLIC  | J642200 |
| GALLBLADDER CALCULUS WITHOUT CHOLECYSTITIS AND OBSTRUCT NOS  | J642z00 |

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| BILE DUCT CALCULUS WITH ACUTE CHOLECYSTITIS                 | J643.00 |
| BILE DUCT CALCULUS + ACUTE CHOLECYSTITIS AND NO OBSTRUCTION | J643000 |
| BILE DUCT CALCULUS + ACUTE CHOLECYSTITIS AND OBSTRUCTION    | J643100 |
| BILE DUCT CALCULUS + ACUTE CHOLECYSTITIS - OBSTRUCT NOS     | J643z00 |
| BILE DUCT CALCULUS WITH OTHER CHOLECYSTITIS                 | J644.00 |
| BILE DUCT CALCULUS + OTHER CHOLECYSTITIS AND NO OBSTRUCTION | J644000 |
| BILE DUCT CALCULUS + OTHER CHOLECYSTITIS AND OBSTRUCTION    | J644100 |
| BILE DUCT CALCULUS + OTHER CHOLECYSTITIS - OBSTRUCTION NOS  | J644z00 |
| BILE DUCT CALCULUS WITHOUT MENTION OF CHOLECYSTITIS         | J645.00 |
| CHOLEDOCHOLITHIASIS   | J645.11 |
| BILE DUCT CALCULUS WITHOUT CHOLECYSTITIS, NO OBSTRUCTION    | J645000 |
| BILE DUCT CALCULUS WITHOUT CHOLECYSTITIS WITH OBSTRUCTION   | J645100 |
| BILE DUCT CALCULUS NOS                                      | J645200 |
| BILE DUCT CALCULUS WITHOUT CHOLECYSTITIS NOS                | J645z00 |
| CALCULUS OF BILE DUCT WITH CHOLANGITIS                      | J646.00 |
| CHOLELITHIASIS NOS  | J64z.00 |
| CHOLELITHIASIS WITHOUT OBSTRUCTION NOS                      | J64z000 |
| CHOLELITHIASIS WITH OBSTRUCTION NOS                         | J64z100 |
| CHOLELITHIASIS NOS  | J64zz00 |
| OTHER GALLBLADDER DISORDERS                                 | J65..00 |
| ACUTE CHOLECYSTITIS   | J650.00 |
| ABSCESS OF GALLBLADDER                                      | J650.11 |
| EMPHYEMA OF GALLBLADDER                                     | J650.12 |
| ACUTE CHOLECYSTITIS UNSPECIFIED                             | J650000 |
| ACUTE ANGIOCHOLECYSTITIS                                    | J650100 |
| ACUTE EMPHYSEMATOUS CHOLECYSTITIS                           | J650200 |
| ACUTE SUPPURATIVE CHOLECYSTITIS                             | J650300 |
| ACUTE GANGRENOUS CHOLECYSTITIS                              | J650400 |
| ACUTE CHOLECYSTITIS NOS                                     | J650z00 |
| OTHER CHOLECYSTITIS   | J651.00 |
| CHRONIC CHOLECYSTITIS                                       | J651000 |
| OTHER CHOLECYSTITIS OS                                      | J651y00 |
| CHOLECYSTITIS NOS   | J651z00 |
| OBSTRUCTION OF GALLBLADDER                                  | J652.00 |
| OCCLUSION OF GALLBLADDER                                    | J652000 |
| STENOSIS OF GALLBLADDER                                     | J652100 |
| OCCLUSION OF CYSTIC DUCT                                    | J652200 |
| STENOSIS OF CYSTIC DUCT                                     | J652300 |
| OBSTRUCTION OF GALLBLADDER NOS                              | J652z00 |
| MUCOCELE OF GALLBLADDER                                     | J653.00 |
| HYDROPS OF GALLBLADDER                                      | J653.11 |
| PERFORATION OF GALLBLADDER                                  | J654.00 |
| RUPTURE OF GALLBLADDER                                      | J654000 |
| RUPTURE OF CYSTIC DUCT                                      | J654100 |
| PERFORATION OF GALLBLADDER NOS                              | J654z00 |
| FISTULA OF GALLBLADDER                                      | J655.00 |

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| BILIARY FISTULA                          | J655000 |
| CHOLECYSTOGASTRIC FISTULA                | J655100 |
| CHOLECYSTODUODENAL FISTULA               | J655200 |
| CHOLECYSTOENTERIC FISTULA                | J655300 |
| FISTULA OF GALLBLADDER NOS               | J655z00 |
| CHOLESTEROLOSIS OF GALLBLADDER           | J656.00 |
| STRAWBERRY GALLBLADDER                   | J656.11 |
| OTHER SPECIFIED GALLBLADDER DISORDERS    | J65y.00 |
| ADHESIONS OF GALLBLADDER                 | J65y000 |
| ADHESIONS OF CYSTIC DUCT                 | J65y100 |
| ATROPHY OF GALLBLADDER                   | J65y200 |
| ATROPHY OF CYSTIC DUCT                   | J65y300 |
| CYST OF GALLBLADDER                      | J65y400 |
| CYST OF CYSTIC DUCT                      | J65y500 |
| HYPERTROPHY OF GALLBLADDER               | J65y600 |
| HYPERTROPHY OF CYSTIC DUCT               | J65y700 |
| ULCER OF GALLBLADDER                     | J65y800 |
| ULCER OF CYSTIC DUCT                     | J65y900 |
| NONFUNCTIONING GALLBLADDER               | J65yA00 |
| BILIARY DYSKINESIA                       | J65yB00 |
| POLYP OF GALLBLADDER                     | J65yC00 |
| OTHER SPECIFIED GALLBLADDER DISORDER NOS | J65yz00 |
| OTHER GALLBLADDER DISORDERS NOS          | J65z.00 |
| OTHER BILIARY TRACT DISORDERS            | J66..00 |
| POSTCHOLECYSTECTOMY SYNDROME             | J660.00 |
| CHOLANGITIS                              | J661.00 |
| ACUTE CHOLANGITIS                        | J661000 |
| CHRONIC CHOLANGITIS                      | J661100 |
| RECURRENT CHOLANGITIS                    | J661200 |
| SUPPURATIVE CHOLANGITIS                  | J661300 |
| ASCENDING CHOLANGITIS                    | J661400 |
| CHOLANGITIS LENTA                        | J661500 |
| OBLITERATIVE CHOLANGITIS                 | J661600 |
| PRIMARY SCLEROSING CHOLANGITIS           | J661700 |
| SECONDARY SCLEROSING CHOLANGITIS         | J661800 |
| SCLEROSING CHOLANGITIS UNSPECIFIED       | J661900 |
| OTHER CHOLANGITIS                        | J661y00 |
| CHOLANGITIS NOS                          | J661z00 |
| OBSTRUCTION OF BILE DUCT                 | J662.00 |
| OCCCLUSION OF BILE DUCT                  | J662000 |
| STRICTURE OF BILE DUCT                   | J662100 |
| OBSTRUCTION OF BILE DUCT NOS             | J662z00 |
| PERFORATION OF BILE DUCT                 | J663.00 |
| FISTULA OF BILE DUCT                     | J664.00 |
| FISTULA OF BILE DUCT NOS                 | J664z00 |
| SPASM OF SPHINCTER OF ODDI               | J665.00 |

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| OTHER BILE DUCT DISORDERS                                   | J66y.00 |
| ADHESIONS OF BILE DUCT                                      | J66y000 |
| ATROPHY OF BILE DUCT  | J66y100 |
| CYST OF BILE DUCT   | J66y200 |
| HYPERTROPHY OF BILE DUCT                                    | J66y300 |
| STASIS OF BILE DUCT   | J66y400 |
| ULCER OF BILE DUCT  | J66y500 |
| OBSTRUCTIVE JAUNDICE NOS                                    | J66y600 |
| POST CHOLECYSTECTOMY BILE LEAKAGE                           | J66y700 |
| OTHER BILE DUCT DISORDER NOS                                | J66yz00 |
| BILE DUCT DISORDER NOS                                      | J66z.00 |
| [X]DISEASES OF THE LIVER                                    | Jyu7.00 |
| [X]TOXIC LIVER DISEASE WITH OTHER DISORDERS OF LIVER        | Jyu7000 |
| [X]OTHER AND UNSPECIFIED CIRRHOSIS OF LIVER                 | Jyu7100 |
| [X]OTHER SPECIFIED INFLAMMATORY LIVER DISEASES              | Jyu7200 |
| [X]OTHER SPECIFIED DISEASES OF LIVER                        | Jyu7300 |
| [X]LIVER DISORDERS IN INFECTIOUS AND PARASITIC DISEASES CE  | Jyu7400 |
| [X]LIVER DISORDERS IN OTHER DISEASES CLASSIFIED ELSEWHERE   | Jyu7500 |
| [X]TOXIC LIVER DISEASE, UNSPECIFIED                         | Jyu7600 |
| [X]GRANULOMATOUS HEPATITIS, NOT ELSEWHERE CLASSIFIED        | Jyu7700 |
| [X]DISORDERS OF THE GALLBLADDER, BILIARY TRACT AND PANCREAS | Jyu8.00 |
| [X]OTHER CHOLELITHIASIS                                     | Jyu8000 |
| [X]OTHER CHOLECYSTITIS                                      | Jyu8100 |
| [X]OTHER SPECIFIED DISEASES OF GALLBLADDER                  | Jyu8200 |
| [X]OTHER SPECIFIED DISEASES OF BILIARY TRACT                | Jyu8300 |
| [X]DISORDERS OF GALLBLADDER+BILIARY TRACT IN DISEASES CE    | Jyu8600 |
| NEPHROTIC SYNDROME IN AMYLOIDOSIS                           | K01x000 |
| FUND HOLDING OP OESOPHAGEAL VARICES                         | K298 FH |
| LIGATION OESOPHAGEAL VARICES                                | K2981   |
| INJECTION OESOPHAGEAL VARICES                               | K2982   |
| HEPATECTOMY   | K500    |
| EXCISION HEPATIC ABSCESS                                    | K5001   |
| REMOVAL HYDATID CYST  | K5001C  |
| TRANSPLANTATION LIVER                                       | K5005   |
| HEPATORRHAPHY   | K502    |
| LIVER OPERATION   | K509    |
| HEPATOSTOMY   | K5091   |
| HEPATOTOMY  | K5092   |
| EXPLORATION BILE DUCT                                       | K510 AA |
| CRUSHING CALCULUS BILIARY                                   | K511    |
| LITHOTOMY HEPATIC DUCT                                      | K511 AA |
| LITHOTOMY BILE DUCT   | K511 AB |
| REMOVAL CALCULUS BILE DUCT                                  | K511 AC |
| DRAINAGE BILE DUCT  | K512    |
| ROUX- Y ANASTOMOSIS BILE DUCT TO BOWEL                      | K513 AA |
| OPERATION ON THE BILE DUCTS                                 | K519    |

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| FUND HOLDING OP BILE DUCT                                    | K519 FH |
| INSERTION TUBE HEPATIC DUCT                                  | K519 H  |
| REMOVAL STONES GALLBLADDER                                   | K521 AB |
| CHOLECYSTECTOMY  | K522    |
| CHOLECYSTECTOMY PLANNED                                      | K522 X  |
| CHOLECYSTENTEROSTOMY   | K524 B  |
| GASTROCHOLECYSTOSTOMY  | K524 G  |
| CHOLECYSTOSTOMY  | K529    |
| ACUTE LIVER NECROSIS FOLLOWING ABORTIVE PREGNANCY            | L09y000 |
| HELLP - SYNDROME HAEMOLYSIS, ELEV LIVER ENZYME LOW PLATELETS | L12A.00 |
| LIVER DISORDER IN PREGNANCY                                  | L167.00 |
| LIVER DISORDER IN PREGNANCY UNSPECIFIED                      | L167000 |
| LIVER DISORDER IN PREGNANCY - DELIVERED                      | L167100 |
| LIVER DISORDER IN PREGNANCY - NOT DELIVERED                  | L167200 |
| LIVER DISORDER IN PREGNANCY NOS                              | L167z00 |
| VIRAL HEPATITIS COMP PREGNANCY, CHILDBIRTH & THE PUERPERIUM  | L176500 |
| LIVER FUNCTION TEST ABNORMAL                                 | L3260AB |
| LIVER BIOCHEMICAL DYSFUNCTION                                | L3262AB |
| LIVER ENZYMES ABNORMAL                                       | L3263AB |
| RAISED LIVER ENZYMES   | L3263H  |
| HEPATIC FUNCTION ABNORMAL                                    | L3264AB |
| PUERPERAL PERITONITIS - DELIVERED WITH POSTNATAL COMP        | L402100 |
| ANTIBODIES ANTI-MITOCHONDRIAL PRESENT                        | L6652DM |
| ANTIBODIES HEPATITIS B CORE PRESENT                          | L6652DV |
| ANTIBODIES HEPATITIS B E PRESENT                             | L6652DW |
| ANTIBODIES HEPATITIS E PRESENT                               | L6652DY |
| CHLOASMA HEPATICUM   | M290400 |
| AMYLOIDOSIS OF SKIN  | M2y9.00 |
| ARTHROPATHY IN AMYLOIDOSIS                                   | N030200 |
| MYOSITIS IN SARCOIDOSIS                                      | N233200 |
| [X]MYOSITIS IN SARCOIDOSIS CLASSIFIED ELSEWHERE              | Nyu8900 |
| ANOMALOUS PORTAL VEIN TERMINATION                            | P743.00 |
| PORTAL VEIN - HEPATIC ARTERY FISTULA                         | P744.00 |
| LIVER AND BILIARY SYSTEM ANOMALIES                           | PB6..00 |
| BILE DUCT ANOMALIES  | PB6..11 |
| BILIARY ANOMALIES  | PB6..12 |
| GALLBLADDER ANOMALIES  | PB6..13 |
| LIVER ANOMALIES  | PB6..14 |
| LIVER AND BILIARY SYSTEM ANOMALIES, UNSPECIFIED              | PB60.00 |
| LIVER ANOMALY, UNSPECIFIED                                   | PB60000 |
| GALLBLADDER ANOMALY, UNSPECIFIED                             | PB60100 |
| BILE DUCT ANOMALY, UNSPECIFIED                               | PB60200 |
| UNSPECIFIED LIVER AND BILIARY SYSTEM ANOMALY NOS             | PB60z00 |
| BILIARY ATRESIA  | PB61.00 |
| BILE DUCT ATRESIA  | PB61.11 |
| CONGENITAL ABSENCE OF BILE DUCT                              | PB61000 |

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| AGENESIS OF BILE DUCT                       | PB61011 |
| CONGENITAL HYPOPLASIA OF BILE DUCT          | PB61100 |
| CONGENITAL OBSTRUCTION OF BILE DUCT         | PB61200 |
| CONGENITAL STRICTURE OF BILE DUCT           | PB61300 |
| CONGENITAL STRICTURE OF COMMON BILE DUCT    | PB61311 |
| ATRESIA OF BILE DUCT                        | PB61400 |
| INTRAHEPATIC ATRESIA OF BILE DUCT           | PB61411 |
| EXTRAHEPATIC ATRESIA OF BILE DUCT           | PB61412 |
| CONGENITAL ABSENCE OF HEPATIC DUCTS         | PB61500 |
| AGENESIS OF HEPATIC DUCTS                   | PB61511 |
| ATRESIA OF HEPATIC DUCTS                    | PB61600 |
| BILIARY ATRESIA NOS                         | PB61z00 |
| CONGENITAL CYSTIC LIVER DISEASE             | PB62.00 |
| CONGENITAL HEPATIC CYST                     | PB62.11 |
| CONGENITAL POLYCYSTIC LIVER DISEASE         | PB62000 |
| FIBROCYSTIC LIVER DISEASE                   | PB62100 |
| CONGENITAL CYSTIC LIVER DISEASE NOS         | PB62z00 |
| CONGENITAL ABSENCE OF LIVER AND GALLBLADDER | PB63.00 |
| CONGENITAL ABSENCE OF GALLBLADDER           | PB63000 |
| AGENESIS OF GALLBLADDER                     | PB63011 |
| CONGENITAL ABSENCE OF LIVER LOBE            | PB63100 |
| CONGENITAL AGENESIS OF LIVER LOBE           | PB63111 |
| CONGENITAL ABSENCE OF LIVER,TOTAL           | PB63400 |
| CONGENITAL AGENESIS LIVER,TOTAL             | PB63411 |
| ABSENCE OF LIVER OR GALLBLADDER NOS         | PB63z00 |
| LIVER AND BILIARY DUPLICATION               | PB64.00 |
| DUPLICATION OF BILIARY DUCT                 | PB64000 |
| DUPLICATION OF CYSTIC DUCT                  | PB64100 |
| DUPLICATION OF GALLBLADDER                  | PB64200 |
| DUPLICATION OF LIVER                        | PB64300 |
| ACCESSORY LIVER                             | PB64311 |
| ACCESSORY HEPATIC DUCTS                     | PB64400 |
| LIVER OR BILIARY DUPLICATION NOS            | PB64z00 |
| OTHER LIVER AND BILIARY ANOMALIES           | PB6y.00 |
| CONGENITAL CHOLEDOCHAL CYST                 | PB6y000 |
| CONGENITAL HEPATOMEGALY                     | PB6y100 |
| CONGENITAL FLOATING GALLBLADDER             | PB6y200 |
| INTRAHEPATIC GALLBLADDER                    | PB6y400 |
| HYPOPLASIA OF GALLBLADDER                   | PB6y500 |
| ATROPHY OF LEFT LOBE OF LIVER               | PB6y600 |
| CONGENITAL DILATION OF BILE DUCT            | PB6y700 |
| CONGENITAL DIVERTICULUM OF BILE DUCT        | PB6y800 |
| LIVER HYPERPLASIA                           | PB6y900 |
| OTHER CONGENITAL ANOMALY OF LIVER           | PB6yw00 |
| LIVER HAMARTOMA                             | PB6yw11 |
| TRILOBULAR LIVER                            | PB6yw13 |

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| OTHER CONGENITAL ANOMALY OF GALLBLADDER                      | PB6yx00 |
| OTHER CONGENITAL ANOMALY OF HEPATIC OR BILE DUCTS            | PB6yy00 |
| CONGENITAL KINK OF CYSTIC DUCT                               | PB6yy11 |
| OTHER LIVER OR BILIARY SYSTEM ANOMALIES NOS                  | PB6yz00 |
| LIVER OR BILIARY SYSTEM ANOMALIES NOS                        | PB6z.00 |
| [X]OTHER CONGENITAL MALFORMATIONS OF GALLBLADDER             | Pyu5C00 |
| [X]OTHER CONGENITAL MALFORMATIONS OF BILE DUCTS              | Pyu5D00 |
| [X]OTHER CONGENITAL MALFORMATIONS OF LIVER                   | Pyu5E00 |
| LIVER SUBCAPSULAR HAEMATOMA DUE TO BIRTH TRAUMA              | Q20y100 |
| LIVER RUPTURE DUE TO BIRTH TRAUMA                            | Q20y400 |
| CONGENITAL VIRAL HEPATITIS                                   | Q409.00 |
| CONGENITAL HEPATITIS A INFECTION                             | Q409000 |
| CONGENITAL HEPATITIS B INFECTION                             | Q409100 |
| OTHER SPECIFIED CONGENITAL VIRAL HEPATITIS                   | Q409y00 |
| CONGENITAL VIRAL HEPATITIS NOS                               | Q409z00 |
| KERNICTERUS DUE TO ISOIMMUNISATION                           | Q424.00 |
| OTHER PERINATAL JAUNDICE                                     | Q43..00 |
| PERINATAL JAUNDICE FROM HEREDITARY HAEMOLYTIC ANAEMIAS       | Q430.00 |
| NEONATAL JAUNDICE + GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFIC. | Q430000 |
| PERINATAL JAUNDICE FROM HEREDITARY HAEMOLYTIC ANAEMIA NOS    | Q430z00 |
| PERINATAL JAUNDICE FROM OTHER EXCESSIVE HAEMOLYSIS           | Q431.00 |
| PERINATAL JAUNDICE FROM BRUISING                             | Q431000 |
| PERINATAL JAUNDICE FROM MATERNAL TRANSMISSION DRUG OR TOXIN  | Q431100 |
| PERINATAL JAUNDICE FROM INFECTION                            | Q431200 |
| PERINATAL JAUNDICE FROM POLYCYTHAEMIA                        | Q431300 |
| PERINATAL JAUNDICE FROM SWALLOWED MATERNAL BLOOD             | Q431400 |
| PERINATAL JAUNDICE FROM BLEEDING                             | Q431500 |
| PERINATAL JAUNDICE FROM OTHER SPECIFIED HAEMOLYSIS           | Q431y00 |
| PERINATAL JAUNDICE FROM HAEMOLYSIS NOS                       | Q431z00 |
| PRETERM DELIVERY ASSOCIATED JAUNDICE                         | Q432.00 |
| OTHER NEONATAL JAUNDICE - DELAYED CONJUGATION OTHER CAUSE    | Q433.00 |
| DELAYED CONJUGATION CAUSING NEONATAL JAUNDICE, UNSPECIFIED   | Q433000 |
| DELAYED CONJUGATION CAUSING NEONATAL JAUNDICE + DISEASE EC   | Q433100 |
| BREAST FEEDING INHIBITORS CAUSING NEONATAL JAUNDICE          | Q433200 |
| NEONATAL JAUNDICE WITH CRIGLER-NAJJAR SYNDROME               | Q433400 |
| NEONATAL JAUNDICE WITH DUBIN-JOHNSON SYNDROME                | Q433500 |
| NEONATAL JAUNDICE WITH GILBERT'S SYNDROME                    | Q433600 |
| NEONATAL JAUNDICE WITH CONGENITAL HYPOTHYROIDISM             | Q433700 |
| NEONATAL JAUNDICE WITH PORPHYRIA                             | Q433800 |
| NEONATAL JAUNDICE WITH ROTOR'S SYNDROME                      | Q433900 |
| NEONATAL JAUNDICE FROM BREAST MILK INHIBITOR                 | Q433A00 |
| DELAYED CONJUGATION CAUSING NEONATAL JAUNDICE OS             | Q433y00 |
| NEONATAL JAUNDICE - DEFICIENCY ENZYME FOR BILIRUBIN CONJUG.  | Q433y11 |
| DELAYED CONJUGATION CAUSING NEONATAL JAUNDICE NOS            | Q433z00 |
| PERINATAL JAUNDICE DUE TO HEPATOCELLULAR DAMAGE              | Q434.00 |
| PERINATAL HEPATITIS CAUSING JAUNDICE, UNSPECIFIED            | Q434000 |



|  |         |
|--|---------|
| GIANT CELL HEPATITIS CAUSING NEONATAL JAUNDICE               | Q434100 |
| PERINATAL JAUNDICE DUE TO HEPATOCELLULAR DAMAGE NOS          | Q434z00 |
| PERINATAL JAUNDICE DUE TO OTHER CAUSE                        | Q435.00 |
| PERINATAL JAUNDICE DUE TO CONGENITAL OBSTRUCTION BILE DUCT   | Q435000 |
| PERINATAL JAUNDICE DUE TO GALACTOSAEMIA                      | Q435100 |
| PERINATAL JAUNDICE DUE TO MUCOVISCIDOSIS                     | Q435200 |
| PERINATAL JAUNDICE DUE TO OTHER SPECIFIED CAUSE              | Q435z00 |
| FETAL AND NEONATAL JAUNDICE, UNSPECIFIED                     | Q436.00 |
| ICTERUS NEONATORUM, UNSPECIFIED                              | Q436000 |
| NEWBORN PHYSIOLOGICAL JAUNDICE NOS                           | Q436200 |
| UNSPECIFIED FETAL OR NEONATAL JAUNDICE NOS                   | Q436z00 |
| KERNICTERUS NOT DUE TO ISOIMMUNISATION                       | Q437.00 |
| KERNICTERUS OF NEWBORN NOS                                   | Q437z00 |
| PERINATAL JAUNDICE NOS                                       | Q43z.00 |
| BRONZE BABY  | Q47y100 |
| CONGENITAL HEPATIC FIBROSIS                                  | Q48yz11 |
| [X]OTHER SPECIFIED KERNICTERUS                               | Qyu5700 |
| [X]NEONATAL JAUNDICE DUE/OTHER SPECIFD EXCESSIVE HAEMOLYSIS  | Qyu5900 |
| [X]NEONATAL JAUNDICE FROM OTHER+UNSPCF HEPATOCELLULAR DAMAGE | Qyu5A00 |
| [X]NEONATAL JAUNDICE FROM OTHER SPECIFIED CAUSES             | Qyu5B00 |
| [D]JAUNDICE (NOT OF NEWBORN)                                 | R024.00 |
| [D]ICTERUS NOS   | R024100 |
| [D]JAUNDICE  | R024111 |
| [D]JAUNDICE (NOT OF NEWBORN) NOS                             | R024z00 |
| [D]LIVER ENLARGEMENT   | R091000 |
| [D]BILIARY TRACT X-RAY OR SCAN ABNORMALITY                   | R133.00 |
| [D]BILIARY X-RAY OR SCAN ABNORMALITY NOS                     | R133z00 |
| [D]ABNORMAL LIVER FUNCTION TEST                              | R148.00 |
| [D]ABNORMAL LIVER SCAN                                       | R148000 |
| [D]ABNORMAL LIVER FUNCTION TEST NOS                          | R148z00 |
| INJURY TO LIVER  | S74..00 |
| CLOSED INJURY OF LIVER                                       | S740.00 |
| LIVER INJURY WITHOUT OPEN WOUND INTO CAVITY, UNSPECIFIED     | S740000 |
| LIVER HAEMATOMA AND CONTUSION WITHOUT OPEN WOUND INTO CAVITY | S740100 |
| LIVER MINOR LACERATION WITHOUT OPEN WOUND INTO CAVITY        | S740200 |
| LIVER MODERATE LACERATION WITHOUT OPEN WOUND INTO CAVITY     | S740300 |
| LIVER MAJOR LACERATION WITHOUT OPEN WOUND INTO CAVITY        | S740400 |
| OTHER LIVER LACERATION WITHOUT OPEN WOUND INTO CAVITY        | S740y00 |
| LIVER INJURIES WITHOUT OPEN WOUND INTO CAVITY, NOS           | S740z00 |
| OPEN INJURY OF LIVER   | S741.00 |
| LIVER INJURY WITH OPEN WOUND INTO CAVITY, UNSPECIFIED        | S741000 |
| LIVER HAEMATOMA AND CONTUSION WITH OPEN WOUND INTO CAVITY    | S741100 |
| LIVER MINOR LACERATION WITH OPEN WOUND INTO CAVITY           | S741200 |
| LIVER MODERATE LACERATION WITH OPEN WOUND INTO CAVITY        | S741300 |
| LIVER MAJOR LACERATION WITH OPEN WOUND INTO CAVITY           | S741400 |
| OTHER LIVER INJURY WITH OPEN WOUND INTO CAVITY               | S741y00 |

|   |         |
|---|---------|
| LIVER INJURY WITH OPEN WOUND INTO CAVITY, NOS               | S741z00 |
| INJURY TO LIVER, NOS  | S74z.00 |
| RUPTURED LIVER NOS  | S74z.11 |
| BILE DUCT/GALLBLADDER INJURY WITHOUT OPEN WOUND INTO CAVITY | S780200 |
| BILE DUCT INJURY WITHOUT OPEN WOUND INTO CAVITY             | S780211 |
| GALLBLADDER INJURY WITHOUT OPEN WOUND INTO CAVITY           | S780212 |
| BILE DUCT/GALLBLADDER INJURY WITH OPEN WOUND INTO CAVITY    | S781200 |
| BILE DUCT INJURY WITH OPEN WOUND INTO CAVITY                | S781211 |
| GALLBLADDER INJURY WITH OPEN WOUND INTO CAVITY              | S781212 |
| HEPATIC VEIN INJURY   | SB21100 |
| HEPATIC ARTERY INJURY                                       | SB22200 |
| PORTAL AND SPLENIC VEIN INJURY                              | SB23.00 |
| PORTAL VEIN INJURY  | SB23200 |
| PORTAL AND SPLENIC VEIN INJURY NOS                          | SB23z00 |
| MECHANICAL COMPLICATION OF BILE DUCT PROSTHESIS             | SP05100 |
| LIVER TRANSPLANT FAILURE AND REJECTION                      | SP08600 |
| HEPATIC FAILURE AS A COMPLICATION OF CARE                   | SP14200 |
| LIVER FAILURE AS A COMPLICATION OF CARE                     | SP14211 |
| HEPATORENAL SYNDROME AS A COMPLICATION OF CARE              | SP14300 |
| LIVER TRANSPLANT WITH COMPLICATION, WITHOUT BLAME           | TB00200 |
| CONTACT SERUM HEPATITIS                                     | Y409 E  |
| CHOLECYSTOGRAM ABNORMAL                                     | Y500 BA |
| DIETARY ADVICE FOR HEPATIC DISORDER                         | ZC2CH00 |
| DIETARY ADVICE FOR LIVER DISEASE                            | ZC2CH11 |
| [V]VIRAL HEPATITIS CARRIER                                  | ZV02600 |
| [V]HEPATITIS AUSTRALIA ANTIGEN CARRIER                      | ZV02612 |
| [V]PERSONAL HISTORY OF MALIGNANT NEOPLASM OF LIVER          | ZV10015 |
| [V]LIVER TRANSPLANTED                                       | ZV42700 |
| [V]ASSESSMENT FOR LIVER TRANSPLANT                          | ZV7C000 |

