

Identifying People with Dementia for Epidemiological Analysis in Electronic Primary Care Records in the UK

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Declaration of originality

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List of Abbreviations

AHTs	Antihypertensive treatments
AMR	Acceptable Mortality Reporting
ARBs	Angiotensin Receptor Blockers
BPSD	Behavioural and psychological symptoms of dementia
BNF	British National Formulary
CDR	Clinical Dementia Rating
CPRD	Clinical Practice Research Datalink
CJD	Creutzfeldt Jakob disease
DEM	Dementia
DSM	Diagnostic and Statistical Manual of Mental Disorders
FAST	Functional Assessment Staging
GDS	Global Deterioration Scale
GPCOG	General Practitioner Assessment of Cognition
HES	Hospital Episode Statistics
ICD-10	10th revision of the International Statistical Classification of Diseases and Related Health Problems
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
NDS	National Dementia Strategy
NICE guidelines	The National Institute for Health and Care Excellence guidelines
QOF	Quality and Outcomes Framework
RCTs	Randomised controlled trials
THIN	The Health Improvement Network

Abstract

There are many epidemiological questions that need to be answered regarding dementia, including the causes, prognosis, comorbidities, and treatment of the condition and complications. Routine data sources including a large electronic primary care dataset provide a way of investigating some of the complicated factors with rich information. However, there has been concern regarding whether dementia is recorded well enough. It has been reported that dementia is often poorly recorded in primary care and so it would be expected to be potentially difficult to identify people with dementia. Before the data sources can be used satisfactorily, it will be important to understand how dementia is recorded, and whether the records on dementia, related symptoms or use of related medications are the most appropriate ways of identifying people with dementia.

This study has therefore explored this by conducting a systematic review to understand how dementia has been identified previously in primary care databases in the UK, and added to this by exploring additional terms and symptoms, and medications that might be helpful in identifying people with dementia. The codes from the literature were not very consistent, taking into account the differing study objectives and populations.

The incidence rates from the longitudinal study which used reliable measurement techniques to identify dementia with a verified process and a recruitment strategy were higher than the rates from the study using primary care databases in the UK. This implies the method of dementia diagnosis may influence the rates. To identify people with dementia in primary care records, a careful alternative identification method for the study population seems to be required.

This study estimated and compared the prevalence and incidence of dementia in the UK using the alternative ways of identifying people with dementia in The Health Improvement Network (THIN) database. The method of comparison of the estimated rates with other studies was employed using the comprehensive list of diagnostic codes.

Since the Quality and Outcomes Framework (QOF) was introduced in 2004, there were slight and steady increasing trends in both prevalence and incidence rates up to a recent date. The estimated incidence rates per 1,000 person-years for the 60+ age group who had any of the first diagnosis among the QOF defined codes, *Other diagnoses, Dementia symptoms* and *Prescribed medication* were 2.5, 4.7, and 15.9 in 1995, 2004, and 2015 respectively. The estimated prevalence rates per 1,000 persons for those aged 60+ who had any of the first diagnosis among the QOF defined codes, *Other diagnoses* and *Prescribed medication* were 2.8, 3.2, and 10.2 in 1995, 2004, and 2015

respectively. The prevalence rates with those codes including the *Dementia symptoms* were 3.0, 4.3 and 19.4 in 1995, 2004 and 2015 respectively.

At least, using of the other dementia diagnostic codes (*Other diagnoses)* in addition to the QOF defined ones, (and treatments (*Prescribed medication)* for Alzheimer's disease or various other memory impairments for verification) was evidenced that will not missing out a number of people with dementia, in the comparison of the incidence and prevalence rates of dementia with the other estimates. The codes related to dementia symptoms (including memory loss/forgets, cognitive decline/impairment) seem to cover a broad definition of dementia or pre-existing dementia population in primary care records in the UK which need to be considered furthermore for study designs in epidemiology. They seem to identify the very elderly population with dementia, implying the codes related to dementia symptoms may cover important cases or the related information of dementia in primary care records. Nevertheless, the codes about non-specific or temporary symptoms may need to be used carefully as it is possible for memory or cognitive function to be impaired temporarily due to stress or medications.

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Chapter 1. Introduction

1-1. Background

1-1-1. Dementia in primary care in the UK

Definition of dementia and impact on life

Dementia is a clinical syndrome characterised by the progressive loss of global cognitive functioning in a time frame of at least 6 months [1]. The kinds of cognitive impairments seen in dementia include short term loss of memory (i.e., amnesia), communication and language problems (i.e., aphasia), inability to recognize things (i.e., agnosia), inability to perform particular purposive actions (apraxia) and loss of a sense of direction and loss of judgement ability. Neuropsychiatric symptoms, i.e., behavioural and psychological symptoms of dementia (BPSD), such as hyperactivity, delusions, hallucinations, depression, anxiety, apathy and agitation, are present in many cases of dementia [2]. There is little effective treatment currently, and with a progressive condition, it makes people very weak and vulnerable. Dementia can lead to difficulties with activities of daily living and has a big impact on the families of the person with dementia. Due to their inability to look after themselves, many people need to move into institutional care. People with dementia are noticeably over-represented in hospitals, and it poses a heavy socioeconomic burden to the state, generating great annual costs (of more than £23 billion) in health and social care, UK [3].

Type of dementia and progression

Alzheimer's (62%) and vascular dementia (17%) are two greater prevalence subtypes of dementia [4]. This clinical classification is based upon the presumption that Alzheimer's pathology and vascular brain damage are, respectively, the main pathological processes underlying these disorders. Other less common subtypes include Lewy Bodies (4%), Parkinson's (2%), Fronto-temporal dementia (2%) and mixed dementia (10%), which is more than one type of dementia, such as Alzheimer's with vascular dementia [5, 6] [1]. Dementia with Lewy bodies, in which microscopic deposits are found in the brain and sometimes develop as an end result of Parkinson's disease, is characterised by marked fluctuation

[1] There are cases related to brain tumour, hydrocephalus (build-up of fluid on the brain) and subdural haemorrhage (blood collects between the skull and the surface of the brain) which cause cognitive impairment.

of impairment and frequent hallucinations, and features similar to Parkinson's disease. Alzheimer's disease is more considered as vascular related dementia following the results of the longitudinal Nun Study of Aging and Alzheimer's disease, which showed that blocked small blood vessels were found in brains of people with Alzheimer's disease [7]. It is increasingly understood that these pathological processes often occur in combination and vary from person to person, and the classification of the type of dementia is of limited value. Nevertheless, in terms of its progression, Alzheimer's dementia seems to have a fairly steady and gradual progression, whereas the classic description of vascular dementia such as stroke-related dementia, has shown a step-wise pattern of progress and often with physical symptoms, e.g., impairment of mobility. It has been reported that dementia with Lewy bodies has a slow and gradual progress [8].

Causes of dementia

Up to date research suggests that there are many other risk factors, not only a build-up of β-amyloid protein plaques in the brain cells [9], such as tauopathy (i.e., pathological aggregation of tau protein), inflammation, neuronal and synaptic protein loss, vascular change and genetic evidence [10][2]. Several different brain pathologies can cause the dementia syndrome, the most common being Alzheimer's disease, vascular disease, and Lewy Body disease. It is known that vascular dementia is caused by repeated cerebrovascular diseases such as cerebral apoplexy (bleeding), cerebral stroke, and stroke in general, which cause either cerebral hemorrhage (bleeding) or cerebral infarction (i.e., area of necrotic tissue in the brain). Vascular dementia is more commonly caused by cerebral infarction, which results from blocked great or small blood vessels [11].

The UK's initiatives to improve identification and care of people with dementia

Prior to the description about diagnosis of dementia in primary care, this section will introduce the UK's initiatives to improve recognition and care of dementia including the Quality and Outcomes Framework (QOF). The OQF was introduced in 2004 by NHS England to improve the quality of patient care. It is a voluntary reward scheme providing a financial incentive for GP practices to carry out a range of activities, which includes creating and maintaining a register of patients with dementia [12]. It is the world's largest healthcare related pay-for-performance scheme into primary care [13]. A report states that the QOF dementia diagnosis rates were highly correlated with the prescribed medications to treat dementia [12]. A significant increase in dementia diagnosis rates and the

[2] It has been considered that Alzheimer's pathology is caused by a problem whereby β-amyloid protein plaques build up in the brain cells (Murphy *et al*., 2010) and it is believed currently there is no remedy to remove them.

prescribed medications to treat dementia have been reported since the launch of the National Dementia Strategy, joint commissioning framework for dementia (NDS, 2009) and incentives to GPs from the NHS, i.e., dementia Enhanced Service (ES) and the QOF [12]. NDS is first UK government initiative to focus on improving dementia care through raising public and professional (GPs) awareness about dementia, encouraging earlier diagnosis (by increased access to specialist diagnostic services), and intervention and increasing the quality of care [12, 14]. Dementia ES (which ceased in 2016) had been designed to reward GP practices for undertaking a proactive approach to the timely assessment and for improvements in services [15]. In 2013, the National Institute for Health and Clinical Excellence (NICE) consulted on potential new indicators for developing a register of carers and providing carers with an annual assessment, and for referring patients with suspected dementia to a memory clinic prior to diagnosis [16].

Dementia diagnosis rates rely on GPs' records via diagnostic codes onto their databases [12]. Required dementia diagnostic codes (such as Read codes that the clinical terminology system used in GP practices, i.e., primary care records, in the UK) have been reported via The Logical Query Indicator Specification and the Dataset and Business Rules (which support the reporting requirements of the QOF based on Read codes and associated dates) [17, 18]. The QOF indicator codes, points and payment stages have been changed over time (Appendix Table 3)[3]. The QOF has reflected the changed definition of dementia over time and symptoms or diseases have been newly included in the QOF dementia diagnostic codes (in 2014) such as sporadic Creutzfeldt-Jakob disease (CJD) [17].

Diagnosis of dementia in primary care in the UK

Missed and delayed diagnoses of dementia in primary care are common due to multiple barriers in the UK. In such cases, dementia has not been diagnosed until late into the illness [19]. The estimated dementia diagnosis rate in practice (within UK Clinical Commissioning Groups (CCGs), NHS organization) was 67.4% by January 2017, and this varies between regions[4] (according to a secondary analysis of the QOF monthly dementia register data by the HSCIC) [20]. This implies more than 30% of patients (i.e., the remainder) in hospital with dementia had not been diagnosed beforehand. The reasons for this may vary. Many patients may not present to their doctors. Part of the dementia process includes lack of awareness and memory, so those people may not know there is anything wrong. Some patients may not wish to accept that there is something wrong due to the stigma still

[3] The value of a QOF point, number of points available for indicator and actual achievement are used to calculate the achievement of indicators in the clinical domain. All payments are weighted by the Contractor Population Index (CPI) and in the clinical domain by disease prevalence (2015/16 GMS contract QOF).