## Appendix III-b Codes for death

| Description                           | medcode |
|---------------------------------------|---------|
| O/E - dead                            | 22J..00 |
| O/E - dead - condition fatal          | 22J..11 |
| Death                                 | 22J..12 |
| Died                                  | 22J..13 |
| Patient died                          | 22J..14 |
| O/E - dead - unexpected               | 22J1.00 |
| O/E - dead - expected                 | 22J2.00 |
| O/E - dead - unattended death         | 22J3.00 |
| O/E - dead - sudden death             | 22J4.00 |
| O/E - dead - cot death                | 22J5.00 |
| O/E - dead - suspicious death         | 22J6.00 |
| Postneonatal death                    | 22J7.00 |
| O/E - dead NOS                        | 22JZ.00 |
| O/E - respiratory death               | 236..12 |
| DELIVERY SUDDEN DEATH (MOTHER)        | 661 DH  |
| SUDDEN DEATH CHILDBIRTH CAUSE UNKNOWN | 661 DN  |
| DELIVERY DEATH DUE ANAESTHETIC        | 662 N   |
| SUDDEN DEATH PUERPERIUM CAUSE UNKNOWN | 6770AD  |
| NEONATAL DEATH                        | 7789ND  |
| DEATH IN UTERO                        | 7799A   |
| STILLBIRTH                            | 7799B   |
| SUDDEN DEATH INFANT SYNDROME          | 795 B   |
| COT DEATH                             | 795 C   |
| DROPPED DEAD                          | 795 DR  |
| SUDDEN DEATH NONVIOLENT               | 795 N   |
| FOUND DEAD                            | 7962    |
| UNKNOWN CAUSE DEATH                   | 7963    |
| Preoperative anaesthetic death        | 7L1M000 |
| Died in hospital                      | 8HG..00 |
| Death in hospital                     | 8HG..11 |
| Registration ghost - deceased         | 9134    |
| Registration ghost - dead             | 9134.11 |
| Registration ghost - died             | 9134.12 |
| FP22-death                            | 9234    |
| Death administration                  | 94...00 |
| Administration after pat. died        | 94...11 |
| Death certificate form Med A          | 941..00 |
| Death cert. Med A due                 | 9411    |
| Death cert. Med A signed              | 9412    |
| Med A given to family                 | 9413    |
| Med A not signed-coroner case         | 9414    |
| Death cert. Med A NOS                 | 941Z.00 |
| Medical cert. of still-birth          | 942..00 |

|                                    |         |
|------------------------------------|---------|
| Report for Coroner                 | 943..00 |
| Coroner's post-mortem report       | 944..00 |
| Hospital death discharge notif     | 945..00 |
| Death notif. from hospital         | 9451    |
| Await hosp death disch letter      | 9452    |
| Receiv hosp death disch letter     | 9453    |
| Ask for hosp death disch lett.     | 9454    |
| Hospital death disch. NOS          | 945Z.00 |
| Death notif.- non.hosp source      | 946..00 |
| Cause of death clarif. SD17/18     | 947..00 |
| SD17 - cause of death clarif       | 947..11 |
| SD18 - cause of death clarif       | 947..12 |
| SD17/18 received-death clarif.     | 9471    |
| SD17/18 completed                  | 9472    |
| SD17/18-no details, returned       | 9473    |
| SD17/18 cause of death NOS         | 947Z.00 |
| Cremation certification            | 948..00 |
| Stat B,C and F cremation certs     | 948..11 |
| Patient died - to record place     | 949..00 |
| Dead - place patient died          | 949..11 |
| Deceased - place patient died      | 949..12 |
| Died - place patient died          | 949..13 |
| Place of death                     | 949..14 |
| Patient died at home               | 9491    |
| Patient died in part 3 accom.      | 9492    |
| Patient died in nursing home       | 9493    |
| Patient died in resid.inst.NOS     | 9494    |
| Patient died in hospital           | 9495    |
| Patient died in street             | 9496    |
| Patient died in publ.place NOS     | 9497    |
| Dead on arrival at hospital        | 9498    |
| Found dead at accident site        | 9499    |
| Patient died in hospice            | 949A.00 |
| Patient died in place NOS          | 949Z.00 |
| Unexpected death-Coroner told      | 94A..00 |
| Referral to coroner                | 94A..11 |
| Cause of death                     | 94B..00 |
| Condition fatal-cause of death     | 94B..11 |
| Post mortem report                 | 94C..00 |
| Hospital notified of death         | 94D..00 |
| Death administration NOS           | 94Z..00 |
| DEATH ANAESTHETIC                  | 9681D   |
| Sudden cardiac death, so described | G575100 |
| Intrauterine death                 | L264.00 |
| Fetal death in utero               | L264.11 |
| Intrauterine death unspecified     | L264000 |

|   |         |
|---|---------|
| Intrauterine death - delivered                              | L264100 |
| Intrauterine death with antenatal problem                   | L264200 |
| Intrauterine death NOS                                      | L264z00 |
| Death obst cse occur more 42 day less than one yr aft deliv | L39A.00 |
| Death from sequelae of direct obstetric causes              | L39B.00 |
| Obstetric death of unspecified cause                        | L39X.00 |
| [X]Obstetric death of unspecified cause                     | Lyu7500 |
| Fetal death due to prelabour anoxia                         | Q210.00 |
| Fetal death due to labour anoxia                            | Q211.00 |
| [X] Stillbirth  | Q48D.00 |
| Early neonatal death  | Q48y600 |
| Late neonatal death   | Q48y700 |
| Infant death  | Q4z..11 |
| Neonatal death  | Q4z..12 |
| Newborn death   | Q4z..13 |
| Perinatal death   | Q4z..14 |
| Stillbirth NEC  | Q4z..15 |
| [D]Mortality, cause unsure                                  | R2...12 |
| [D]Sudden death, cause unknown                              | R21..00 |
| [D]Sudden infant death syndrome                             | R210.00 |
| [D]Cot death  | R210000 |
| [D]Crib death   | R210100 |
| [D]Nonspecific sudden infant death                          | R210200 |
| [D]Sudden infant death syndrome NOS                         | R210z00 |
| [D]Instantaneous death                                      | R211.00 |
| [D]Death less than 24 hours from onset of illness           | R212.00 |
| [D]Death, not instantaneous cause unknown                   | R212000 |
| [D]Died, with no sign of disease                            | R212100 |
| [D]Death less than 24 hours from onset of illness NOS       | R212z00 |
| [D]Unattended death   | R213.00 |
| [D]Found after death, unknown cause of death                | R213000 |
| [D]Found dead   | R213100 |
| [D]Unattended death NOS                                     | R213z00 |
| [D]Sudden death, cause unknown NOS                          | R21z.00 |
| [X]Ill-defined and unknown causes of mortality              | RyuC.00 |
| [X]Sudden infant death syndrome                             | RyuC000 |
| [X]Other sudden death, cause unknown                        | RyuC100 |
| [X]Other ill-defined and unspecified causes of death        | RyuC200 |
| Found dead on railway right-of-way unspecified              | T0y0.00 |
| Found dead on railway unspec - railway employee             | T0y0000 |
| Found dead on railway unspecified - passenger               | T0y0100 |
| Found dead on railway unspecified - pedestrian              | T0y0200 |
| Found dead on railway unspecified - cyclist                 | T0y0300 |
| Found dead on railway unspecified - other spec person       | T0y0y00 |
| Found dead on railway unspecified - unspecified person      | T0y0z00 |
| DEATH   | T140 F  |

|                               |         |
|-------------------------------|---------|
| DEATH AT HOME                 | T140 FH |
| DEATH IN HOSPITAL             | T140 FP |
| POST MORTEM RESULT            | T140 G  |
| DIED                          | T1400M  |
| SUDDEN INFANT DEATH           | T1400SI |
| PATIENT DIED                  | T400    |
| VIOLENT DEATH                 | T4001   |
| SUDDEN DEATH                  | T4002   |
| [V]Issue of death certificate | ZV68011 |

### Appendix III-c Codes for alcohol use

| Description                                       | medcode | Assigned alcohol status |
|---|---------|-------------------------|
| Teetotaller                                       | 1361    | Non-drinker             |
| Non drinker alcohol                               | 1361.11 | Non-drinker             |
| Non-drinker alcohol                               | 1361.12 | Non-drinker             |
| Current non drinker                               | 136M.00 | Non-drinker             |
| NON-DRINKER ALCOHOL                               | L5154NI | Non-drinker             |
| ALCOHOL NONE                                      | L5154NO | Non-drinker             |
| Alcohol consumption                               | 136..00 | Drinker                 |
| Drinks rarely                                     | 1362.11 | Drinker                 |
| Drinks occasionally                               | 1362.12 | Drinker                 |
| Stopped drinking alcohol                          | 1367    | Drinker                 |
| Spirit drinker                                    | 136F.00 | Drinker                 |
| Beer drinker                                      | 136G.00 | Drinker                 |
| Drinks beer and spirits                           | 136H.00 | Drinker                 |
| Drinks wine                                       | 136I.00 | Drinker                 |
| Social drinker                                    | 136J.00 | Drinker                 |
| Alcohol intake within recommended sensible limits | 136L.00 | Drinker                 |
| Light drinker                                     | 136N.00 | Drinker                 |
| Moderate drinker                                  | 136O.00 | Drinker                 |
| Heavy drinker                                     | 136P.00 | Drinker                 |
| Very heavy drinker                                | 136Q.00 | Drinker                 |
| Alcohol consumption NOS                           | 136Z.00 | Drinker                 |
| O/E - breath - alcohol smell                      | 2577    | Drinker                 |
| O/E - alcoholic breath                            | 2577.11 | Drinker                 |
| INTOXICATION ALCOHOL ACUTE                        | 3039AC  | Drinker                 |
| INTOXICATION ALCOHOL                              | 3039AD  | Drinker                 |
| PIXILLATED  | 3039AE  | Drinker                 |
| HUNG OVER (HANGOVER)                              | 3039HR  | Drinker                 |
| ALCOHOL BINGES                                    | 3039PB  | Drinker                 |
| Health ed. - alcohol                              | 6792    | Drinker                 |
| Pregnancy alcohol advice                          | 67A5.00 | Drinker                 |
| Patient advised about alcohol                     | 8CAM.00 | Drinker                 |
| Alcohol leaflet given                             | 8CE1.00 | Drinker                 |
| Referral to community alcohol team                | 8H7p.00 | Drinker                 |
| INGESTION ALCOHOL                                 | 9890A   | Drinker                 |
| Hangover (alcohol)                                | E250.12 | Drinker                 |
| Inebriety NOS                                     | E250.13 | Drinker                 |
| Intoxication - alcohol                            | E250.14 | Drinker                 |
| ADVISED TO STOP DRINKING                          | L2621ST | Drinker                 |
| ALCOHOL CONSUMPTION                               | L5150C  | Drinker                 |
| ALCOHOL BEER                                      | L5154B  | Drinker                 |
| ALCOHOL MIXED WINE BEER & SPIRITS                 | L5154M  | Drinker                 |

|  |         |           |
|--|---------|-----------|
| ALCOHOL SPIRITS                                  | L5154S  | Drinker   |
| ALCOHOL WINE                                     | L5154W  | Drinker   |
| [D]Alcohol blood level excessive                 | R103.00 | Drinker   |
| HEAVY DRINKER                                    | T514    | Drinker   |
| ALCOHOL RARELY                                   | T5151   | Drinker   |
| ALCOHOL MODERATE                                 | T5152   | Drinker   |
| ALCOHOL OCCASIONALLY                             | T5153   | Drinker   |
| SOCIAL DRINKER ALCOHOL                           | T5154   | Drinker   |
| STOPPED DRINKING ALCOHOL                         | T5156   | Drinker   |
| Planned reduction of alcohol consumption         | Z191200 | Drinker   |
| Self-monitoring of alcohol intake                | Z191400 | Drinker   |
| Removal of alcohol                               | Z9KF400 | Drinker   |
| Removing alcohol from home                       | Z9KF600 | Drinker   |
| Advice to change alcoholic drink intake          | ZC22200 | Drinker   |
| Advice to change alcohol intake                  | ZC2H.00 | Drinker   |
| Advice on alcohol consumption                    | ZG23100 | Drinker   |
| [V] Alcohol use                                  | ZV4KC00 | Drinker   |
| Ex-trivial drinker (<1u/day)                     | 136A.00 | Drinker   |
| Ex-light drinker - (1-2u/day)                    | 136B.00 | Drinker   |
| Ex-moderate drinker - (3-6u/d)                   | 136C.00 | Drinker   |
| Ex-heavy drinker - (7-9u/day)                    | 136D.00 | Drinker   |
| Ex-very heavy drinker-(>9u/d)                    | 136E.00 | Drinker   |
| Trivial drinker - <1u/day                        | 1362    | Drinker   |
| Light drinker - 1-2u/day                         | 1363    | Drinker   |
| Moderate drinker - 3-6u/day                      | 1364    | Drinker   |
| Heavy drinker - 7-9u/day                         | 1365    | Drinker   |
| Very heavy drinker - >9u/day                     | 1366    | Drinker   |
| Alcohol intake above recommended sensible limits | 136K.00 | Alcoholic |
| Alcoholics anonymous                             | 13Y8.00 | Alcoholic |
| H/O: alcoholism                                  | 1462    | Alcoholic |
| ALCOHOL DRINKING EXCESSIVE                       | 3031    | Alcoholic |
| ALCOHOL ADDICTION                                | 3032    | Alcoholic |
| SYMPTOMS ALCOHOLIC WITHDRAWAL                    | 3032B   | Alcoholic |
| ALCOHOL DEPENDENCE                               | 3032D   | Alcoholic |
| ALCOHOL ABUSE INTOXICATION CHRONIC               | 3032NA  | Alcoholic |
| INTOXICATION ALCOHOL CHRONIC                     | 3032NB  | Alcoholic |
| ABUSE ALCOHOL                                    | 3032NC  | Alcoholic |
| WINE ADDICTION                                   | 3032WN  | Alcoholic |
| ALCOHOLISM                                       | 3039A   | Alcoholic |
| ABSINTHISM                                       | 3039AB  | Alcoholic |
| PROBLEMS ALCOHOL RELATED                         | 3039AP  | Alcoholic |
| FALLS ALCOHOLIC                                  | 3039FL  | Alcoholic |
| ALCOHOL ABUSE                                    | 3039PA  | Alcoholic |
| PROBLEM DRINKING STRAIN ON SPOUSE                | 3039PP  | Alcoholic |
| PROBLEM DRINKING (ALCOHOL)                       | 3039PR  | Alcoholic |
| CIRRHOSIS ALCOHOLIC                              | 5710CA  | Alcoholic |



|   |         |                 |
|---|---------|-----------------|
| SICKNESS AFTER ALCOHOL ABUSE                          | 7841LA  | Alcoholic       |
| Alcohol detoxification                                | 8BA8.00 | Alcoholic       |
| Admitted to alcohol detoxification centre             | 8H35.00 | Alcoholic       |
| Under care of community alcohol team                  | 9NN2.00 | Alcoholic       |
| Pathological alcohol intoxication                     | E014.00 | Alcoholic       |
| Drunkenness - pathological                            | E014.11 | Alcoholic       |
| Alcohol dependence syndrome                           | E23..00 | Alcoholic       |
| Alcoholism  | E23..11 | Alcoholic       |
| Alcohol problem drinking                              | E23..12 | Alcoholic       |
| Alcohol dependence with acute alcoholic intoxication  | E230.11 | Alcoholic       |
| Continuous acute alcoholic intoxication in alcoholism | E230100 | Alcoholic       |
| Episodic acute alcoholic intoxication in alcoholism   | E230200 | Alcoholic       |
| Chronic alcoholism                                    | E231.00 | Alcoholic       |
| Dipsomania  | E231.11 | Alcoholic       |
| Unspecified chronic alcoholism                        | E231000 | Alcoholic       |
| Continuous chronic alcoholism                         | E231100 | Alcoholic       |
| Episodic chronic alcoholism                           | E231200 | Alcoholic       |
| Chronic alcoholism in remission                       | E231300 | Alcoholic       |
| Chronic alcoholism NOS                                | E231z00 | Alcoholic       |
| Alcohol dependence syndrome NOS                       | E23z.00 | Alcoholic       |
| Nondependent alcohol abuse                            | E250.00 | Alcoholic       |
| Drunkenness NOS                                       | E250.11 | Alcoholic       |
| Nondependent alcohol abuse, unspecified               | E250000 | Alcoholic       |
| Nondependent alcohol abuse, continuous                | E250100 | Alcoholic       |
| Nondependent alcohol abuse, episodic                  | E250200 | Alcoholic       |
| Nondependent alcohol abuse in remission               | E250300 | Alcoholic       |
| Nondependent alcohol abuse NOS                        | E250z00 | Alcoholic       |
| [X]Acute alcoholic drunkenness                        | Eu10011 | Alcoholic       |
| [X]Alcohol addiction                                  | Eu10211 | Alcoholic       |
| [X]Chronic alcoholism                                 | Eu10212 | Alcoholic       |
| [X]Dipsomania   | Eu10213 | Alcoholic       |
| Alcoholic cirrhosis of the liver                      | J612.00 | Alcoholic       |
| HIGH RISK ALCOHOLISM                                  | T185    | Alcoholic       |
| ALCOHOLICS ANONYMOUS ATTENDED                         | T3810   | Alcoholic       |
| DETOXIFICATION ALCOHOL                                | T3821   | Alcoholic       |
| Alcohol detoxification                                | Z191.00 | Alcoholic       |
| Drying out  | Z191111 | Alcoholic       |
| Alcohol reduction programme                           | Z191211 | Alcoholic       |
| Alcoholism counselling                                | Z4B1.00 | Alcoholic       |
| [V]Personal history of alcoholism                     | ZV11300 | Alcoholic       |
| [V]Problems related to lifestyle alcohol use          | ZV11311 | Alcoholic       |
| [V]Alcohol rehabilitation                             | ZV57A00 | Alcoholic       |
| [V]Alcohol abuse counselling and surveillance         | ZV6D600 | Alcoholic       |
| SHAKES ALCOHOLIC                                      | 2910    | Problem drinker |
| KORSAKOV'S PSYCHOSIS ALCOHOLIC                        | 2911    | Problem drinker |

|  |         |                 |
|--|---------|-----------------|
| HALLUCINATIONS ALCOHOLIC                                     | 2912    | Problem drinker |
| ALCOHOLIC PSYCHOSIS PARANOID                                 | 2913    | Problem drinker |
| DEMENTIA ALCOHOLIC   | 2919    | Problem drinker |
| PSYCHOSIS ALCOHOLIC  | 2919P   | Problem drinker |
| ALCOHOLIC CARDIOPATHY  | 3032C   | Problem drinker |
| EPILEPSY ALCOHOLIC   | 3032EP  | Problem drinker |
| ALCOHOLIC GASTRITIS  | 3032G   | Problem drinker |
| ALCOHOLIC GASTRITIS CHRONIC                                  | 3032GC  | Problem drinker |
| NEUROPATHY ALCOHOLIC   | 3032R   | Problem drinker |
| ALCOHOL RELATED DISTURBANCES                                 | 3039AR  | Problem drinker |
| ALCOHOLIC GASTRITIS ACUTE                                    | 3039G   | Problem drinker |
| POLYNEURITIS ALCOHOLIC                                       | 3039PN  | Problem drinker |
| HEPATITIS ALCOHOLIC  | 5710HA  | Problem drinker |
| MICRONODULAR CIRRHOSIS                                       | 5710MC  | Problem drinker |
| Alcohol-induced pseudo-Cushing's syndrome                    | C150500 | Problem drinker |
| Alcoholic psychoses  | E01..00 | Problem drinker |
| Alcohol withdrawal delirium                                  | E010.00 | Problem drinker |
| Alcohol amnestic syndrome                                    | E011.00 | Problem drinker |
| Korsakov's alcoholic psychosis                               | E011000 | Problem drinker |
| Korsakov's alcoholic psychosis with peripheral neuritis      | E011100 | Problem drinker |
| Alcohol amnestic syndrome NOS                                | E011z00 | Problem drinker |
| Other alcoholic dementia                                     | E012.00 | Problem drinker |
| Alcoholic dementia NOS                                       | E012.11 | Problem drinker |
| Chronic alcoholic brain syndrome                             | E012000 | Problem drinker |
| Alcohol withdrawal hallucinosis                              | E013.00 | Problem drinker |
| Alcoholic paranoia   | E015.00 | Problem drinker |
| Other alcoholic psychosis                                    | E01y.00 | Problem drinker |
| Alcohol withdrawal syndrome                                  | E01y000 | Problem drinker |
| Other alcoholic psychosis NOS                                | E01yz00 | Problem drinker |
| Alcoholic psychosis NOS                                      | E01z.00 | Problem drinker |
| Acute alcoholic intoxication in alcoholism                   | E230.00 | Problem drinker |
| Acute alcoholic intoxication, unspecified, in alcoholism     | E230000 | Problem drinker |
| Acute alcoholic intoxication in remission, in alcoholism     | E230300 | Problem drinker |
| Acute alcoholic intoxication in alcoholism NOS               | E230z00 | Problem drinker |
| [X]Mental and behavioural disorders due to use of alcohol    | Eu10.00 | Problem drinker |
| [X]Mental & behav dis due to use alcohol: acute intoxication | Eu10000 | Problem drinker |
| [X]Mental and behav dis due to use of alcohol: harmful use   | Eu10100 | Problem drinker |
| [X]Mental and behav dis due to use alcohol: dependence syndr | Eu10200 | Problem drinker |
| [X]Mental and behav dis due to use alcohol: withdrawal state | Eu10300 | Problem drinker |
| [X]Men & behav dis due alcohol: withdrawl state              | Eu10400 | Problem drinker |

|   |         |                 |
|---|---------|-----------------|
| with delirium   |         |                 |
| [X]Delirium tremens, alcohol induced                            | Eu10411 | Problem drinker |
| [X]Mental & behav dis due to use alcohol:<br>psychotic disorder | Eu10500 | Problem drinker |
| [X]Alcoholic hallucinosis                                       | Eu10511 | Problem drinker |
| [X]Alcoholic jealousy   | Eu10512 | Problem drinker |
| [X]Alcoholic paranoia   | Eu10513 | Problem drinker |
| [X]Alcoholic psychosis NOS                                      | Eu10514 | Problem drinker |
| [X]Mental and behav dis due to use alcohol:<br>amnesic syndrome | Eu10600 | Problem drinker |
| [X]Korsakov's psychosis, alcohol induced                        | Eu10611 | Problem drinker |
| [X]Men & behav dis due alcoh: resid & late-onset<br>psychot dis | Eu10700 | Problem drinker |
| [X]Alcoholic dementia NOS                                       | Eu10711 | Problem drinker |
| [X]Chronic alcoholic brain syndrome                             | Eu10712 | Problem drinker |
| [X]Men & behav dis due to use alcohol: oth men &<br>behav dis   | Eu10y00 | Problem drinker |
| [X]Ment & behav dis due use alcohol: unsp ment &<br>behav dis   | Eu10z00 | Problem drinker |
| Cerebral degeneration due to alcoholism                         | F11x000 | Problem drinker |
| Alcoholic encephalopathy  | F11x011 | Problem drinker |
| Cerebellar ataxia due to alcoholism                             | F144000 | Problem drinker |
| Alcoholic polyneuropathy  | F375.00 | Problem drinker |
| Alcoholic myopathy  | F394100 | Problem drinker |
| Alcoholic cardiomyopathy  | G555.00 | Problem drinker |
| Alcoholic gastritis   | J153.00 | Problem drinker |
| Alcoholic fatty liver   | J610.00 | Problem drinker |
| Acute alcoholic hepatitis                                       | J611.00 | Problem drinker |
| Alcoholic cirrhosis of liver                                    | J612.00 | Problem drinker |
| Alcoholic fibrosis and sclerosis of liver                       | J612000 | Problem drinker |
| Alcoholic liver damage unspecified                              | J613.00 | Problem drinker |
| Alcoholic hepatic failure                                       | J613000 | Problem drinker |
| Alcoholic hepatitis   | J617.00 | Problem drinker |
| Chronic alcoholic hepatitis                                     | J617000 | Problem drinker |
| Alcohol-induced chronic pancreatitis                            | J671000 | Problem drinker |
| Alcohol causing toxic effect                                    | SM0..00 | Problem drinker |
| Alcohol causing toxic effect NOS                                | SM0z.00 | Problem drinker |
| Alcohol withdrawal regime                                       | Z191100 | Problem drinker |

## Appendix III-d Codes for viral hepatitis

| description   | medcode |
|---|---------|
| HERPES VIRUS HEPATITIS                                      | 054 H   |
| VIRUS HEPATITIS TYPE A                                      | 070 A   |
| HEPATITIS C   | 070 AC  |
| HEPATITIS TYPE C  | 070 AD  |
| VIRUS HEPATITIS TYPE B                                      | 070 B   |
| HEPATITIS TYPE NON- A NON- B                                | 070 N   |
| VIRUS HEPATITIS   | 070 RL  |
| HEPATITIS COXSACKIE VIRUS                                   | 0749H   |
| HEPATITIS ADENOVIRUS  | 0788H   |
| HEPATITIS CYTOMEGALIC INCLUSION VIRUS                       | 0795H   |
| Hepatitis C status  | 2J1..00 |
| Hepatitis A status  | 2J2..00 |
| Hepatitis A - current infection                             | 2J23.00 |
| Hepatitis B antibody present                                | 43B2.11 |
| Hepatitis B surface antig +ve                               | 43B4.00 |
| Hepatitis e antigen present                                 | 43B5.00 |
| Hepatitis A test positive                                   | 43M2.00 |
| Hepatitis C antibody test positive                          | 43X3.00 |
| Viral hepatitis carrier                                     | 65Q7.00 |
| Viral hepatitis   | A70..00 |
| Viral hepatitis A with coma                                 | A700.00 |
| Viral (infectious) hepatitis A                              | A701.00 |
| Viral hepatitis B with coma                                 | A702.00 |
| Viral (serum) hepatitis B                                   | A703.00 |
| Other specified viral hepatitis with coma                   | A704.00 |
| Viral hepatitis C with coma                                 | A704000 |
| Other specified viral hepatitis with hepatic coma NOS       | A704z00 |
| Other specified viral hepatitis without coma                | A705.00 |
| Viral hepatitis C without mention of hepatic coma           | A705000 |
| Acute delta-(super)infection of hepatitis B carrier         | A705100 |
| Acute hepatitis E   | A705200 |
| Hepatitis non A non B                                       | A705400 |
| Other specified viral hepatitis without mention of coma NOS | A705z00 |
| Unspecified viral hepatitis with coma                       | A706.00 |
| Chronic viral hepatitis                                     | A707.00 |
| Chronic viral hepatitis B with delta-agent                  | A707000 |
| Chronic viral hepatitis B without delta-agent               | A707100 |
| Chronic viral hepatitis C                                   | A707200 |
| Chronic viral hepatitis, unspecified                        | A707X00 |
| Unspecified viral hepatitis                                 | A70z.00 |
| Hepatitis C   | A70z000 |
| Cytomegaloviral hepatitis                                   | A785200 |
| [X]Viral hepatitis  | AyuB.00 |

|   |         |
|---|---------|
| [X]Other specified acute viral hepatitis                    | AyuB000 |
| [X]Other chronic viral hepatitis                            | AyuB100 |
| [X]Chronic viral hepatitis, unspecified                     | AyuB200 |
| [X]Unspecified viral hepatitis with coma                    | AyuB300 |
| [X]Unspecified viral hepatitis without coma                 | AyuB400 |
| Hepatitis in viral diseases EC                              | J631.00 |
| Hepatitis in coxsackie virus                                | J631000 |
| Hepatitis in cytomegalic inclusion virus                    | J631100 |
| Hepatitis in other viral disease                            | J631500 |
| Hepatitis in viral diseases EC NOS                          | J631z00 |
| Viral hepatitis comp pregnancy, childbirth & the puerperium | L176500 |
| ANTIBODIES HEPATITIS B CORE PRESENT                         | L6652DV |
| ANTIBODIES HEPATITIS B E PRESENT                            | L6652DW |
| ANTIBODIES HEPATITIS SURFACE PRESENT                        | L6652DX |
| ANTIBODIES HEPATITIS E PRESENT                              | L6652DY |
| Congenital viral hepatitis                                  | Q409.00 |
| Congenital hepatitis A infection                            | Q409000 |
| Congenital hepatitis B infection                            | Q409100 |
| Other specified congenital viral hepatitis                  | Q409y00 |
| Congenital viral hepatitis NOS                              | Q409z00 |
| [V]Hepatitis B carrier                                      | ZV02B00 |

### **Appendix III-e Codes for autoimmune liver disease**

| Description                         | medcode |
|-------------------------------------|---------|
| PRIMARY BILIARY CIRRHOSIS (LIVER)   | 5719PB  |
| SCLEROSING CHOLANGITIS PRIMARY      | 575 AL  |
| Autoimmune chronic active hepatitis | J614111 |
| Primary biliary cirrhosis           | J616000 |
| Primary sclerosing cholangitis      | J661700 |

### **Appendix III-f Codes for metabolic liver disease**

| Description                                      | medcode |
|--|---------|
| HAEMOCHROMATOSIS                                 | 2732    |
| DIABETES BRONZE (HAEMOCHROMATOSIS)               | 2732B   |
| HAEMOCHROMATOSIS IDIOPATHIC                      | 2732HI  |
| WILSON'S DISEASE                                 | 2733W   |
| ANTITRYPSIN DEFICIENCY                           | 2790AD  |
| Alpha-1-antitrypsin phenotype                    | 4L00.00 |
| Haemochromatosis                                 | C350000 |
| Bronzed diabetes                                 | C350011 |
| Von Recklinghausen - Applebaum disease           | C350013 |
| Hepatolenticular degeneration (Wilson's disease) | C351000 |
| Wilson's disease                                 | C351011 |
| Alpha-1-antitrypsin hepatitis                    | C376100 |
| Alpha-1-antitrypsin deficiency                   | C376200 |

### Appendix III-g Codes for encephalopathy

| description                | medcode |
|----------------------------|---------|
| WERNICKE'S ENCEPHALOPATHY  | 2639WN  |
| ENCEPHALOPATHY             | 7817    |
| Wernicke's encephalopathy  | C251.11 |
| Wernicke's encephalopathy  | C253.00 |
| Alcoholic encephalopathy   | F11x011 |
| Unspecified encephalopathy | F283.00 |
| Hepatic coma               | J622.00 |
| Encephalopathy - hepatic   | J622.11 |
| Hepatorenal syndrome       | J624.00 |
| [X] Hepatic failure        | J625.00 |
| [X] Liver failure          | J625.11 |
| Liver failure NOS          | J62y.12 |
| Hepatic failure            | J62y.13 |
| Bilirubin encephalopathy   | Q437000 |



## Appendix III-h Codes for smoking

| Description  | medcode | Assigned smoking status |
|--|---------|-------------------------|
| Never smoked tobacco   | 1371    | Non-smoker              |
| Non-smoker   | 1371.11 | Non-smoker              |
| Current non-smoker   | 137L.00 | Non-smoker              |
| SMOKER NON   | T5093   | Non-smoker              |
| SMOKED NEVER   | T5093N  | Non-smoker              |
| Ex-trivial smoker (<1/day)                                   | 1377    | Ex-Smoker               |
| Ex-light smoker (1-9/day)                                    | 1378    | Ex-Smoker               |
| Ex-moderate smoker (10-19/day)                               | 1379    | Ex-Smoker               |
| Ex-heavy smoker (20-39/day)                                  | 137A.00 | Ex-Smoker               |
| Ex-very heavy smoker (40+/day)                               | 137B.00 | Ex-Smoker               |
| Ex-smoker - amount unknown                                   | 137F.00 | Ex-Smoker               |
| Stopped smoking  | 137K.00 | Ex-Smoker               |
| Ex pipe smoker   | 137N.00 | Ex-Smoker               |
| Ex cigar smoker  | 137O.00 | Ex-Smoker               |
| Ex smoker  | 137S.00 | Ex-Smoker               |
| Date ceased smoking  | 137T.00 | Ex-Smoker               |
| Smoking free weeks   | 13p4.00 | Ex-Smoker               |
| [X]Mental and behav dis due to use tobacco: withdrawal state | Eu17300 | Ex-Smoker               |
| [X]Men & behav dis due tobacco: withdrawl state wth delirium | Eu17400 | Ex-Smoker               |
| STOPPED SMOKING  | T5091   | Ex-Smoker               |
| FORMER SMOKER  | T5091ES | Ex-Smoker               |
| EX HEAVY SMOKER  | T5091HS | Ex-Smoker               |
| Smoker - amount smoked                                       | 137..11 | Smoker                  |
| Trivial smoker - < 1 cig/day                                 | 1372    | Smoker                  |
| Occasional smoker  | 1372.11 | Smoker                  |
| Light smoker - 1-9 cigs/day                                  | 1373    | Smoker                  |
| Moderate smoker - 10-19 cigs/d                               | 1374    | Smoker                  |
| Heavy smoker - 20-39 cigs/day                                | 1375    | Smoker                  |
| Very heavy smoker - 40+cigs/d                                | 1376    | Smoker                  |
| Keeps trying to stop smoking                                 | 137C.00 | Smoker                  |
| Trying to give up smoking                                    | 137G.00 | Smoker                  |
| Pipe smoker  | 137H.00 | Smoker                  |
| Cigar smoker   | 137J.00 | Smoker                  |
| Rolls own cigarettes   | 137M.00 | Smoker                  |
| Cigarette smoker   | 137P.00 | Smoker                  |
| Smoker   | 137P.11 | Smoker                  |
| Smoking started  | 137Q.00 | Smoker                  |
| Smoking restarted  | 137Q.11 | Smoker                  |
| Current smoker   | 137R.00 | Smoker                  |
| Smoking reduced  | 137V.00 | Smoker                  |

|  |         |        |
|--|---------|--------|
| Cigarette consumption  | 137X.00 | Smoker |
| Cigar consumption  | 137Y.00 | Smoker |
| Tobacco consumption NOS                                      | 137Z.00 | Smoker |
| Pipe tobacco consumption                                     | 137a.00 | Smoker |
| Ready to stop smoking  | 137b.00 | Smoker |
| Thinking about stopping smoking                              | 137c.00 | Smoker |
| Not interested in stopping smoking                           | 137d.00 | Smoker |
| Smoking restarted  | 137e.00 | Smoker |
| Reason for restarting smoking                                | 137f.00 | Smoker |
| Negotiated date for cessation of smoking                     | 13p0.00 | Smoker |
| Smoking cessation programme start date                       | 13p5.00 | Smoker |
| Health ed. - smoking   | 6791    | Smoker |
| Smoking cessation advice                                     | 8CAL.00 | Smoker |
| Referral to smoking cessation advisor                        | 8H7i.00 | Smoker |
| Seen by smoking cessation advisor                            | 9N2k.00 | Smoker |
| Attends stop smoking monitor.                                | 9O01.00 | Smoker |
| Refuses stop smoking monitor                                 | 9O02.00 | Smoker |
| Stop smoking monitor verb.inv.                               | 9O07.00 | Smoker |
| Stop smoking monitor phone inv                               | 9O08.00 | Smoker |
| Tobacco dependence   | E251.00 | Smoker |
| Tobacco dependence, unspecified                              | E251000 | Smoker |
| Tobacco dependence, continuous                               | E251100 | Smoker |
| Tobacco dependence, episodic                                 | E251200 | Smoker |
| Tobacco dependence in remission                              | E251300 | Smoker |
| Tobacco dependence NOS                                       | E251z00 | Smoker |
| [X]Mental and behavioural disorder due to use of tobacco     | Eu17.00 | Smoker |
| [X]Mental and behav dis due to use of tobacco: harmful use   | Eu17100 | Smoker |
| [X]Mental and behav dis due to use tobacco: dependence syndr | Eu17200 | Smoker |
| [X]Mental & behav dis due to use tobacco: psychotic disorder | Eu17500 | Smoker |
| [X]Mental and behav dis due to use tobacco: amnesic syndrome | Eu17600 | Smoker |
| [X]Men & beh dis due tobacco: resid & late-onset psychot dis | Eu17700 | Smoker |
| [X]Men & behav dis due to use tobacco: oth men & behav dis   | Eu17y00 | Smoker |
| [X]Ment & behav dis due use tobacco: unsp ment & behav dis   | Eu17z00 | Smoker |
| SMOKING STARTED  | L5091S  | Smoker |
| Toxic effect of tobacco and nicotine                         | SMC..00 | Smoker |
| SMOKER   | T509    | Smoker |
| SMOKING RESTARTED  | T509 SR | Smoker |
| SMOKER OWN ROLLED  | T5090OR | Smoker |
| SMOKER CIGARETTES  | T5090XC | Smoker |
| SMOKING ADVISED TO STOP                                      | T5092   | Smoker |

|  |         |         |
|--|---------|---------|
| SMOKING WISHES TO STOP                 | T5092S  | Smoker  |
| SMOKING WANTS TO STOP                  | T5092SA | Smoker  |
| EXCESSIVE SMOKING                      | T510    | Smoker  |
| HEAVY SMOKER (20-PLUS PER DAY)         | T510 HS | Smoker  |
| SMOKING EXCESSIVE                      | T510 SE | Smoker  |
| SMOKER HEAVY (Ex-Smoker0-PLUS PER DAY) | T510 SH | Smoker  |
| SMOKER MODERATE (LESS THAN 20 PER DAY) | T511    | Smoker  |
| SMOKER (20 PER DAY)                    | T5112   | Smoker  |
| SMOKER (15 PER DAY)                    | T5113   | Smoker  |
| SMOKER (10 PER DAY)                    | T5114   | Smoker  |
| SMOKER (LESS THAN 10 PER DAY)          | T5115   | Smoker  |
| SMOKER MILD (5 OR LESS PER DAY)        | T5115M  | Smoker  |
| SMOKER(OCCASIONAL)                     | T5116   | Smoker  |
| SMOKER (30 PER DAY)                    | T5117   | Smoker  |
| SMOKER PIPE                            | T512    | Smoker  |
| SMOKER CIGARS                          | T513    | Smoker  |
| [V]Tobacco use                         | ZV4K000 | Smoker  |
| [V]Tobacco abuse counselling           | ZV6D800 | Smoker  |
| Tobacco consumption                    | 137..00 | Unknown |
| Tobacco consumption unknown            | 137E.00 | Unknown |

## **Appendix III-j Codes for comorbidity**

Table j-i Codes for myocardial infarct

Table j-ii Codes for Congestive heart failure

Table j-iii Codes for Peripheral vascular disease

Table j-iv Codes for Cerebrovascular disease

Table j-v Codes for Dementia

Table j-vi Codes for Chronic pulmonary disease

Table j-vii Codes for Connective tissue disease

Table j-viii Codes for Ulcer disease

Table j-ix Codes for Diabetes (not specifying end organ damage)

Table j-x Codes for Hemiplegia

Table j-xi Codes for Moderate or severe renal disease

Table j-xii Codes for Diabetes with end organ damage

Table j-xiii Codes for Any tumour

Table j-xiv Codes for Leukaemia

Table j-xv Codes for Lymphoma

Table j-xvi Codes for Metastatic solid tumour

Table j-xvii Codes for AIDS

Table j-i Codes for myocardial infarct

| description  | medcode |
|--|---------|
| H/O: myocardial infarct <60                          | 14A3.00 |
| H/O: myocardial infarct >60                          | 14A4.00 |
| H/O: angina pectoris                                 | 14A5.00 |
| H/O: heart disease NOS                               | 14AA.00 |
| H/O: Myocardial infarction in last year              | 14AH.00 |
| H/O: Angina in last year                             | 14AJ.00 |
| H/O: atrial fibrillation                             | 14AN.00 |
| H/O: CVS disease NOS                                 | 14AZ.00 |
| Special CVS test abnormal                            | 3154    |
| ECG: myocardial ischaemia                            | 322..00 |
| ECG:shows myocardial ischaemia                       | 3222    |
| ECG: myocardial ischaemia NOS                        | 322Z.00 |
| ECG: myocardial infarction                           | 323..00 |
| ECG: old myocardial infarction                       | 3232    |
| ECG: antero-septal infarct.                          | 3233    |
| ECG:posterior/inferior infarct                       | 3234    |
| ECG: subendocardial infarct                          | 3235    |
| ECG: lateral infarction                              | 3236    |
| ECG: myocardial infarct NOS                          | 323Z.00 |
| ECG: heart block                                     | 329..00 |
| Acute myocardial infarction                          | G30..00 |
| Attack - heart                                       | G30..11 |
| Coronary thrombosis                                  | G30..12 |
| Cardiac rupture following myocardial infarction (MI) | G30..13 |
| Heart attack   | G30..14 |
| MI - acute myocardial infarction                     | G30..15 |
| Thrombosis - coronary                                | G30..16 |
| Silent myocardial infarction                         | G30..17 |
| Acute anterolateral infarction                       | G300.00 |
| Other specified anterior myocardial infarction       | G301.00 |
| Acute anteroapical infarction                        | G301000 |
| Acute anteroseptal infarction                        | G301100 |
| Anterior myocardial infarction NOS                   | G301z00 |
| Acute inferolateral infarction                       | G302.00 |
| Acute inferoposterior infarction                     | G303.00 |
| Posterior myocardial infarction NOS                  | G304.00 |
| Lateral myocardial infarction NOS                    | G305.00 |
| True posterior myocardial infarction                 | G306.00 |
| Acute subendocardial infarction                      | G307.00 |
| Acute non-Q wave infarction                          | G307000 |
| Acute non-ST segment elevation myocardial infarction | G307100 |
| Inferior myocardial infarction NOS                   | G308.00 |
| Acute Q-wave infarct                                 | G309.00 |

|  |         |
|--|---------|
| Mural thrombosis   | G30A.00 |
| Acute posterolateral myocardial infarction                 | G30B.00 |
| Acute transmural myocardial infarction of unspecif site    | G30X.00 |
| Acute ST segment elevation myocardial infarction           | G30X000 |
| Other acute myocardial infarction                          | G30y.00 |
| Acute atrial infarction                                    | G30y000 |
| Acute papillary muscle infarction                          | G30y100 |
| Acute septal infarction                                    | G30y200 |
| Other acute myocardial infarction NOS                      | G30yz00 |
| Acute myocardial infarction NOS                            | G30z.00 |
| Other acute and subacute ischaemic heart disease           | G31..00 |
| Postmyocardial infarction syndrome                         | G310.00 |
| Dressler's syndrome  | G310.11 |
| Preinfarction syndrome                                     | G311.00 |
| Crescendo angina   | G311.11 |
| Impending infarction                                       | G311.12 |
| Unstable angina  | G311.13 |
| Angina at rest   | G311.14 |
| Unstable angina  | G311100 |
| Angina at rest   | G311200 |
| Refractory angina  | G311300 |
| Worsening angina   | G311400 |
| Acute coronary syndrome                                    | G311500 |
| Preinfarction syndrome NOS                                 | G311z00 |
| Coronary thrombosis not resulting in myocardial infarction | G312.00 |
| Other acute and subacute ischaemic heart disease           | G31y.00 |
| Acute coronary insufficiency                               | G31y000 |
| Microinfarction of heart                                   | G31y100 |
| Subendocardial ischaemia                                   | G31y200 |
| Transient myocardial ischaemia                             | G31y300 |
| Other acute and subacute ischaemic heart disease NOS       | G31yz00 |
| Old myocardial infarction                                  | G32..00 |
| Healed myocardial infarction                               | G32..11 |
| Personal history of myocardial infarction                  | G32..12 |
| Angina pectoris  | G33..00 |
| Status anginosus   | G33z000 |
| Stenocardia  | G33z100 |
| Syncope anginosa   | G33z200 |
| Angina on effort   | G33z300 |
| Ischaemic chest pain                                       | G33z400 |
| Post infarct angina  | G33z500 |
| New onset angina   | G33z600 |
| Stable angina  | G33z700 |
| Angina pectoris NOS  | G33zz00 |
| Other chronic ischaemic heart disease                      | G34..00 |
| Coronary atherosclerosis                                   | G340.00 |

|  |         |
|--|---------|
| Triple vessel disease of the heart                           | G340.11 |
| Coronary artery disease                                      | G340.12 |
| Aneurysm of heart  | G341.00 |
| Cardiac aneurysm   | G341.11 |
| Atherosclerotic cardiovascular disease                       | G342.00 |
| Ischaemic cardiomyopathy                                     | G343.00 |
| Silent myocardial ischaemia                                  | G344.00 |
| Other specified chronic ischaemic heart disease              | G34y.00 |
| Chronic coronary insufficiency                               | G34y000 |
| Chronic myocardial ischaemia                                 | G34y100 |
| Other specified chronic ischaemic heart disease NOS          | G34yz00 |
| Other chronic ischaemic heart disease NOS                    | G34z.00 |
| Subsequent myocardial infarction                             | G35..00 |
| Subsequent myocardial infarction of anterior wall            | G350.00 |
| Subsequent myocardial infarction of inferior wall            | G351.00 |
| Subsequent myocardial infarction of other sites              | G353.00 |
| Subsequent myocardial infarction of unspecified site         | G35X.00 |
| Certain current complication follow acute myocardial infarct | G36..00 |
| Haemopericardium/current comp folow acut myocard infarct     | G360.00 |
| Atrial septal defect/curr comp folow acut myocardal infarct  | G361.00 |
| Ventric septal defect/curr comp fol acut myocardal infarctn  | G362.00 |
| Ruptur cardiac wall w'out haemopericard/cur comp fol ac MI   | G363.00 |
| Ruptur chordae tendinae/curr comp fol acute myocard infarct  | G364.00 |
| Rupture papillary muscle/curr comp fol acute myocard infarct | G365.00 |
| Thrombosis atrium,auric append&vent/curr comp foll acute MI  | G366.00 |
| Postoperative myocardial infarction                          | G38..00 |
| Postoperative transmural myocardial infarction anterior wall | G380.00 |
| Postoperative transmural myocardial infarction inferior wall | G381.00 |
| Postoperative transmural myocardial infarction other sites   | G382.00 |
| Postoperative transmural myocardial infarction unspec site   | G383.00 |
| Postoperative subendocardial myocardial infarction           | G384.00 |
| Postoperative myocardial infarction, unspecified             | G38z.00 |
| Other specified ischaemic heart disease                      | G3y..00 |
| Ischaemic heart disease NOS                                  | G3z..00 |
| Acute cor pulmonale  | G400.00 |
| Acute pericarditis in diseases EC                            | G500.00 |
| Post infarction pericarditis                                 | G501.00 |
| Other and unspecified acute pericarditis                     | G50z.00 |
| Rupture of papillary muscle                                  | G5y6.00 |
| [X]Other current complicatns following acute myocard infarct | Gyu3100 |
| [X]Acute transmural myocardial infarction of unspecif site   | Gyu3400 |
| [X]Subsequent myocardial infarction of other sites           | Gyu3500 |
| [X]Subsequent myocardial infarction of unspecified site      | Gyu3600 |

Table j-ii Codes for Congestive heart failure

| description   | medcode |
|---|---------|
| Suspected heart failure                                     | 1J60.00 |
| Heart failure confirmed                                     | 1O1..00 |
| O/E - pulmonary oedema                                      | 23E1.00 |
| New York Heart Assoc classification heart failure symptoms  | 388D.00 |
| New York Heart Association classification - class I         | 662f.00 |
| New York Heart Association classification - class II        | 662g.00 |
| New York Heart Association classification - class III       | 662h.00 |
| New York Heart Association classification - class IV        | 662i.00 |
| Malignant hypertensive heart disease with CCF               | G210100 |
| Benign hypertensive heart disease with CCF                  | G211100 |
| Hypertensive heart disease NOS with CCF                     | G21z100 |
| Hypertensive heart&renal dis wth (congestive) heart failure | G232.00 |
| Hyperten heart&renal dis+both(congestv)heart and renal fail | G234.00 |
| Aneurysm of heart   | G341.00 |
| Congestive cardiomyopathy                                   | G554000 |
| Congestive obstructive cardiomyopathy                       | G554011 |
| Heart failure   | G58..00 |
| Cardiac failure   | G58..11 |
| Congestive heart failure                                    | G580.00 |
| Congestive cardiac failure                                  | G580.11 |
| Right heart failure   | G580.12 |
| Right ventricular failure                                   | G580.13 |
| Biventricular failure                                       | G580.14 |
| Acute congestive heart failure                              | G580000 |
| Chronic congestive heart failure                            | G580100 |
| Left ventricular failure                                    | G581.00 |
| Pulmonary oedema - acute                                    | G581.12 |
| Acute heart failure   | G582.00 |
| Heart failure NOS   | G58z.00 |
| Cardiac failure NOS   | G58z.12 |
| Pulmonary oedema NOS  | H541z00 |
| Acute pulmonary oedema unspecified                          | H584.00 |
| Acute oedema of lung, unspecified                           | H584.11 |
| Acute pulmonary oedema NOS                                  | H584z00 |
| [D]Dropsy   | R023200 |
| Heart failure as a complication of care                     | SP11111 |
| New York Heart Assoc classification heart failure symptoms  | ZRad.00 |



Table j-iii Codes for Peripheral vascular disease

| description  | medcode |
|--|---------|
| Diabetes mellitus with peripheral circulatory disorder       | C107.00 |
| Diabetes mellitus, juvenile +peripheral circulatory disorder | C107000 |
| Diabetes mellitus, adult, + peripheral circulatory disorder  | C107100 |
| IDDM with peripheral circulatory disorder                    | C107300 |
| NIDDM with peripheral circulatory disorder                   | C107400 |
| Diabetes mellitus NOS with peripheral circulatory disorder   | C107z00 |
| Insulin dependent diab mell with peripheral angiopathy       | C108G00 |
| Type I diabetes mellitus with peripheral angiopathy          | C108G11 |
| Type 1 diabetes mellitus with peripheral angiopathy          | C108G12 |
| Non-insulin-dependent d m with peripheral angiopath          | C109F00 |
| Type II diabetes mellitus with peripheral angiopathy         | C109F11 |
| Type 2 diabetes mellitus with peripheral angiopathy          | C109F12 |
| Type 1 diabetes mellitus with peripheral angiopathy          | C10EG00 |
| Type I diabetes mellitus with peripheral angiopathy          | C10EG11 |
| Insulin dependent diab mell with peripheral angiopathy       | C10EG12 |
| Type 2 diabetes mellitus with peripheral angiopathy          | C10FF00 |
| Type II diabetes mellitus with peripheral angiopathy         | C10FF11 |
| Pulmonary arteritis  | G42y000 |
| Pulmonary vessel rupture                                     | G42y100 |
| Pulmonary vessel stricture                                   | G42y200 |
| Other specified pulmonary circulation disease NOS            | G42yz00 |
| Cardiovascular arteriosclerosis unspecified                  | G5y2.00 |
| Arteriosclerosis   | G70..11 |
| Aorto-iliac disease  | G700.11 |
| Renal artery atherosclerosis                                 | G701.00 |
| Extremity artery atheroma                                    | G702.00 |
| Monckeberg's medial sclerosis                                | G702000 |
| Other specified artery atheroma                              | G70y.00 |
| Carotid artery atherosclerosis                               | G70y000 |
| Arteriosclerotic vascular disease NOS                        | G70z.00 |
| Other aneurysm   | G72..00 |
| Other peripheral vascular disease                            | G73..00 |
| Peripheral ischaemic vascular disease                        | G73..11 |
| Ischaemia of legs  | G73..12 |
| Peripheral ischaemia   | G73..13 |
| Buerger's disease  | G731000 |
| Peripheral gangrene  | G732.00 |
| Other specified peripheral vascular disease                  | G73y.00 |
| Diabetic peripheral angiopathy                               | G73y000 |
| Erythrocyanosis  | G73y700 |
| Spasm of peripheral artery                                   | G73z100 |
| Arterial embolism and thrombosis                             | G74..00 |
| Arterial embolus and thrombosis                              | G74..11 |

|  |         |
|--|---------|
| Thrombosis - arterial  | G74..12 |
| Arterial embolic and thrombotic occlusion                    | G74..13 |
| Polyarteritis nodosa and allied conditions                   | G75..00 |
| Polyarteritis nodosa   | G750.00 |
| Necrotising angiitis   | G750.11 |
| Wegener's granulomatosis                                     | G754.00 |
| Giant cell arteritis   | G755.00 |
| Cranial arteritis  | G755000 |
| Temporal arteritis   | G755100 |
| Horton's disease   | G755200 |
| Giant cell arteritis NOS                                     | G755z00 |
| Thrombotic microangiopathy                                   | G756.00 |
| Takayasu's disease   | G757.00 |
| Aortic arch arteritis  | G757.11 |
| Pulseless disease  | G757.12 |
| Churg-Strauss vasculitis                                     | G758.00 |
| Juvenile polyarteritis                                       | G759.00 |
| Necrotising vasculopathy, unspecified                        | G75X.00 |
| Polyarteritis nodosa and allied conditions NOS               | G75z.00 |
| Other disorders of arteries and arterioles                   | G76..00 |
| Acquired arteriovenous fistula                               | G760.00 |
| Stricture of artery  | G761.00 |
| Rupture of artery  | G762.00 |
| Hyperplasia of renal artery                                  | G763.00 |
| Coeliac artery compression syndrome                          | G764.00 |
| Marable's syndrome   | G764.11 |
| Necrosis of artery   | G765.00 |
| Arteritis unspecified  | G766.00 |
| Aortitis   | G766.11 |
| Aortitis - syphilitic  | G767.00 |
| Other disorders of arteries and arterioles                   | G768.00 |
| Anterior spinal and vertebral artery compression syndromes   | G769.00 |
| Arterial insufficiency                                       | G76A.00 |
| Vasculitis   | G76B.00 |
| Disorders of arteries and arterioles NOS                     | G76z.00 |
| Diseases of capillaries                                      | G77..00 |
| Other specified arterial, arteriole or capillary disease     | G7y..00 |
| Arterial, arteriole and capillary diseases NOS               | G7z..00 |
| Phlebosclerosis  | G8yy200 |
| [X]Atherosclerosis of other arteries                         | Gyu7000 |
| [X]Other specified peripheral vascular diseases              | Gyu7400 |
| [X]Embolism and thrombosis of other arteries                 | Gyu7500 |
| [X]Other specified disorders of arteries and arterioles      | Gyu7600 |
| [X]Other diseases of capillaries                             | Gyu7700 |
| [X]Peripheral angiopathy in diseases classified elsewhere    | Gyu7A00 |
| [X]Oth disorders/arteries,arterioles+capillaries/diseases CE | Gyu7B00 |

|  |         |
|--|---------|
| Vascular insufficiency of the intestine                    | J42..00 |
| Acute intestinal vascular insufficiency                    | J420.00 |
| Acute intestinal vascular insufficiency NOS                | J420z00 |
| Chronic intestinal vascular insufficiency                  | J421.00 |
| Chronic intestinal vascular insufficiency NOS              | J421z00 |
| Intestinal vascular insufficiency NOS                      | J42z.00 |
| Vascular disorders of intestine                            | J577.00 |
| Gastric antral vascular ectasia                            | J577100 |
| [X]Other vascular disorders of intestine                   | Jyu5000 |
| Vascular disorders of kidney                               | K138.00 |
| Renal vascular disorders                                   | K138.11 |
| Renal vascular disorders NOS                               | K138z00 |
| Vascular disorders of penis                                | K275.00 |
| Penile vascular disorder NOS                               | K275z00 |
| Male genital organ vascular diseases                       | K286.00 |
| Male genital vascular diseases NOS                         | K286z00 |
| Giant cell arteritis with polymyalgia rheumatica           | N200.00 |
| [X]Other conditions related to polyarteritis nodosa        | Nyu4000 |
| [X]Other giant cell arteritis                              | Nyu4100 |
| [X]Other specified necrotizing vasculopathies              | Nyu4200 |
| [X]Necrotising vasculopathy, unspecified                   | Nyu4D00 |
| Other peripheral vascular system anomalies                 | P76..00 |
| Peripheral arterio-venous aneurysm                         | P766.00 |
| Peripheral arterio-venous malformation                     | P766.11 |
| Congenital peripheral aneurysm                             | P767.00 |
| Congenital anomaly of peripheral vascular system OS        | P76y.00 |
| Other congenital anomaly of peripheral vascular system NOS | P76yz00 |
| Peripheral vascular system anomaly NOS                     | P76z.00 |
| Cerebrovascular system anomaly NOS                         | P7y0z00 |
| Other cardiovascular system anomaly NOS                    | P7yz.00 |
| Other cardiovascular system anomaly NOS                    | P7yzz00 |
| [D]Failure of peripheral circulation                       | R055000 |
| [D]Peripheral circulatory failure                          | R055011 |
| Peripheral vascular complications of care                  | SP12.00 |
| Peripheral vascular complications of care NOS              | SP12z00 |

Table j-iv Codes for Cerebrovascular disease

| description  | medcode |
|--|---------|
| Diabetes mellitus with peripheral circulatory disorder       | C107.00 |
| Diabetes mellitus, juvenile +peripheral circulatory disorder | C107000 |
| Diabetes mellitus, adult, + peripheral circulatory disorder  | C107100 |
| IDDM with peripheral circulatory disorder                    | C107300 |
| NIDDM with peripheral circulatory disorder                   | C107400 |
| Diabetes mellitus NOS with peripheral circulatory disorder   | C107z00 |
| Insulin dependent diab mell with peripheral angiopathy       | C108G00 |
| Type I diabetes mellitus with peripheral angiopathy          | C108G11 |
| Type 1 diabetes mellitus with peripheral angiopathy          | C108G12 |
| Non-insulin-dependent d m with peripheral angiopath          | C109F00 |
| Type II diabetes mellitus with peripheral angiopathy         | C109F11 |
| Type 2 diabetes mellitus with peripheral angiopathy          | C109F12 |
| Type 1 diabetes mellitus with peripheral angiopathy          | C10EG00 |
| Type I diabetes mellitus with peripheral angiopathy          | C10EG11 |
| Insulin dependent diab mell with peripheral angiopathy       | C10EG12 |
| Type 2 diabetes mellitus with peripheral angiopathy          | C10FF00 |
| Type II diabetes mellitus with peripheral angiopathy         | C10FF11 |
| Pulmonary arteritis  | G42y000 |
| Pulmonary vessel rupture                                     | G42y100 |
| Pulmonary vessel stricture                                   | G42y200 |
| Other specified pulmonary circulation disease NOS            | G42yz00 |
| Cardiovascular arteriosclerosis unspecified                  | G5y2.00 |
| Arteriosclerosis   | G70..11 |
| Aorto-iliac disease  | G700.11 |
| Renal artery atherosclerosis                                 | G701.00 |
| Extremity artery atheroma                                    | G702.00 |
| Monckeberg's medial sclerosis                                | G702000 |
| Other specified artery atheroma                              | G70y.00 |
| Carotid artery atherosclerosis                               | G70y000 |
| Arteriosclerotic vascular disease NOS                        | G70z.00 |
| Other aneurysm   | G72..00 |
| Other peripheral vascular disease                            | G73..00 |
| Peripheral ischaemic vascular disease                        | G73..11 |
| Ischaemia of legs  | G73..12 |
| Peripheral ischaemia   | G73..13 |
| Buerger's disease  | G731000 |
| Peripheral gangrene  | G732.00 |
| Other specified peripheral vascular disease                  | G73y.00 |
| Diabetic peripheral angiopathy                               | G73y000 |
| Erythrocyanosis  | G73y700 |
| Spasm of peripheral artery                                   | G73z100 |
| Arterial embolism and thrombosis                             | G74..00 |
| Arterial embolus and thrombosis                              | G74..11 |

|  |         |
|--|---------|
| Thrombosis - arterial  | G74..12 |
| Arterial embolic and thrombotic occlusion                    | G74..13 |
| Polyarteritis nodosa and allied conditions                   | G75..00 |
| Polyarteritis nodosa   | G750.00 |
| Necrotising angiitis   | G750.11 |
| Wegener's granulomatosis                                     | G754.00 |
| Giant cell arteritis   | G755.00 |
| Cranial arteritis  | G755000 |
| Temporal arteritis   | G755100 |
| Horton's disease   | G755200 |
| Giant cell arteritis NOS                                     | G755z00 |
| Thrombotic microangiopathy                                   | G756.00 |
| Takayasu's disease   | G757.00 |
| Aortic arch arteritis  | G757.11 |
| Pulseless disease  | G757.12 |
| Churg-Strauss vasculitis                                     | G758.00 |
| Juvenile polyarteritis                                       | G759.00 |
| Necrotising vasculopathy, unspecified                        | G75X.00 |
| Polyarteritis nodosa and allied conditions NOS               | G75z.00 |
| Other disorders of arteries and arterioles                   | G76..00 |
| Acquired arteriovenous fistula                               | G760.00 |
| Stricture of artery  | G761.00 |
| Rupture of artery  | G762.00 |
| Hyperplasia of renal artery                                  | G763.00 |
| Coeliac artery compression syndrome                          | G764.00 |
| Marable's syndrome   | G764.11 |
| Necrosis of artery   | G765.00 |
| Arteritis unspecified  | G766.00 |
| Aortitis   | G766.11 |
| Aortitis - syphilitic  | G767.00 |
| Other disorders of arteries and arterioles                   | G768.00 |
| Anterior spinal and vertebral artery compression syndromes   | G769.00 |
| Arterial insufficiency                                       | G76A.00 |
| Vasculitis   | G76B.00 |
| Disorders of arteries and arterioles NOS                     | G76z.00 |
| Diseases of capillaries                                      | G77..00 |
| Other specified arterial, arteriole or capillary disease     | G7y..00 |
| Arterial, arteriole and capillary diseases NOS               | G7z..00 |
| Phlebosclerosis  | G8yy200 |
| [X]Atherosclerosis of other arteries                         | Gyu7000 |
| [X]Other specified peripheral vascular diseases              | Gyu7400 |
| [X]Embolism and thrombosis of other arteries                 | Gyu7500 |
| [X]Other specified disorders of arteries and arterioles      | Gyu7600 |
| [X]Other diseases of capillaries                             | Gyu7700 |
| [X]Peripheral angiopathy in diseases classified elsewhere    | Gyu7A00 |
| [X]Oth disorders/arteries,arterioles+capillaries/diseases CE | Gyu7B00 |

|  |         |
|--|---------|
| Vascular insufficiency of the intestine                    | J42..00 |
| Acute intestinal vascular insufficiency                    | J420.00 |
| Acute intestinal vascular insufficiency NOS                | J420z00 |
| Chronic intestinal vascular insufficiency                  | J421.00 |
| Chronic intestinal vascular insufficiency NOS              | J421z00 |
| Intestinal vascular insufficiency NOS                      | J42z.00 |
| Vascular disorders of intestine                            | J577.00 |
| Gastric antral vascular ectasia                            | J577100 |
| [X]Other vascular disorders of intestine                   | Jyu5000 |
| Vascular disorders of kidney                               | K138.00 |
| Renal vascular disorders                                   | K138.11 |
| Renal vascular disorders NOS                               | K138z00 |
| Vascular disorders of penis                                | K275.00 |
| Penile vascular disorder NOS                               | K275z00 |
| Male genital organ vascular diseases                       | K286.00 |
| Male genital vascular diseases NOS                         | K286z00 |
| Giant cell arteritis with polymyalgia rheumatica           | N200.00 |
| [X]Other conditions related to polyarteritis nodosa        | Nyu4000 |
| [X]Other giant cell arteritis                              | Nyu4100 |
| [X]Other specified necrotizing vasculopathies              | Nyu4200 |
| [X]Necrotising vasculopathy, unspecified                   | Nyu4D00 |
| Other peripheral vascular system anomalies                 | P76..00 |
| Peripheral arterio-venous aneurysm                         | P766.00 |
| Peripheral arterio-venous malformation                     | P766.11 |
| Congenital peripheral aneurysm                             | P767.00 |
| Congenital anomaly of peripheral vascular system OS        | P76y.00 |
| Other congenital anomaly of peripheral vascular system NOS | P76yz00 |
| Peripheral vascular system anomaly NOS                     | P76z.00 |
| Cerebrovascular system anomaly NOS                         | P7y0z00 |
| Other cardiovascular system anomaly NOS                    | P7yz.00 |
| Other cardiovascular system anomaly NOS                    | P7yzz00 |
| [D]Failure of peripheral circulation                       | R055000 |
| [D]Peripheral circulatory failure                          | R055011 |
| Peripheral vascular complications of care                  | SP12.00 |
| Peripheral vascular complications of care NOS              | SP12z00 |

Table j-v Codes for Dementia

| description  | medcode |
|--|---------|
| H/O: dementia  | 1461    |
| Senile dementia  | E00..11 |
| Senile/presenile dementia                                    | E00..12 |
| Uncomplicated senile dementia                                | E000.00 |
| Presenile dementia   | E001.00 |
| Uncomplicated presenile dementia                             | E001000 |
| Presenile dementia with delirium                             | E001100 |
| Presenile dementia with paranoia                             | E001200 |
| Presenile dementia with depression                           | E001300 |
| Presenile dementia NOS                                       | E001z00 |
| Senile dementia with depressive or paranoid features         | E002.00 |
| Senile dementia with paranoia                                | E002000 |
| Senile dementia with depression                              | E002100 |
| Senile dementia with depressive or paranoid features NOS     | E002z00 |
| Senile dementia with delirium                                | E003.00 |
| Arteriosclerotic dementia                                    | E004.00 |
| Multi infarct dementia                                       | E004.11 |
| Uncomplicated arteriosclerotic dementia                      | E004000 |
| Arteriosclerotic dementia with delirium                      | E004100 |
| Arteriosclerotic dementia with paranoia                      | E004200 |
| Arteriosclerotic dementia with depression                    | E004300 |
| Arteriosclerotic dementia NOS                                | E004z00 |
| Dementia in conditions EC                                    | E041.00 |
| Chronic confusional state                                    | E042.00 |
| [X]Dementia in Alzheimer's disease                           | Eu00.00 |
| [X]Dementia in Alzheimer's disease with early onset          | Eu00000 |
| [X]Presenile dementia,Alzheimer's type                       | Eu00011 |
| [X]Primary degen dementia, Alzheimer's type, presenile onset | Eu00012 |
| [X]Alzheimer's disease type 2                                | Eu00013 |
| [X]Dementia in Alzheimer's disease with late onset           | Eu00100 |
| [X]Alzheimer's disease type 1                                | Eu00111 |
| [X]Senile dementia,Alzheimer's type                          | Eu00112 |
| [X]Primary degen dementia of Alzheimer's type, senile onset  | Eu00113 |
| [X]Dementia in Alzheimer's dis, atypical or mixed type       | Eu00200 |
| [X]Dementia in Alzheimer's disease, unspecified              | Eu00z00 |
| [X]Alzheimer's dementia unspec                               | Eu00z11 |
| [X]Vascular dementia   | Eu01.00 |
| [X]Arteriosclerotic dementia                                 | Eu01.11 |
| [X]Vascular dementia of acute onset                          | Eu01000 |
| [X]Multi-infarct dementia                                    | Eu01100 |
| [X]Predominantly cortical dementia                           | Eu01111 |
| [X]Subcortical vascular dementia                             | Eu01200 |
| [X]Mixed cortical and subcortical vascular dementia          | Eu01300 |

|  |         |
|--|---------|
| [X]Other vascular dementia                                   | Eu01y00 |
| [X]Vascular dementia, unspecified                            | Eu01z00 |
| [X]Dementia in other diseases classified elsewhere           | Eu02.00 |
| [X]Dementia in Pick's disease                                | Eu02000 |
| [X]Dementia in Creutzfeldt-Jakob disease                     | Eu02100 |
| [X]Dementia in Huntington's disease                          | Eu02200 |
| [X]Dementia in Parkinson's disease                           | Eu02300 |
| [X]Dementia in human immunodeficiency virus [HIV] disease    | Eu02400 |
| [X]Dementia in other specified diseases classified elsewhere | Eu02y00 |
| [X] Unspecified dementia                                     | Eu02z00 |
| [X] Presenile dementia NOS                                   | Eu02z11 |
| [X] Primary degenerative dementia NOS                        | Eu02z13 |
| [X] Senile dementia NOS                                      | Eu02z14 |
| [X] Senile dementia, depressed or paranoid type              | Eu02z16 |
| [X]Delirium superimposed on dementia                         | Eu04100 |