[4] GPs should record all diagnoses of dementia on dementia registers (Living Well with Dementia, 2009 [14]).

attached to dementia. They do not tell their GPs about the symptoms. Some patients and their families may simply put the changes down to old age and may simply adapt their lifestyles in which cases they may not think of seeking a medical opinion. Current lack of effective treatments may be one of barriers. Some GPs or other doctors may be reluctant to diagnose or may not recognise it. It is not easy to detect the early signs of dementia [19].

Dementia diagnosis in the UK

Often people get diagnosed with dementia by presenting with something else at a crisis point, often in hospital. It is preferable for the diagnosis to be made by referral to a memory clinic in the UK although it is also diagnosed in other settings. The UK Guidelines emphasize a careful history-taking in suspected dementia prior to referral. As pre-referral assessment in primary care, history checking of a GP including onset, progression, pattern of memory problems, and medical, psychiatric and family history are recommended in suspected dementia by NICE-SCIE Guideline [1, 21]. The Scottish Intercollegiate Guidelines Network [22] underlined that individual's subjective memory complaints should be taken seriously as they may be associated with the earliest sign of the syndrome, and even with Alzheimer's biomarkers [23]. In addition, a brief cognitive assessment test is recommended as an initial assessment of memory problems (using the Mini–Mental State Examination (MMSE), the General Practitioner assessment of Cognition (GPCOG), Six-item Cognitive Impairment Test (6CIT), 7-min screen and clock drawing test) [21, 24, 25][5]. Physical examinations such as basic neurological examinations, blood tests or other investigations (e.g., MSU, CXR or ECG and MRI or CT) are also recommended although these examinations are not always feasible [21].

Role of primary care in dementia in the UK

In terms of early diagnosis and management in the early stages of dementia, the role of primary care, especially a GP, is very important. The roles of a GP include monitoring mild cognitive impairment (which can develop to late-onset dementia), prompt onward referral to relevant services in secondary care (e.g., referral to a dementia specialist and memory clinic) when a GP is unsure about the diagnosis, and providing feedback about the diagnosis [21]. Primary care electronic health records

[5] A number of assessments measuring the stage of cognitive impairment have been developed and used in research, or to help describe the diagnosis in practice (rather than being used as a clinical tool). These include The Global Deterioration Scale (GDS) (Reisberg *et al.,* 1982), Functional Assessment Staging (FAST), Clinical Dementia Rating (CDR), The Mini–Mental State Examination (MMSE), and Psychometric tests (Reisberg *et al.*, 2001) (Brooke *et al*., 1999).

are useful source for dementia research with rich information of medical history, and the information related to its treatments is relatively well recorded. This study will conduct some of the early work to find out how well dementia is recorded and how to identify dementia in primary care records in the UK.

Estimated prevalence of dementia in the UK

Prevalence measures the proportion of people in a population with a disease at a specific point in time [26, 27]. The estimated number of people with dementia was 815,827 (i.e., 1.3% of the UK adult population) in 2013, of whom 95% were aged 65+ years [6]. This figure was based on an estimated prevalence by the Delphi consensus process which used an average estimation calculated from each research panel's response for all the available evidence [6]. Prevalence of dementia was 7.1% for the total age-standardised 65+ years population based on 2013 data. The prevalence of dementia increased exponentially with increasing age, approximately doubling every five years (Table 1-1) [6, 28-30]. The MRC CFA (Cognitive Function and Ageing) is a longitudinal cohort study (CFAS, which estimated 209,600 new dementia cases each year) based on the large population data in the UK. In CFAS I, 7,635 people aged 65+ years were interviewed and 1,459 were being diagnostically assessed in Cambridgeshire, Newcastle, and Nottingham (1990-93). Of these individuals 900 took part in the 2 year follow-up (1993-95) [28]. In the CFAS II, 7,762 individuals were in the baseline and assessment interviews in the same geographical areas (2008-11). Of these individuals 5,288 took part in the re-interview (2011-13). With the two-waves of data 2 years apart, the study has the biggest observational design to quantify dementia. Nevertheless, only individuals who consented to take part in the study were included and it seems unlikely to be completely representative of the general elderly population. Another study (2010) [31] reported the prevalence rates of dementia for aged 65–104 years patients (who have been registered with their general practice for at least 90 days) using the UK's primary care database, The Health Improvement Network (THIN), were 40.8% (95% CIs: 37.5–44.1, N=4,269) in nursing care home and 37.4% (95% CIs: 34.7–39.8, N=4,715) in residential care homes compared to 3.4% (95% CIs: 3.1-3.6, N=403,259) in community. The study was in a fairly small subset of people from the primary care database, and limited or narrowly defined dementia diagnostic codes were used.

Table 1-1. Consensus estimates of the prevalence (%) of dementia in the UK

Age in years		Dementia UK 2007 report	Dementia UK 2014 report	CFAS I (1993-1995)	CFAS II (2011-2013)
		(Prince *et al*., 2014 [6])		(Matthews *et al*., 2016 [28])	
Up to 60 years	45-49	0.03	-	-	-
	50-54	0.06	-	-	-
	55-59	0.14	-	-	-
60+ years	60-64	-	0.9	-	-
	65-69	-	1.7	1.5	1.5
	70-74	-	3.0	2.6	2.7
	75-79	-	6.0	6.3	5.7
	80-84	-	11.1	13	10
	85-89	-	18.3	25.3	16.1
	90-94	-	29.9	-	30.1
	95+	-	41.1	-	-

Estimated incidences of dementia in the UK

The incidence rate is the number of new cases of disease in a population per unit of person-time during a specific time period [26, 27]. Incidences of dementia can be estimated using various data sources such as the primary care database and Hospital Episode Statistics (HES) (i.e., records of all admissions, appointments and attendances for patients admitted to NHS hospitals in England). A study of comparison of dementia recorded (Brown *et al.*, 2016) reported the age-specific rates of dementia per 1,000 women-year using the primary care database, Clinical Practice Research Datalink (CPRD, i.e., the new English NHS observational data) for the period of 1990-2012, and HES for the period of 1997-2011 [32] (Table 1-2).

Overall incidence rates reported per 1,000 person-years for ages 65+ was 20.1 (95% CIs: 16.8-24.0, N= 1,805) in CFAS I for the period of 1993-95, and 17.7 (95% CIs: 15.2-20.6, N= 5,288) in CFAS II for the period of 2011-13 in England and Wales. Overall, the incidence rate increased substantially with age (Table 1-2). Incidence rates of the CFAS were higher than the figures from the study using the primary care database. A number of factors could have led to these outcomes. Using a robust diagnostic technique for dementia to estimate the incidence rates of the population would be one of them.

Table 1-2. Age-specific incidence rates of dementia per 1,000 women-years in the UK

Age in years	CPRD (1990-2012)	HES (1997-2011)	CFAS I (1993-1995)	CFAS II (2011-2013)
	(Brown *et al*., 2016 [32])		(Matthews *et al*., 2016 [28])	
65-69	1.18	0.76	6.3	4.6
70-74	3.53	2.37	7.4	6.4
75-79	8.06	6.96	17.6	16.1
80-84	-	-	35.6	39.6
85+	-	-	59.5	55.3

1-1-2. Dementia in global primary care

Diagnosis of dementia in global studies

Global studies reported the prevalence and incidences of dementia in regional populations, having used various study designs and diagnostic evaluations. These longitudinal studies used various standardised or reliable dementia diagnostic techniques with additional verified processes or two-phase procedures, and recruitment strategies. The German [33, 34] and Canadian [35] studies used ICD-9/10. More specifically, the former used ICD-10, or cholinesterase inhibitors/memantine, with a developed internal validation procedure to deal with false-positive diagnoses (as the health claims tend to overestimate the true prevalence of dementia). The latter used ICD-9/10, or cholinesterase inhibitor prescription and with an additional verified process (i.e., one hospitalization with any field diagnosis of dementia, one physician visit with diagnosis of dementia, or one prescription for cholinesterase inhibitor within the previous year) [35] (Appendix Table 1 and 2).
Most of the other studies used DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised) or DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition) by a panel of a neurologist (e.g., Hisayama, the Japan [36] study), neuropsychologist, or research physician (e.g., the Rotterdam, Netherlands [37] study), or research psychiatrists (e.g., the Zaragoza, Spain [38] study), or a specialist in geriatrics (e.g., the Umea [39] study). DSM-III or DSM-IV was also used in the China, Japan, and South Korea studies and NIA-AA (National Institute on Aging-Alzheimer's Association criteria) was used in the Twain study [40-44]. In addition to DSM-IV, the Framingham, MA, US [45] study used NINCDS-ADRDA (National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association) [46] and NINDS-AIREN (National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences) [47]. Studies also used a two-stage design with screening followed by extensive clinical evaluation with DSM-III(-R) or DSM-IV.

The Ibadan, Nigeria [48], the Stockholm, Sweden [49] and the Umea [39] studies used the MMSE (to assess the level of cognitive impairment and to document cognitive changes) in the screening phase. Furthermore, some studies used algorithmic diagnosis. The Framingham, MA, US [45] study used the diagnostic algorithm to allow participants to have more than one subtype of dementia, and the Bordeaux, France [50]) study used it to avoid a measurement bias (with MMSE and IADL (Instrumental Activities of Daily Living)). The CFAS, UK [51] study used GMS (Geriatric Mental State Examination)-AGECAT for computer assisted taxonomy screening and diagnostic assessment (which is commonly used for elderly people).

The Goteborg, Sweden [52] study used dementia historical criteria (described by Kay *et al*., 1964) in 1976–77 and performed the measurement agreement with the DSM-III-R in 2000–01(Cohen's kappa=0.81). In addition, the Indianapolis, IN, African Americans [53] study, the ad hoc criteria similar to those of the DSM-III-R and clinical criteria for the diagnosis of Alzheimer's disease were used [54] (as the data was collected as part of routine medical care where the diagnostic criteria were not fully standardized and not all of the subjects had psychometric, imaging, or other research tests).

Global prevalence of dementia

Age-specific prevalence (%) of dementia in Western European populations are presented in Figure 1-1 [55]. The studies are the CFAS, UK [51] study (with two cohorts of aged 65+ years, N=7,635, 1993-95 and N=7,796, 2008-11), the Stockholm [49] study (with two cohorts of aged 75+ years, N=1,810, 1987 and N=1,575, 2001) and the Zaragoza, Spain [38, 56] study (with two cohorts of aged 65+ years, N=1,080, 1987-89 and N=3,715, 1994-96). The estimated prevalence (%) of dementia in the populations showed increasing patterns with age. The (crude) prevalence (%) of dementia in East Asian countries was 5.1% (N=10,276, 2008-09) in China [41], 6.3% (N=10,432, 2011-13) in Taiwan [40], 22.5% (N=3,394, 2009) in Japan [42] and 9.2% (N=6,141, 2008) in South Korea for all aged 65+ years [43, 44].

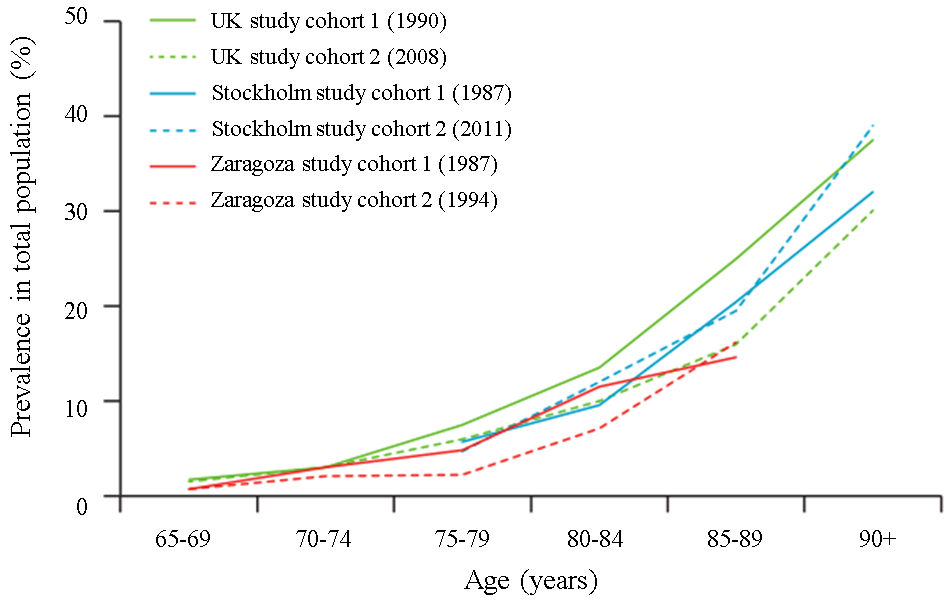


Figure 1-1. Estimated Age-specific prevalence (%) of dementia in Western Europe, Wu *et al*., 2016 [55]; approved by authors to be presented in this dissertation.

1-1-3. Recording of dementia in primary care in the UK

Dementia records in primary care in the UK

It has been mentioned that primary care plays an important role in the identification of people with dementia (including people with suspected dementia). Therefore, primary care records may provide a vital source of data to address some of the evidence gaps that other studies could not fulfil. However, it is acknowledged that records on dementia in primary care databases also have limitations. Firstly, people with dementia may not see GPs or ever tell GPs about their symptoms. Secondly, there are multiple potential codes which are not yet systematically organized to define dementia. It was reported that only 48% of those who were predicted to have dementia (based on the population prevalence rates) are recorded on GP practice dementia registers in London (QOF data in 2010/11) [57]. One of the putative reasons of the low diagnosis rate is a lack of accurate coding since there has been confusion with the available codes [57]. Thirdly, there are possible coding (human) errors although they are expected to be relatively small. Lastly, a GP's attitude can lead to a result of not identifying disease in records due to incomplete coding (for example, some of them have more clearly indicative signs of dementia whereas some of them may less clear). In addition, GPs might

worry about making a diagnosis of dementia, fearing that doing so may do no good to or may overly distress the patient. In addition, in an unusual case, GPs may think that they are not supposed to diagnose dementia, and should refer the patient to a memory clinic. However, referral to a memory clinic to diagnosis takes time; it requires minimum two times to diagnose. Patients also could refuse to visit a memory clinic. Visiting a memory clinic does not guarantee a clear diagnosis as well; it can be uncertain. The diagnosis should be recorded by a GP in primary care records after the diagnosis made in the memory clinic and it normally takes time. Care home patients are also in the primary care database system, but they have more difficulty in seeing a GP than the general population.
A recent higher prevalence of dementia may not indicate the actual rate was increased; it may be recent GP's education or policy (e.g. financial incentives) changes related to dementia diagnosis encouraged these figures. It is assumed that those people with dementia, who haven't firmly or officially been diagnosed constitute more than a half the number in the primary care database.
In summary, primary care records may be a good source on dementia research. Primary care data may be useful as it reflects the real-world cohorts for the UK population. This will control the limitations of those epidemiological and research cohorts, or RCT design studies. However, the records on dementia diagnosis may not be accurate. The records may have changed over time as education and incentives for GPs have changed. Codes related to dementia which are used in practice haven't yet been clearly established or systematically managed. Therefore, alternative or additional methods to identify dementia will be needed in primary care records.

1-2. Rationale and Objective

1-2-1. Rational

Dementia is one of the major public health problems in the UK and globally, with major implications for the individual, families and society. There is much that is not yet known about the causes and lifetime history of dementia, prognosis, and how to manage and treat the condition. Randomised controlled trials (RCTs) are probably not feasible to answer many of those questions and its comorbidities and treatments, as people with dementia are often excluded from RCTs. Previous observational studies of dementia have been small in size. Therefore, an alternative approach, i.e., an observational study with a large primary care database, is believed to address those research questions.

Electronic primary care databases provide data on diagnoses and prescriptions. There are several UK primary care databases such as the Clinical Practice Research Datalink (CPRD) (new name of the General Practice Research Database (GPRD)) and The Health Improvement Network (THIN). Nevertheless, recording of dementia in primary care databases may have limitations. For a wide range of reasons discussed in the previous sections, dementia may not be well recorded, and it is not clear how dementia should be identified in those records. In order to perform epidemiological research into dementia using these datasets, firstly, it is necessary to understand how dementia is recorded in primary care, which codes are used, and whether related symptoms and medications are additionally needed to the codes to identify people with dementia. Dementia prevalence and incidence in the UK have been estimated previously using various data sources, but those estimates have limitations. They were often derived from small or non-representative datasets. The UK's electronic primary care datasets are reasonably representative and are extremely large. There is therefore an opportunity to estimate the prevalence and incidence of dementia in the UK population, to examine how this has changed over time, and to look at how the rates vary depending on the codes that have been used.

1-2-2. Study objectives

The main research aims of this study are to investigate how people with dementia should be identified for epidemiological work using primary care records, and the implications of this for estimates of prevalence and incidence of dementia as recorded in primary care.
More specific objectives of the study are firstly, to systematically search for the diagnosis and symptom codes for dementia which have been used in previous research in electronic primary care records in the UK. Secondly, to collate and update the code lists to create alternative categories of codes to identify dementia, or its associated symptoms or medication use. Thirdly, to apply these definitions to provide estimates of the prevalence and incidence of dementia in the UK from a large electronic primary care database, i.e., THIN.

Chapter 2. Systematic review of the codes used to identify dementia in electronic primary care records

2-1. Identification of studies and search the codes

In this chapter, the methods of a systematic review of diagnostic codes which have been used in the UK primary care database will be described were described.

Background

A clear understanding of the population defined as dementia in primary care is required to perform research on the topics. To perform a quantitative analysis using a primary dataset, examination of how previous studies have identified people with dementia (or related conditions), and the codes that have been used to extract the population is important as a reference, and for the justification of the study population.

Objectives

The review question was how previous studies using primary care databases have identified people with dementia or related conditions. There are two objectives in this review: firstly, to identify dementia related studies which used electronic primary care records in the UK. Secondly, to locate the codes which have been used in those studies as a reference for a primary care database analysis.

Method

Electronic searches including the medical database – PubMed (Medline) and the non-Medical database – EMBASE, and the social science database – PsychINFO, social science citation index (IBSS, sociological abstracts), Cochrane Library were performed (lastly confirmed on 27/04/2017) for the studies using the main primary care datasets in the UK (i.e., Clinical Practice Research Datalink (CPRD), General practice Research Database (GPRD), The Health Improvement Network (THIN) and QResearch) involving people with ‘dementia’ or ‘Alzheimer’ or ‘cognitive’ or ‘memory’ problems (Figure 2-1). Abstracts and titles were then reviewed with eligible articles read in full including appendices. Supplementary documents were examined for the codes have used in the study.

The final selection of studies was then analysed and appraised to combine the codes. Types of study included were observational studies including Quasi-experimental or Mix method (i.e., Quantitative and Qualitative) studies. RCTs, CCTs (controlled clinical trials), Open-label or Qualitative studies (e.g., systematic reviews) were excluded.

Figure 2-1. Search keywords in PUBMED

(dementia OR alzheim* OR cognit* OR memory) AND ("Clinical Practice Research Datalink" OR CPRD OR "General Practice Research Database" OR GPRD OR "The Health Improvement Network" OR QResearch)

Results

92 papers in PUBMED, 50 papers in EMBASE, and 27 papers in PsychINFO were identified by the search keywords. 43 papers were identified containing the 'code' keyword after removing 57 duplicated papers (30 papers in EMBASE, and 27 papers in PsychINFO). 13 papers provided 'code' lists (including Appendix and supplementary documents) which have been used in the primary care databases; therefore 30 papers not provide a code list were excluded. As 1 paper provided the seizure code list [58] which is not exactly a dementia-related code, 12 studies were used for analysis (Figure 2-2 and Table 2-1).

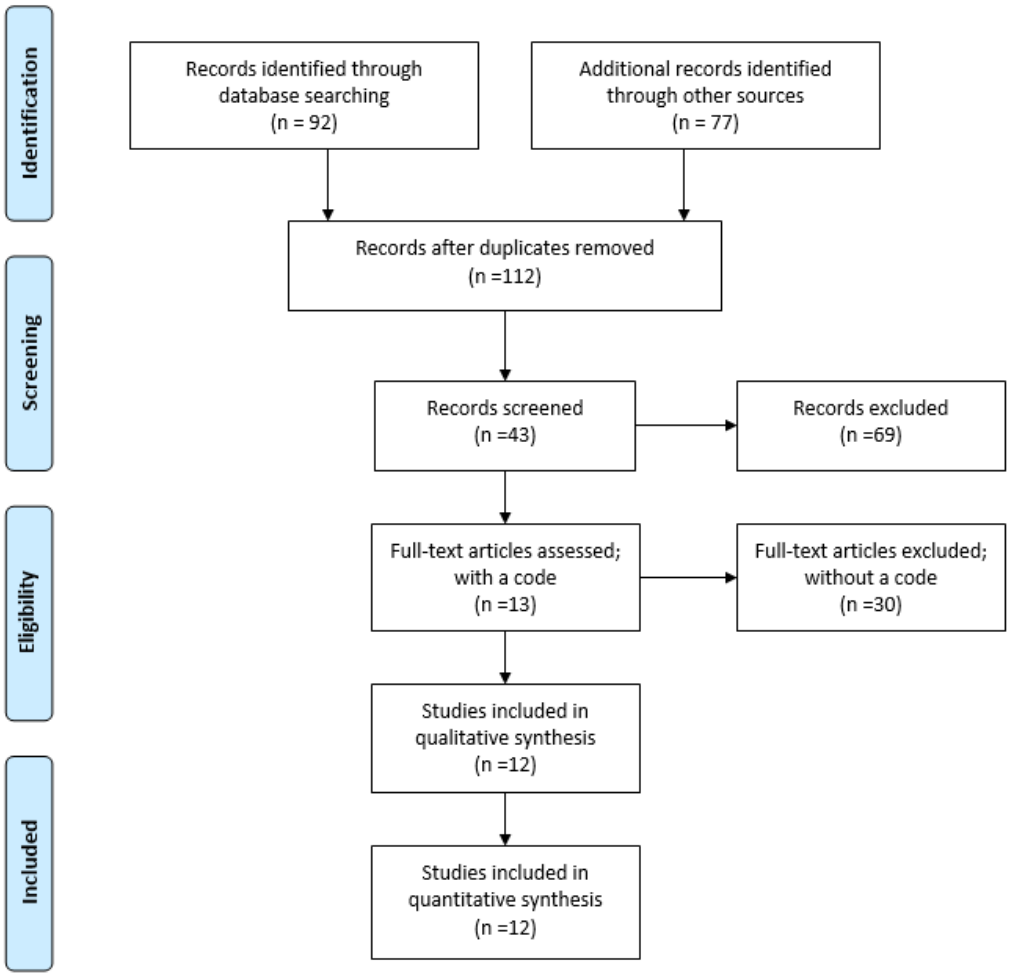


Figure 2-2. Flow diagram for a systematic review (PRISMA) [59]