Table j-vi Codes for Chronic pulmonary disease

| description   | medcode |
|---|---------|
| Recurrent wheezy bronchitis                               | H30..12 |
| Chronic bronchitis  | H31..00 |
| Chronic asthmatic bronchitis                              | H312000 |
| Chronic wheezy bronchitis                                 | H312011 |
| Emphysematous bronchitis                                  | H312100 |
| Acute exacerbation of chronic obstructive airways disease | H312200 |
| Bronchiolitis obliterans                                  | H312300 |
| Obstructive chronic bronchitis NOS                        | H312z00 |
| Emphysema   | H32..00 |
| Chronic bullous emphysema                                 | H320.00 |
| Segmental bullous emphysema                               | H320000 |
| Zonal bullous emphysema                                   | H320100 |
| Giant bullous emphysema                                   | H320200 |
| Bullous emphysema with collapse                           | H320300 |
| Chronic bullous emphysema NOS                             | H320z00 |
| Panlobular emphysema                                      | H321.00 |
| Centrilobular emphysema                                   | H322.00 |
| Other emphysema   | H32y.00 |
| Atrophic (senile) emphysema                               | H32y100 |
| MacLeod's unilateral emphysema                            | H32y200 |
| Other emphysema NOS                                       | H32yz00 |
| Emphysema NOS   | H32z.00 |
| Asthma  | H33..00 |
| Bronchial asthma  | H33..11 |
| Bronchiectasis  | H34..00 |
| Extrinsic allergic alveolitis                             | H35..00 |
| Other allergic alveolitis                                 | H35y.00 |
| Other allergic alveolitis NOS                             | H35yz00 |
| Allergic alveolitis and pneumonitis NOS                   | H35z.00 |
| Allergic extrinsic alveolitis NOS                         | H35z000 |
| Allergic alveolitis and pneumonitis NOS                   | H35zz00 |
| Mild chronic obstructive pulmonary disease                | H36..00 |
| Moderate chronic obstructive pulmonary disease            | H37..00 |
| Severe chronic obstructive pulmonary disease              | H38..00 |
| Other specified chronic obstructive airways disease       | H3y..00 |
| Other specified chronic obstructive pulmonary disease     | H3y..11 |
| Chronic obstructive airways disease NOS                   | H3z..00 |
| Chronic obstructive pulmonary disease NOS                 | H3z..11 |
| Chronic emphysema due to chemical fumes                   | H464000 |
| Obliterative bronchiolitis due to chemical fumes          | H464100 |
| Chronic pulmonary fibrosis due to chemical fumes          | H464200 |
| Chronic respiratory conditions due to chemical fumes NOS  | H464z00 |
| Idiopathic fibrosing alveolitis                           | H563.00 |

|  |         |
|--|---------|
| Cryptogenic fibrosing alveolitis                         | H563.12 |
| Idiopathic fibrosing alveolitis NOS                      | H563z00 |
| Other lung disease NEC                                   | H58y.00 |
| Lung disease NOS   | H58z.00 |
| [X]Other emphysema                                       | Hyu3000 |
| [X]Other specified chronic obstructive pulmonary disease | Hyu3100 |

Table j-vii Codes for Connective tissue disease

| description   | medcode |
|---|---------|
| Behcet's syndrome                                     | AD61.00 |
| Polyneuropathy in collagen vascular disease           | F371.00 |
| Polyneuropathy in disseminated lupus erythematosus    | F371000 |
| Polyneuropathy in polyarteritis nodosa                | F371100 |
| Polyneuropathy in collagen vascular disease NOS       | F371z00 |
| Muscular dystrophies and other myopathies             | F39..00 |
| Symptomatic inflammatory myopathy in disease EC       | F396.00 |
| Myopathy due to disseminated lupus erythematosus      | F396100 |
| Myopathy due to polyarteritis nodosa                  | F396300 |
| Eyelid discoid lupus erythematosus                    | F4D3300 |
| Arterial, arteriole and capillary disease             | G7...00 |
| Capillary disease                                     | G7...11 |
| Polyarteritis nodosa and allied conditions            | G75..00 |
| Polyarteritis nodosa                                  | G750.00 |
| Wegener's granulomatosis                              | G754.00 |
| Juvenile polyarteritis                                | G759.00 |
| Polyarteritis nodosa and allied conditions NOS        | G75z.00 |
| Lung disease with systemic lupus erythematosus        | H57y400 |
| Nephrotic syndrome in polyarteritis nodosa            | K01x300 |
| Lupus erythematosus                                   | M154.00 |
| Lupus erythematosus chronicus                         | M154000 |
| Discoid lupus erythematosus                           | M154100 |
| Lupus erythematosus migrans                           | M154200 |
| Lupus erythematosus nodularis                         | M154300 |
| Lupus erythematosus profundus                         | M154400 |
| Lupus erythematosus tumidus                           | M154500 |
| Lupus erythematosus unguium mutilans                  | M154600 |
| Subacute cutaneous lupus erythematosus                | M154700 |
| Lupus erythematosus NOS                               | M154z00 |
| [X]Other local lupus erythematosus                    | Myu7800 |
| Musculoskeletal and connective tissue diseases        | N....00 |
| Connective tissue diseases                            | N....11 |
| Arthropathies and related disorders                   | NO...00 |
| Diffuse diseases of connective tissue                 | N00..00 |
| Collagen diseases                                     | N00..11 |
| Systemic lupus erythematosus                          | N000.00 |
| Disseminated lupus erythematosus                      | N000000 |
| Drug-induced systemic lupus erythematosus             | N000200 |
| Systemic lupus erythematosus with organ or sys involv | N000300 |
| Systemic lupus erythematosus with pericarditis        | N000400 |
| Systemic lupus erythematosus NOS                      | N000z00 |
| Other specified diffuse collagen diseases             | N00y.00 |
| Collagen disease NOS                                  | N00z.00 |

|  |         |
|--|---------|
| Arthropathy in Behcet's syndrome                             | N012.00 |
| Arthropathy in Behcet's syndrome of unspecified site         | N012000 |
| Behcet's syndrome arthropathy                                | N012011 |
| Arthropathy in Behcet's syndrome of the shoulder region      | N012100 |
| Arthropathy in Behcet's syndrome of the upper arm            | N012200 |
| Arthropathy in Behcet's syndrome of the forearm              | N012300 |
| Arthropathy in Behcet's syndrome of the hand                 | N012400 |
| Arthropathy in Behcet's syndrome of the pelvis/thigh         | N012500 |
| Arthropathy in Behcet's syndrome of the lower leg            | N012600 |
| Arthropathy in Behcet's syndrome of the ankle and foot       | N012700 |
| Arthropathy in Behcet's syndrome of multiple sites           | N012x00 |
| Arthropathy in Behcet's syndrome of other specified sites    | N012y00 |
| Arthropathy in Behcet's syndrome NOS                         | N012z00 |
| Rheumatism, excluding the back                               | N2...00 |
| Polymyalgia rheumatica                                       | N20..00 |
| Polymyalgia  | N20..11 |
| Giant cell arteritis with polymyalgia rheumatica             | N200.00 |
| Scoliosis in connective tissue anomalies                     | N374D00 |
| Musculoskeletal or connective tissue diseases OS             | Ny...00 |
| [X]Addtnl muscelskeletal+connectv tissue dis classfctn terms | Nyu..00 |
| [X]Systemic connective tissue disorders                      | Nyu4.00 |
| [X]Other conditions related to polyarteritis nodosa          | Nyu4000 |
| [X]Other forms of systemic lupus erythematosus               | Nyu4300 |
| [X]Other systemic diseases of connective tissue              | Nyu4700 |
| [X]Systemic disorders/connective tissue in other diseases CE | Nyu4C00 |
| [X]Other disord musculoskeletal system and connective tissue | NyuE.00 |
| Musculoskeletal and connective tissue diseases NOS           | Nz...00 |
| Unspecified anomaly of connective tissue                     | PGz4.00 |

Table j-viii Codes for Ulcer disease

| description   | medcode |
|---|---------|
| Peptic ulcer symptoms                                       | 1956    |
| Oesophageal, stomach and duodenal diseases                  | J1...00 |
| Duodenal diseases   | J1...11 |
| Ulcerative oesophagitis                                     | J101600 |
| Ulcer of oesophagus   | J102.00 |
| Peptic ulcer of oesophagus                                  | J102000 |
| Oesophageal ulcer due to aspirin                            | J102200 |
| Oesophageal ulcer due to chemicals                          | J102300 |
| Oesophageal ulcer due to medicines                          | J102400 |
| Barrett's ulcer of oesophagus                               | J102500 |
| Ulcer of oesophagus NOS                                     | J102z00 |
| Gastric ulcer - (GU)  | J11..00 |
| Prepyloric ulcer  | J11..11 |
| Pyloric ulcer   | J11..12 |
| Acute gastric ulcer   | J110.00 |
| Acute gastric ulcer without mention of complication         | J110000 |
| Acute gastric ulcer with haemorrhage                        | J110100 |
| Bleeding acute gastric ulcer                                | J110111 |
| Acute gastric ulcer with perforation                        | J110200 |
| Acute gastric ulcer with haemorrhage and perforation        | J110300 |
| Acute gastric ulcer with obstruction                        | J110400 |
| Acute gastric ulcer unspecified                             | J110y00 |
| Acute gastric ulcer NOS                                     | J110z00 |
| Chronic gastric ulcer                                       | J111.00 |
| Chronic gastric ulcer without mention of complication       | J111000 |
| Chronic gastric ulcer with haemorrhage                      | J111100 |
| Bleeding chronic gastric ulcer                              | J111111 |
| Chronic gastric ulcer with perforation                      | J111200 |
| Perforated chronic gastric ulcer                            | J111211 |
| Chronic gastric ulcer with haemorrhage and perforation      | J111300 |
| Chronic gastric ulcer with obstruction                      | J111400 |
| Chronic gastric ulcer unspecified                           | J111y00 |
| Chronic gastric ulcer NOS                                   | J111z00 |
| Unspecified gastric ulcer                                   | J11y.00 |
| Unspecified gastric ulcer without mention of complication   | J11y000 |
| Unspecified gastric ulcer with haemorrhage                  | J11y100 |
| Unspecified gastric ulcer with perforation                  | J11y200 |
| Unspecified gastric ulcer with haemorrhage and perforation  | J11y300 |
| Unspecified gastric ulcer with obstruction                  | J11y400 |
| Unspec gastric ulcer; unspec haemorrhage and/or perforation | J11yy00 |
| Unspecified gastric ulcer NOS                               | J11yz00 |
| Gastric ulcer NOS   | J11z.00 |
| Multiple gastric ulcers                                     | J11z.12 |

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|--|---------|
| Duodenal ulcer - (DU)  | J12..00 |
| Acute duodenal ulcer   | J120.00 |
| Acute duodenal ulcer without mention of complication         | J120000 |
| Acute duodenal ulcer with haemorrhage                        | J120100 |
| Acute duodenal ulcer with perforation                        | J120200 |
| Acute duodenal ulcer with haemorrhage and perforation        | J120300 |
| Acute duodenal ulcer with obstruction                        | J120400 |
| Acute duodenal ulcer unspecified                             | J120y00 |
| Acute duodenal ulcer NOS                                     | J120z00 |
| Chronic duodenal ulcer                                       | J121.00 |
| Chronic duodenal ulcer without mention of complication       | J121000 |
| Chronic duodenal ulcer with haemorrhage                      | J121100 |
| Bleeding chronic duodenal ulcer                              | J121111 |
| Chronic duodenal ulcer with perforation                      | J121200 |
| Perforated chronic duodenal ulcer                            | J121211 |
| Chronic duodenal ulcer with haemorrhage and perforation      | J121300 |
| Chronic duodenal ulcer with obstruction                      | J121400 |
| Chronic duodenal ulcer unspecified                           | J121y00 |
| Chronic duodenal ulcer NOS                                   | J121z00 |
| Duodenal ulcer disease                                       | J122.00 |
| Recurrent duodenal ulcer                                     | J124.00 |
| Unspecified duodenal ulcer                                   | J12y.00 |
| Unspecified duodenal ulcer without mention of complication   | J12y000 |
| Unspecified duodenal ulcer with haemorrhage                  | J12y100 |
| Unspecified duodenal ulcer with perforation                  | J12y200 |
| Unspecified duodenal ulcer with haemorrhage and perforation  | J12y300 |
| Unspecified duodenal ulcer with obstruction                  | J12y400 |
| Unspec duodenal ulcer; unspec haemorrhage and/or perforation | J12yy00 |
| Unspecified duodenal ulcer NOS                               | J12yz00 |
| Duodenal ulcer NOS   | J12z.00 |
| Peptic ulcer - (PU) site unspecified                         | J13..00 |
| Stress ulcer NOS   | J13..11 |
| Acute peptic ulcer   | J130.00 |
| Acute peptic ulcer without mention of complication           | J130000 |
| Acute peptic ulcer with haemorrhage                          | J130100 |
| Acute peptic ulcer with perforation                          | J130200 |
| Acute peptic ulcer with haemorrhage and perforation          | J130300 |
| Acute peptic ulcer with obstruction                          | J130400 |
| Acute peptic ulcer unspecified                               | J130y00 |
| Acute peptic ulcer NOS                                       | J130z00 |
| Chronic peptic ulcer   | J131.00 |
| Chronic peptic ulcer without mention of complication         | J131000 |
| Chronic peptic ulcer with haemorrhage                        | J131100 |
| Chronic peptic ulcer with perforation                        | J131200 |
| Chronic peptic ulcer with haemorrhage and perforation        | J131300 |
| Chronic peptic ulcer with obstruction                        | J131400 |

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|--|---------|
| Chronic peptic ulcer unspecified                             | J131y00 |
| Chronic peptic ulcer NOS                                     | J131z00 |
| Unspecified peptic ulcer                                     | J13y.00 |
| Unspecified peptic ulcer without mention of complication     | J13y000 |
| Unspecified peptic ulcer with haemorrhage                    | J13y100 |
| Unspecified peptic ulcer with perforation                    | J13y200 |
| Unspecified peptic ulcer with haemorrhage and perforation    | J13y300 |
| Unspecified peptic ulcer with obstruction                    | J13y400 |
| Unspec peptic ulcer; unspec haemorrhage and/or perforation   | J13yy00 |
| Unspecified peptic ulcer NOS                                 | J13yz00 |
| Peptic ulcer NOS   | J13z.00 |
| Gastrojejunal ulcer (GJU)                                    | J14..00 |
| Gastrocolic ulcer  | J14..12 |
| Jejunal ulcer  | J14..13 |
| Marginal ulcer   | J14..14 |
| Stomal ulcer   | J14..15 |
| Acute gastrojejunal ulcer                                    | J140.00 |
| Acute gastrojejunal ulcer without mention of complication    | J140000 |
| Acute gastrojejunal ulcer with haemorrhage                   | J140100 |
| Acute gastrojejunal ulcer with perforation                   | J140200 |
| Acute gastrojejunal ulcer with haemorrhage and perforation   | J140300 |
| Acute gastrojejunal ulcer with obstruction                   | J140400 |
| Acute gastrojejunal ulcer unspecified                        | J140y00 |
| Acute gastrojejunal ulcer NOS                                | J140z00 |
| Chronic gastrojejunal ulcer                                  | J141.00 |
| Chronic gastrojejunal ulcer without mention of complication  | J141000 |
| Chronic gastrojejunal ulcer with haemorrhage                 | J141100 |
| Chronic gastrojejunal ulcer with perforation                 | J141200 |
| Chronic gastrojejunal ulcer with haemorrhage and perforation | J141300 |
| Chronic gastrojejunal ulcer with obstruction                 | J141400 |
| Chronic gastrojejunal ulcer unspecified                      | J141y00 |
| Chronic gastrojejunal ulcer NOS                              | J141z00 |
| Unspecified gastrojejunal ulcer                              | J14y.00 |
| Unspecified gastrojejunal ulcer without mention complication | J14y000 |
| Unspecified gastrojejunal ulcer with haemorrhage             | J14y100 |
| Unspecified gastrojejunal ulcer with perforation             | J14y200 |
| Unspec gastrojejunal ulcer with haemorrhage and perforation  | J14y300 |
| Unspecified gastrojejunal ulcer with obstruction             | J14y400 |
| Unspec gastrojejunal ulcer; unspec haemorrhage/perforation   | J14yy00 |
| Unspecified gastrojejunal ulcer NOS                          | J14yz00 |
| Gastrojejunal ulcer NOS                                      | J14z.00 |
| Other stomach and duodenal disorders                         | J17..00 |
| Other stomach and duodenal disorders                         | J17y.00 |
| Primary ulcer of intestine                                   | J57y800 |
| Ulceration of colon  | J57y900 |
| Ulceration of intestine NOS                                  | J57yA00 |

Table j-ix Codes for Diabetes (not specifying end organ damage)

| description  | medcode |
|--|---------|
| Initial diabetic assessment                                  | 66A1.00 |
| Follow-up diabetic assessment                                | 66A2.00 |
| Diabetic on diet only  | 66A3.00 |
| Diabetic on oral treatment                                   | 66A4.00 |
| Diabetic on insulin  | 66A5.00 |
| Has seen dietician - diabetes                                | 66A8.00 |
| Unstable diabetes  | 66AJ.11 |
| Diabetic - poor control NOS                                  | 66AJz00 |
| Diabetes: practice programme                                 | 66AP.00 |
| Diabetes: shared care programme                              | 66AQ.00 |
| Diabetes care by hospital only                               | 66AU.00 |
| Diabetic on insulin and oral treatment                       | 66AV.00 |
| Diabetic monitoring NOS                                      | 66AZ.00 |
| Under care of diabetologist                                  | 9NN8.00 |
| Under care of diabetes specialist nurse                      | 9NN9.00 |
| Diabetes mellitus  | C10..00 |
| Diabetes mellitus with no mention of complication            | C100.00 |
| Diabetes mellitus, juvenile type, no mention of complication | C100000 |
| Insulin dependent diabetes mellitus                          | C100011 |
| Diabetes mellitus, adult onset, no mention of complication   | C100100 |
| Maturity onset diabetes                                      | C100111 |
| Non-insulin dependent diabetes mellitus                      | C100112 |
| Diabetes mellitus NOS with no mention of complication        | C100z00 |
| Insulin dependent diabetes mellitus                          | C108.00 |
| IDDM-Insulin dependent diabetes mellitus                     | C108.11 |
| Type 1 diabetes mellitus                                     | C108.12 |
| Type I diabetes mellitus                                     | C108.13 |
| Unstable insulin dependent diabetes mellitus                 | C108400 |
| Unstable type I diabetes mellitus                            | C108411 |
| Unstable type 1 diabetes mellitus                            | C108412 |
| Insulin dependent diabetes mellitus - poor control           | C108800 |
| Type I diabetes mellitus - poor control                      | C108811 |
| Type 1 diabetes mellitus - poor control                      | C108812 |
| Insulin dependent diabetes maturity onset                    | C108900 |
| Type I diabetes mellitus maturity onset                      | C108911 |
| Type 1 diabetes mellitus maturity onset                      | C108912 |
| Insulin-dependent diabetes without complication              | C108A00 |
| Type I diabetes mellitus without complication                | C108A11 |
| Type 1 diabetes mellitus without complication                | C108A12 |
| Non-insulin dependent diabetes mellitus                      | C109.00 |
| NIDDM - Non-insulin dependent diabetes mellitus              | C109.11 |
| Type 2 diabetes mellitus                                     | C109.12 |



|  |         |
|--|---------|
| Type II diabetes mellitus                                    | C109.13 |
| Non-insulin dependent diabetes mellitus - poor control       | C109700 |
| Type II diabetes mellitus - poor control                     | C109711 |
| Type 2 diabetes mellitus - poor control                      | C109712 |
| Reaven's syndrome  | C109800 |
| Non-insulin-dependent diabetes mellitus without complication | C109900 |
| Type II diabetes mellitus without complication               | C109911 |
| Type 2 diabetes mellitus without complication                | C109912 |
| Insulin treated Type 2 diabetes mellitus                     | C109J00 |
| Insulin treated non-insulin dependent diabetes mellitus      | C109J11 |
| Insulin treated Type II diabetes mellitus                    | C109J12 |
| Malnutrition-related diabetes mellitus                       | C10A.00 |
| Diabetes mellitus induced by steroids                        | C10B.00 |
| Steroid induced diabetes mellitus without complication       | C10B000 |
| Diabetes mellitus autosomal dominant                         | C10C.00 |
| Maturity onset diabetes in youth                             | C10C.11 |
| Maturity onset diabetes in youth type 1                      | C10C.12 |
| Diabetes mellitus autosomal dominant type 2                  | C10D.00 |
| Maturity onset diabetes in youth type 2                      | C10D.11 |
| Type 1 diabetes mellitus                                     | C10E.00 |
| Type I diabetes mellitus                                     | C10E.11 |
| Insulin dependent diabetes mellitus                          | C10E.12 |
| Unstable type 1 diabetes mellitus                            | C10E400 |
| Unstable type I diabetes mellitus                            | C10E411 |
| Unstable insulin dependent diabetes mellitus                 | C10E412 |
| Type 1 diabetes mellitus - poor control                      | C10E800 |
| Type I diabetes mellitus - poor control                      | C10E811 |
| Insulin dependent diabetes mellitus - poor control           | C10E812 |
| Type 1 diabetes mellitus maturity onset                      | C10E900 |
| Type I diabetes mellitus maturity onset                      | C10E911 |
| Insulin dependent diabetes maturity onset                    | C10E912 |
| Type 1 diabetes mellitus without complication                | C10EA00 |
| Type I diabetes mellitus without complication                | C10EA11 |
| Insulin-dependent diabetes without complication              | C10EA12 |
| Type 2 diabetes mellitus                                     | C10F.00 |
| Type II diabetes mellitus                                    | C10F.11 |
| Type 2 diabetes mellitus - poor control                      | C10F700 |
| Type II diabetes mellitus - poor control                     | C10F711 |
| Reaven's syndrome  | C10F800 |
| Metabolic syndrome X   | C10F811 |
| Type 2 diabetes mellitus without complication                | C10F900 |
| Type II diabetes mellitus without complication               | C10F911 |
| Secondary pancreatic diabetes mellitus                       | C10G.00 |
| Secondary pancreatic diabetes mellitus without complication  | C10G000 |
| Diabetes mellitus induced by non-steroid drugs               | C10H.00 |
| Insulin autoimmune syndrome                                  | C10J.00 |

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|--|---------|
| Type A insulin resistance                                    | C10K.00 |
| Fibrocalculous pancreatopathy                                | C10L.00 |
| Lipoatrophic diabetes mellitus                               | C10M.00 |
| Lipoatrophic diabetes mellitus without complication          | C10M000 |
| Secondary diabetes mellitus                                  | C10N.00 |
| Secondary diabetes mellitus without complication             | C10N000 |
| Diabetes mellitus with other specified manifestation         | C10y.00 |
| Diabetes mellitus, juvenile, + other specified manifestation | C10y000 |
| Diabetes mellitus, adult, + other specified manifestation    | C10y100 |
| Steroid induced diabetes                                     | C11y000 |
| [X]Diabetes mellitus   | Cyu2.00 |
| [X]Other specified diabetes mellitus                         | Cyu2000 |
| Diabetes mellitus during pregnancy/childbirth/puerperium     | L180.00 |
| Diabetes mellitus - unspec whether in pregnancy/puerperium   | L180000 |
| Diabetes mellitus during pregnancy - baby delivered          | L180100 |
| Diabetes mellitus in puerperium - baby delivered             | L180200 |
| Diabetes mellitus during pregnancy - baby not yet delivered  | L180300 |
| Diabetes mellitus in puerperium - baby previously delivered  | L180400 |
| Pre-existing diabetes mellitus, insulin-dependent            | L180500 |
| Pre-existing diabetes mellitus, non-insulin-dependent        | L180600 |
| Pre-existing malnutrition-related diabetes mellitus          | L180700 |
| Diabetes mellitus arising in pregnancy                       | L180800 |
| Gestational diabetes mellitus                                | L180811 |
| Gestational diabetes mellitus                                | L180900 |
| Pre-existing diabetes mellitus, unspecified                  | L180X00 |
| Diabetes mellitus in pregnancy/childbirth/puerperium NOS     | L180z00 |
| Abnormal glucose tolerance test in pregnancy/childb/puerp    | L188.00 |
| GTT - glucose tolerance test abnormal in preg/childb/puerp   | L188.11 |
| [X]Pre-existing diabetes mellitus, unspecified               | Lyu2900 |
| [D]Drug induced hyperglycaemia                               | R10C.00 |
| [D]Elevated blood glucose level                              | R10D.00 |
| [D]Impaired glucose tolerance                                | R10E.00 |
| Dietary advice for type I diabetes                           | ZC2C900 |
| Diet advice for insulin-dependent diabetes                   | ZC2C911 |
| Dietary advice for type II diabetes                          | ZC2CA00 |
| Dietary advice non-insulin-dependent diabetes                | ZC2CA11 |
| Dietary advice for gestational diabetes                      | ZC2CB00 |
| Referral to diabetes nurse                                   | ZL62500 |
| Referral to diabetic liaison nurse                           | ZL62600 |
| [V]Dietary counselling in diabetes mellitus                  | ZV65312 |

Table j-x Codes for Hemiplegia

| description              | medcode |
|--------------------------|---------|
| O/E - hemiplegia         | 2833    |
| Hemiplegia               | F22..00 |
| Flaccid hemiplegia       | F220.00 |
| Spastic hemiplegia       | F221.00 |
| Left hemiplegia          | F222.00 |
| Right hemiplegia         | F223.00 |
| Hemiplegia NOS           | F22z.00 |
| Paraplegia - congenital  | F230.11 |
| Congenital hemiplegia    | F231.00 |
| Infantile hemiplegia NOS | F234.00 |

Table j-xi Codes for Moderate or severe renal disease

| description  | medcode |
|--|---------|
| Renal colic  | 1A52.00 |
| Renal colic, symptom   | 1A52.11 |
| Ureteric colic   | 1A54.00 |
| Dysuria  | 1A55.00 |
| Strangury  | 1A56.00 |
| O/E - kidney palpated  | 262..00 |
| O/E - renal palpation  | 262..11 |
| O/E - left kidney palpable                                   | 2622    |
| O/E - right kidney palpable                                  | 2623    |
| O/E - renal angle tenderness                                 | 2624    |
| O/E - kidney palpable NOS                                    | 262Z.00 |
| O/E - bladder palpated                                       | 263..00 |
| O/E - bladder palpable                                       | 263..11 |
| O/E: renal calculus  | 4G4..00 |
| O/E: kidney stone  | 4G4..11 |
| O/E: oxalate renal calculus                                  | 4G41.00 |
| Phosphate kidney stone                                       | 4G42.11 |
| O/E: uric acid renal calculus                                | 4G43.00 |
| O/E: cystine renal calculus                                  | 4G44.00 |
| O/E: renal stone NOS   | 4G4Z.00 |
| O/E - ureteric calculus                                      | 4G6..00 |
| O/E - urethral calculus                                      | 4G7..00 |
| O/E - bladder calculus                                       | 4G8..00 |
| Dialysis for renal failure                                   | 7L1A.11 |
| Renal dialysis   | 7L1A000 |
| Thomas intravascular shunt for dialysis                      | 7L1A011 |
| Peritoneal dialysis  | 7L1A100 |
| Haemodialysis NEC  | 7L1A200 |
| Other specified compensation for renal failure               | 7L1Ay00 |
| Compensation for renal failure NOS                           | 7L1Az00 |
| Placement ambulatory apparatus compensation renal failure    | 7L1B.00 |
| Placement ambulatory dialysis apparatus - compens renal fail | 7L1B.11 |
| Insertion of ambulatory peritoneal dialysis catheter         | 7L1B000 |
| Placement ambulatory apparatus- compensate renal failure OS  | 7L1By00 |
| Placement ambulatory apparatus- compensate renal failure NOS | 7L1Bz00 |
| Placement other apparatus for compensation for renal failure | 7L1C.00 |
| Insertion of temporary peritoneal dialysis catheter          | 7L1C000 |
| Placement other apparatus- compensate for renal failure OS   | 7L1Cy00 |
| Placement other apparatus- compensate for renal failure NOS  | 7L1Cz00 |
| Tuberculosis of kidney                                       | A160.00 |
| Renal tuberculosis   | A160.11 |
| Tuberculosis of bladder                                      | A161.00 |
| Tuberculosis of ureter                                       | A162.00 |

|   |         |
|---|---------|
| Tuberculosis of other urinary organs                        | A163.00 |
| Tuberculosis of urinary tract                               | A168.00 |
| Syphilis of kidney  | A954.00 |
| Renal syphilis  | A954.11 |
| Hypertensive renal disease                                  | G22..00 |
| Nephrosclerosis   | G22..11 |
| Malignant hypertensive renal disease                        | G220.00 |
| Benign hypertensive renal disease                           | G221.00 |
| Hypertensive renal disease with renal failure               | G222.00 |
| Hypertensive renal disease NOS                              | G22z.00 |
| Renal hypertension  | G22z.11 |
| Hypertensive heart and renal disease                        | G23..00 |
| Malignant hypertensive heart and renal disease              | G230.00 |
| Benign hypertensive heart and renal disease                 | G231.00 |
| Hypertensive heart&renal dis wth (congestive) heart failure | G232.00 |
| Hypertensive heart and renal disease with renal failure     | G233.00 |
| Hyperten heart&renal dis+both(congestv)heart and renal fail | G234.00 |
| Hypertensive heart and renal disease NOS                    | G23z.00 |
| Aneurysm of renal artery                                    | G721.00 |
| Hyperplasia of renal artery                                 | G763.00 |
| Embolism and thrombosis of the renal vein                   | G823.00 |
| Acute glomerulonephritis                                    | K00..00 |
| Acute nephritis   | K00..11 |
| Bright's disease  | K00..12 |
| Nephrotic syndrome  | K01..00 |
| Chronic glomerulonephritis                                  | K02..00 |
| Nephritis - chronic   | K02..11 |
| Nephropathy - chronic                                       | K02..12 |
| Nephritis and nephropathy unspecified                       | K03..00 |
| Nephritis and nephropathy unspecified                       | K03..11 |
| Nephropathy, unspecified                                    | K03..12 |
| Proliferative nephritis unspecified                         | K030.00 |
| Membranous nephritis unspecified                            | K031.00 |
| Membranoproliferative nephritis unspecified                 | K032.00 |
| Rapidly progressive nephritis unspecified                   | K033.00 |
| Renal cortical necrosis unspecified                         | K034.00 |
| Renal medullary necrosis unspecified                        | K035.00 |
| Tubulo-interstit nephritis, not specif as acute or chron    | K03T.00 |
| Unspecif nephr synd, diff concentric glomerulonephritis     | K03U.00 |
| Unspecified nephritic syndrome, dense deposit disease       | K03V.00 |
| Unsp nephrit synd, diff endocap prolif glomerulonephritis   | K03W.00 |
| Unsp nephrit synd, diff mesang prolif glomerulonephritis    | K03X.00 |
| Other nephritis and nephrosis unspecified                   | K03y.00 |
| Unspecified glomerulonephritis NOS                          | K03z.00 |
| Acute renal failure   | K04..00 |
| Acute renal tubular necrosis                                | K040.00 |

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| Acute renal cortical necrosis                              | K041.00 |
| Acute renal medullary necrosis                             | K042.00 |
| Necrotising renal papillitis                               | K042.11 |
| Acute drug-induced renal failure                           | K043.00 |
| Other acute renal failure                                  | K04y.00 |
| Acute renal failure NOS                                    | K04z.00 |
| Chronic renal failure                                      | K05..00 |
| Chronic uraemia  | K05..11 |
| End stage renal failure                                    | K05..12 |
| End stage renal failure                                    | K050.00 |
| Renal failure unspecified                                  | K06..00 |
| Uraemia NOS  | K06..11 |
| Renal impairment   | K060.00 |
| Impaired renal function                                    | K060.11 |
| Renal sclerosis unspecified                                | K07..00 |
| Atrophy of kidney  | K070.00 |
| Renal fibrosis   | K071.00 |
| Glomerulosclerosis   | K072.00 |
| Renal sclerosis NOS  | K07z.00 |
| Impaired renal function disorder                           | K08..00 |
| Renal osteodystrophy                                       | K080.00 |
| Phosphate-losing tubular disorders                         | K080000 |
| Renal osteodystrophy NOS                                   | K080z00 |
| Nephrogenic diabetes insipidus                             | K081.00 |
| Other impaired renal function disorder                     | K08y.00 |
| Hypokalaemic nephropathy                                   | K08y000 |
| Lightwood - Albright syndrome                              | K08y200 |
| Albright's renal tubular acidosis                          | K08y211 |
| Renal function impairment with growth failure              | K08y300 |
| Renal tubular acidosis                                     | K08y400 |
| Renal tubular acidaemia                                    | K08y412 |
| Acute interstitial nephritis                               | K08y500 |
| Other impaired renal function disorder NOS                 | K08yz00 |
| Renal acidaemia  | K08yz11 |
| Renotubular acidaemia                                      | K08yz12 |
| Impaired renal function disorder NOS                       | K08z.00 |
| Small kidney of unknown cause                              | K09..00 |
| Glomerular disease   | K0A..00 |
| Renal tubulo-interstitial disorders in diseases EC         | K0B..00 |
| Ren tubulo-interstitial disord infect and parasitic dis EC | K0B0.00 |
| Renal tubulo-interstitial disorder/ neoplastic diseases    | K0B1.00 |
| Ren tub-interst disordr/blood dis+disordr inv immune mech  | K0B2.00 |
| Renal tubulo-interstitial disorders in metabolic diseases  | K0B3.00 |
| Ren tub-interstitl disordr/systemc connectv tiss disorder  | K0B4.00 |
| Renal tubulo-interstitial disorder in SLE                  | K0B4000 |
| Renal tubulo-interstitial disorders in transplant rejectn  | K0B5.00 |