The first study, ① Goh *et al*., 2015 [60], is a cohort study with 45, 541 persons in the CPRD who were exposed to angiotensin receptor blockers (ARBs) (with 380,548 persons exposed to angiotensin-converting enzyme inhibitors) and compared the risk of dementia incidence. The study provided 63 Read codes representing dementia outcomes of interest in the study with 19 codes for dementia subtypes and 33 indicative codes for pre-existing dementia or cognitive impairment. The second study, ②Cook *et al.*, 2015 [61], is a retrospective cohort study using electronic medical records (EMRs) from primary care practices that participated in THIN database (01/1990-07/2009). The study estimated the incidence rates of ischaemic and haemorrhagic stroke and seizure, and compared among cohorts with and without dementia in Alzheimer's disease. The third study, ③ Strom *et al.*, 2015 [62], is a retrospective cohort study using THIN database (01/1987-12/2013) examining statin therapy and risk of acute memory impairment via comparisons of statin users with two control groups (i.e., matched nonusers of any LLDs and users of non-statin LLDs). The fourth study, ④ Browne *et al.*, 2017 [63], is a retrospective cohort study based on the CPRD, with incident cases of dementia

diagnosed in 2008 and followed for up to 5 years. The study is about to identify subgroups with higher healthcare needs, by analysing the association of comorbidity and health service usage among patients with dementia in the UK. The fifth study, ⑤ Davies *et al.,* 2011 [64], performed a nested case-control analysis within the GP research database, i.e., GPRD (with dementia diagnosed persons aged 60+ years, 1997-2008) to investigated whether angiotensin II receptor blockers (ARBs) and angiotensin converting enzyme inhibitors (ACE-Is) are more strongly associated with dementias than other antihypertensive drugs. The sixth case-control study, ⑥ Schrag, *et al.*, 2014 [65], used THIN database to examine the association between the first presentation of several pre-diagnostic features in primary care (1996-2012) and a subsequent diagnosis of Parkinson's disease, and to chart the timeline of the first presentations (before diagnosis). The seventh study, ⑦ Brown *et al.,* 2016 [32], provided a comparison of dementia recorded in routinely collected hospital admission data in England, i.e., HES with dementia recorded in two sources of CPRD (N=340) and a survey of study participants' GPs (N=244) in primary care. The eighth study, ⑧ Happich *et al.,* 2016 [66], investigated whether prior diagnosis with Alzheimer's disease among patients with vascular dementia is associated with excess costs in the CPRD population. The study used patients with a final vascular dementia diagnosis and linkage to HES data which retrospectively selected from de-identified CPRD data. The ninth study, ⑨ Grant *et al*., 2013 [67], is a cohort study with data (on 54,816 people aged 60-89 with dementia and an age-gender stratified 205,795 people without dementia, 2001-10) from THIN. The study examined the first diagnosis and management of incontinence in older people with and without dementia. The tenth study, ⑩ Shah *et al*., 2010 [68], performed a cross-sectional analysis using THIN (435,568 patients aged 65+ years care home residents from 326 English and Welsh general practices) in order to enhance identification of older nursing and residential home residents in a national sample, and to describe their chronic disease prevalence. The eleventh study, ⑪ Khosrow-Khavar *et al.,* 2017 [69], used the CPRD, a cohort of 30,903 men who newly diagnosed with nonmetastatic prostate cancer (04/1988- 04/2015) to determine whether the use of androgen deprivation therapy (ADT) is associated with an increased risk of dementia including Alzheimer's disease, in patients with prostate cancer. The twelfth study, ⑫ Emdin *et al*., 2016 [70], is a prospective population-based cohort study (with 11,114 initial presentations of vascular dementia were observed for a median 7 years follow-up using the CPRD). The study examined associations between blood pressure and risk of vascular dementia both in individuals prior to and after transient ischemic attack or stroke (Oxford Vascular Study).

Most studies have used codes representing dementia diagnosis, and prescribed medications depends on the study objectives. Some studies included indicative codes of pre-existing dementia, cognitive impairment or acute memory loss, but there was no evidence of using the codes related symptoms. The studies examining therapies of hypertension in systematic reviews (① Goh *et al*., 2015 [60], ③ Strom *et al.,* 2015 [62], ⑤ Davies *et al.,* 2011 [64], ⑫ Emdin *et al*., 2016 [70] and the study

examined comorbidity with dementia, ④ Browne *et al.*, 2017 [63]) have used codes representing dementia and codes indicative of pre-existing dementia, cognitive impairment and acute memory loss in primary care databases (Table 2-1).

Table 2-1. Lists of studies provided codes

Studies		Code lists	N*	Main Findings of incidence/prevalence rates
①	Goh *et al*., 2015 [60]	1. Read codes representing dementia outcomes of interest in the study 2. Read codes for dementia subtypes where ARBs are not expected to have an effect 3. Read codes indicative of pre-existing dementia or cognitive impairment	115	Incidence rate per 1,000 person-years (95%CIs): ACE-I use only 3.91 (3.81-4.01) and ever ARB use 3.46 (3.20-3.73).
②	Cook *et al.*, 2015 [61]	Alzheimer's codes	16	Incidence rates of stroke: 15.9/1,000 person-years among AD dementia patients, 12.0/1,000 person-years among non-AD dementia patients; RR (95% CIs) 1.33 (1.15-1.53).
③	Strom *et al.*, 2015 [62]	Read medical codes (Clinical Terms Version 2) for acute memory loss: distribution occurring within 30-days after first statin exposure	30	The prevalence of statin exposure immediately preceding the first diagnosis of acute memory loss: 18.9%. (18.5% during 31–60 days prior, 18.9% during 150–180 days prior, and 17.7% during 270–300 days prior).
④	Browne *et al.*, 2017 [63]	Case definition of dementia (dementia diagnosis in primary care clinical charts or referrals to secondary care recorded between 03/2008 and 02/2009).	63	The prevalence of comorbidity: 91.7%. (Review: 94.7% of those with dementia have another chronic disease in the Scottish population [71]).
⑤	Davies *et al.*, 2011 [64]	Read/OXMIS codes used to define dementia (from 73 studies)	39	Review: ARBs were associated with lower rates of dementia incidence and slower progression of AD compared to ACE-I and other antihypertensive treatments [72].
⑥	Schrag, *et al.*, 2014 [65]	Read codes used for cognitive decline and memory problems were extracted from the pre-diagnostic presentations (and a subsequent diagnosis of Parkinson's disease)	108	RR (95% CIs) for patients with Parkinson's: incidence of balance impairments 2.19 (1.09-4.16), hypotension 3.23 (1.85-5.52), dizziness 1.99 (1.67-2.37), fatigue 1.56 (1.27-1.91), depression 1.76 (1.41-2.17), anxiety 1.41 (1.09-1.79).
⑦	Brown *et al.*, 2016 [32]	1. CPRD Read codes and terms for dementia 2. Additional read terms compatible with, but not defining, dementia	189	Table 1-2, Age-specific incidence rates of dementia per 1,000 women-years in the UK, CPRD (1990-2012): 0.37 (60-64 years), 1.18 (65-69 years), 3.53 (70-74 years), 8.06 (75-79 years).
⑧	Happich *et al.*, 2016 [66]	Read codes and ICD-10 used to identify dementias of interest	147	6% (among N=9,311 with vascular dementia) had prior Alzheimer's disease with a median time to vascular dementia exceeding 2 years from index date of the first dementia(-like condition) diagnosis.
⑨	Grant *et al*., 2013[67]	Read codes identifying dementia	54	No estimates
⑩	Shah *et al*., 2010 [68]	Read codes used for care home residence and disease definitions of all type of dementia	51	Prevalence ratios for dementia (95% CIs): 14.8 (13.4-16.4) for nursing and 13.5 (12.4-14.8) for residential homes versus controls.
⑪	Khosrow-Khavar *et al.*, 2017 [69]	Read codes and read terms for dementia	66	During a mean (SD) follow-up of 4.3 (3.6) years, 799 patients were newly diagnosed with dementia (incidence 95% CIs, 6.0 (5.6-6.4) per 1,000 person-years.
⑫	Emdin *et al*., 2016 [70]	Read codes used to identify vascular dementia cases in primary care records	16	No estimates

* The number of codes provided.

Tables 2-2 to Table 2-7 will present the collected codes from the 12 studies. Further information about the categorized codes are in the next chapter (3-1-3).

The QOF defined dementia codes

QOF is considered to be the ultimate definitive category as that is what is used in incentives to GPs. The QOF based dementia codes (i.e., DEM_COD, version 28[6] (28/03/2014) to version 33 (27/10/2015) [17, 73-77]) were combined with other categorised diagnostic codes. If a QOF code appears more than once in other categories (Table 2-3 and Table 2-5), it was counted as a QOF code in the analysis stage. The QOF based codes (Table 2-2) include dementia in Alzheimer's disease, vascular dementia, Lewy body disease, arteriosclerotic dementia, dementia in other classified diseases, presenile/senile dementia, pick's disease, other alcoholic dementia and drug-induced dementia.

The *Other diagnoses* codes

The *Other diagnoses* (Table 2-3) codes are dementia diagnosis codes other than or alternative of the QOF based dementia codes. Except the QOF based codes [7], the codes include presenile/ senile dementia related, alcoholic dementia NOS, moderate and severe cognitive impairment/decline (GDS level 4-7), dementia monitoring, annual review, medication review, and additionally, language disorder of dementia, presbyophrenic psychosis, dementia (advanced) care plan related codes (which not used in the 12 literature studies). The third study, ③ Strom et al., 2015 [65] (which examined risk of acute memory impairment), and the sixth study, ⑥ Schrag, et al., 2014 [68] (which examined the first presentation of pre-diagnostic features and a subsequent diagnosis of Parkinson's disease with codes about cognitive decline and memory problems), did not use both the QOF based (Table 2-2) and *Other diagnoses* codes. The codes used in the two studies appeared instead in *Dementia symptoms* (Table 2-4), *Vague indicators* (Table 2-5), and *Likely MCI* (Table 2-7).

Codes suggest *Dementia symptoms*

The codes suggest *Dementia symptoms* (Table 2-4) consist of referral to memory clinic, memory loss/forgets and its assessment (e.g., AMI), cognitive decline/impairment and its assessment (e.g.,

[6] version 20 to 27 are identical to version 28.
[7] The codes initially included some of the QOF (DEM_COD) (version 28-33) codes associated with presenile dementia, senile dementia, arteriosclerotic dementia, other alcoholic dementia, drug-induced dementia, Alzheimer's disease, pick's disease, and Lewy body disease in Table 2-2.

CFG, LOTCA, MEANS, MMSE), dementia tests (e.g., GPCOG, CDR, DRS, BDRS) or Alzheimer's disease test/screening (e.g., ADAS), and cerebral degeneration. The studies (except ③ Strom et al., 2015 [65] and ⑥ Schrag, et al., 2014 [68]) appeared in *Dementia symptoms* were ① Goh *et al*., 2015 [60] which examined risk of dementia incidence using the codes representing dementia outcomes, dementia subtypes and indicative of pre-existing dementia or cognitive impairment, ⑦ Brown *et al.*, 2016 [32] which provided a comparison of dementia recorded in primary care sources and ⑧ Happich *et al.*, 2016 [66] which investigated prior diagnosis with Alzheimer's disease among patients with vascular dementia using Read codes and ICD-10.

Vague indicators

Vague indicators that could be dementia related (Table 2-5) consist of codes related to (poor) memory or forgetfulness, memory scales (e.g., WMS) and alcoholic encephalopathy. The study, ⑩ Shah *et al*., 2010 [68] which used the codes to define all types of dementia (to enhance identification of older nursing and residential home residents) appeared in *Vague indicators* with the studies appearing in *Dementia symptoms* (Table 2-4).

Likely MCI

Likely MCI (Table 2-7) is about mild memory disturbance, mild cognitive decline levels (GDS level 2-3), mild cognitive disorder, mild cognitive impairment and at risk of dementia. The studies of ③ Strom et al., 2015 [65] and ⑥ Schrag, et al., 2014 [68], ⑦ Brown *et al.*, 2016 [32] and ⑧ Happich *et al.*, 2016 [66] appeared in *Likely MCI.*

Table 2-2. QOF

Code (N=54)	Description	Studies provided Read codes [32, 60-70] (Table 2-1) ①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	TC*
Eu00.00	[X]Dementia in Alzheimer's disease	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00000	[X]Dementia in Alzheimer's disease with early onset	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00100	[X]Dementia in Alzheimer's disease with late onset	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00200	[X]Dementia in Alzheimer's dis, atypical or mixed type	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00z00	[X]Dementia in Alzheimer's disease, unspecified	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu01.00	[X]Vascular dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01000	[X]Vascular dementia of acute onset	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01100	[X]Multi-infarct dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01200	[X]Subcortical vascular dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01300	[X]Mixed cortical and subcortical vascular dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01y00	[X]Other vascular dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01z00	[X]Vascular dementia, unspecified	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
E004z00	Arteriosclerotic dementia NOS	✓			✓	✓		✓	✓	✓		✓	✓	8
Eu02z00	[X] Unspecified dementia	✓			✓	✓		✓	✓	✓	✓	✓		8
Eu04100	[X]Delirium superimposed on dementia	✓			✓	✓		✓	✓	✓	✓	✓		8
F110.00	Alzheimer's disease	✓	✓		✓			✓	✓	✓	✓	✓		8
F110000	Alzheimer's disease with early onset	✓	✓		✓			✓	✓	✓	✓	✓		8
F110100	Alzheimer's disease with late onset	✓	✓		✓			✓	✓	✓	✓	✓		8
E002z00	Senile dementia with depressive or paranoid features NOS	✓			✓	✓		✓	✓	✓		✓		7
E004.00	Arteriosclerotic dementia	✓			✓			✓	✓	✓		✓	✓	7
E004000	Uncomplicated arteriosclerotic dementia	✓			✓			✓	✓	✓		✓	✓	7
E004100	Arteriosclerotic dementia with delirium	✓			✓			✓	✓	✓		✓	✓	7
E004200	Arteriosclerotic dementia with paranoia	✓			✓			✓	✓	✓		✓	✓	7
E004300	Arteriosclerotic dementia with depression	✓			✓			✓	✓	✓		✓	✓	7
E041.00	Dementia in conditions EC	✓			✓			✓	✓	✓	✓	✓		7
Eu02.00	[X]Dementia in other diseases classified elsewhere	✓			✓	✓		✓	✓		✓	✓		7
Eu02300	[X]Dementia in Parkinson's disease	✓			✓	✓		✓	✓		✓	✓		7
E000.00	Uncomplicated senile dementia	✓			✓			✓	✓	✓		✓		6
E001.00	Presenile dementia	✓			✓			✓	✓	✓		✓		6
E001000	Uncomplicated presenile dementia	✓			✓			✓	✓	✓		✓		6
E001100	Presenile dementia with delirium	✓			✓			✓	✓	✓		✓		6
E001200	Presenile dementia with paranoia	✓			✓			✓	✓	✓		✓		6
E001300	Presenile dementia with depression	✓			✓			✓	✓	✓		✓		6
E001z00	Presenile dementia NOS	✓				✓		✓	✓	✓		✓		6
E002.00	Senile dementia with depressive or paranoid features	✓			✓			✓	✓	✓		✓		6
E002000	Senile dementia with paranoia	✓			✓			✓	✓	✓		✓		6
E002100	Senile dementia with depression	✓			✓			✓	✓	✓		✓		6
E003.00	Senile dementia with delirium	✓			✓			✓	✓	✓		✓		6
E012.00	Other alcoholic dementia	✓			✓			✓	✓		✓	✓		6
Eu02000	[X]Dementia in Pick's disease	✓			✓			✓	✓		✓	✓		6
Eu02500	[X]Lewy body dementia	✓				✓		✓	✓		✓	✓		6
Eu02y00	[X]Dementia in other specified diseases class if elsewhere	✓			✓	✓		✓			✓	✓		6
Eu02100	[X]Dementia in Creutzfeldt-Jakob disease	✓			✓			✓			✓	✓		5
Eu02200	[X]Dementia in Huntington's disease	✓			✓			✓			✓	✓		5
Eu02400	[X]Dementia in human immunodef virus [HIV] disease	✓			✓			✓			✓	✓		5
F111.00	Pick's disease	✓			✓			✓	✓		✓			5
E012000	Chronic alcoholic brain syndrome	✓						✓	✓		✓			4
E02y100	Drug-induced dementia	✓							✓		✓	✓		4
F116.00	Lewy body disease	✓						✓	✓		✓			4
F112.00	Senile degeneration of brain	✓						✓			✓			3
E00..00	Senile and presenile organic psychotic conditions								✓		✓			2
E00y.00	Other senile and presenile organic psychoses					✓			✓					2
E00z.00	Senile or presenile psychoses NOS					✓			✓					2
A411000	Sporadic Creutzfeldt-Jakob disease													0
Total		50	8	0	44	23	0	49	48	36	33	46	13	

* Total Count: The number of studies included the code.

Table 2-3. *Other diagnoses*

Code (N=98)	Description	Studies provided Read codes [32, 60-70] (Table 2-1) ①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	TC *
Eu00011	[X]Presenile dementia, Alzheimer's type	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00012	[X]Primary degen dementia, Alzheimer's type, presenile onset	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00013	[X]Alzheimer's disease type 2	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00111	[X]Alzheimer's disease type 1	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00112	[X]Senile dementia, Alzheimer's type	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00113	[X]Primary degen dementia of Alzheimer's type, senile onset	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu00z11	[X]Alzheimer's dementia unspec	✓	✓		✓	✓		✓	✓	✓	✓	✓		9
Eu01.11	[X]Arteriosclerotic dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu01111	[X]Predominantly cortical dementia	✓			✓	✓		✓	✓	✓	✓	✓	✓	9
Eu02z11	[X] Presenile dementia NOS	✓			✓	✓		✓	✓	✓	✓	✓		8
Eu02z13	[X] Primary degenerative dementia NOS	✓			✓	✓		✓	✓	✓	✓	✓		8
Eu02z14	[X] Senile dementia NOS	✓			✓	✓		✓	✓	✓	✓	✓		8
Eu02z16	[X] Senile dementia, depressed or paranoid type	✓			✓	✓		✓	✓	✓	✓	✓		8
E00..11	Senile dementia	✓			✓			✓	✓	✓	✓	✓		7
E00..12	Senile/presenile dementia	✓			✓			✓	✓	✓	✓	✓		7
E004.11	Multi infarct dementia	✓			✓			✓	✓	✓		✓	✓	7
Fyu3000	[X]Other Alzheimer's disease	✓	✓		✓	✓			✓	✓		✓		7
1461	H/O: dementia	✓			✓			✓	✓	✓				5
E012.11	Alcoholic dementia NOS	✓						✓	✓		✓	✓		5
Eu10711	[X]Alcoholic dementia NOS	✓			✓			✓	✓			✓		5
3AE3.00	GDS level 4 - moderate cognitive decline	✓						✓	✓					3
3AE4.00	GDS level 5 - moderately severe cognitive decline	✓						✓	✓					3
3AE5.00	GDS level 6 - severe cognitive decline	✓						✓	✓					3
3AE6.00	GDS level 7 - very severe cognitive decline	✓						✓	✓					3
6AB..00	Dementia annual review	✓						✓	✓					3
66h..00	Dementia monitoring	✓						✓						2
9Ou..00	Dementia monitoring administration	✓						✓						2
9Ou1.00	Dementia monitoring first letter	✓						✓						2
9Ou2.00	Dementia monitoring second letter	✓						✓						2
9Ou3.00	Dementia monitoring third letter	✓						✓						2
9Ou4.00	Dementia monitoring verbal invite	✓						✓						2
9Ou5.00	Dementia monitoring telephone invite	✓						✓						2
F118.00	Frontotemporal degeneration							✓	✓					2
ZS7C500	Language disorder of dementia	✓							✓					2
28E1.00	Moderate cognitive impairment								✓					1
28E2.00	Severe cognitive impairment								✓					1
8Hla.00	Referral to dementia care advisor							✓						1
E00y.11	Presbyophrenic psychosis								✓					1
8BM0200	Dementia medication review													0
8CMZ.00	Dementia care plan													0
8CMZ000	Dementia care plan agreed													0
8CMZ100	Dementia care plan reviewed													0
8CMZ200	Dementia care plan declined													0
8CMZ300	Dementia care plan review declined													0
8CMe000	Dementia advance care plan													0
8CSA.00	Dementia advance care plan agreed													0
8IAe000	Dementia advance care plan declined													0
8IAe200	Dementia advance care plan review declined													0
Z59..00	Reminiscence therapy													0
Total		33	8	0	19	14	0	33	30	18	16	19	3	

* Total Count: The number of studies included the code.