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|--|---------|
| Balkan nephropathy   | K0B6.00 |
| Drug/heavy-metal-induced tubulo-interstitial and tub conditn | K0C..00 |
| End-stage renal disease                                      | K0D..00 |
| Other specified nephritis, nephrosis or nephrotic syndrome   | K0y..00 |
| Nephritis, nephrosis and nephrotic syndrome NOS              | K0z..00 |
| Infections of kidney   | K10..00 |
| Renal infections   | K10..11 |
| Chronic pyelonephritis                                       | K100.00 |
| Acute pyelonephritis   | K101.00 |
| Renal and perinephric abscess                                | K102.00 |
| Renal abscess  | K102000 |
| Perinephric abscess  | K102100 |
| Renal carbuncle  | K102200 |
| Renal and perinephric abscess NOS                            | K102z00 |
| Pyeloureteritis cystica                                      | K103.00 |
| Ureteritis cystica   | K103.11 |
| Infestation of renal pelvis with ureter                      | K103.12 |
| Xanthogranulomatous pyelonephritis                           | K104.00 |
| Pyelonephritis and pyonephrosis unspecified                  | K10y.00 |
| Infection of kidney NOS                                      | K10z.00 |
| Hydronephrosis   | K11..00 |
| Hydrocalycosis   | K110.00 |
| Hydroureteronephrosis  | K111.00 |
| Hydronephrosis with renal and ureteral calculous obstruction | K112.00 |
| Hydronephrosis with ureteropelvic junction obstruction       | K113.00 |
| Hydronephrosis with pelviureteric junction obstruction       | K113.11 |
| Hydronephrosis with ureteral stricture NEC                   | K11X.00 |
| Hydronephrosis NOS   | K11z.00 |
| Calculus of kidney and ureter                                | K12..00 |
| Kidney calculus  | K12..11 |
| Urinary calculus   | K12..12 |
| Calculus of kidney   | K120.00 |
| Nephrolithiasis NOS  | K120.11 |
| Renal calculus   | K120.12 |
| Renal stone  | K120.13 |
| Staghorn calculus  | K120000 |
| Renal calculus NOS   | K120z00 |
| Calculus of ureter   | K121.00 |
| Ureteric calculus  | K121.11 |
| Ureteric stone   | K121.12 |
| Ureterolithiasis   | K121.13 |
| Calculus of kidney with calculus of ureter                   | K122.00 |
| Urinary calculus NOS   | K12z.00 |
| Other kidney and ureter disorders                            | K13..00 |
| Other kidney disorders                                       | K13..11 |
| Other ureter disorders                                       | K13..12 |

|  |         |
|--|---------|
| Nephroptosis                               | K130.00 |
| Floating kidney                            | K130.11 |
| Mobile kidney                              | K130.12 |
| Hypertrophy of kidney                      | K131.00 |
| Acquired cyst of kidney                    | K132.00 |
| Stricture of ureter                        | K133.00 |
| Other ureteric obstruction                 | K134.00 |
| Hydroureter                                | K135.00 |
| Benign postural proteinuria                | K136.00 |
| Orthostatic proteinuria                    | K136.11 |
| Vesicoureteric reflux                      | K137.00 |
| Ureteric reflux                            | K137.11 |
| Vascular disorders of kidney               | K138.00 |
| Renal vascular disorders                   | K138.11 |
| Renal artery embolism                      | K138000 |
| Renal artery embolus                       | K138011 |
| Renal artery haemorrhage                   | K138100 |
| Renal artery thrombosis                    | K138200 |
| Intrarenal haematoma                       | K138300 |
| Renal vascular disorders NOS               | K138z00 |
| Renal infarction                           | K138z11 |
| Other kidney and ureteric disorders        | K13y.00 |
| Ureteric fistula                           | K13y000 |
| Adhesions of kidney                        | K13y100 |
| Adhesions of ureter                        | K13y200 |
| Periureteritis                             | K13y300 |
| Pyelectasia                                | K13y400 |
| Polyp of ureter                            | K13y500 |
| Ureterocele - acquired                     | K13y600 |
| Idiopathic dilation of ureter              | K13y611 |
| Megaloureter - acquired                    | K13y700 |
| Perirenal haematoma                        | K13y800 |
| Ureteric neuromuscular incoordination      | K13y900 |
| Other kidney and ureteric disorders NOS    | K13yz00 |
| Salt-losing nephritis                      | K13yz11 |
| Kidney and ureter disease NOS              | K13z.00 |
| Lower urinary tract calculus               | K14..00 |
| Cystitis                                   | K15..00 |
| Other disorders of bladder                 | K16..00 |
| Urethritis due to non venereal causes      | K17..00 |
| Periurethritis                             | K17..11 |
| Urethral stricture                         | K18..00 |
| Pinhole meatus                             | K18..11 |
| Other urethral and urinary tract disorders | K19..00 |
| Other urethral disorders                   | K19..11 |
| Urinary calculus in schistosomiasis        | K1A..00 |



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| Other specified diseases of urinary system                       | K1y..00 |
| Other urinary system diseases NOS                                | K1z..00 |
| [X]Glomerular diseases   | Kyu0.00 |
| [X]Renal tubulo-interstitial diseases                            | Kyu1.00 |
| [X]Other chronic tubulo-interstitial nephritis                   | Kyu1000 |
| [X]Other and unspecified hydronephrosis                          | Kyu1100 |
| [X]Other obstructive and reflux uropathy                         | Kyu1200 |
| [X]Obstructive and reflux uropathy, unspecified                  | Kyu1300 |
| [X]Nephropathy induced by other drugs+biological substances      | Kyu1400 |
| [X]Toxic nephropathy, not elsewhere classified                   | Kyu1500 |
| [X]Other specified renal tubulo-interstitial diseases            | Kyu1600 |
| [X]Renal tubulo-interstitial disorder/infect+parasitic dis CE    | Kyu1700 |
| [X]Renal tubulo-interstitial disorders/neoplastic diseases CE    | Kyu1800 |
| [X]Renal tub-interstl disorder/bld dis+disorder incl imm mech CE | Kyu1900 |
| [X]Renal tubulo-interstitial disorders/metabolic diseases CE     | Kyu1A00 |
| [X]Renal tubul-interstitl disorders/connectiv tissu disorder CE  | Kyu1B00 |
| [X]Renal tubulo-interstitial disorders/transplant rejection      | Kyu1C00 |
| [X]Renal tubulo-interstitial disorders in other diseases CE      | Kyu1D00 |
| [X]Tubulo-interstit nephritis, not specif as acute or chron      | Kyu1E00 |
| [X]Hydronephrosis with ureteral stricture NEC                    | Kyu1F00 |
| [X]Renal failure   | Kyu2.00 |
| [X]Other acute renal failure                                     | Kyu2000 |
| [X]Other chronic renal failure                                   | Kyu2100 |
| [X]Urolithiasis  | Kyu3.00 |
| [X]Other disorders of kidney and ureter                          | Kyu4.00 |
| [X]Other disorders resulting/impaired renal tubular function     | Kyu4000 |
| [X]Other specified disorders of kidney and ureter                | Kyu4100 |
| [X]Oth disorders/kidney+ureter/infects+parasitic diseases CE     | Kyu4200 |
| [X]Other disorders of kidney+ureter in other diseases CE         | Kyu4300 |
| [X]Other diseases of urinary system                              | Kyu5.00 |
| [X]Other disorders of genitourinary tract                        | KyuA.00 |
| Incomplete spontaneous abortion with renal failure               | L041300 |
| Complete spontaneous abortion with renal failure                 | L042300 |
| Unspecified legal abortion with renal failure                    | L050300 |
| Incomplete legal abortion with renal failure                     | L051300 |
| Complete legal abortion with renal failure                       | L052300 |
| Unspecified illegal abortion with renal failure                  | L060300 |
| Incomplete illegal abortion with renal failure                   | L061300 |
| Complete illegal abortion with renal failure                     | L062300 |
| Unspecified abortion with renal failure                          | L070300 |
| Unspecified abortion with metabolic disorder                     | L070400 |
| Unspecified abortion with shock                                  | L070500 |
| Unspecified abortion with embolism                               | L070600 |
| Unspecified abortion with other specified complication           | L070w00 |
| Unspecified abortion with complication NOS                       | L070x00 |
| Unspecified abortion with no mention of complication             | L070y00 |

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| Unspecified abortion NOS                                     | L070z00 |
| Unspecified incomplete abortion +genital tract/pelvic infect | L071000 |
| Unspecified incomplete abortion + delayed/excess haemorrhage | L071100 |
| Unspecified complete abortion with renal failure             | L072300 |
| Failed attempted abortion with renal failure                 | L083.00 |
| Renal failure following abortive pregnancy                   | L093.00 |
| Oliguria following abortive pregnancy                        | L093000 |
| Acute renal failure following abortive pregnancy             | L093100 |
| Renal shutdown following abortive pregnancy                  | L093200 |
| Renal tubular necrosis following abortive pregnancy          | L093300 |
| Uraemia following abortive pregnancy                         | L093400 |
| Renal failure NOS following abortive pregnancy               | L093z00 |
| Renal hypertension in pregnancy/childbirth/puerperium        | L121.00 |
| Renal hypertension in pregnancy/childbirth/puerp unspecified | L121000 |
| Renal hypertension in pregnancy/childbirth/puerp - delivered | L121100 |
| Renal hypertension in preg/childb/puerp -deliv with p/n comp | L121200 |
| Renal hypertension in preg/childbirth/puerp - not delivered  | L121300 |
| Renal hypertension in preg/childb/puerp + p/n complication   | L121400 |
| Renal hypertension in pregnancy/childbirth/puerperium NOS    | L121z00 |
| Other pre-existing hypertension in preg/childbirth/puerp     | L122.00 |
| Pre-exist hyperten heart renal dis comp preg chldbirth/puerp | L128100 |
| Unspecified renal disease in pregnancy                       | L162.00 |
| Unspecified renal disease in pregnancy unspecified           | L162000 |
| Unspecified renal disease in pregnancy - delivered           | L162100 |
| Unspecified renal disease in pregnancy - del with p/n comp   | L162200 |
| Unspecified renal disease in pregnancy - not delivered       | L162300 |
| Unspecified renal disease in pregnancy with p/n complication | L162400 |
| Unspecified renal disease in pregnancy NOS                   | L162z00 |
| Acute renal failure following labour and delivery            | L393.00 |
| Post-delivery acute renal failure unspecified                | L393000 |
| Post-delivery acute renal failure - delivered with p/n prob  | L393100 |
| Post-delivery acute renal failure with postnatal problem     | L393200 |
| Post-delivery acute renal failure NOS                        | L393z00 |
| Renal agenesis and dysgenesis                                | PD0..00 |
| Renal agenesis, unspecified                                  | PD00.00 |
| Bilateral renal agenesis                                     | PD00000 |
| Unilateral renal agenesis                                    | PD00100 |
| Renal agenesis, unspecified NOS                              | PD00z00 |
| Congenital renal atrophy                                     | PD01.00 |
| Congenital absence of kidney                                 | PD02.00 |
| Hypoplasia of kidney   | PD03.00 |
| Bilateral renal hypoplasia                                   | PD03000 |
| Potter's syndrome  | PD03011 |
| Unilateral renal hypoplasia                                  | PD03100 |
| Dysplasia of kidney  | PD04.00 |
| Bilateral renal dysplasia                                    | PD04000 |

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| Bilateral renal dysgenesis                                   | PD04011 |
| Unilateral renal dysplasia                                   | PD04100 |
| Unilateral renal dysgenesis                                  | PD04111 |
| Dysplasia of kidney NOS                                      | PD04z00 |
| Renal agenesis or dysgenesis NOS                             | PD0z.00 |
| Congenital cystic kidney disease                             | PD1..00 |
| Congenital cystic renal disease                              | PD1..11 |
| Fibrocystic kidney   | PD1..12 |
| Polycystic kidney  | PD1..13 |
| Sponge kidney  | PD1..14 |
| Congenital renal cyst, single                                | PD10.00 |
| Polycystic kidney disease                                    | PD11.00 |
| Medullary cystic disease                                     | PD12.00 |
| Multicystic renal dysplasia                                  | PD13.00 |
| Multicystic kidney   | PD13.11 |
| Other specified congenital cystic kidney disease             | PD1y.00 |
| Fibrocystic kidney disease                                   | PD1y000 |
| Fibrocystic renal degeneration                               | PD1y011 |
| Other congenital cystic kidney disease NOS                   | PD1yz00 |
| Congenital cystic kidney disease NOS                         | PD1z.00 |
| Renal pelvis and ureter obstructive defects                  | PD2..00 |
| Atresia of ureter  | PD20.00 |
| Occlusion of ureter  | PD21.00 |
| Congenital ureteric valves                                   | PD21.11 |
| Congenital stricture of ureter                               | PD22.00 |
| Congenital stenosis of ureter                                | PD22.11 |
| Congenital hydronephrosis                                    | PD23.00 |
| Congenital dilated renal pelvis                              | PD23.11 |
| Congenital dilatation of ureter                              | PD24.00 |
| Hydroureter - congenital                                     | PD25.00 |
| Megaloureter - congenital                                    | PD26.00 |
| Ureterocele - congenital                                     | PD27.00 |
| Impervious ureter  | PD28.00 |
| Other specified obstructive defect of renal pelvis or ureter | PD2y.00 |
| Obstructive defect of renal pelvis or ureter NOS             | PD2z.00 |
| Other specified renal anomaly                                | PD3..00 |
| Accessory kidney   | PD30.00 |
| Duplication of kidney  | PD30.11 |
| Renal duplication NEC  | PD30.12 |
| Supernumerary kidney   | PD30.13 |
| Congenital calculus of kidney                                | PD31.00 |
| Congenital displaced kidney                                  | PD32.00 |
| Discoid kidney   | PD33.00 |
| Double kidney with double pelvis                             | PD34.00 |
| Duplex kidneys   | PD34.11 |
| Pyelon duplex  | PD34.12 |

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| Ectopic kidney                                 | PD35.00 |
| Pelvic kidney                                  | PD35.11 |
| Fusion of kidneys                              | PD36.00 |
| Giant kidney                                   | PD37.00 |
| Horseshoe kidney                               | PD38.00 |
| Hyperplasia of kidney                          | PD39.00 |
| Lobulation of kidney                           | PD3A.00 |
| Ren arcuatus                                   | PD3A.11 |
| Ren unguiformis                                | PD3A.12 |
| Malrotation of kidney                          | PD3B.00 |
| Triple kidney with triple pelvis               | PD3C.00 |
| Trifid kidney                                  | PD3C.11 |
| Pyelon triplex                                 | PD3C.12 |
| Enlarged kidney                                | PD3D.00 |
| Other specified renal anomaly NOS              | PD3z.00 |
| Other specified ureter anomalies               | PD4..00 |
| Absent ureter                                  | PD40.00 |
| Accessory ureter                               | PD41.00 |
| Deviation of ureter                            | PD42.00 |
| Displaced ureteric orifice                     | PD43.00 |
| Double ureter                                  | PD44.00 |
| Duplication of ureter                          | PD44.11 |
| Ectopic ureter                                 | PD45.00 |
| Congenital displacement of opening of ureter   | PD45.11 |
| Ectopic insertion of ureter                    | PD45.12 |
| Anomalous ureter implantation                  | PD46.00 |
| Congenital vesico-uretero-renal reflux         | PD47.00 |
| Other specified ureter anomaly NOS             | PD4z.00 |
| Exstrophy of urinary bladder                   | PD5..00 |
| Ectopia vesicae                                | PD5..11 |
| Ectopic bladder                                | PD5..12 |
| Urethra and bladder neck atresia and stenosis  | PD6..00 |
| Other specified bladder and urethral anomalies | PDy..00 |
| Urinary system anomalies NOS                   | PDz..00 |
| [D]Renal colic                                 | R080.00 |
| [D]Renal colic, unspecified                    | R080000 |
| [D]Ureteric colic                              | R080100 |
| [D]Renal colic NOS                             | R080z00 |
| [D]Dysuria                                     | R081.00 |
| [D]Retention of urine                          | R082.00 |
| [D]Incontinence of urine                       | R083.00 |
| [D]Micturition frequency and polyuria          | R084.00 |
| [D]Oliguria and anuria                         | R085.00 |
| [D]Other urination abnormality                 | R086.00 |
| [D]Difficulty with micturition                 | R086.11 |
| [D]Urethral discharge                          | R087.00 |

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| [D]Extravasation of urine                                   | R088.00 |
| [D]Other urinary system symptom                             | R08z.00 |
| [D]Urinary system symptoms NOS                              | R08zz00 |
| [D]Bladder filling defect                                   | R135000 |
| [D]Kidney filling defect                                    | R135100 |
| [D]Ureter filling defect                                    | R135200 |
| [D]Renal scarring   | R135300 |
| [D]Genitourinary x-ray or scan abnormality NOS              | R135z00 |
| [D]Renal function test abnormal                             | R144.00 |
| [D]Kidney function test abnormal                            | R144.11 |
| Kidney injury without open wound into cavity, unspecified   | S760000 |
| Kidney haematoma without mention of open wound into cavity  | S760100 |
| Renal haematoma without mention of open wound into cavity   | S760111 |
| Kidney laceration without mention of open wound into cavity | S760200 |
| Kidney parenchyma disruption without open wound to cavity   | S760300 |
| Kidney injury without mention of open wound into cavity NOS | S760z00 |
| Kidney injury with open wound into cavity, unspecified      | S761000 |
| Kidney haematoma with open wound into cavity                | S761100 |
| Renal haematoma with open wound into cavity                 | S761111 |
| Kidney laceration with open wound into cavity               | S761200 |
| Kidney parenchyma disruption with open wound into cavity    | S761300 |
| Kidney injury with open wound into cavity NOS               | S761z00 |
| Renal failure following crush syndrome                      | SK05.00 |
| Renal failure after crushing                                | SK05.11 |
| Traumatic anuria - crush syndrome                           | SK05.12 |
| Oliguria as a complication of care                          | SP15200 |
| Anuria as a complication of care                            | SP15300 |
| Renal failure as a complication of care                     | SP15400 |
| Kidney failure as a complication of care                    | SP15411 |
| Post operative renal failure                                | SP15412 |
| Uraemia - post operative                                    | SP15413 |
| Kidney transplant with complication, without blame          | TB00100 |
| Renal transplant with complication, without blame           | TB00111 |
| Kidney dialysis with complication, without blame            | TB11.00 |
| Renal dialysis with complication, without blame             | TB11.11 |

Table j-xii Codes for Diabetes with end organ damage

| description  | medcode |
|--|---------|
| Retinal abnormality - diabetes related                   | 2BBF.00 |
| O/E - diabetic maculopathy present both eyes             | 2BBL.00 |
| O/E - diabetic maculopathy absent both eyes              | 2BBM.00 |
| O/E - right eye background diabetic retinopathy          | 2BBP.00 |
| O/E - left eye background diabetic retinopathy           | 2BBQ.00 |
| O/E - right eye preproliferative diabetic retinopathy    | 2BBR.00 |
| O/E - left eye preproliferative diabetic retinopathy     | 2BBS.00 |
| O/E - right eye proliferative diabetic retinopathy       | 2BBT.00 |
| O/E - left eye proliferative diabetic retinopathy        | 2BBV.00 |
| O/E - right eye diabetic maculopathy                     | 2BBW.00 |
| O/E - left eye diabetic maculopathy                      | 2BBX.00 |
| O/E - sight threatening diabetic retinopathy             | 2BBo.00 |
| Foot abnormality - diabetes related                      | 2G51000 |
| O/E - Right diabetic foot at risk                        | 2G5A.00 |
| O/E - Left diabetic foot at risk                         | 2G5B.00 |
| Foot abnormality - diabetes related                      | 2G5C.00 |
| O/E - Right diabetic foot at low risk                    | 2G5E.00 |
| O/E - Right diabetic foot at moderate risk               | 2G5F.00 |
| O/E - Right diabetic foot at high risk                   | 2G5G.00 |
| O/E - Right diabetic foot - ulcerated                    | 2G5H.00 |
| O/E - Left diabetic foot at low risk                     | 2G5I.00 |
| O/E - Left diabetic foot at moderate risk                | 2G5J.00 |
| O/E - Left diabetic foot at high risk                    | 2G5K.00 |
| O/E - Left diabetic foot - ulcerated                     | 2G5L.00 |
| O/E - right chronic diabetic foot ulcer                  | 2G5V.00 |
| O/E - left chronic diabetic foot ulcer                   | 2G5W.00 |
| Pan retinal photocoagulation for diabetes                | 7276    |
| Diabetes mellitus with ketoacidosis                      | C101.00 |
| Diabetes mellitus, juvenile type, with ketoacidosis      | C101000 |
| Diabetes mellitus, adult onset, with ketoacidosis        | C101100 |
| Other specified diabetes mellitus with ketoacidosis      | C101y00 |
| Diabetes mellitus NOS with ketoacidosis                  | C101z00 |
| Diabetes mellitus with hyperosmolar coma                 | C102.00 |
| Diabetes mellitus, juvenile type, with hyperosmolar coma | C102000 |
| Diabetes mellitus, adult onset, with hyperosmolar coma   | C102100 |
| Diabetes mellitus NOS with hyperosmolar coma             | C102z00 |
| Diabetes mellitus with ketoacidotic coma                 | C103.00 |
| Diabetes mellitus, juvenile type, with ketoacidotic coma | C103000 |
| Diabetes mellitus, adult onset, with ketoacidotic coma   | C103100 |
| Other specified diabetes mellitus with coma              | C103y00 |
| Diabetes mellitus NOS with ketoacidotic coma             | C103z00 |
| Diabetes mellitus with renal manifestation               | C104.00 |
| Diabetic nephropathy                                     | C104.11 |

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| Diabetes mellitus, juvenile type, with renal manifestation   | C104000 |
| Diabetes mellitus, adult onset, with renal manifestation     | C104100 |
| Other specified diabetes mellitus with renal complications   | C104y00 |
| Diabetes mellitus with nephropathy NOS                       | C104z00 |
| Diabetes mellitus with ophthalmic manifestation              | C105.00 |
| Diabetes mellitus, juvenile type, + ophthalmic manifestation | C105000 |
| Diabetes mellitus, adult onset, + ophthalmic manifestation   | C105100 |
| Other specified diabetes mellitus with ophthalmic complicatn | C105y00 |
| Diabetes mellitus NOS with ophthalmic manifestation          | C105z00 |
| Diabetes mellitus with neurological manifestation            | C106.00 |
| Diabetic amyotrophy  | C106.11 |
| Diabetes mellitus with neuropathy                            | C106.12 |
| Diabetes mellitus with polyneuropathy                        | C106.13 |
| Diabetes mellitus, juvenile, + neurological manifestation    | C106000 |
| Diabetes mellitus, adult onset, + neurological manifestation | C106100 |
| Other specified diabetes mellitus with neurological comps    | C106y00 |
| Diabetes mellitus NOS with neurological manifestation        | C106z00 |
| Diabetes mellitus with peripheral circulatory disorder       | C107.00 |
| Diabetes mellitus with gangrene                              | C107.11 |
| Diabetes with gangrene                                       | C107.12 |
| Diabetes mellitus, juvenile +peripheral circulatory disorder | C107000 |
| Diabetes mellitus, adult, + peripheral circulatory disorder  | C107100 |
| Diabetes mellitus, adult with gangrene                       | C107200 |
| IDDM with peripheral circulatory disorder                    | C107300 |
| NIDDM with peripheral circulatory disorder                   | C107400 |
| Other specified diabetes mellitus with periph circ comps     | C107y00 |
| Insulin-dependent diabetes mellitus with renal complications | C108000 |
| Type I diabetes mellitus with renal complications            | C108011 |
| Type 1 diabetes mellitus with renal complications            | C108012 |
| Insulin-dependent diabetes mellitus with ophthalmic comps    | C108100 |
| Type I diabetes mellitus with ophthalmic complications       | C108111 |
| Type 1 diabetes mellitus with ophthalmic complications       | C108112 |
| Insulin-dependent diabetes mellitus with neurological comps  | C108200 |
| Type I diabetes mellitus with neurological complications     | C108211 |
| Type 1 diabetes mellitus with neurological complications     | C108212 |
| Insulin dependent diabetes mellitus with multiple complicatn | C108300 |
| Type I diabetes mellitus with multiple complications         | C108311 |
| Type 1 diabetes mellitus with multiple complications         | C108312 |
| Insulin dependent diabetes mellitus with ulcer               | C108500 |
| Type I diabetes mellitus with ulcer                          | C108511 |
| Type 1 diabetes mellitus with ulcer                          | C108512 |
| Insulin dependent diabetes mellitus with gangrene            | C108600 |
| Type I diabetes mellitus with gangrene                       | C108611 |
| Type 1 diabetes mellitus with gangrene                       | C108612 |
| Insulin dependent diabetes mellitus with retinopathy         | C108700 |
| Type I diabetes mellitus with retinopathy                    | C108711 |

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| Type 1 diabetes mellitus with retinopathy                   | C108712 |
| Insulin dependent diabetes mellitus with mononeuropathy     | C108B00 |
| Type I diabetes mellitus with mononeuropathy                | C108B11 |
| Type 1 diabetes mellitus with mononeuropathy                | C108B12 |
| Insulin dependent diabetes mellitus with polyneuropathy     | C108C00 |
| Type I diabetes mellitus with polyneuropathy                | C108C11 |
| Type 1 diabetes mellitus with polyneuropathy                | C108C12 |
| Insulin dependent diabetes mellitus with nephropathy        | C108D00 |
| Type I diabetes mellitus with nephropathy                   | C108D11 |
| Type 1 diabetes mellitus with nephropathy                   | C108D12 |
| Insulin dependent diabetes mellitus with hypoglycaemic coma | C108E00 |
| Type I diabetes mellitus with hypoglycaemic coma            | C108E11 |
| Type 1 diabetes mellitus with hypoglycaemic coma            | C108E12 |
| Insulin dependent diabetes mellitus with diabetic cataract  | C108F00 |
| Type I diabetes mellitus with diabetic cataract             | C108F11 |
| Type 1 diabetes mellitus with diabetic cataract             | C108F12 |
| Insulin dependent diab mell with peripheral angiopathy      | C108G00 |
| Type I diabetes mellitus with peripheral angiopathy         | C108G11 |
| Type 1 diabetes mellitus with peripheral angiopathy         | C108G12 |
| Insulin dependent diabetes mellitus with arthropathy        | C108H00 |
| Type I diabetes mellitus with arthropathy                   | C108H11 |
| Type 1 diabetes mellitus with arthropathy                   | C108H12 |
| Insulin dependent diab mell with neuropathic arthropathy    | C108J00 |
| Type I diabetes mellitus with neuropathic arthropathy       | C108J11 |
| Type 1 diabetes mellitus with neuropathic arthropathy       | C108J12 |
| Other specified diabetes mellitus with multiple comps       | C108y00 |
| Unspecified diabetes mellitus with multiple complications   | C108z00 |
| Non-insulin-dependent diabetes mellitus with renal comps    | C109000 |
| Type II diabetes mellitus with renal complications          | C109011 |
| Type 2 diabetes mellitus with renal complications           | C109012 |
| Non-insulin-dependent diabetes mellitus with ophthalm comps | C109100 |
| Type II diabetes mellitus with ophthalmic complications     | C109111 |
| Type 2 diabetes mellitus with ophthalmic complications      | C109112 |
| Non-insulin-dependent diabetes mellitus with neuro comps    | C109200 |
| Type II diabetes mellitus with neurological complications   | C109211 |
| Type 2 diabetes mellitus with neurological complications    | C109212 |
| Non-insulin-dependent diabetes mellitus with multiple comps | C109300 |
| Type II diabetes mellitus with multiple complications       | C109311 |
| Type 2 diabetes mellitus with multiple complications        | C109312 |
| Non-insulin dependent diabetes mellitus with ulcer          | C109400 |
| Type II diabetes mellitus with ulcer                        | C109411 |
| Type 2 diabetes mellitus with ulcer                         | C109412 |
| Non-insulin dependent diabetes mellitus with gangrene       | C109500 |
| Type II diabetes mellitus with gangrene                     | C109511 |
| Type 2 diabetes mellitus with gangrene                      | C109512 |
| Non-insulin-dependent diabetes mellitus with retinopathy    | C109600 |



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| Type II diabetes mellitus with retinopathy                   | C109611 |
| Type 2 diabetes mellitus with retinopathy                    | C109612 |
| Non-insulin dependent diabetes mellitus with mononeuropathy  | C109A00 |
| Type II diabetes mellitus with mononeuropathy                | C109A11 |
| Type 2 diabetes mellitus with mononeuropathy                 | C109A12 |
| Non-insulin dependent diabetes mellitus with polyneuropathy  | C109B00 |
| Type II diabetes mellitus with polyneuropathy                | C109B11 |
| Type 2 diabetes mellitus with polyneuropathy                 | C109B12 |
| Non-insulin dependent diabetes mellitus with nephropathy     | C109C00 |
| Type II diabetes mellitus with nephropathy                   | C109C11 |
| Type 2 diabetes mellitus with nephropathy                    | C109C12 |
| Non-insulin dependent diabetes mellitus with hypoglyca coma  | C109D00 |
| Type II diabetes mellitus with hypoglycaemic coma            | C109D11 |
| Type 2 diabetes mellitus with hypoglycaemic coma             | C109D12 |
| Non-insulin depend diabetes mellitus with diabetic cataract  | C109E00 |
| Type II diabetes mellitus with diabetic cataract             | C109E11 |
| Type 2 diabetes mellitus with diabetic cataract              | C109E12 |
| Non-insulin-dependent d m with peripheral angiopath          | C109F00 |
| Type II diabetes mellitus with peripheral angiopathy         | C109F11 |
| Type 2 diabetes mellitus with peripheral angiopathy          | C109F12 |
| Non-insulin dependent diabetes mellitus with arthropathy     | C109G00 |
| Type II diabetes mellitus with arthropathy                   | C109G11 |
| Type 2 diabetes mellitus with arthropathy                    | C109G12 |
| Non-insulin dependent d m with neuropathic arthropathy       | C109H00 |
| Type II diabetes mellitus with neuropathic arthropathy       | C109H11 |
| Type 2 diabetes mellitus with neuropathic arthropathy        | C109H12 |
| Hyperosmolar non-ketotic state in type 2 diabetes mellitus   | C109K00 |
| Malnutrition-related diabetes mellitus with coma             | C10A000 |
| Malnutrition-related diabetes mellitus with ketoacidosis     | C10A100 |
| Malnutrition-related diabetes mellitus with renal complicatn | C10A200 |
| Malnutrit-related diabetes mellitus wth ophthalmic complicat | C10A300 |
| Malnutrition-related diabetes mellitus wth neuro complicatns | C10A400 |
| Malnutritn-relat diabetes melitus wth periph circul complctn | C10A500 |
| Malnutrition-related diabetes mellitus with multiple comps   | C10A600 |
| Malnutrition-related diabetes mellitus without complications | C10A700 |
| Malnutrit-related diabetes mellitus with unspec complics     | C10AW00 |
| Malnutrit-relat diabetes mellitus with other spec comps      | C10AX00 |
| Type 1 diabetes mellitus with renal complications            | C10E000 |
| Type I diabetes mellitus with renal complications            | C10E011 |
| Insulin-dependent diabetes mellitus with renal complications | C10E012 |
| Type 1 diabetes mellitus with ophthalmic complications       | C10E100 |
| Type I diabetes mellitus with ophthalmic complications       | C10E111 |
| Insulin-dependent diabetes mellitus with ophthalmic comps    | C10E112 |
| Type 1 diabetes mellitus with neurological complications     | C10E200 |
| Type I diabetes mellitus with neurological complications     | C10E211 |
| Insulin-dependent diabetes mellitus with neurological comps  | C10E212 |