Table 2-4. *Dementia symptoms*

Code (N=171)	Description	Studies provided Read codes [32, 60-70] (Table 2-1) ①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	TC*
8HTY.00	Referral to memory clinic			✓			✓	✓	✓					4
3A...12	Dementia assessment	✓						✓	✓					3
3A30.00	Memory: present place not known			✓			✓	✓						3
3AE..00	Global deterioration scale: assessment of prim deg dementia	✓						✓	✓					3
F11x900	Cerebral degeneration in Parkinson's disease	✓						✓	✓					3
Z7CE615	Loss of memory			✓			✓		✓					3
Z7CEH00	Memory impairment			✓			✓	✓						3
Z7CEH15	Poor memory			✓			✓		✓					3
ZR3V.12	CDR - Clinical dementia rating scale	✓						✓	✓					3
1B1A100	Short-term memory loss			✓				✓						2
28E..00	Cognitive decline						✓		✓					2
388V.00	Mini mental state score							✓	✓					2
388m.00	Mini-mental state examination							✓	✓					2
388m.11	MMSE score							✓	✓					2
3A20.00	Memory: present time not known						✓	✓						2
3A40.00	Memory: present year not known						✓	✓						2
3A60.00	Memory: present month not known						✓	✓						2
3A80.00	Memory: import.person not known						✓	✓						2
3A91.00	Memory: count down unsuccess.						✓	✓						2
3AD1.00	Ten item dementia test							✓	✓					2
3AD2.00	Thirty seven item dementia test							✓	✓					2
3AD3.00	Six item cognitive impairment test							✓	✓					2
3AF..00	Addenbrooke's cognitive examination revised							✓	✓					2
9Nk1.00	Seen in memory clinic			✓			✓							2
E2A1100	Organic memory impairment						✓		✓					2
F11x700	Cerebral degeneration due to Jakob - Creutzfeldt disease	✓						✓						2
R00z011	[D]Memory deficit			✓			✓							2
Z7CE616	LOM - Loss of memory						✓		✓					2
Z7CEA11	Impairment of working memory						✓		✓					2
Z7CEA13	Impairment of primary memory						✓		✓					2
Z7CEH13	Bad memory						✓		✓					2
Z7CEH14	Memory problem			✓			✓							2
Z7CEJ00	Memory lapses			✓			✓							2
Z7CF800	Poor short-term memory			✓			✓							2
Z7CF811	Short-term memory loss			✓			✓							2
Z7CFO00	Poor long-term memory						✓		✓					2
Z7CFO11	Long-term memory loss						✓		✓					2
ZR1H.00	Allen cognitive level screening tool							✓	✓					2
ZR1T.00	Arizona battery for communication disorders of dementia	✓							✓					2
ZR2X.12	BDRS - Blessed dementia rating scale	✓							✓					2
ZR3V.00	Clinical dementia rating scale	✓							✓					2
ZR3V.11	DRS - Clinical dementia rating scale	✓							✓					2
ZRaA.11	MMSE - Mini-mental state examination							✓	✓					2
ZRaA200	Modified mini-mental state examination							✓	✓					2
1B1Y.00	Poor visual sequential memory						✓							1
1B1a.00	Poor auditory sequential memory						✓							1
1JA2.00	Suspected dementia							✓						1
1S21.00	Disturbance of memory for order of events						✓							1
28G..00	Forgetful						✓							1
2JR..00	Lack mental capacity make decision Mental Capacity Act 2005							✓						1
38Dv.00	GPCOG - general practitioner assessment of cognition							✓						1
38Dv000	GPCOG (GP assessment of cognition) patient examination							✓						1
38Dv100	GPCOG (GP assessment of cognition) informant interview							✓						1
3A...11	Memory assessment							✓						1
3A1..00	Memory: own age							✓						1
3A10.00	Memory: own age not known						✓							1
3A3..00	Memory: present place							✓						1
3A4..00	Memory: present year							✓						1
3A50.00	Memory: own DOB not known						✓							1
3A70.00	Memory: important event not known						✓							1
3A9..00	Memory: count down							✓						1
3AA..00	Memory: address recall							✓						1
3AA1.00	Memory: address recall unsucc.						✓							1
3AD..00	Dementia test							✓						1

Table to be continued

7P10400	Neuropsychology test of memory				✓	1
F11..00	Other cerebral degenerations			✓		1
F11x.00	Cerebral degeneration in other disease EC	✓				1
F11x200	Cerebral degeneration due to cerebrovascular disease	✓				1
F11x400	Cerebral degeneration due to neoplastic disease	✓				1
F11x500	Cerebral degeneration due to myxoedema	✓				1
F11x600	Cerebral degeneration due to vitamin B12 deficiency	✓				1
F11xz00	Cerebral degeneration other disease NOS	✓				1
F11y.00	Other cerebral degeneration	✓				1
F11yz00	Other cerebral degeneration NOS	✓				1
F11z.00	Cerebral degeneration NOS			✓		1
F11z.11	Cerebral atrophy			✓		1
Z7A1300	Memory skills training		✓			1
Z7CE612	Memory gone		✓			1
Z7CEA00	Impairment of registration		✓			1
Z7CEA12	Impairment of immediate recall		✓			1
Z7CEB11	Loss of memory for remote events		✓			1
Z7CEH11	Memory dysfunction		✓			1
Z7CEH12	Memory deficit		✓			1
Z7CEI00	Mixes past with present		✓			1
Z7CFH00	Forgets recent activities		✓			1
Z7CFI00	Forgets what has just done		✓			1
Z7CFJ00	Forgets what has just said		✓			1
Z7CFK00	Forgets what has just read		✓			1
Z7CFL00	Forgets what has just seen		✓			1
Z7CFM00	Forgets what has just heard		✓			1
Z7CFQ00	Unable to remember own date of birth		✓			1
Z7CFS00	Unable to remember own age		✓			1
Z7CFS11	Cannot remember own age		✓			1
Z7CFU00	Unable to remember day of the week		✓			1
Z7CFW00	Unable to remember today's date		✓			1
Z7CFW11	Cannot remember today's date		✓			1
Z7CFY00	Unable to remember month of year		✓			1
Z7CFa00	Unable to remember current year		✓			1
Z7CFc00	Unable to remember name of reigning monarch		✓			1
Z7CFc11	Cannot remember reigning monarch		✓			1
Z7CFc12	Unable to remember name of current monarch		✓			1
Z7CFe00	Unable to remember name of current prime minister		✓			1
Z7CFe11	Cannot remember current prime minister		✓			1
Z7CFf00	Cannot remember name of school		✓			1
Z7CFg00	Cannot remember names of intimates		✓			1
Z7CFh00	Cannot remember birth dates of children		✓			1
Z7CFi00	Cannot remember wedding anniversary		✓			1
Z7CFk00	Unable to remember objects		✓			1
Z7CFm00	Unable to remember faces		✓			1
Z7CFo00	Unable to remember sounds		✓			1
Z7CFq00	Unable to remember motor skills		✓			1
Z7CFs00	Unable to remember new motor skills		✓			1
Z7CFu00	Unable to remember old motor skills		✓			1
Z7CFw00	Memory aided by use of diary		✓			1
Z7CFx00	Memory aided by use of labels		✓			1
Z7CFz00	Memory aided by use of lists		✓			1
Z7CGP00	Delayed verbal memory		✓			1
ZD11300	Auditory memory therapy		✓			1
ZR16.00	Abbreviated mental test			✓		1
ZR16.11	AMT - Abbreviated mental test			✓		1
ZR1I.00	Allen cognitive performance test				✓	1
ZR1K.00	Alzheimer's disease assessment scale	✓				1
ZR1K.11	ADAS - Alzheimer's disease assessment scale	✓				1
ZR2X.00	Blessed dementia rating scale				✓	1
ZR2X.11	Memory concentration test			✓		1
ZR2X.13	Information-memory-concentration test				✓	1
ZR3V.13	Dementia rating scale	✓				1
ZR3a.00	Cognitions questionnaire			✓		1
ZRBg.00	Everyday memory questionnaire			✓		1
ZRV9.00	Kendrick battery for detection of dementia in the elderly				✓	1
ZRV9.11	Kendrick cognitive tests for the elderly				✓	1
ZRVa.00	Lowenstein OT cognitive assessment				✓	1
ZRVa.11	LOTCA - Lowenstein OT cognitive assessment				✓	1
ZRa2.00	Microcog - assessment of cognitive function			✓		1
ZRa3.00	Middlesex elderly assessment of mental state				✓	1
ZRa3.11	MEAMS - Middlesex elderly assessment of mental state				✓	1
ZRaA.00	Mini-mental state examination				✓	1
ZRaA100	Modified mini-mental state 3MS examination				✓	1

Table to be continued

ZRaY.00	Neurobehavioural cognitive status examination								✓					1
28E3.00	Cognitive impairment													0
28H..00	Mentally vague													0
311B.00	Cognitive assessment													0
3A2..00	Memory: present time													0
3A5..00	Memory: own DOB													0
3A6..00	Memory: present month													0
3A7..00	Memory: important event													0
3A8..00	Memory: important person													0
3AB..00	Behaviour assessment													0
8CET.00	Dementia leaflet given													0
8IBB000	Dementia assessment not indicated													0
8IEn.00	Referral to memory clinic declined													0
8IEu.00	Dementia screening declined													0
8IEu000	Dementia screening questionnaire declined													0
9OqD.00	Dementia screening questionnaire sent to patient													0
9OqE.00	Dementia screening questionnaire completed													0
9OqF.00	No response to dementia screening invitation													0
9OqG.00	Everyday Cognition questionnaire completed													0
9OqG.11	ECog (Everyday Cognition) questionnaire completed													0
Z59..11	RT - Reminiscence therapy													0
Z7A1.00	Cognitive skills training													0
ZR16.12	Hodkinson's mental test													0
ZR16.13	Hodkinson's test													0
ZR1J.00	Alphabet number alteration test													0
ZR1N.00	Anomalous sentences repetition test													0
ZR1n.00	Autobiographical memory interview													0
ZR1n.11	Autobiographical memory inventory													0
ZR1n.12	AMI - Autobiographical memory interview													0
ZR3T.00	Clifton assessment procedures for the elderly													0
ZR3b.00	Cognitive failures questionnaire													0
ZR3b.11	CFQ - Cognitive failures questionnaire													0
ZR3k.00	Consonant trigrams test													0
Total		20	0	12	0	0	74	45	42	0	0	0	0	

* Total Count: The number of studies included the code.

Table 2-5. *Vague indicators*

Code	Description	Studies provide d Read codes [32, 60-70] (Table 2-1)												
(N=76)		①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	TC*
1B1A.12	Memory loss symptom			✓			✓	✓	✓					4
1B1A.13	Memory disturbance			✓			✓	✓						3
E011000	Korsakov's alcoholic psychosis	✓						✓	✓					3
E011100	Korsakov's alcoholic psychosis with peripheral neuritis	✓						✓	✓					3
Eu02z15	[X] Senile psychosis NOS							✓	✓		✓			3
F11x000	Cerebral degeneration due to alcoholism	✓						✓	✓					3
Z7CE611	Memory loss			✓			✓		✓					3
3A11.00	Memory: own age known			✓				✓						2
E040.11	Korsakoff's non-alcoholic psychosis	✓						✓						2
Eu10712	[X]Chronic alcoholic brain syndrome	✓						✓						2
Z7C1.00	Impaired cognition						✓		✓					2
Z7CE415	Loss of memory						✓		✓					2
Z7CE500	Forgetful			✓			✓							2
Z7CEC11	Loss of memory for recent events			✓			✓							2
1479	H/O: disturbance of consciousness							✓						1
147F.00	History of Parkinson's disease							✓						1
1B6..00	Disturbance of consciousness							✓						1
1BN..00	Wandering							✓						1
1BN0.00	Wanders during the day							✓						1
1BN2.00	Wanders during the day and at night							✓						1
2232	O/E - mentally confused							✓						1
2232.11	O/E - confused							✓						1
2233	O/E - delirious							✓						1
2841.11	Confusion							✓						1
3A21.00	Memory: present time known							✓						1
3A31.00	Memory: present place known							✓						1
3A41.00	Memory: present year known							✓						1
3A51.00	Memory: own DOB known							✓						1
3A61.00	Memory: present month known							✓						1
3A71.00	Memory: important event known							✓						1
3A81.00	Memory: important person known							✓						1
3AA0.00	Memory: address recall success							✓						1
E010.12	Delirium tremens							✓						1
E02y200	Drug-induced amnestic syndrome								✓					1
E030.00	Acute confusional state							✓						1
E030.11	Delirium - acute organic							✓						1
E031.00	Subacute confusional state			✓										1
F11x011	Alcoholic encephalopathy							✓						1
Ryu5.00	[X]Symptoms/signs inv cognit, percept, emotion state & behav						✓							1
Ryu5100	[X]Oth & unspec symptom/sign involv cognit funct/awareness						✓							1
Z7A1500	Memory retraining						✓							1
Z7CA100	Isolated memory skills						✓							1
Z7CE412	Memory loss symptom						✓							1
Z7CE414	Memory disturbance						✓							1
Z7CEB12	Poor memory for remote events						✓							1
Z7CEC12	No memory for recent events						✓							1
Z7CEK00	Minor memory lapses						✓							1
Z7CEL00	Mild memory disturbance						✓							1
Z7CEM00	Distortion of memory						✓							1
Z7CEN00	Confabulation						✓							1
Z7CEN11	Invents experiences to compensate for loss of memory						✓							1
Z7CEO00	Momentary confabulation						✓							1
Z7CEP00	Fantastical confabulation						✓							1
Z7CF200	Has delayed recall						✓							1
Z7CFA00	Unable to recall random address at five minutes						✓							1
Z7CFC00	Unable to recall five digit number at five minutes						✓							1
Z7CFE00	Unable to reproduce geometric figure at five minutes						✓							1
Z7CFF00	Forgets what was going to do						✓							1
Z7CFG00	Forgets what was going to say						✓							1

Table to be continued

ZRhS.00	Rivermead behavioural memory test								✓				1
ZRhS.11	RBMT - Rivermead behavioural memory test								✓				1
ZRhS100	Rivermead behavioural memory test - adult version								✓				1
ZRrO.00	Wechsler memory scale								✓				1
ZRrO.11	WMS - Wechsler memory scale								✓				1
ZRrg.00	Wechsler memory scale revised								✓				1
ZRrh.00	Williams memory assessment scales								✓				1
28D..00	Confabulation												0
E042.00	Chronic confusional state												0
Z7C..00	Cognitive function observations												0
Z7D..00	Awareness of self												0
Z7D..11	Personal awareness												0
Z7D..12	Self awareness												0
ZR3T.11	CAPE - Clifton assessment procedures for the elderly												0
Total		5	0	7	0	0	28	31	16	0	1	0	0

* Total Count: The number of studies included the code.

Table 2-6. *Possible additional information*

Code (N=2)	Description	Studies provided Read codes [32, 60-70] (Table 2-1) ①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫
13Y7.00	Alzheimer's disease society member												
3AC..00	Mental disability assess score												

Table 2-7. *Likely MCI*

Code (N=6)	Description	Studies provided Read codes [32, 60-70] (Table 2-1) ①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫	TC*
E2A1000	Mild memory disturbance			✓			✓	✓	✓					4
3AE1.00	GDS level 2 - very mild cognitive decline						✓	✓	✓					3
3AE2.00	GDS level 3 - mild cognitive decline						✓	✓	✓					3
Eu05700	[X]Mild cognitive disorder						✓	✓	✓					3
14Od.00	At risk of dementia							✓						1
28E0.00	Mild cognitive impairment								✓					1
Total		0	0	1	0	0	4	5	5	0	0	0	0	

* Total Count: The number of studies included the code.

Discussion

Systematic literature sources of dementia diagnostic codes in the UK primary care databases (from the primary care practices that participated) were examined. This ensures the codes for dementia have been used. Risk of bias assessment was performed with more than one researchers for the internal validity of the included studies whether the code definition seems to fit with what we expected for dementia. However, the definition of a risk of bias (quality) or a quality score was not presented in this study. In general, risks of bias could have been assessed with very questions. The criteria could include a selection bias (e.g., uniform inclusion/ exclusion criteria to all the groups, accounting for important confounding variables in the design/ analysis), a performance bias (e.g., excluding any impacts from a concurrent or an unintended exposure), an attrition bias (e.g., appropriate missing data handling), a detection bias (e.g., whether confounding/interventions/exposures variables were assessed using valid and reliable measures, and implemented consistently across all the participants) and a reporting bias (e.g. whether all pre-specified outcomes were reported)[78].

Some of the studies may have used very conservative or narrow definitions of dementia and therefore they may have omitted definitive dementia codes. Otherwise, some of the studies may have been too general in the definition of dementia and they have used codes that are not very definitive. The

estimates of prevalence and incidence rates from those studies will be affected by the definitions have used and the overall quality of the studies. It would have been possible to access quality by a standard quality assessment tool, or by simply looking at how extensive their code lists were, however that was beyond the scope of the study. The purpose of this literature review was a part of collecting codes used from all other sources. The validation of the codes was examined in Chapter 4, with the estimates of prevalence and incidence rates.

Considering the difficulty in identifying the clinical syndrome in a study from a primary care database as compared to a study using randomized cohort datasets (which diagnosis can be obtained from a screening or a test), it is important to use adequate diagnostic codes to define the study population with dementia. This would be the first time attempt to try to pull the list of comprehensive codes together from the literature review. However, the limitations of this attempt would be the inclusion of selected sources of data, i.e., the UK primary care data, only since there are other sources of medical records. In addition, the search criteria could have some limitations in particular that the search method used specific keywords. For instance, specific the UK primary care databases such as 'Clinical Practice Research Datalink or CPRD', 'General Practice Research Database or GPRD', 'The Health Improvement Network' and 'QResearch' were used, instead of 'primary care database' or 'hospital database'. Studies using Intercontinental Marketing Services (IMS) Health and the SystmOne GP databases, which might potentially provide codes, could be missing out, even though the outcome would be the same. The Medical Subject Headings (MeSH) could use as additional search engine for Medline records. Therefore, the process of searching for the codes from other sources of data, and combing and categorizing all the collected codes will be described in the next chapter. Moreover, the code lists that have been used in those studies have not been very comprehensive, for example, many of the (pre-) symptom or (pre-) diagnostic codes, or even some of the QOF based codes have not been included (Table 2-2 to Table 2-7). Codes to identify dementia across the studies were not very consistent even though different study objectives and populations were taken into consideration.

The aim of this study is seeking to identify the codes used elsewhere, and to identity the codes need to use for epidemiological analysis. The relevant codes will depend on the study objectives. For instance, some studies are focusing on the population truly have diseases and some studies such as prevalence studies are more interested in identifying population who had all the related symptoms. The code lists were not to be compared against those study objectives. As the code lists were evolving over time, it would be important to examine identifying codes newly included. The code lists were similar over time among studies, except that the very few QOF codes which were used in more recent studies. All the codes lists from the past will be used in this study including the more recent codes. How those codes changed over time was not examined in detail in this study. Many of these studies have been conducted using either THIN or CPRD with the same authors or organizations. Although there have

been some differences, it seems that the same lists of diagnostic codes have tended to be used which supports to continue to use those codes to identify dementia for the UK primary care database.

A low incidence of disease is often occurs following long latency periods and this could be reflected into codes. Nevertheless, there is no gold standard whether the codes used elsewhere were the right ones. Therefore, what other codes should be included will be examined in the next chapters. The codes related to the dementia symptoms, the codes from the database, and prescribed medication will be examined.

Chapter 3. Methods

The codes identified in the previous section were used to identify dementia for the subsequent work which was conducted in THIN primary care database. In this chapter, THIN database and also the use of a dictionary of the codes, specially designed for THIN database, will be described to explore whether there are any further codes for dementia or its symptoms that should be added to the list of codes already identified in the previous chapter. The codes were put into categories as some of the collective list of codes provide definitive evidence for dementia whilst other codes are about a symptom or a related prognosis which may be indicative of dementia but less specific. This chapter described the categories of the codes with the methods that were used to put the codes into categories. The methods used to estimate of prevalence and incidence in THIN database will now be described.

3-1. The Health Improvement Network (THIN) database

The Health Improvement Network (THIN) primary care database contains anonymised longitudinal data on about 6.2% of the UK population records (i.e., 12 million patients) from nearly 600 practices [79]; it derives data from routine clinical practice in the UK which has been collected since 2003 [80, 81]. THIN database represents a collaboration between In Practice Systems (INPS), a company developed Vision software that GPs use in their practice and IMS Health which provide access to the data [82]. THIN database was approved by the nationally accredited ethics committee and separate ethical approval was not required to use the anonymised longitudinal data for individual studies [83]. The data has been shown to have high standards of validity [81]. The data includes medical diagnoses, all prescriptions with the date issued, consultation, referrals and additional health information such as smoking, birth, death, height, weight. Dementia diagnoses received by the practice are coded and entered in hierarchical Read codes. The codes also include terms relating to symptoms, procedures, and laboratory tests. Prescriptions can be easily linked to British National Formulary (BNF) codes [82, 84]. THIN database is updated continuously, permitting investigation of the effects of new treatments. The data is linked by postal code to population census data, including quintiles of the Townsend deprivation index (neighbourhood deprivation) [80, 85]. Some patient level information such as ethnicity, occupation, employment, and socio-economic status are not available [82]. In terms of representativeness, THIN database is considered to be generalizable to the UK in terms of demographics, chronic disease prevalence and mortality rates when it was compared with national statistical and 2006/07 QOF data, adjusting for demographics and Townsend deprivation [86].

3-1-1. Identification of additional codes in THIN dataset

A cohort study in a large UK population of primary care patients was designed using THIN database (version 16.01). All practices in England, North Island and Wales had been using the GP computer system. In total, 949 codes were identified from a THIN data dictionary file (Read codes1601.dta) with keywords (which is in line with literature search keywords in Figure 2-1), 'dementia' or 'Alzheimer' or 'cognitive' or' memory' problems. STATA/SE (version 15.0, StataCorp LLC) was used with the 'searchrc' package.