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| Type 1 diabetes mellitus with multiple complications        | C10E300 |
| Type I diabetes mellitus with multiple complications        | C10E311 |
| Insulin dependent diabetes mellitus with multiple complicat | C10E312 |
| Type 1 diabetes mellitus with ulcer                         | C10E500 |
| Type I diabetes mellitus with ulcer                         | C10E511 |
| Insulin dependent diabetes mellitus with ulcer              | C10E512 |
| Type 1 diabetes mellitus with gangrene                      | C10E600 |
| Type I diabetes mellitus with gangrene                      | C10E611 |
| Insulin dependent diabetes mellitus with gangrene           | C10E612 |
| Type 1 diabetes mellitus with retinopathy                   | C10E700 |
| Type I diabetes mellitus with retinopathy                   | C10E711 |
| Insulin dependent diabetes mellitus with retinopathy        | C10E712 |
| Type 1 diabetes mellitus with mononeuropathy                | C10EB00 |
| Type I diabetes mellitus with mononeuropathy                | C10EB11 |
| Insulin dependent diabetes mellitus with mononeuropathy     | C10EB12 |
| Type 1 diabetes mellitus with polyneuropathy                | C10EC00 |
| Type I diabetes mellitus with polyneuropathy                | C10EC11 |
| Insulin dependent diabetes mellitus with polyneuropathy     | C10EC12 |
| Type 1 diabetes mellitus with nephropathy                   | C10ED00 |
| Type I diabetes mellitus with nephropathy                   | C10ED11 |
| Insulin dependent diabetes mellitus with nephropathy        | C10ED12 |
| Type 1 diabetes mellitus with hypoglycaemic coma            | C10EE00 |
| Type I diabetes mellitus with hypoglycaemic coma            | C10EE11 |
| Insulin dependent diabetes mellitus with hypoglycaemic coma | C10EE12 |
| Type 1 diabetes mellitus with diabetic cataract             | C10EF00 |
| Type I diabetes mellitus with diabetic cataract             | C10EF11 |
| Insulin dependent diabetes mellitus with diabetic cataract  | C10EF12 |
| Type 1 diabetes mellitus with peripheral angiopathy         | C10EG00 |
| Type I diabetes mellitus with peripheral angiopathy         | C10EG11 |
| Insulin dependent diab mell with peripheral angiopathy      | C10EG12 |
| Type 1 diabetes mellitus with arthropathy                   | C10EH00 |
| Type I diabetes mellitus with arthropathy                   | C10EH11 |
| Insulin dependent diabetes mellitus with arthropathy        | C10EH12 |
| Type 1 diabetes mellitus with neuropathic arthropathy       | C10EJ00 |
| Type I diabetes mellitus with neuropathic arthropathy       | C10EJ11 |
| Insulin dependent diab mell with neuropathic arthropathy    | C10EJ12 |
| Type 1 diabetes mellitus with persistent proteinuria        | C10EK00 |
| Type I diabetes mellitus with persistent proteinuria        | C10EK11 |
| Type 1 diabetes mellitus with persistent microalbuminuria   | C10EL00 |
| Type I diabetes mellitus with persistent microalbuminuria   | C10EL11 |
| Type 1 diabetes mellitus with ketoacidosis                  | C10EM00 |
| Type I diabetes mellitus with ketoacidosis                  | C10EM11 |
| Type 1 diabetes mellitus with ketoacidotic coma             | C10EN00 |
| Type I diabetes mellitus with ketoacidotic coma             | C10EN11 |
| Type 1 diabetes mellitus with exudative maculopathy         | C10EP00 |
| Type I diabetes mellitus with exudative maculopathy         | C10EP11 |

|  |         |
|--|---------|
| Type 2 diabetes mellitus with renal complications            | C10F000 |
| Type II diabetes mellitus with renal complications           | C10F011 |
| Type 2 diabetes mellitus with ophthalmic complications       | C10F100 |
| Type II diabetes mellitus with ophthalmic complications      | C10F111 |
| Type 2 diabetes mellitus with neurological complications     | C10F200 |
| Type II diabetes mellitus with neurological complications    | C10F211 |
| Type 2 diabetes mellitus with multiple complications         | C10F300 |
| Type II diabetes mellitus with multiple complications        | C10F311 |
| Type 2 diabetes mellitus with ulcer                          | C10F400 |
| Type II diabetes mellitus with ulcer                         | C10F411 |
| Type 2 diabetes mellitus with gangrene                       | C10F500 |
| Type II diabetes mellitus with gangrene                      | C10F511 |
| Type 2 diabetes mellitus with retinopathy                    | C10F600 |
| Type II diabetes mellitus with retinopathy                   | C10F611 |
| Type 2 diabetes mellitus with mononeuropathy                 | C10FA00 |
| Type II diabetes mellitus with mononeuropathy                | C10FA11 |
| Type 2 diabetes mellitus with polyneuropathy                 | C10FB00 |
| Type II diabetes mellitus with polyneuropathy                | C10FB11 |
| Type 2 diabetes mellitus with nephropathy                    | C10FC00 |
| Type II diabetes mellitus with nephropathy                   | C10FC11 |
| Type 2 diabetes mellitus with hypoglycaemic coma             | C10FD00 |
| Type II diabetes mellitus with hypoglycaemic coma            | C10FD11 |
| Type 2 diabetes mellitus with diabetic cataract              | C10FE00 |
| Type II diabetes mellitus with diabetic cataract             | C10FE11 |
| Type 2 diabetes mellitus with peripheral angiopathy          | C10FF00 |
| Type II diabetes mellitus with peripheral angiopathy         | C10FF11 |
| Type 2 diabetes mellitus with arthropathy                    | C10FG00 |
| Type II diabetes mellitus with arthropathy                   | C10FG11 |
| Type 2 diabetes mellitus with neuropathic arthropathy        | C10FH00 |
| Type II diabetes mellitus with neuropathic arthropathy       | C10FH11 |
| Hyperosmolar non-ketotic state in type 2 diabetes mellitus   | C10FK00 |
| Type 2 diabetes mellitus with persistent proteinuria         | C10FL00 |
| Type II diabetes mellitus with persistent proteinuria        | C10FL11 |
| Type 2 diabetes mellitus with persistent microalbuminuria    | C10FM00 |
| Type II diabetes mellitus with persistent microalbuminuria   | C10FM11 |
| Type 2 diabetes mellitus with ketoacidosis                   | C10FN00 |
| Type II diabetes mellitus with ketoacidosis                  | C10FN11 |
| Type 2 diabetes mellitus with ketoacidotic coma              | C10FP00 |
| Type II diabetes mellitus with ketoacidotic coma             | C10FP11 |
| Type 2 diabetes mellitus with exudative maculopathy          | C10FQ00 |
| Type II diabetes mellitus with exudative maculopathy         | C10FQ11 |
| Other specified diabetes mellitus with other spec comps      | C10yy00 |
| Diabetes mellitus NOS with other specified manifestation     | C10yz00 |
| Diabetes mellitus with unspecified complication              | C10z.00 |
| Diabetes mellitus, juvenile type, + unspecified complication | C10z000 |
| Diabetes mellitus, adult onset, + unspecified complication   | C10z100 |

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|---|---------|
| Other specified diabetes mellitus with unspecified comps    | C10zy00 |
| Diabetes mellitus NOS with unspecified complication         | C10zz00 |
| [X]Malnutrit-relat diabetes mellitus with other spec comps  | Cyu2100 |
| [X]Malnutrit-related diabetes mellitus with unspec complics | Cyu2200 |
| [X]Unspecified diabetes mellitus with renal complications   | Cyu2300 |
| [X]Glomerular disorders in diabetes mellitus                | Kyu0300 |

Table j-xiii Codes for Any tumour

| description  | medcode |
|--|---------|
| Malignant neoplasm of eye                                    | B50..00 |
| Malignant neoplasm of brain                                  | B51..00 |
| Cerebral tumour - malignant                                  | B51..11 |
| Malig neop of other and unspecified parts of nervous system  | B52..00 |
| Malignant neoplasm of thyroid gland                          | B53..00 |
| Malig neop of other endocrine glands and related structures  | B54..00 |
| Malignant neoplasm of other and ill-defined sites            | B55..00 |
| Malignant neoplasm of unspecified site                       | B59..00 |
| Malignant neoplasm of other and unspecified site OS          | B5y..00 |
| Malignant neoplasm of other and unspecified site NOS         | B5z..00 |
| Malignant neoplasms of lymphoid and histiocytic tissue NOS   | B62z.00 |
| Benign neoplasm of parotid gland                             | B702000 |
| Adenoma of parotid gland                                     | B702011 |
| Benign neoplasm of submandibular gland                       | B702100 |
| Benign neoplasm of sublingual gland                          | B702200 |
| Warthin's tumour   | B702300 |
| Benign neoplasm of major salivary gland NOS                  | B702z00 |
| Benign islet cell tumour                                     | B717000 |
| Endocrine tumour of pancreas                                 | B717011 |
| Benign neoplasm of islets of Langerhans NOS                  | B717z00 |
| Benign neoplasm of brain                                     | B7F0.00 |
| Cerebral tumour - benign                                     | B7F0.11 |
| Benign neoplasm of cranial nerves                            | B7F1.00 |
| Benign neoplasm of cerebral meninges                         | B7F2.00 |
| Benign neoplasm of spinal cord                               | B7F3.00 |
| Benign neoplasm of spinal meninges                           | B7F4.00 |
| Benign neoplasm of meninges, unspecified                     | B7FX.00 |
| Benign neoplasm of other part of nervous system              | B7Fy.00 |
| Benign neoplasm of brain or other nervous system NOS         | B7Fz.00 |
| Haemangioma  | B7J0.00 |
| Glomus tumour  | B7J0.11 |
| Lymphangioma   | B7J1.00 |
| Congenital lymphangioma                                      | B7J1.11 |
| Naevus - lymphatic   | B7J1.12 |
| Haemangioma or lymphangioma NOS                              | B7Jz.00 |
| Neoplasm of uncertain behaviour of parotid gland             | B900000 |
| Mixed parotid tumour   | B900011 |
| Neoplasm of uncertain behaviour of sublingual gland          | B900100 |
| Neoplasm of uncertain behaviour of submandibular gland       | B900200 |
| Neoplasm of uncertain behaviour of major salivary gland NOS  | B900z00 |
| Neop of uncertain behaviour of bone and articular cartilage  | B930.00 |
| Neop of uncertain behaviour connective and other soft tissue | B931.00 |
| Neoplasm of uncertain behaviour of skin                      | B932.00 |

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|---|---------|
| Neoplasm of uncertain behaviour of breast                     | B933.00 |
| Cystosarcoma phyllodes  | B933.11 |
| Neoplasm of uncertain behaviour of histiocytic and mast cell  | B935.00 |
| Histiocytic tumour NOS  | B935.11 |
| Mastocytoma NOS   | B935.12 |
| Neoplasm of uncertain behaviour of plasma cells               | B936.00 |
| Myeloma - solitary  | B936.11 |
| Plasmacytoma NOS  | B936.12 |
| Neop uncertain behaviour other lymphatic/haematopoietic tiss  | B937.00 |
| Neoplasm of uncertain behaviour of blood                      | B937.11 |
| Neo/uncertain+unknown behav/lymph,h'ematopetc+rel tiss,unspcf | B93X.00 |
| Neoplasm of uncertain behaviour of other specified sites      | B93y.00 |
| Neop uncertain behaviour other unspec site and tissue NOS     | B93z.00 |
| [M]Tumour morphology  | BB...11 |
| [M]Neoplasms NOS  | BB0..00 |
| [M]Neoplasm, benign   | BB00.00 |
| [M]Neoplasm, uncertain whether benign or malignant            | BB01.00 |
| [M]Neoplasm, malignant  | BB02.00 |
| [M]Neoplasm, metastatic                                       | BB03.00 |
| [M]Secondary neoplasm   | BB03.11 |
| [M]Neoplasm, malig, uncertain whether primary or metastatic   | BB04.00 |
| [M]Tumour cells, benign                                       | BB05.00 |
| [M]Tumour cells, uncertain whether benign or malignant        | BB06.00 |
| [M]Tumour cells, malignant                                    | BB07.00 |
| [M]Malignant tumour, small cell type                          | BB08.00 |
| [M]Malignant tumour, giant cell type                          | BB09.00 |
| [M]Malignant tumour, fusiform cell type                       | BB0A.00 |
| [M]Unspecified tumour cell NOS                                | BB0z.00 |
| [M]Epithelial neoplasms NOS                                   | BB1..00 |
| [M]Epithelial tumour, benign                                  | BB10.00 |
| [M]Carcinoma in situ NOS                                      | BB11.00 |
| [M]Intraepithelial carcinoma NOS                              | BB11.11 |
| [M]Carcinoma NOS  | BB12.00 |
| [M]Carcinoma, metastatic, NOS                                 | BB13.00 |
| [M]Secondary carcinoma  | BB13.11 |
| [M]Carcinomatosis   | BB14.00 |
| [M]Epithelioma, benign  | BB15.00 |
| [M]Epithelioma, malignant                                     | BB16.00 |
| [M]Large cell carcinoma NOS                                   | BB17.00 |
| [M]Carcinoma, undifferentiated type, NOS                      | BB18.00 |
| [M]Carcinoma, anaplastic type, NOS                            | BB19.00 |
| [M]Pleomorphic carcinoma                                      | BB1A.00 |
| [M]Giant cell and spindle cell carcinoma                      | BB1B.00 |
| [M]Giant cell carcinoma                                       | BB1C.00 |
| [M]Spindle cell carcinoma                                     | BB1D.00 |
| [M]Pseudosarcomatous carcinoma                                | BB1E.00 |

|  |         |
|--|---------|
| [M]Polygonal cell carcinoma                    | BB1F.00 |
| [M]Spheroidal cell carcinoma                   | BB1G.00 |
| [M]Small cell carcinoma NOS                    | BB1J.00 |
| [M]Reserve cell carcinoma                      | BB1J.11 |
| [M]Round cell carcinoma                        | BB1J.12 |
| [M]Oat cell carcinoma                          | BB1K.00 |
| [M]Small cell carcinoma, fusiform cell type    | BB1L.00 |
| [M]Small cell carcinoma, intermediate cell     | BB1M.00 |
| [M]Small cell-large cell carcinoma             | BB1N.00 |
| [M]Unspecified epithelial neoplasm             | BB1z.00 |
| [M]Papillary and squamous cell neoplasms       | BB2..00 |
| [M]Papillary neoplasms                         | BB2..11 |
| [M]Squamous cell neoplasms                     | BB2..12 |
| [M]Basal cell neoplasms                        | BB3..00 |
| [M]Basal cell tumour                           | BB30.00 |
| [M]Basal cell carcinoma NOS                    | BB31.00 |
| [M]Multicentric basal cell carcinoma           | BB32.00 |
| [M]Basal cell carcinoma, morphoea type         | BB33.00 |
| [M]Basal cell carcinoma, fibroepithelial type  | BB34.00 |
| [M]Basosquamous carcinoma                      | BB35.00 |
| [M]Metatypical carcinoma                       | BB36.00 |
| [M]Intraepidermal epithelioma of Jadassohn     | BB37.00 |
| [M]Trichoepithelioma                           | BB38.00 |
| [M]Brooke's tumour                             | BB38.11 |
| [M]Epithelioma adenoides cyst                  | BB38.12 |
| [M]Trichofolliculoma                           | BB39.00 |
| [M]Tricholemmoma                               | BB3A.00 |
| [M]Pilomatrixoma                               | BB3B.00 |
| [M]Malherbe's calcified epithelioma            | BB3B.11 |
| [M]Basal cell neoplasm NOS                     | BB3z.00 |
| [M]Transitional cell papillomas and carcinomas | BB4..00 |
| [M]Adenomas and adenocarcinomas                | BB5..00 |
| [M]Adenocarcinomas                             | BB5..11 |
| [M]Adenomas                                    | BB5..12 |
| [M]Adenoma NOS                                 | BB50.00 |
| [M]Adenocarcinoma in situ                      | BB51.00 |
| [M]Adenocarcinoma NOS                          | BB52.00 |
| [M]Adenocarcinoma, metastatic, NOS             | BB53.00 |
| [M]Scirrhus adenocarcinoma                     | BB54.00 |
| [M]Linitis plastica                            | BB55.00 |
| [M]Superficial spreading adenocarcinoma        | BB56.00 |
| [M]Adenocarcinoma, intestinal type             | BB57.00 |
| [M]Carcinoma, diffuse type                     | BB58.00 |
| [M]Monomorphic adenoma                         | BB59.00 |
| [M]Basal cell adenoma                          | BB5A.00 |
| [M]Pancreatic adenomas and carcinomas          | BB5B.00 |

|   |         |
|---|---------|
| [M]Islet cell adenoma                                 | BB5B000 |
| [M]Nesidioblastoma                                    | BB5B011 |
| [M]Islet cell carcinoma                               | BB5B100 |
| [M]Insulinoma NOS                                     | BB5B200 |
| [M]Beta-cell adenoma                                  | BB5B211 |
| [M]Insulinoma, malignant                              | BB5B300 |
| [M]Beta-cell tumour, malignant                        | BB5B311 |
| [M]Glucagonoma NOS                                    | BB5B400 |
| [M]Alpha-cell adenoma                                 | BB5B411 |
| [M]Glucagonoma, malignant                             | BB5B500 |
| [M]Alpha-cell tumour,malignant                        | BB5B511 |
| [M]Mixed islet cell and exocrine adenocarcinoma       | BB5B600 |
| [M]Pancreatic adenoma or carcinoma NOS                | BB5Bz00 |
| [M]Gastrinoma and carcinomas                          | BB5C.00 |
| [M]Gastrinoma NOS                                     | BB5C000 |
| [M]G cell tumour NOS                                  | BB5C011 |
| [M]Gastrinoma, malignant                              | BB5C100 |
| [M]G cell tumour, malignant                           | BB5C111 |
| [M]Gastrinoma or carcinoma NOS                        | BB5Cz00 |
| [M]Hepatobiliary tract adenomas and carcinomas        | BB5D.00 |
| [M]Biliary tract adenomas and adenocarcinomas         | BB5D.11 |
| [M]Trabecular adenoma                                 | BB5E.00 |
| [M]Trabecular adenocarcinoma                          | BB5F.00 |
| [M]Embryonal adenoma                                  | BB5G.00 |
| [M]Eccrine dermal cylindroma                          | BB5H.00 |
| [M]Turban tumour                                      | BB5H.11 |
| [M]Adenoid cystic carcinoma                           | BB5J.00 |
| [M]Cylindroid adenocarcinoma                          | BB5J.11 |
| [M]Cylindroid bronchial adenoma                       | BB5J.12 |
| [M]Cylindroma NOS                                     | BB5J.13 |
| [M]Cribriform carcinoma                               | BB5K.00 |
| [M]Adenomatous and adenocarcinomatous polyps          | BB5L.00 |
| [M]Tubular adenomas and adenocarcinomas               | BB5M.00 |
| [M]Adenomatous and adenocarcinomatous polyps of colon | BB5N.00 |
| [M]Adenoma or or adenocarcinoma in polyposis coli     | BB5N.11 |
| [M]Solid carcinoma NOS                                | BB5P.00 |
| [M]Carcinoma simplex                                  | BB5Q.00 |
| [M]Carcinoid tumours                                  | BB5R.00 |
| [M]Carcinoid tumour NOS                               | BB5R000 |
| [M]Carcinoid tumour, malignant                        | BB5R100 |
| [M]Carcinoid bronchial adenoma                        | BB5R111 |
| [M]Carcinoid tumour, argentaffin, NOS                 | BB5R200 |
| [M]Argentaffinoma NOS                                 | BB5R211 |
| [M]Carcinoid tumour, argentaffin, malignant           | BB5R300 |
| [M]Carcinoid tumour, nonargentaffin, NOS              | BB5R400 |
| [M]Carcinoid tumour, nonargentaffin, malignant        | BB5R500 |



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| [M]Mucocarcinoid tumour, malignant                     | BB5R600 |
| [M]Goblet cell tumour                                  | BB5R611 |
| [M]Composite carcinoid                                 | BB5R700 |
| [M]Adenocarcinoid tumour                               | BB5R800 |
| [M]Neuroendocrine carcinoma                            | BB5R900 |
| [M]Merkel cell carcinoma                               | BB5RA00 |
| [M]Carcinoid tumours NOS                               | BB5Rz00 |
| [M]Respiratory tract adenomas and adenocarcinomas      | BB5S.00 |
| [M]Papillary adenomas and adenocarcinomas              | BB5T.00 |
| [M]Villous adenomas and adenocarcinomas                | BB5U.00 |
| [M]Pituitary adenomas and carcinomas                   | BB5V.00 |
| [M]Oxyphilic adenomas and adenocarcinomas              | BB5W.00 |
| [M]Clear cell adenomas and adenocarcinomas             | BB5X.00 |
| [M]Hypernephroid tumour                                | BB5Y.00 |
| [M]Clear cell adenofibroma                             | BB5Z.00 |
| [M]Renal adenoma and carcinoma                         | BB5a.00 |
| [M]Renal cell carcinoma                                | BB5a000 |
| [M]Grawitz tumour                                      | BB5a011 |
| [M]Hypernephroma                                       | BB5a012 |
| [M]Juxtaglomerular tumour                              | BB5a100 |
| [M]Reninoma  | BB5a111 |
| [M]Renal adenoma or carcinoma NOS                      | BB5az00 |
| [M]Granular cell carcinoma                             | BB5b.00 |
| [M]Parathyroid adenomas and adenocarcinomas            | BB5c.00 |
| [M]Mixed cell adenoma and adenocarcinoma               | BB5d.00 |
| [M]Lipoadenoma   | BB5e.00 |
| [M]Thyroid adenoma and adenocarcinoma                  | BB5f.00 |
| [M]Multiple endocrine adenomas                         | BB5g.00 |
| [M]Adrenal cortical tumours                            | BB5h.00 |
| [M]Adrenal cortical adenoma NOS                        | BB5h000 |
| [M]Adrenal cortical carcinoma                          | BB5h100 |
| [M]Adrenal cortical adenoma, compact cell type         | BB5h200 |
| [M]Adrenal cortical adenoma, heavily pigmented variant | BB5h300 |
| [M]Black adenoma                                       | BB5h311 |
| [M]Adrenal cortical adenoma, clear cell type           | BB5h400 |
| [M]Adrenal cortical adenoma, glomerulosa cell type     | BB5h500 |
| [M]Adrenal cortical adenoma, mixed cell type           | BB5h600 |
| [M]Adrenal cortical tumours NOS                        | BB5hz00 |
| [M]Endometrioid adenomas and carcinomas                | BB5j.00 |
| [M]Adenoma and adenocarcinoms OS                       | BB5y.00 |
| [M]Basal cell adenocarcinoma                           | BB5y000 |
| [M]Vipoma  | BB5y100 |
| [M]Klatskin's tumour                                   | BB5y200 |
| [M]Apudoma   | BB5y300 |
| [M]Prolactinoma  | BB5y400 |
| [M]Lipid-rich carcinoma                                | BB5y500 |

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|--|---------|
| [M]Glycogen-rich carcinoma                               | BB5y600 |
| [M]Adenoma or adenocarcinoma NOS                         | BB5z.00 |
| [M]Adnexal and skin appendage neoplasms                  | BB6..00 |
| [M]Sweat gland adenoma                                   | BB61000 |
| [M]Hidradenoma NOS                                       | BB61011 |
| [M]Nodular hidradenoma                                   | BB61012 |
| [M]Syringadenoma NOS                                     | BB61013 |
| [M]Sweat gland tumour NOS                                | BB61100 |
| [M]Sweat gland adenocarcinoma                            | BB61200 |
| [M]Sweat gland adenoma or adenocarcinoma NOS             | BB61z00 |
| [M]Mucoepidermoid neoplasms                              | BB7..00 |
| [M]Mucoepidermoid tumour                                 | BB70.00 |
| [M]Mucoepidermoid carcinoma                              | BB71.00 |
| [M]Mucoepidermoid neoplasm NOS                           | BB7z.00 |
| [M]Cystic, mucinous and serous neoplasms                 | BB8..00 |
| [M]Cystadenoma and carcinoma                             | BB80.00 |
| [M]Ovarian cystic, mucinous and serous neoplasms         | BB81.00 |
| [M]Ovarian cystadenoma or carcinoma                      | BB81.11 |
| [M]Ovarian mucinous tumour                               | BB81.12 |
| [M]Ovarian papillary tumour                              | BB81.13 |
| [M]Ovarian serous tumour                                 | BB81.14 |
| [M]Serous cystadenoma NOS                                | BB81000 |
| [M]Serous cystadenoma, borderline malignancy             | BB81100 |
| [M]Serous cystadenocarcinoma, NOS                        | BB81200 |
| [M]Papillary cystadenoma NOS                             | BB81300 |
| [M]Papillary cystadenoma, borderline malignancy          | BB81400 |
| [M]Papillary cystadenocarcinoma, NOS                     | BB81500 |
| [M]Papillary serous cystadenoma NOS                      | BB81600 |
| [M]Papillary serous cystadenoma, borderline malignancy   | BB81700 |
| [M]Papillary serous cystadenocarcinoma                   | BB81800 |
| [M]Serous surface papilloma NOS                          | BB81900 |
| [M]Serous surface papilloma, borderline malignancy       | BB81A00 |
| [M]Serous surface papillary carcinoma                    | BB81B00 |
| [M]Mucinous cystadenoma NOS                              | BB81C00 |
| [M]Pseudomucinous cystadenoma NOS                        | BB81C11 |
| [M]Mucinous cystadenoma, borderline malignancy           | BB81D00 |
| [M]Mucinous cystadenocarcinoma NOS                       | BB81E00 |
| [M]Pseudomucinous adenocarcinoma                         | BB81E11 |
| [M]Papillary mucinous cystadenoma NOS                    | BB81F00 |
| [M]Papillary mucinous cystadenoma, borderline malignancy | BB81G00 |
| [M]Papillary mucinous cystadenocarcinoma                 | BB81H00 |
| [M]Serous cystadenoma, borderline malignancy             | BB81J00 |
| [M]Papillary cystadenoma, borderline malignancy          | BB81K00 |
| [M]Papillary cystic tumour                               | BB81L00 |
| [M]Papillary serous cystadenoma, borderline malignancy   | BB81M00 |
| [M]Ovarian cystic, mucinous or serous neoplasm NOS       | BB81z00 |

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| [M]Mucinous adenoma and adenocarcinoma                      | BB82.00 |
| [M]Pseudomyxoma peritonei                                   | BB83.00 |
| [M]Mucin-producing adenocarcinoma                           | BB84.00 |
| [M]Signet ring carcinoma                                    | BB85.00 |
| [M]Signet ring cell carcinoma                               | BB85000 |
| [M]Metastatic signet ring cell carcinoma                    | BB85100 |
| [M]Krukenberg tumour  | BB85111 |
| [M]Signet ring carcinoma NOS                                | BB85z00 |
| [M]Cystic, mucinous or serous neoplasm NOS                  | BB8z.00 |
| [M]Ductal, lobular and medullary neoplasms                  | BB9..00 |
| [M]Acinar cell neoplasms                                    | BBA..00 |
| [M]Acinar cell adenoma                                      | BBA0.00 |
| [M]Acinar cell tumour                                       | BBA1.00 |
| [M]Acinar cell carcinoma                                    | BBA2.00 |
| [M]Acinar cell neoplasm NOS                                 | BBAz.00 |
| [M]Complex epithelial neoplasms                             | BBB..00 |
| [M]Adenosquamous carcinoma                                  | BBB0.00 |
| [M]Adenolymphoma  | BBB1.00 |
| [M]Warthin's tumour   | BBB1.11 |
| [M]Adenocarcinoma with squamous metaplasia                  | BBB2.00 |
| [M]Adenoacanthoma   | BBB2.11 |
| [M]Adenocarcinoma with cartilaginous and osseous metaplasia | BBB3.00 |
| [M]Adenocarcinoma with spindle cell metaplasia              | BBB4.00 |
| [M]Adenocarcinoma with apocrine metaplasia                  | BBB5.00 |
| [M]Thymoma  | BBB6.00 |
| [M]Epithelial-myoepithelial carcinoma                       | BBB7.00 |
| [M]Complex epithelial neoplasm NOS                          | BBBz.00 |
| [M]Specialised gonadal neoplasms                            | BBC..00 |
| [M]Sex cord-stromal tumour                                  | BBC0.00 |
| [M]Gonadal stromal tumour                                   | BBC0.11 |
| [M]Ovarian stromal tumour                                   | BBC0.12 |
| [M]Testicular stromal tumour                                | BBC0.13 |
| [M]Sex cord tumour with annular tubules                     | BBC0000 |
| [M]Thecal cell neoplasms                                    | BBC1.00 |
| [M]Luteoma NOS  | BBC2.00 |
| [M]Luteinoma  | BBC2.11 |
| [M]Granulosa cell tumour NOS                                | BBC3.00 |
| [M]Juvenile granulosa cell tumour                           | BBC3000 |
| [M]Granulosa cell tumour, malignant                         | BBC4.00 |
| [M]Granulosa cell-theca cell tumour                         | BBC5.00 |
| [M]Androblastoma  | BBC6.00 |
| [M]Sertoli-Leydig cell tumour                               | BBC7.00 |
| [M]Gynandroblastoma   | BBC8.00 |
| [M]Tubular androblastoma NOS                                | BBC9.00 |
| [M]Pick's tubular adenoma                                   | BBC9.11 |
| [M]Sertoli cell adenoma                                     | BBC9.12 |

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| [M]Sertoli cell tumour                      | BBC9.13 |
| [M]Testicular adenoma                       | BBC9.14 |
| [M]Sertoli cell carcinoma                   | BBCA.00 |
| [M]Tubular androblastoma with lipid storage | BBCB.00 |
| [M]Sertoli cell tumour with lipid storage   | BBCB.11 |
| [M]Leydig cell tumour                       | BBCC.00 |
| [M]Leydig cell tumour, benign               | BBCC000 |
| [M]Interstitial cell tumour, benign         | BBCC011 |
| [M]Leydig cell tumour, malignant            | BBCC100 |
| [M]Interstitial cell tumour, malignant      | BBCC111 |
| [M]Leydig cell tumour NOS                   | BBCCz00 |
| [M]Interstitial cell tumour NOS             | BBCCz11 |
| [M]Hilar cell tumour                        | BBCD.00 |
| [M]Lipid cell tumour of ovary               | BBCE.00 |
| [M]Masculinovoblastoma                      | BBCE.11 |
| [M]Adrenal rest tumour                      | BBCF.00 |
| [M]Sclerosing stromal tumour                | BBCG.00 |
| [M]Specialised gonadal neoplasm NOS         | BBCz.00 |
| [M]Paragangliomas and glomus tumours        | BBD..00 |
| [M]Paraganglioma NOS                        | BBD0.00 |
| [M]Paraganglioma, malignant                 | BBD1.00 |
| [M]Sympathetic paraganglioma                | BBD2.00 |
| [M]Parasympathetic paraganglioma            | BBD3.00 |
| [M]Glomus jugulare tumour                   | BBD4.00 |
| [M]Jugular paraganglioma                    | BBD4.11 |
| [M]Aortic body tumour                       | BBD5.00 |
| [M]Carotid body tumour                      | BBD6.00 |
| [M]Extra-adrenal paraganglioma, NOS         | BBD7.00 |
| [M]Chemodectoma                             | BBD7.11 |
| [M]Extra-adrenal paraganglioma, malignant   | BBD8.00 |
| [M]Pheochromocytoma NOS                     | BBD9.00 |
| [M]Chromaffin paraganglioma                 | BBD9.11 |
| [M]Chromaffin tumour                        | BBD9.12 |
| [M]Chromaffinoma                            | BBD9.13 |
| [M]Pheochromocytoma, malignant              | BBDA.00 |
| [M]Pheochromoblastoma                       | BBDA.11 |
| [M]Glomangiosarcoma                         | BBDB.00 |
| [M]Glomoid sarcoma                          | BBDB.11 |
| [M]Glomus tumour                            | BBDC.00 |
| [M]Glomangioma                              | BBDD.00 |
| [M]Gangliocytic paraganglioma               | BBDE.00 |
| [M]Glomangiomyoma                           | BBDF.00 |
| [M]Paraganglioma or glomus tumour NOS       | BBDz.00 |
| [M]Naevi and melanomas                      | BBE..00 |
| [M]Soft tissue tumours and sarcomas NOS     | BBF..00 |
| [M]Soft tissue tumour, benign               | BBF0.00 |

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| [M]Sarcoma NOS                           | BBF1.00 |
| [M]Sarcomatosis NOS                      | BBF2.00 |
| [M]Spindle cell sarcoma                  | BBF3.00 |
| [M]Giant cell sarcoma (except of bone)   | BBF4.00 |
| [M]Pleomorphic cell sarcoma              | BBF4.11 |
| [M]Small cell sarcoma                    | BBF5.00 |
| [M]Round cell sarcoma                    | BBF5.11 |
| [M]Epithelioid cell sarcoma              | BBF6.00 |
| [M]Soft tissue tumour or sarcoma NOS     | BBFz.00 |
| [M]Fibromatous neoplasms                 | BBG..00 |
| [M]Myxomatous neoplasms                  | BBH..00 |
| [M]Lipomatous neoplasms                  | BBJ..00 |
| [M]Lipoma NOS                            | BBJ0.00 |
| [M]Liposarcoma NOS                       | BBJ1.00 |
| [M]Fibroliposarcoma                      | BBJ1.11 |
| [M]Fibrolipoma                           | BBJ2.00 |
| [M]Fibroma molle                         | BBJ2.11 |
| [M]Soft fibroma                          | BBJ2.12 |
| [M]Liposarcoma, well differentiated type | BBJ3.00 |
| [M]Fibromyxolipoma                       | BBJ4.00 |
| [M]Myxolipoma                            | BBJ4.11 |
| [M]Myxoid liposarcoma                    | BBJ5.00 |
| [M]Embryonal liposarcoma                 | BBJ5.11 |
| [M]Myxoliposarcoma                       | BBJ5.12 |
| [M]Round cell liposarcoma                | BBJ6.00 |
| [M]Pleomorphic liposarcoma               | BBJ7.00 |
| [M]Mixed type liposarcoma                | BBJ8.00 |
| [M]Intramuscular lipoma                  | BBJ9.00 |
| [M]Infiltrating lipoma                   | BBJ9.11 |
| [M]Spindle cell lipoma                   | BBJA.00 |
| [M]Angiolipomatous neoplasms             | BBJB.00 |
| [M]Myelolipoma                           | BBJC.00 |
| [M]Hibernoma                             | BBJD.00 |
| [M]Brown fat tumour                      | BBJD.11 |
| [M]Fetal fat cell lipoma                 | BBJD.12 |
| [M]Lipoblastomatosis                     | BBJE.00 |
| [M]Fetal lipoma NOS                      | BBJE.11 |
| [M]Pleomorphic lipoma                    | BBJF.00 |
| [M]Dedifferentiated liposarcoma          | BBJH.00 |
| [M]Lipomatous neoplasms NOS              | BBJz.00 |
| [M]Myomatous neoplasms                   | BBK..00 |
| [M]Rhabdomyoma NOS                       | BBK3000 |
| [M]Rhabdomyosarcoma NOS                  | BBK3100 |
| [M]Pleomorphic rhabdomyosarcoma          | BBK3200 |
| [M]Mixed cell rhabdomyosarcoma           | BBK3300 |
| [M]Fetal rhabdomyoma                     | BBK3400 |

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| [M]Adult rhabdomyoma                     | BBK3500 |
| [M]Glycogenic rhabdomyoma                | BBK3511 |
| [M]Embryonal rhabdomyosarcoma            | BBK3600 |
| [M]Sarcoma botryoides                    | BBK3611 |
| [M]Alveolar rhabdomyosarcoma             | BBK3700 |
| [M]Smooth muscle tumour NOS              | BBK3800 |
| [M]Rhabdomyomatous neoplasm NOS          | BBK3z00 |
| [M]Complex mixed and stromal neoplasms   | BBL..00 |
| [M]Endometrial stromal sarcoma           | BBL0.00 |
| [M]Endolymphatic stromal myosis          | BBL1.00 |
| [M]Stromal endometriosis                 | BBL1.11 |
| [M]Adenomyoma                            | BBL2.00 |
| [M]Pleomorphic adenoma                   | BBL3.00 |
| [M]Chondroid syringoma                   | BBL3.11 |
| [M]Mixed tumour NOS                      | BBL3.12 |
| [M]Mixed tumour, malignant, NOS          | BBL4.00 |
| [M]Mullerian mixed tumour                | BBL5.00 |
| [M]Mesodermal mixed tumour               | BBL6.00 |
| [M]Mixed and stromal renal neoplasms     | BBL7.00 |
| [M]Nephromas and nephroblastomas         | BBL7.11 |
| [M]Mesoblastic nephroma                  | BBL7000 |
| [M]Nephroblastoma NOS                    | BBL7100 |
| [M]Adenosarcoma                          | BBL7111 |
| [M]Wilms' tumour                         | BBL7112 |
| [M]Epithelial nephroblastoma             | BBL7200 |
| [M]Mesenchymal nephroblastoma            | BBL7300 |
| [M]Mixed or stromal renal neoplasm NOS   | BBL7z00 |
| [M]Hepatoblastoma                        | BBL8.00 |
| [M]Embryonal hepatoma                    | BBL8.11 |
| [M]Carcinosarcoma NOS                    | BBL9.00 |
| [M]Carcinosarcoma, embryonal type        | BBLA.00 |
| [M]Pneumoblastoma                        | BBLA.11 |
| [M]Myoepithelioma                        | BBLB.00 |
| [M]Mesenchymomas                         | BBLC.00 |
| [M]Embryonal sarcoma                     | BBLD.00 |
| [M]Adenosarcoma                          | BBLE.00 |
| [M]Endometrial stromal nodule            | BBLF.00 |
| [M]Carcinoma in pleomorphic adenoma      | BBLG.00 |
| [M]Rhabdoid sarcoma                      | BBLH.00 |
| [M]Clear cell sarcoma of kidney          | BBLJ.00 |
| [M]Pancreatoblastoma                     | BBLK.00 |
| [M]Pulmonary blastoma                    | BBLM.00 |
| [M]Complex mixed or stromal neoplasm NOS | BBLz.00 |
| [M]Fibroepithelial neoplasms             | BBM..00 |
| [M]Brenner tumours                       | BBM0.00 |
| [M]Brenner tumour, borderline malignancy | BBM0000 |

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| [M]Brenner tumour, malignant              | BBM0100 |
| [M]Brenner tumour NOS                     | BBM0z00 |
| [M]Fibroadenoma NOS                       | BBM1.00 |
| [M]Intracanalicular fibroadenoma NOS      | BBM2.00 |
| [M]Pericanalicular fibroadenoma           | BBM3.00 |
| [M]Adenofibroma NOS                       | BBM4.00 |
| [M]Cystadenofibroma NOS                   | BBM4.11 |
| [M]Serous adenofibroma                    | BBM5.00 |
| [M]Mucinous adenofibroma                  | BBM6.00 |
| [M]Cellular intracanalicular fibroadenoma | BBM7.00 |
| [M]Cystosarcoma phyllodes, benign         | BBM7.11 |
| [M]Fibroadenoma phyllodes                 | BBM7.12 |
| [M]Giant fibroadenoma NOS                 | BBM7.13 |
| [M]Giant intracanalicular fibroadenoma    | BBM7.14 |
| [M]Cystosarcoma phyllodes NOS             | BBM8.00 |
| [M]Cystosarcoma phyllodes, malignant      | BBM9.00 |
| [M]Juvenile fibroadenoma                  | BBMA.00 |
| [M]Giant fibroadenoma                     | BBMB.00 |
| [M]Fibroepithelial neoplasm NOS           | BBMz.00 |
| [M]Synovial neoplasms                     | BBN..00 |
| [M]Mesothelial neoplasms                  | BBP..00 |
| [M]Mesothelioma, benign                   | BBP0.00 |
| [M]Mesothelioma, malignant                | BBP1.00 |
| [M]Fibrous mesothelioma, benign           | BBP2.00 |
| [M]Fibrous mesothelioma, malignant        | BBP3.00 |
| [M]Epithelioid mesothelioma, benign       | BBP4.00 |
| [M]Epithelioid mesothelioma, malignant    | BBP5.00 |
| [M]Mesothelioma, biphasic type, benign    | BBP6.00 |
| [M]Mesothelioma, biphasic type, malignant | BBP7.00 |
| [M]Adenomatoid tumour NOS                 | BBP8.00 |
| [M]Cystic mesothelioma                    | BBP9.00 |
| [M]Mesothelioma, unspecified              | BBPX.00 |
| [M]Mesothelial neoplasm NOS               | BBPz.00 |
| [M]Germ cell neoplasms                    | BBQ..00 |
| [M]Dysgerminoma                           | BBQ0.00 |
| [M]Seminomas                              | BBQ1.00 |
| [M]Germinoma                              | BBQ2.00 |
| [M]Embryonal carcinoma NOS                | BBQ3.00 |
| [M]Endodermal sinus tumour                | BBQ4.00 |
| [M]Infantile embryonal carcinoma          | BBQ4.11 |
| [M]Orchioblastoma                         | BBQ4.12 |
| [M]Polyvesicular vitelline tumour         | BBQ4.13 |
| [M]Yolk sac tumour                        | BBQ4.14 |
| [M]Polyembryoma                           | BBQ5.00 |
| [M]Polyembryonal embryonal carcinoma      | BBQ5.11 |
| [M]Gonadoblastoma                         | BBQ6.00 |

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| [M]Gonocytoma                                 | BBQ6.11 |
| [M]Teratomas                                  | BBQ7.00 |
| [M]Dermoid cyst                               | BBQ8.00 |
| [M]Dermoid NOS                                | BBQ8.11 |
| [M]Dermoid cyst with malignant transformation | BBQ9.00 |
| [M]Strumal neoplasms                          | BBQA.00 |
| [M]Mixed germ cell tumour                     | BBQB.00 |
| [M]Germ cell neoplasm NOS                     | BBQz.00 |
| [M]Trophoblastic neoplasms                    | BBR..00 |
| [M]Hydatidiform mole NOS                      | BBR0.00 |
| [M]Hydatid mole                               | BBR0.11 |
| [M]Invasive hydatidiform mole                 | BBR1.00 |
| [M]Chorioadenoma                              | BBR1.11 |
| [M]Chorioadenoma destruens                    | BBR1.12 |
| [M]Invasive mole NOS                          | BBR1.13 |
| [M]Choriocarcinoma                            | BBR2.00 |
| [M]Chorioepithelioma                          | BBR2.11 |
| [M]Choriocarcinoma combined with teratoma     | BBR3.00 |
| [M]Malignant teratoma, trophoblastic          | BBR4.00 |
| [M]Partial hydatidiform mole                  | BBR5.00 |
| [M]Placental site trophoblastic tumour        | BBR6.00 |
| [M]Classical hydatidiform mole                | BBR7.00 |
| [M]Complete hydatidiform mole                 | BBR8.00 |
| [M]Trophoblastic neoplasm NOS                 | BBRz.00 |
| [M]Mesonephromas                              | BBS..00 |
| [M]Mesonephroma, benign                       | BBS0.00 |
| [M]Wolffian duct adenoma                      | BBS0.11 |
| [M]Mesonephric tumour                         | BBS1.00 |
| [M]Mesonephroma, malignant                    | BBS2.00 |
| [M]Wolffian duct carcinoma                    | BBS2.11 |
| [M]Endosalpingioma                            | BBS3.00 |
| [M]Mesonephroma NOS                           | BBSz.00 |
| [M]Blood vessel tumours                       | BBT..00 |
| [M]Haemangiomas tumours                       | BBT..11 |
| [M]Haemangioma NOS                            | BBT0.00 |
| [M]Angioma NOS                                | BBT0.11 |
| [M]Chorioangioma                              | BBT0.12 |
| [M]Haemangiosarcoma                           | BBT1.00 |
| [M]Angiosarcoma                               | BBT1.11 |
| [M]Cavernous haemangioma                      | BBT2.00 |
| [M]Venous haemangioma                         | BBT3.00 |
| [M]Racemose haemangioma                       | BBT4.00 |
| [M]Arteriovenous haemangioma                  | BBT4.11 |
| [M]Kupffer cell sarcoma                       | BBT5.00 |
| [M]Haemangioendothelioma                      | BBT7.00 |
| [M]Capillary haemangioma                      | BBT8.00 |



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| [M]Haemangioma simplex                          | BBT8.11 |
| [M]Infantile haemangioma                        | BBT8.12 |
| [M]Juvenile haemangioma                         | BBT8.13 |
| [M]Plexiform haemangioma                        | BBT8.14 |
| [M]Intramuscular haemangioma                    | BBT9.00 |
| [M]Kaposi's sarcoma                             | BBTA.00 |
| [M]Multiple haemorrhagic sarcoma                | BBTA.11 |
| [M]Angiokeratoma                                | BBTB.00 |
| [M]Verrucous keratotic haemangioma              | BBTC.00 |
| [M]Haemangiopericytic neoplasms                 | BBTD.00 |
| [M]Angiofibroma NOS                             | BBTE.00 |
| [M]Juvenile angiofibroma                        | BBTE.11 |
| [M]Haemangioblastoma                            | BBTF.00 |
| [M]Angioblastoma                                | BBTF.11 |
| [M]Epithelioid haemangioma                      | BBTG.00 |
| [M]Histiocytoid haemangioma                     | BBTH.00 |
| [M]Epithelioid haemangioendothelioma NOS        | BBTJ.00 |
| [M]Epithelioid haemangioendothelioma, malignant | BBTK.00 |
| [M]Intravascular bronchial alveolar tumour      | BBTL.00 |
| [M]Blood vessel tumour NOS                      | BBTz.00 |
| [M]Lymphatic vessel tumours                     | BBU..00 |
| [M]Lymphangiomatous tumours                     | BBU..11 |
| [M]Lymphangioma NOS                             | BBU0.00 |
| [M]Lymphangiosarcoma                            | BBU1.00 |
| [M]Capillary lymphangioma                       | BBU2.00 |
| [M]Cavernous lymphangioma                       | BBU3.00 |
| [M]Cystic lymphangioma                          | BBU4.00 |
| [M]Cystic hygroma                               | BBU4.11 |
| [M]Hygroma                                      | BBU4.12 |
| [M]Lymphangiomyoma                              | BBU5.00 |
| [M]Lymphangiomyomatosis                         | BBU6.00 |
| [M]Haemolymphangioma                            | BBU7.00 |
| [M]Lymphatic vessel tumour NOS                  | BBUz.00 |
| [M]Osteomas and osteosarcomas                   | BBV..00 |
| [M]Juxtacortical osteogenic sarcoma             | BBV..11 |
| [M]Parosteal osteosarcoma                       | BBV..12 |
| [M]Periosteal osteogenic sarcoma                | BBV..13 |
| [M]Chondromatous neoplasms                      | BBW..00 |
| [M]Osteochondroma                               | BBW0.00 |
| [M]Cartilaginous exostosis                      | BBW0.11 |
| [M]Ecchondroma                                  | BBW0.12 |
| [M]Osteocartilaginous exostosis                 | BBW0.13 |
| [M]Osteochondromatosis NOS                      | BBW1.00 |
| [M]Ecchondrosis                                 | BBW1.11 |
| [M]Chondroma NOS                                | BBW2.00 |
| [M]Enchondroma                                  | BBW2.11 |

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| [M]Chondromatosis NOS                        | BBW3.00 |
| [M]Chondrosarcoma NOS                        | BBW4.00 |
| [M]Fibrochondrosarcoma                       | BBW4.11 |
| [M]Juxtacortical chondroma                   | BBW5.00 |
| [M]Periosteal chondroma                      | BBW5.11 |
| [M]Juxtacortical chondrosarcoma              | BBW6.00 |
| [M]Chondroblastoma NOS                       | BBW7.00 |
| [M]Chondromatous giant cell tumour           | BBW7.11 |
| [M]Codman's tumour                           | BBW7.12 |
| [M]Chondroblastoma, malignant                | BBW8.00 |
| [M]Mesenchymal chondrosarcoma                | BBW9.00 |
| [M]Chondromyxoid fibroma                     | BBWA.00 |
| [M]Chondromatous neoplasm NOS                | BBWz.00 |
| [M]Giant cell tumours                        | BBX..00 |
| [M]Giant cell tumour of bone NOS             | BBX0.00 |
| [M]Osteoclastoma                             | BBX0.11 |
| [M]Giant cell tumour of bone, malignant      | BBX1.00 |
| [M]Giant cell bone sarcoma                   | BBX1.11 |
| [M]Osteoclastoma, malignant                  | BBX1.12 |
| [M]Giant cell tumour of soft parts NOS       | BBX2.00 |
| [M]Malignant giant cell tumour of soft parts | BBX3.00 |
| [M]Giant cell tumour NOS                     | BBXz.00 |
| [M]Miscellaneous bone tumours                | BBY..00 |
| [M]Ewing's sarcoma                           | BBY0.00 |
| [M]Endothelial bone sarcoma                  | BBY0.11 |
| [M]Adamantinoma of long bones                | BBY1.00 |
| [M]Tibial adamantinoma                       | BBY1.11 |
| [M]Ossifying fibroma                         | BBY2.00 |
| [M]Ossifying fibroma                         | BBY2.11 |
| [M]Osteofibroma                              | BBY2.12 |
| [M]Miscellaneous bone tumour NOS             | BBYz.00 |
| [M]Odontogenic tumours                       | BBZ..00 |
| [M]Odontogenic tumour, benign                | BBZ0.00 |
| [M]Odontogenic tumour NOS                    | BBZ1.00 |
| [M]Odontogenic tumour, malignant             | BBZ2.00 |
| [M]Intraosseous carcinoma                    | BBZ2.11 |
| [M]Dentinoma                                 | BBZ3.00 |
| [M]Cementoma NOS                             | BBZ4.00 |
| [M]Cementoblastoma, benign                   | BBZ5.00 |
| [M]Cementifying fibroma                      | BBZ6.00 |
| [M]Gigantiform cementoma                     | BBZ7.00 |
| [M]Odontoma NOS                              | BBZ8.00 |
| [M]Compound odontoma                         | BBZ9.00 |
| [M]Complex odontoma                          | BBZA.00 |
| [M]Ameloblastic fibro-odontoma               | BBZB.00 |
| [M]Ameloblastic odontosarcoma                | BBZC.00 |

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| [M]Adenomatoid odontogenic tumour           | BBZD.00 |
| [M]Adenoameloblastoma                       | BBZD.11 |
| [M]Calcifying odontogenic cyst              | BBZE.00 |
| [M]Ameloblastoma NOS                        | BBZF.00 |
| [M]Adamantinoma NOS                         | BBZF.11 |
| [M]Ameloblastoma, malignant                 | BBZG.00 |
| [M]Adamantinoma, malignant                  | BBZG.11 |
| [M]Odontoameloblastoma                      | BBZH.00 |
| [M]Squamous odontogenic tumour              | BBZJ.00 |
| [M]Odontogenic myxoma                       | BBZK.00 |
| [M]Odontogenic myxofibroma                  | BBZK.11 |
| [M]Odontogenic fibroma NOS                  | BBZL.00 |
| [M]Ameloblastic fibroma                     | BBZM.00 |
| [M]Ameloblastic fibrosarcoma                | BBZN.00 |
| [M]Odontogenic fibrosarcoma                 | BBZN.11 |
| [M]Calcifying epithelial odontogenic tumour | BBZP.00 |
| [M]Odontogenic tumour NOS                   | BBZz.00 |
| [M]Miscellaneous tumours                    | BBa..00 |
| [M]Craniopharyngioma                        | BBa0.00 |
| [M]Rathke's pouch tumour                    | BBa0.11 |
| [M]Pinealoma                                | BBa1.00 |
| [M]Pineocytoma                              | BBa2.00 |
| [M]Pineoblastoma                            | BBa3.00 |
| [M]Melanotic neuroectodermal tumour         | BBa4.00 |
| [M]Melanoameloblastoma                      | BBa4.11 |
| [M]Melanotic progonoma                      | BBa4.12 |
| [M]Retinal angle tumour                     | BBa4.13 |
| [M]Chordoma                                 | BBa5.00 |
| [M]Miscellaneous tumour NOS                 | BBaz.00 |
| [M]Gliomas                                  | BBb..00 |
| [M]Glioma, malignant                        | BBb0.00 |
| [M]Glioma NOS                               | BBb0.11 |
| [M]Gliosarcoma                              | BBb0.12 |
| [M]Gliomatosis cerebri                      | BBb1.00 |
| [M]Mixed glioma                             | BBb2.00 |
| [M]Mixed glioma                             | BBb2.11 |
| [M]Subependymal glioma                      | BBb3.00 |
| [M]Subependymal astrocytoma NOS             | BBb3.11 |
| [M]Subependymal astrocytoma NOS             | BBb3.12 |
| [M]Subependymoma                            | BBb3.13 |
| [M]Subependymal giant cell astrocytoma      | BBb4.00 |
| [M]Choroid plexus papilloma NOS             | BBb5.00 |
| [M]Choroid plexus papilloma, malignant      | BBb6.00 |
| [M]Ependymoma NOS                           | BBb7.00 |
| [M]Ependymoma, anaplastic type              | BBb8.00 |
| [M]Ependymoblastoma                         | BBb8.11 |

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| [M]Papillary ependymoma                    | BBb9.00 |
| [M]Myxopapillary ependymoma                | BBbA.00 |
| [M]Astrocytoma NOS                         | BBbB.00 |
| [M]Astrocytic glioma                       | BBbB.11 |
| [M]Astroganglioma                          | BBbB.12 |
| [M]Astrocytoma, anaplastic type            | BBbC.00 |
| [M]Protoplasmic astrocytoma                | BBbD.00 |
| [M]Gemistocytic astrocytoma                | BBbE.00 |
| [M]Gemistocytoma                           | BBbE.11 |
| [M]Fibrillary astrocytoma                  | BBbF.00 |
| [M]Pilocytic astrocytoma                   | BBbG.00 |
| [M]Juvenile astrocytoma                    | BBbG.11 |
| [M]Piloid astrocytoma                      | BBbG.12 |
| [M]Spongioblastoma NOS                     | BBbH.00 |
| [M]Spongioblastoma polare                  | BBbJ.00 |
| [M]Astroblastoma                           | BBbK.00 |
| [M]Glioblastoma NOS                        | BBbL.00 |
| [M]Glioblastoma multiforme                 | BBbL.11 |
| [M]Spongioblastoma multiforme              | BBbL.12 |
| [M]Giant cell glioblastoma                 | BBbM.00 |
| [M]Glioblastoma with sarcomatous component | BBbN.00 |
| [M]Primitive polar spongioblastoma         | BBbP.00 |
| [M]Oligodendroglioma NOS                   | BBbQ.00 |
| [M]Oligodendroglioma, anaplastic type      | BBbR.00 |
| [M]Oligodendroblastoma                     | BBbS.00 |
| [M]Medulloblastoma NOS                     | BBbT.00 |
| [M]Desmoplastic medulloblastoma            | BBbU.00 |
| [M]Medullomyoblastoma                      | BBbV.00 |
| [M]Cerebellar sarcoma NOS                  | BBbW.00 |
| [M]Monstrocellular sarcoma                 | BBbX.00 |
| [M]Pleomorphic xanthoastrocytoma           | BBbZ.00 |
| [M]Primitive neuroectodermal tumour        | BBba.00 |
| [M]Glioma NOS                              | BBbz.00 |
| [M]Neuroepitheliomatous neoplasms          | BBc..00 |
| [M]Ganglioneuromatous neoplasms            | BBc0.00 |
| [M]Neuroblastoma NOS                       | BBc1.00 |
| [M]Sympathicoblastoma                      | BBc1.11 |
| [M]Sympathicogonioma                       | BBc1.12 |
| [M]Sympathogonioma                         | BBc1.13 |
| [M]Medulloepithelioma NOS                  | BBc2.00 |
| [M]Diktyoma                                | BBc2.11 |
| [M]Teratoid medulloepithelioma             | BBc3.00 |
| [M]Neuroepithelioma NOS                    | BBc4.00 |
| [M]Spongioneuroblastoma                    | BBc5.00 |
| [M]Ganglioglioma                           | BBc6.00 |
| [M]Glioneuroma                             | BBc6.11 |

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| [M]Neurocytoma   | BBc7.00 |
| [M]Neuroastrocytoma  | BBc7.11 |
| [M]Pacinian tumour   | BBc8.00 |
| [M]Retinoblastomas   | BBc9.00 |
| [M]Olfactory neurogenic tumour                               | BBcA.00 |
| [M]Aesthesioneurocytoma                                      | BBcB.00 |
| [M]Aesthesioneuroblastoma                                    | BBcC.00 |
| [M]Olfactory neuroblastoma                                   | BBcC.11 |
| [M]Aesthesioneuroepithelioma                                 | BBcD.00 |
| [M]Olfactory neuroepithelioma                                | BBcD.11 |
| [M]Neuroepitheliomatous neoplasm NOS                         | BBcz.00 |
| [M]Meningiomas   | BBd..00 |
| [M]Nerve sheath tumour                                       | BBe..00 |
| [M]Neurofibromas   | BBe..11 |
| [M]Neurofibroma NOS  | BBe0.00 |
| [M]Neurofibromatosis NOS                                     | BBe1.00 |
| [M]Multiple neurofibromatosis                                | BBe1.11 |
| [M]Von Recklinghausen's disease                              | BBe1.12 |
| [M]Neurofibrosarcoma   | BBe2.00 |
| [M]Melanotic neurofibroma                                    | BBe3.00 |
| [M]Plexiform neurofibroma                                    | BBe4.00 |
| [M]Neurilemmoma NOS  | BBe5.00 |
| [M]Acoustic neuroma  | BBe5.11 |
| [M]Neurinoma   | BBe5.12 |
| [M]Schwannoma NOS  | BBe5.13 |
| [M]Neurinomatosis  | BBe6.00 |
| [M]Neurilemmoma, malignant                                   | BBe7.00 |
| [M]Schwannoma, malignant                                     | BBe7.11 |
| [M]Neuroma NOS   | BBe8.00 |
| [M]Triton tumour, malignant                                  | BBe9.00 |
| [M]Neurothekeoma   | BBeA.00 |
| [M]Nerve sheath tumour NOS                                   | BBez.00 |
| [M]Granular cell tumours and alveolar soft part sarcoma      | BBf..00 |
| [M]Granular cell tumour NOS                                  | BBf0.00 |
| [M]Granular cell tumour, malignant                           | BBf1.00 |
| [M]Alveolar soft part sarcoma                                | BBf2.00 |
| [M]Granular cell tumour or alveolar soft part sarcoma NOS    | BBfz.00 |
| Tumour of uterine body in pregnancy/childbirth/puerperium    | L241.00 |
| Uterine fibroids in pregnancy, childbirth and the puerperium | L241.11 |
| Tumour of uterine body affecting obstetric care              | L241000 |
| Uterine fibroid affecting obstetric care                     | L241011 |
| Tumour of uterine body - baby delivered                      | L241100 |
| Uterine fibroid - baby delivered                             | L241111 |
| Tumour of uterine body - baby delivered + p/n complication   | L241200 |
| Uterine fibroid - baby delivered + postpartum complication   | L241211 |
| Tumour of uterine body complicating a/n care, baby not deliv | L241300 |

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| Uterine fibroid complicating a/n care, baby not delivered    | L241311 |
| Tumour of uterine body complic p/n care, baby prev delivered | L241400 |
| Uterine fibroid complicating p/n care - baby delivered prev  | L241411 |
| Uterine body tumour in pregnancy/childbirth/puerperium NOS   | L241z00 |
| Uterine fibroid in pregnancy/childbirth/puerperium NOS       | L241z11 |
| Polyp of cervix in pregnancy, childbirth and the puerperium  | L246.11 |
| Pelvic soft tissue abnormality in pregnancy/childbirth/puerp | L24z.00 |
| Monostotic fibrous dysplasia                                 | N332300 |
| Fibrous cortical defect                                      | N332400 |
| Brown tumour of hyperparathyroidism                          | N332500 |

Table j-xiv Codes for Leukaemia

| description                            | medcode |
|--|---------|
| H/O: * leukaemia                       | 1429    |
| Suspected leukaemia                    | 1J02.00 |
| Plasma cell leukaemia                  | B631.00 |
| Lymphoid leukaemia                     | B64..00 |
| Lymphatic leukaemia                    | B64..11 |
| Acute lymphoid leukaemia               | B640.00 |
| Chronic lymphoid leukaemia             | B641.00 |
| Chronic lymphatic leukaemia            | B641.11 |
| Subacute lymphoid leukaemia            | B642.00 |
| Other lymphoid leukaemia               | B64y.00 |
| Aleukaemic lymphoid leukaemia          | B64y000 |
| Prolymphocytic leukaemia               | B64y100 |
| Adult T-cell leukaemia                 | B64y200 |
| Other lymphoid leukaemia NOS           | B64yz00 |
| Lymphoid leukaemia NOS                 | B64z.00 |
| Myeloid leukaemia                      | B65..00 |
| Acute myeloid leukaemia                | B650.00 |
| Chronic myeloid leukaemia              | B651.00 |
| Chronic granulocytic leukaemia         | B651.11 |
| Chronic eosinophilic leukaemia         | B651000 |
| Chronic neutrophilic leukaemia         | B651200 |
| Chronic myeloid leukaemia NOS          | B651z00 |
| Subacute myeloid leukaemia             | B652.00 |
| Other myeloid leukaemia                | B65y.00 |
| Aleukaemic myeloid leukaemia           | B65y000 |
| Acute promyelocytic leukaemia          | B65y100 |
| Other myeloid leukaemia NOS            | B65yz00 |
| Myeloid leukaemia NOS                  | B65z.00 |
| Monocytic leukaemia                    | B66..00 |
| Histiocytic leukaemia                  | B66..11 |
| Monoblastic leukaemia                  | B66..12 |
| Acute monocytic leukaemia              | B660.00 |
| Chronic monocytic leukaemia            | B661.00 |
| Subacute monocytic leukaemia           | B662.00 |
| Other monocytic leukaemia              | B66y.00 |
| Aleukaemic monocytic leukaemia         | B66y000 |
| Other monocytic leukaemia NOS          | B66yz00 |
| Monocytic leukaemia NOS                | B66z.00 |
| Other specified leukaemia              | B67..00 |
| Acute erythraemia and erythroleukaemia | B670.00 |
| Megakaryocytic leukaemia               | B672.00 |
| Thrombocytic leukaemia                 | B672.11 |
| Mast cell leukaemia                    | B673.00 |

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|--|---------|
| Other and unspecified leukaemia          | B67y.00 |
| Lymphosarcoma cell leukaemia             | B67y000 |
| Other and unspecified leukaemia NOS      | B67yz00 |
| Other specified leukaemia NOS            | B67z.00 |
| Leukaemia of unspecified cell type       | B68..00 |
| Acute leukaemia NOS                      | B680.00 |
| Chronic leukaemia NOS                    | B681.00 |
| Subacute leukaemia NOS                   | B682.00 |
| Other leukaemia of unspecified cell type | B68y.00 |
| Leukaemia NOS                            | B68z.00 |
| Myelomonocytic leukaemia                 | B69..00 |
| Acute myelomonocytic leukaemia           | B690.00 |
| Chronic myelomonocytic leukaemia         | B691.00 |
| Subacute myelomonocytic leukaemia        | B692.00 |
| [M]Leukaemias                            | BBr..00 |
| [M]Leukaemias unspecified                | BBr0.00 |
| [M]Leukaemia NOS                         | BBr0000 |
| [M]Acute leukaemia NOS                   | BBr0100 |
| [M]Blast cell leukaemia                  | BBr0111 |
| [M]Blastic leukaemia                     | BBr0112 |
| [M]Stem cell leukaemia                   | BBr0113 |
| [M]Subacute leukaemia NOS                | BBr0200 |
| [M]Chronic leukaemia NOS                 | BBr0300 |
| [M]Aleukaemic leukaemia NOS              | BBr0400 |
| [M]Leukaemia unspecified, NOS            | BBr0z00 |
| [M]Compound leukaemias                   | BBr1.00 |
| [M]Compound leukaemia                    | BBr1000 |
| [M]Mixed leukaemia                       | BBr1011 |
| [M]Compound leukaemia NOS                | BBr1z00 |
| [M]Lymphoid leukaemias                   | BBr2.00 |
| [M]Lymphoid leukaemia NOS                | BBr2000 |
| [M]Lymphatic leukaemia                   | BBr2011 |
| [M]Acute lymphoid leukaemia              | BBr2100 |
| [M]Subacute lymphoid leukaemia           | BBr2200 |
| [M]Chronic lymphoid leukaemia            | BBr2300 |
| [M]Aleukaemic lymphoid leukaemia         | BBr2400 |
| [M]Prolymphocytic leukaemia              | BBr2500 |
| [M]Burkitt's cell leukaemia              | BBr2600 |
| [M]Adult T-cell leukaemia/lymphoma       | BBr2700 |
| [M]Other lymphoid leukaemia NOS          | BBr2z00 |
| [M]Plasma cell leukaemias                | BBr3.00 |
| [M]Plasma cell leukaemia                 | BBr3000 |
| [M]Plasma cell leukaemia NOS             | BBr3z00 |
| [M]Erythroleukaemias                     | BBr4.00 |
| [M]Erythroleukaemia                      | BBr4000 |
| [M]Erythraemic myelosis                  | BBr4011 |



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|---------------------------------------|---------|
| [M]Di Guglielmo's disease             | BBr4111 |
| [M]Chronic erythraemia                | BBr4200 |
| [M]Erythroleukaemia NOS               | BBr4z00 |
| [M]Lymphosarcoma cell leukaemias      | BBr5.00 |
| [M]Lymphosarcoma cell leukaemia       | BBr5000 |
| [M]Lymphosarcoma cell leukaemia NOS   | BBr5z00 |
| [M]Myeloid leukaemias                 | BBr6.00 |
| [M]Myeloid leukaemia NOS              | BBr6000 |
| [M]Granulocytic leukaemia NOS         | BBr6011 |
| [M]Acute myeloid leukaemia            | BBr6100 |
| [M]Subacute myeloid leukaemia         | BBr6200 |
| [M]Chronic myeloid leukaemia          | BBr6300 |
| [M]Naegeli-type monocytic leukaemia   | BBr6311 |
| [M]Aleukaemic myeloid leukaemia       | BBr6400 |
| [M]Neutrophilic leukaemia             | BBr6500 |
| [M]Acute promyelocytic leukaemia      | BBr6600 |
| [M]Acute myelomonocytic leukaemia     | BBr6700 |
| [M]Chronic myelomonocytic leukaemia   | BBr6800 |
| [M]Other myeloid leukaemia NOS        | BBr6z00 |
| [M]Basophilic leukaemias              | BBr7.00 |
| [M]Basophilic leukaemia               | BBr7000 |
| [M]Basophilic leukaemia NOS           | BBr7z00 |
| [M]Eosinophilic leukaemias            | BBr8.00 |
| [M]Eosinophilic leukaemia             | BBr8000 |
| [M]Eosinophilic leukaemia NOS         | BBr8z00 |
| [M]Monocytic leukaemias               | BBr9.00 |
| [M]Monocytic leukaemia NOS            | BBr9000 |
| [M]Histiocytic leukaemia              | BBr9011 |
| [M]Schilling-type monocytic leukaemia | BBr9012 |
| [M]Acute monocytic leukaemia          | BBr9100 |
| [M]Subacute monocytic leukaemia       | BBr9200 |
| [M]Chronic monocytic leukaemia        | BBr9300 |
| [M]Aleukaemic monocytic leukaemia     | BBr9400 |
| [M]Other monocytic leukaemia NOS      | BBr9z00 |
| [M]Miscellaneous leukaemias           | BBrA.00 |
| [M]Mast cell leukaemia                | BBrA000 |
| [M]Megakaryocytic leukaemia           | BBrA100 |
| [M]Thrombocytic leukaemia             | BBrA111 |
| [M]Hairy cell leukaemia               | BBrA400 |
| [M]Leukaemic reticuloendotheliosis    | BBrA411 |
| [M]Acute megakaryoblastic leukaemia   | BBrA500 |
| [M]Leukaemic reticuloendotheliosis    | BBrA800 |
| [M]Miscellaneous leukaemia NOS        | BBrAz00 |
| [M]Leukaemia NOS                      | BBrz.00 |
| [X]Other lymphoid leukaemia           | ByuD500 |
| [X]Other myeloid leukaemia            | ByuD600 |

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| [X]Other monocytic leukaemia                | ByuD700 |
| [X]Other specified leukaemias               | ByuD800 |
| [X]Other leukaemia of unspecified cell type | ByuD900 |
| [V]Personal history of leukaemia            | ZV10600 |
| [V]Personal history of lymphoid leukaemia   | ZV10611 |
| [V]Personal history of monocytic leukaemia  | ZV10612 |
| [V]Personal history of myeloid leukaemia    | ZV10613 |

Table j-xv Codes for Lymphoma

| description  | medcode |
|--|---------|
| Lymphoma stage I   | 4M20.00 |
| Lymphoma stage II  | 4M21.00 |
| Lymphoma stage III   | 4M22.00 |
| Lymphoma stage IV  | 4M23.00 |
| HIV disease resulting in Burkitt's lymphoma                  | A789600 |
| HIV dis resulting oth types of non-Hodgkin's lymphoma        | A789700 |
| [X]HIV disease resulting in other non-Hodgkin's lymphoma     | AyuC600 |
| Lymphosarcoma  | B601.00 |
| Burkitt's lymphoma   | B602.00 |
| Burkitt's lymphoma of unspecified site                       | B602000 |
| Burkitt's lymphoma of lymph nodes of head, face and neck     | B602100 |
| Burkitt's lymphoma of intrathoracic lymph nodes              | B602200 |
| Burkitt's lymphoma of intra-abdominal lymph nodes            | B602300 |
| Burkitt's lymphoma of lymph nodes of axilla and upper limb   | B602400 |
| Burkitt's lymphoma of lymph nodes of inguinal region and leg | B602500 |
| Burkitt's lymphoma of intrapelvic lymph nodes                | B602600 |
| Burkitt's lymphoma of spleen                                 | B602700 |
| Burkitt's lymphoma of lymph nodes of multiple sites          | B602800 |
| Burkitt's lymphoma NOS                                       | B602z00 |
| Other specified reticulosarcoma or lymphosarcoma             | B60y.00 |
| Reticulosarcoma or lymphosarcoma NOS                         | B60z.00 |
| Nodular lymphoma (Brill - Symmers disease)                   | B620.00 |
| Reticulosarcoma - follicular or nodular                      | B620.11 |
| Nodular lymphoma of unspecified site                         | B620000 |
| Nodular lymphoma of lymph nodes of head, face and neck       | B620100 |
| Nodular lymphoma of intrathoracic lymph nodes                | B620200 |
| Nodular lymphoma of intra-abdominal lymph nodes              | B620300 |
| Nodular lymphoma of lymph nodes of axilla and upper limb     | B620400 |
| Nodular lymphoma of lymph nodes of inguinal region and leg   | B620500 |
| Nodular lymphoma of intrapelvic lymph nodes                  | B620600 |
| Nodular lymphoma of spleen                                   | B620700 |
| Nodular lymphoma of lymph nodes of multiple sites            | B620800 |
| Nodular lymphoma NOS   | B620z00 |
| Mycosis fungoides  | B621.00 |
| Sezary's disease   | B622.00 |
| Malignant histiocytosis                                      | B623.00 |
| Malignant histiocytosis of unspecified site                  | B623000 |
| Malignant histiocytosis of lymph nodes head, face and neck   | B623100 |
| Malignant histiocytosis of intrathoracic lymph nodes         | B623200 |
| Malignant histiocytosis of intra-abdominal lymph nodes       | B623300 |
| Malignant histiocytosis of lymph nodes of axilla and arm     | B623400 |
| Malignant histiocytosis of lymph nodes inguinal and leg      | B623500 |
| Malignant histiocytosis of intrapelvic lymph nodes           | B623600 |

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| Malignant histiocytosis of spleen                            | B623700 |
| Malignant histiocytosis of lymph nodes of multiple sites     | B623800 |
| Malignant histiocytosis NOS                                  | B623z00 |
| Leukaemic reticuloendotheliosis                              | B624.00 |
| Leukaemic reticuloendotheliosis                              | B624.11 |
| Letterer-Siwe disease  | B625.00 |
| Histiocytosis X (acute, progressive)                         | B625.11 |
| Malignant mast cell tumours                                  | B626.00 |
| Mast cell malignancy of unspecified site                     | B626000 |
| Mast cell malignancy of lymph nodes of head, face and neck   | B626100 |
| Mast cell malignancy of intrathoracic lymph nodes            | B626200 |
| Mast cell malignancy of intra-abdominal lymph nodes          | B626300 |
| Mast cell malignancy of lymph nodes of axilla and upper limb | B626400 |
| Mast cell malignancy of lymph nodes inguinal region and leg  | B626500 |
| Mast cell malignancy of intrapelvic lymph nodes              | B626600 |
| Mast cell malignancy of spleen                               | B626700 |
| Mast cell malignancy of lymph nodes of multiple sites        | B626800 |
| Malignant mast cell tumour NOS                               | B626z00 |
| Non - Hodgkin's lymphoma                                     | B627.00 |
| Follicular non-Hodgkin's small cleaved cell lymphoma         | B627000 |
| Follicular non-Hodg mixed sml cleavd & lge cell lymphoma     | B627100 |
| Follicular non-Hodgkin's large cell lymphoma                 | B627200 |
| Diffuse non-Hodgkin's small cell (diffuse) lymphoma          | B627300 |
| Diffuse non-Hodgkin's small cleaved cell (diffuse) lymphoma  | B627400 |
| Diffuse non-Hodgkin mixed sml & lge cell (diffuse) lymphoma  | B627500 |
| Diffuse non-Hodgkin's immunoblastic (diffuse) lymphoma       | B627600 |
| Diffuse non-Hodgkin's lymphoblastic (diffuse) lymphoma       | B627700 |
| Diffuse non-Hodgkin's lymphoma undifferentiated (diffuse)    | B627800 |
| Other types of follicular non-Hodgkin's lymphoma             | B627B00 |
| Follicular non-Hodgkin's lymphoma                            | B627C00 |
| Follicular lymphoma NOS                                      | B627C11 |
| Diffuse non-Hodgkin's centroblastic lymphoma                 | B627D00 |
| Unspecified B-cell non-Hodgkin's lymphoma                    | B627W00 |
| Diffuse non-Hodgkin's lymphoma, unspecified                  | B627X00 |
| Malignant lymphoma otherwise specified                       | B62x.00 |
| T-zone lymphoma  | B62x000 |
| Lymphoepithelioid lymphoma                                   | B62x100 |
| Peripheral T-cell lymphoma                                   | B62x200 |
| Malignant reticuloendotheliosis                              | B62x300 |
| Malignant reticulosis  | B62x400 |
| True histiocytic lymphoma                                    | B62x600 |
| Oth and unspecif peripheral & cutaneous T-cell lymphomas     | B62xX00 |
| Malignant lymphoma NOS                                       | B62y.00 |
| Malignant lymphoma NOS of unspecified site                   | B62y000 |
| Malignant lymphoma NOS of lymph nodes of head, face and neck | B62y100 |
| Malignant lymphoma NOS of intrathoracic lymph nodes          | B62y200 |

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| Malignant lymphoma NOS of intra-abdominal lymph nodes        | B62y300 |
| Malignant lymphoma NOS of lymph nodes of axilla and arm      | B62y400 |
| Malignant lymphoma NOS of lymph node inguinal region and leg | B62y500 |
| Malignant lymphoma NOS of intrapelvic lymph nodes            | B62y600 |
| Malignant lymphoma NOS of spleen                             | B62y700 |
| Malignant lymphoma NOS of lymph nodes of multiple sites      | B62y800 |
| Malignant lymphoma NOS                                       | B62yz00 |
| Malignant neoplasms of lymphoid and histiocytic tissue NOS   | B62z.00 |
| Chloroma   | B653000 |
| Neoplasm of uncertain behaviour of histiocytic and mast cell | B935.00 |
| Histiocytic tumour NOS                                       | B935.11 |
| Mastocytoma NOS  | B935.12 |
| Neoplasm of uncertain behaviour of plasma cells              | B936.00 |
| Myeloma - solitary   | B936.11 |
| Plasmacytoma NOS   | B936.12 |
| Neop uncertain behaviour other lymphatic/haematopoietic tiss | B937.00 |
| [M]Adenolymphoma   | BBB1.00 |
| [M]Lymphatic vessel tumours                                  | BBU..00 |
| [M]Lymphangiomatous tumours                                  | BBU..11 |
| [M]Lymphomas, NOS or diffuse                                 | BBg..00 |
| [M]Lymphomatous tumour, benign                               | BBg0.00 |
| [M]Malignant lymphoma NOS                                    | BBg1.00 |
| [M]Lymphoma NOS  | BBg1.11 |
| [M]Malignant lymphoma, diffuse NOS                           | BBg1000 |
| [M]Malignant lymphoma, non Hodgkin's type                    | BBg2.00 |
| [M]Non Hodgkins lymphoma                                     | BBg2.11 |
| [M]Malignant lymphoma, undifferentiated cell type NOS        | BBg3.00 |
| [M]Malignant lymphoma, stem cell type                        | BBg4.00 |
| [M]Malignant lymphoma, convoluted cell type NOS              | BBg5.00 |
| [M]Lymphosarcoma NOS   | BBg6.00 |
| [M]Malignant lymphoma, lymphoplasmacytoid type               | BBg7.00 |
| [M]Malignant lymphoma, immunoblastic type                    | BBg8.00 |
| [M]Malignant lymphoma, mixed lymphocytic-histiocytic NOS     | BBg9.00 |
| [M]Reticulolymphosarcoma NOS                                 | BBg9.11 |
| [M]Reticulolymphosarcoma, diffuse                            | BBg9.12 |
| [M]Malignant lymphoma, centroblastic-centrocytic, diffuse    | BBgA.00 |
| [M]Germinoblastoma, diffuse                                  | BBgA.11 |
| [M]Malignant lymphoma, follicular centre cell NOS            | BBgB.00 |
| [M]Malignant lymphoma, lymphocytic, well differentiated NOS  | BBgC.00 |
| [M]Lymphocytic lymphoma NOS                                  | BBgC.11 |
| [M]Lymphocytic lymphosarcoma NOS                             | BBgC.12 |
| [M]Malig lymphoma, lymphocytic, intermediate different NOS   | BBgD.00 |
| [M]Malignant lymphoma, centrocytic                           | BBgE.00 |
| [M]Malignant lymphoma, follicular centre cell, cleaved NOS   | BBgF.00 |
| [M]Malignant lymphoma, lymphocytic, poorly different NOS     | BBgG.00 |
| [M]Lymphoblastic lymphosarcoma NOS                           | BBgG.11 |

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|---|---------|
| [M]Lymphoblastic lymphoma NOS                                 | BBgG.12 |
| [M]Lymphoblastoma NOS   | BBgG.13 |
| [M]Prolymphocytic lymphosarcoma                               | BBgH.00 |
| [M]Malignant lymphoma, centroblastic type NOS                 | BBgJ.00 |
| [M]Germinoblastic sarcoma NOS                                 | BBgJ.11 |
| [M]Malig lymphoma, follicular centre cell, non-cleaved NOS    | BBgK.00 |
| [M]Malignant lymphoma, small lymphocytic NOS                  | BBgL.00 |
| [M]Malignant lymphoma, small cleaved cell, diffuse            | BBgM.00 |
| [M]Malign lymphoma,lymphocytic,intermediate differrn, diffuse | BBgN.00 |
| [M]Malignant lymphoma, mixed small and large cell, diffuse    | BBgP.00 |
| [M]Malignant lymphomatous polyposis                           | BBgQ.00 |
| [M]Malignant lymphoma, large cell, diffuse NOS                | BBgR.00 |
| [M]Malignant lymphoma, large cell, cleaved, diffuse           | BBgS.00 |
| [M]Malignant lymphoma, large cell, noncleaved, diffuse        | BBgT.00 |
| [M]Malignant lymphoma, small cell, noncleaved, diffuse        | BBgV.00 |
| [M]Lymphoma, diffuse or NOS                                   | BBgz.00 |
| [M]Reticulosarcomas   | BBh..00 |
| [M]Hodgkin's disease  | BBj..00 |
| [M]Lymphomas, nodular or follicular                           | BBk..00 |
| [M]Malignant lymphoma, nodular NOS                            | BBk0.00 |
| [M]Brill - Symmers' disease                                   | BBk0.11 |
| [M]Follicular lymphosarcoma NOS                               | BBk0.12 |
| [M]Giant follicular lymphoma                                  | BBk0.13 |
| [M]Nodular lymphosarcoma NOS                                  | BBk0.14 |
| [M]Malig lymphoma, mixed lymphocytic-histiocytic, nodular     | BBk1.00 |
| [M]Reticulolymphosarcoma, follicular                          | BBk1.11 |
| [M]Reticulolymphosarcoma, nodular                             | BBk1.12 |
| [M]Malignant lymphoma, centroblastic-centrocytic, follicular  | BBk2.00 |
| [M]Germinoblastoma, follicular                                | BBk2.11 |
| [M]Malig lymphoma, lymphocytic, well differentiated,nodular   | BBk3.00 |
| [M]Malig lymph, lymphocytic, intermediate different, nodular  | BBk4.00 |
| [M]Malig lymph, follicular centre cell, cleaved, follicular   | BBk5.00 |
| [M]Malig lymph, lymphocytic, poorly differentiated, nodular   | BBk6.00 |
| [M]Malignant lymphoma, centroblastic type, follicular         | BBk7.00 |
| [M]Germinoblastic sarcoma, follicular                         | BBk7.11 |
| [M]Malig lymph,follicular centre cell,noncleaved,follicular   | BBk8.00 |
| [M]Lymphoma, nodular or follicular NOS                        | BBkz.00 |
| [M]Mycosis fungoides  | BBl..00 |
| [M]Miscellaneous reticuloendothelial neoplasms                | BBm..00 |
| [M]Malignant histiocytosis                                    | BBm1.00 |
| [M]Letterer - Siwe disease                                    | BBm3.00 |
| [M]Acute progressive histiocytosis X                          | BBm3.12 |
| [M]True histiocytic lymphoma                                  | BBm4.00 |
| [M] Peripheral T-cell lymphoma NOS                            | BBm5.00 |
| [M] Monocytoid B-cell lymphoma                                | BBm9.00 |
| [M] Cutaneous lymphoma  | BBmD.00 |

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|--|---------|
| [M] Large cell lymphoma                                      | BBmH.00 |
| [M]Waldenstrom's macroglobulinaemia                          | BBmK.00 |
| [M]Miscellaneous reticuloendothelial neoplasm NOS            | BBmz.00 |
| [M]Plasma cell tumours                                       | BBn..00 |
| [M]Plasma cell myeloma                                       | BBn0.00 |
| [M]Multiple myeloma  | BBn0.11 |
| [M]Myeloma NOS   | BBn0.12 |
| [M]Myelomatosis  | BBn0.13 |
| [M]Plasmacytic myeloma                                       | BBn0.14 |
| [M]Plasma cell tumour, benign                                | BBn1.00 |
| [M]Plasmacytoma, benign                                      | BBn1.11 |
| [M]Plasmacytoma NOS  | BBn2.00 |
| [M]Monostotic myeloma  | BBn2.11 |
| [M]Solitary myeloma  | BBn2.12 |
| [M]Plasma cell tumour, malignant                             | BBn3.00 |
| [M]Plasma cell tumour NOS                                    | BBnz.00 |
| [M]Mast cell tumours   | BBp..00 |
| [M]Mastocytoma NOS   | BBp0.00 |
| [M]Mast cell sarcoma   | BBp1.00 |
| [M]Malignant mastocytosis                                    | BBp2.00 |
| [M]Mast cell tumour NOS                                      | BBpz.00 |
| [M]Burkitt's tumours   | BBq..00 |
| [M]Burkitt's tumour  | BBq0.00 |
| [M]Burkitt's tumour NOS                                      | BBqz.00 |
| [M]Leukaemias  | BBr..00 |
| [M]Other lymphoid leukaemia NOS                              | BBr2z00 |
| [M]Chloroma  | BBrA311 |
| [M]Misc myeloproliferative and lymphoproliferative disorders | BBs..00 |
| [M]Monocytoid B-cell lymphoma                                | BBv0.00 |
| [M]AngiocentricT-cell lymphoma                               | BBv2.00 |
| [X]Other Hodgkin's disease                                   | ByuD000 |
| [X]Other types of follicular non-Hodgkin's lymphoma          | ByuD100 |
| [X]Other types of diffuse non-Hodgkin's lymphoma             | ByuD200 |
| [X]Other specified types of non-Hodgkin's lymphoma           | ByuD300 |
| [X]Other malignant immunoproliferative diseases              | ByuD400 |
| [X]Oth spcf mal neoplsm/lymphoid,haematopoietic+rldt tissue  | ByuDA00 |
| [X]Mal neoplasm/lymphoid,haematopoietic+related tissu,unspcf | ByuDB00 |
| [X]Diffuse non-Hodgkin's lymphoma, unspecified               | ByuDC00 |
| [X]Oth and unspecif peripheral & cutaneous T-cell lymphomas  | ByuDD00 |
| [X]Unspecified B-cell non-Hodgkin's lymphoma                 | ByuDE00 |
| [X]Non-Hodgkin's lymphoma, unspecified type                  | ByuDF00 |
| [X]Non-Hodgkin's lymphoma NOS                                | ByuDF11 |
| Histiocytosis X , chronic                                    | C37y500 |
| Histiocytosis X , unspecified                                | C37y600 |
| Histiocytosis, unspecified                                   | C37y700 |
| Haemophagocytic lymphohistiocytosis                          | C37y800 |

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|--|---------|
| Langerhans' cell histiocytosis                     | C37yB00 |
| Histiocytosis X (chronic)                          | C37yz11 |
| Lipochrome histiocytosis - familial                | D401.12 |
| Familial erythrophagocytic lymph histiocytosis     | D401100 |
| FEL-Familial erythrophagocytic lymph histiocytosis | D401111 |
| [X]Other histiocytosis syndromes                   | Dyu4400 |



Table j-xvi Codes for Metastatic solid tumour

| description  | medcode |
|--|---------|
| Pain from metastases   | 1D18.00 |
| Secondary malignant neoplasm of liver                        | B153.00 |
| Secondary and unspecified malignant neoplasm of lymph nodes  | B56..00 |
| Lymph node metastases  | B56..11 |
| Secondary and unspec malig neop lymph nodes head/face/neck   | B560.00 |
| Secondary and unspec malig neop of superficial parotid LN    | B560000 |
| Secondary and unspec malignant neoplasm mastoid lymph nodes  | B560100 |
| Secondary and unspec malig neop superficial cervical LN      | B560200 |
| Secondary and unspec malignant neoplasm occipital lymph node | B560300 |
| Secondary and unspec malig neop deep parotid lymph nodes     | B560400 |
| Secondary and unspec malig neop submandibular lymph nodes    | B560500 |
| Secondary and unspec malig neop of facial lymph nodes        | B560600 |
| Secondary and unspec malig neop submental lymph nodes        | B560700 |
| Secondary and unspec malig neop anterior cervical LN         | B560800 |
| Secondary and unspec malig neop deep cervical LN             | B560900 |
| Secondary unspec malig neop lymph nodes head/face/neck NOS   | B560z00 |
| Secondary and unspec malig neop intrathoracic lymph nodes    | B561.00 |
| Secondary and unspec malig neop internal mammary lymph nodes | B561000 |
| Secondary and unspec malig neop intercostal lymph nodes      | B561100 |
| Secondary and unspec malig neop diaphragmatic lymph nodes    | B561200 |
| Secondary and unspec malig neop ant mediastinal lymph nodes  | B561300 |
| Secondary and unspec malig neop post mediastinal lymph nodes | B561400 |
| Secondary and unspec malig neop paratracheal lymph nodes     | B561500 |
| Secondary and unspec malig neop superfic tracheobronchial LN | B561600 |
| Secondary and unspec malig neop inferior tracheobronchial LN | B561700 |
| Secondary and unspec malig neop bronchopulmonary lymph nodes | B561800 |
| Secondary and unspec malig neop pulmonary lymph nodes        | B561900 |
| Secondary and unspec malig neop intrathoracic LN NOS         | B561z00 |
| Secondary and unspec malig neop intra-abdominal lymph nodes  | B562.00 |
| Secondary and unspec malig neop coeliac lymph nodes          | B562000 |
| Secondary and unspec malig neop superficial mesenteric LN    | B562100 |
| Secondary and unspec malig neop inferior mesenteric LN       | B562200 |
| Secondary and unspec malig neop common iliac lymph nodes     | B562300 |
| Secondary and unspec malig neop external iliac lymph nodes   | B562400 |
| Secondary and unspec malig neop intra-abdominal LN NOS       | B562z00 |
| Secondary and unspec malig neop axilla and upper limb LN     | B563.00 |
| Secondary and unspec malig neop axillary lymph nodes         | B563000 |
| Secondary and unspec malig neop supratrochlear lymph nodes   | B563100 |
| Secondary and unspec malig neop infraclavicular lymph nodes  | B563200 |
| Secondary and unspec malig neop pectoral lymph nodes         | B563300 |
| Secondary and unspec malig neop axilla and upper limb LN NOS | B563z00 |
| Secondary and unspec malig neop inguinal and lower limb LN   | B564.00 |
| Secondary and unspec malig neop superficial inguinal LN      | B564000 |

|  |         |
|--|---------|
| Secondary and unspec malig neop deep inguinal lymph nodes    | B564100 |
| Secondary and unspec malig neop popliteal lymph nodes        | B564200 |
| Secondary and unspec malig neop of inguinal and leg LN NOS   | B564z00 |
| Secondary and unspec malig neop intrapelvic lymph nodes      | B565.00 |
| Secondary and unspec malig neop internal iliac lymph nodes   | B565000 |
| Secondary and unspec malig neop inferior epigastric LN       | B565100 |
| Secondary and unspec malig neop circumflex iliac LN          | B565200 |
| Secondary and unspec malig neop sacral lymph nodes           | B565300 |
| Secondary and unspec malig neop obturator lymph nodes        | B565400 |
| Secondary and unspec malig neop intrapelvic LN NOS           | B565z00 |
| Secondary and unspec malig neop lymph nodes multiple sites   | B56y.00 |
| Secondary and unspec malig neop lymph nodes NOS              | B56z.00 |
| Secondary malig neop of respiratory and digestive systems    | B57..00 |
| Metastases of respiratory and/or digestive systems           | B57..11 |
| Secondary carcinoma of respiratory and/or digestive systems  | B57..12 |
| Secondary malignant neoplasm of lung                         | B570.00 |
| Secondary malignant neoplasm of mediastinum                  | B571.00 |
| Secondary malignant neoplasm of pleura                       | B572.00 |
| Secondary malignant neoplasm of other respiratory organs     | B573.00 |
| Secondary malignant neoplasm of small intestine and duodenum | B574.00 |
| Secondary malignant neoplasm of duodenum                     | B574000 |
| Secondary malignant neoplasm of jejunum                      | B574100 |
| Secondary malignant neoplasm of ileum                        | B574200 |
| Secondary malig neop of small intestine or duodenum NOS      | B574z00 |
| Secondary malignant neoplasm of large intestine and rectum   | B575.00 |
| Secondary malignant neoplasm of colon                        | B575000 |
| Secondary malignant neoplasm of rectum                       | B575100 |
| Secondary malig neop of large intestine or rectum NOS        | B575z00 |
| Secondary malig neop of retroperitoneum and peritoneum       | B576.00 |
| Secondary malignant neoplasm of retroperitoneum              | B576000 |
| Secondary malignant neoplasm of peritoneum                   | B576100 |
| Secondary malig neop of retroperitoneum or peritoneum NOS    | B576z00 |
| Secondary malignant neoplasm of liver                        | B577.00 |
| Liver metastases   | B577.11 |
| Secondary malignant neoplasm of other digestive organ        | B57y.00 |
| Secondary malig neop of respiratory or digestive system NOS  | B57z.00 |
| Secondary malignant neoplasm of other specified sites        | B58..00 |
| Secondary carcinoma of other specified sites                 | B58..11 |
| Secondary malignant neoplasm of kidney                       | B580.00 |
| Secondary malignant neoplasm of other urinary organs         | B581.00 |
| Secondary malignant neoplasm of ureter                       | B581000 |
| Secondary malignant neoplasm of bladder                      | B581100 |
| Secondary malignant neoplasm of urethra                      | B581200 |
| Secondary malignant neoplasm of other urinary organ NOS      | B581z00 |
| Secondary malignant neoplasm of skin                         | B582.00 |
| Secondary malignant neoplasm of skin of head                 | B582000 |

|  |         |
|--|---------|
| Secondary malignant neoplasm of skin of face                 | B582100 |
| Secondary malignant neoplasm of skin of neck                 | B582200 |
| Secondary malignant neoplasm of skin of trunk                | B582300 |
| Secondary malignant neoplasm of skin of shoulder and arm     | B582400 |
| Secondary malignant neoplasm of skin of hip and leg          | B582500 |
| Secondary malignant neoplasm of skin of breast               | B582600 |
| Secondary malignant neoplasm of skin NOS                     | B582z00 |
| Secondary malignant neoplasm of brain and spinal cord        | B583.00 |
| Secondary malignant neoplasm of brain                        | B583000 |
| Secondary malignant neoplasm of spinal cord                  | B583100 |
| Cerebral metastasis  | B583200 |
| Secondary malignant neoplasm of brain or spinal cord NOS     | B583z00 |
| Secondary malignant neoplasm of other part of nervous system | B584.00 |
| Secondary malignant neoplasm of bone and bone marrow         | B585.00 |
| Pathological fracture due to metastatic bone disease         | B585000 |
| Secondary malignant neoplasm of ovary                        | B586.00 |
| Secondary malignant neoplasm of adrenal gland                | B587.00 |
| Secondary malignant neoplasm of other specified sites        | B58y.00 |
| Secondary malignant neoplasm of breast                       | B58y000 |
| Secondary malignant neoplasm of uterus                       | B58y100 |
| Secondary malignant neoplasm of cervix uteri                 | B58y200 |
| Secondary cancer of the cervix                               | B58y211 |
| Secondary malignant neoplasm of vagina                       | B58y300 |
| Secondary malignant neoplasm of vulva                        | B58y400 |
| Secondary cancer of the vulva                                | B58y411 |
| Secondary malignant neoplasm of prostate                     | B58y500 |
| Secondary malignant neoplasm of testis                       | B58y600 |
| Secondary malignant neoplasm of penis                        | B58y700 |
| Secondary malignant neoplasm of epididymis and vas deferens  | B58y800 |
| Secondary malignant neoplasm of tongue                       | B58y900 |
| Secondary malignant neoplasm of other specified site NOS     | B58yz00 |
| Secondary malignant neoplasm of other specified site NOS     | B58z.00 |
| Secondary malignant neoplasm of unknown site                 | B594.00 |
| [M]Neoplasm, metastatic                                      | BB03.00 |
| [M]Secondary neoplasm  | BB03.11 |
| [M]Neoplasm, malig, uncertain whether primary or metastatic  | BB04.00 |
| [M]Carcinoma, metastatic, NOS                                | BB13.00 |
| [M]Secondary carcinoma                                       | BB13.11 |
| [M]Squamous cell carcinoma, metastatic NOS                   | BB2B.00 |
| [M]Adenocarcinoma, metastatic, NOS                           | BB53.00 |
| [M]Metastatic signet ring cell carcinoma                     | BB85100 |
| [M]No microscopic confirmation tumour, clinically metastatic | BBy2.00 |
| [X]Malignant neoplasm of ill-defined, secondary and unspeci  | ByuC.00 |
| [X]Secondary malignant neoplasm/oth+unspc respiratory organs | ByuC300 |
| [X]Secondary malignant neoplasm/oth+unspcfd digestive organs | ByuC400 |
| [X]Secondary malignant neoplasm of other specified sites     | ByuC700 |

Table j-xvii Codes for AIDS

| description  | medcode |
|--|---------|
| HIV positive   | 43C3.11 |
| AIDS carrier   | 65QA.00 |
| Notification of AIDS   | 65VE.00 |
| Acute human immunodeficiency virus infection                 | A788000 |
| Asymptomatic human immunodeficiency virus infection          | A788100 |
| HIV infection with persistent generalised lymphadenopathy    | A788200 |
| Human immunodeficiency virus with constitutional disease     | A788300 |
| Human immunodeficiency virus with neurological disease       | A788400 |
| Human immunodeficiency virus with secondary infection        | A788500 |
| Human immunodeficiency virus with secondary cancers          | A788600 |
| HIV disease result/haematological+immunologic abnorms,NEC    | A788U00 |
| HIV disease resulting in multiple diseases CE                | A788V00 |
| HIV disease resulting in unspecified malignant neoplasm      | A788W00 |
| HIV disease resulting/unspcf infectious+parasitic disease    | A788X00 |
| Human immunodeficiency virus with other clinical findings    | A788y00 |
| Acquired human immunodeficiency virus infection syndrome NOS | A788z00 |
| HIV disease resulting in mycobacterial infection             | A789000 |
| HIV disease resulting in cytomegaloviral disease             | A789100 |
| HIV disease resulting in candidiasis                         | A789200 |
| HIV disease resulting in Pneumocystis carinii pneumonia      | A789300 |
| HIV disease resulting in multiple infections                 | A789400 |
| HIV disease resulting in Kaposi's sarcoma                    | A789500 |
| HIV disease resulting in Burkitt's lymphoma                  | A789600 |
| HIV dis resulting oth types of non-Hodgkin's lymphoma        | A789700 |
| HIV disease resulting in multiple malignant neoplasms        | A789800 |
| HIV disease resulting in lymphoid interstitial pneumonitis   | A789900 |
| HIV disease resulting in wasting syndrome                    | A789A00 |
| HIV dis reslt/oth mal neopl/lymph,h'matopoetc+reltd tissu    | A789X00 |
| [X]HIV disease resulting in other bacterial infections       | AyuC000 |
| [X]HIV disease resulting in other viral infections           | AyuC100 |
| [X]HIV disease resulting in other mycoses                    | AyuC200 |
| [X]HIV disease resulting in multiple infections              | AyuC300 |
| [X]HIV disease resulting/other infectious+parasitic diseases | AyuC400 |
| [X]HIV disease resulting/unspcf infectious+parasitic disease | AyuC500 |
| [X]HIV disease resulting in other non-Hodgkin's lymphoma     | AyuC600 |
| [X]HIV dis reslt/oth mal neopl/lymph,h'matopoetc+reltd tissu | AyuC700 |
| [X]HIV disease resulting in other malignant neoplasms        | AyuC800 |
| [X]HIV disease resulting in unspecified malignant neoplasm   | AyuC900 |
| [X]HIV disease resulting in multiple diseases CE             | AyuCA00 |
| [X]HIV disease result/haematological+immunologic abnorms,NEC | AyuCB00 |
| [X]HIV disease resulting in other specified conditions       | AyuCC00 |
| [X]Unspecified human immunodeficiency virus [HIV] disease    | AyuCD00 |

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|--|---------|
| [X]Dementia in human immunodeficiency virus [HIV] disease    | Eu02400 |
| [D]Laboratory evidence of human immunodeficiency virus [HIV] | R109.00 |

### **Appendix III-k Codes for liver transplant**

| Description                                       | medcode |
|---|---------|
| Transplantation of liver                          | 7800    |
| Orthotopic transplantation of liver               | 7800000 |
| Heterotopic transplantation of liver              | 7800100 |
| Auxillary liver transplant                        | 7800111 |
| Piggy back liver transplant                       | 7800112 |
| Replacement of previous liver transplant          | 7800200 |
| Other specified transplantation of liver          | 7800y00 |
| Transplantation of liver NOS                      | 7800z00 |
| TRANSPLANTATION LIVER                             | K5005   |
| Liver transplant failure and rejection            | SP08600 |
| Liver transplant with complication, without blame | TB00200 |
| [V]Liver transplanted                             | ZV42700 |