Figure 3-1. Search keyword in a THIN data dictionary

```
searchrc dement* | alzheim* | cognit* | memory using Read codes1601.dta, keepcat nofh nojob clear
```

3-1-2. Use of the *Prescribed medication* as an additional indicator

To identify people who might not be covered by the codes, the *Prescribed medication* to treat dementia in Alzheimer's disease was also considered. Possible dementia patients may not officially be diagnosed as having dementia, but GPs could prescribe related medications to treat. The *Prescribed medication* for a related illness would be one of the ways to verify or support the identification of people with dementia in addition to the diagnostic codes in primary care records. Four treatments of Alzheimer's disease listed in the NICE guidelines were selected as the *Prescribed medication* (Table 3-1) [87]. Donepezil is used in the palliative treatment of mild to moderate dementia in Alzheimer's disease. Galantamine is used in treatment of mild to moderate dementia in Alzheimer's disease and various other memory impairments. Rivastigmine is a parasympathomimetic/cholinergic agent for the treatment of mild to moderate dementia of the Alzheimer's type, and dementia (due to Parkinson's disease). Memantine is used to treat moderate to severe dementia in Alzheimer's disease [84].

Table 3-1. *Prescribed medication*

Prescribed medication	Drug code		N (%)*
Donepezil 5mg tablets	88986998	10,084 (34.0)	19,185 (64.8)
Donepezil 5mg orodispersible tablets sugar free	85091998	318 (1.1)	
Donepezil 5mg orodispersible tablets sugar free	58735979	152 (0.5)	
Donepezil 5mg orodispersible tablets sugar free	85089998	7 (0.0)	
Donepezil 5mg tablets	88984998	1,406 (4.8)	
Donepezil 10mg orodispersible tablets sugar free	85090998	145 (0.5)	
Donepezil 10mg orodispersible tablets sugar free	58737979	47 (0.2)	
Donepezil 10mg orodispersible tablets sugar free	85088998	4 (0.0)	
Donepezil 10mg tablets	88986997	6,385 (21.6)	
Donepezil 10mg tablets	88984997	637 (2.2)	
Galantamine 4mg tablets	88483998	327 (1.1)	3,681 (12.4)
Galantamine 4mg tablets	92579998	40 (0.1)	
Galantamine 8mg modified-release capsules	86819998	1,365 (4.6)	
Galantamine 8mg modified-release capsules	86816998	179 (0.6)	
Galantamine 8mg modified-release capsules	54761979	7 (0.0)	
Galantamine 8mg modified-release capsules	78073978	3 (0.0)	
Galantamine 8mg modified-release capsules	70165978	1 (0.0)	
Galantamine 8mg modified-release capsules	81182998	1 (0.0)	
Galantamine 8mg tablets	88483997	302 (1.0)	
Galantamine 8mg tablets	92579997	37 (0.1)	
Galantamine 12mg tablets	88483996	127 (0.4)	
Galantamine 12mg tablets	92579996	15 (0.1)	
Galantamine 16mg modified-release capsules	86818998	503 (1.7)	
Galantamine 16mg modified-release capsules	86815998	56 (0.2)	
Galantamine 16mg modified-release capsules	54763979	13 (0.0)	
Galantamine 16mg modified-release capsules	78075978	3 (0.0)	
Galantamine 20mg/5ml oral solution sugar free	92457998	30 (0.1)	
Galantamine 20mg/5ml oral solution sugar free	88277998	2 (0.0)	
Galantamine 24mg modified-release capsules	86817998	596 (2.0)	
Galantamine 24mg modified-release capsules	86814998	57 (0.2)	
Galantamine 24mg modified-release capsules	54762979	12 (0.0)	
Galantamine 24mg modified-release capsules	81180998	3 (0.0)	
Galantamine 24mg modified-release capsules	78074978	2 (0.0)	
Rivastigmine 1.5mg capsules	97471998	1,335 (4.5)	3,572 (12.1)
Rivastigmine 1.5mg capsules	90702998	47 (0.2)	
Rivastigmine 13.3mg/24hours transdermal patches	83737978	1 (0.0)	
Rivastigmine 2mg/ml oral solution sugar free	92091998	26 (0.1)	
Rivastigmine 2mg/ml oral solution sugar free	56115979	1 (0.0)	
Rivastigmine 2mg/ml oral solution sugar free	92090998	1 (0.0)	
Rivastigmine 3mg capsules	97471997	478 (1.6)	
Rivastigmine 3mg capsules	90702997	18 (0.1)	
Rivastigmine 4.5mg capsules	97471996	133 (0.5)	
Rivastigmine 4.5mg capsules	90702996	2 (0.0)	
Rivastigmine 4.6mg/24hours transdermal patches	84307998	821 (2.8)	
Rivastigmine 4.6mg/24hours transdermal patches	84305998	52 (0.2)	
Rivastigmine 4.6mg/24hours transdermal patches	83491978	4 (0.0)	
Rivastigmine 4.6mg/24hours transdermal patches	75983978	3 (0.0)	
Rivastigmine 6mg capsules	92301998	103 (0.4)	
Rivastigmine 6mg capsules	90705998	7 (0.0)	
Rivastigmine 9.5mg/24hours transdermal patches	84306998	499 (1.7)	
Rivastigmine 9.5mg/24hours transdermal patches	84304998	40 (0.1)	
Rivastigmine 9.5mg/24hours transdermal patches	84086978	1 (0.0)	
Generic Ebixa tablets treatment initiation pack	83567998	191 (0.6)	3,188 (10.8)
Generic Ebixa tablets treatment initiation pack	83569998	156 (0.5)	
Memantine 10mg tablets	91100998	1,649 (5.6)	
Memantine 10mg tablets	88928998	51 (0.2)	
Memantine 10mg/ml oral solution sugar free	91099998	132 (0.5)	
Memantine 10mg/ml oral solution sugar free	98131998	6 (0.0)	
Memantine 20mg tablets	83574998	989 (3.3)	
Memantine 20mg tablets	83573998	14 (0.1)	
Total			29,626 (100.0)

* Frequencies (percentages) of the first prescribed medication in the therapy data (Chapter 4).

3-1-3. Collation and categorization of the codes

The comprehensive lists of codes which were used in the previous studies (for identification of people with dementia in the UK electronic primary care databases) and additional codes from other sources were collated and categorized (with help from Dr Van Der wardt Veronika and a clinician, Professor John Gladman for additional confirmation). Codes identified were a mixture of definitive codes for dementia (where there is little doubt the individual has dementia, but some of which are included in the QOF definition and some are not), others which were indicative of dementia and symptoms that could be dementia but possibly without diagnosis. It is not clear whether epidemiological studies should just use the definitive codes, or include the codes that might be dementia or even include all the codes including those that are just symptoms of cognitive loss. Codes were categorised to examine how many people definitively had dementia and how many people might have dementia.

Table 3-2. Categories of the comprehensive dementia diagnostic codes and the *Prescribed medication*

- **QOF -** NHS standard Read codes (version 2)[8] suggest dementia
- ***Other diagnoses*** – Codes suggest dementia other than (or alternative of) the QOF based codes
- ***Dementia symptoms*** - Codes suggest dementia symptoms, memory loss/forgets, cognitive decline/impairment (and their tests)
- ***Vague indicators*** - Indefinite indicators that could be dementia related (including functional tests)
- ***Possible additional information* –** Codes possibly dementia related information[9]
- ***Likely MCI* –** Codes about likely Mild Cognitive Impairment (MCI)
- ***Prescribed medication* –** Four treatment of Alzheimer's disease (by the NICE guideline [87])

[8] This is updated twice a year around April and October and are available on the Health and Social Care Information Centre (HSCIC) website.

[9] Only two codes, neither of which supported a diagnosis of dementia were dropped due to lack of relevance.

3-1-4. Combining the categorized codes

In total, 399 codes were obtained (Table 2-2 to Table 2-7), excluding duplications and some irrelevant codes[10] in the QOF based codes. (12 studies which provided Read codes are presented in Table 2-1.) STATA/SE (version 15.0, StataCorp LLC) was used to combine the categorized codes (excluding duplicated codes) to examine incidence and prevalence rates by categories of the codes.

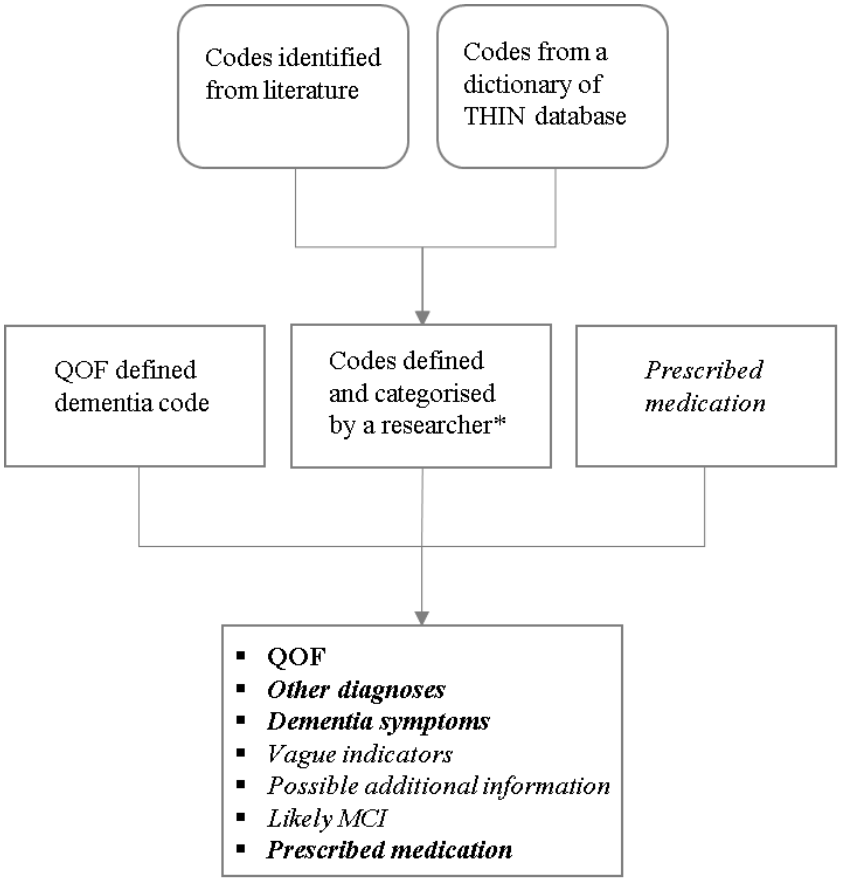


Figure 3-2. Flow diagram for combining the dementia diagnostic codes

[10] 1 case of QOF code, Sporadic Creutzfeldt-Jakob disease (A411000), 3 cases of vague indicators that could be dementia related (Other senile and presenile organic psychoses (E00y.00), Senile or presenile psychoses NOS ((E00z.00) and Chronic alcoholic brain syndrome (E012000).

* Dr Van Der Wardt Veronika, Faculty of Medicine & Health Sciences, University of Nottingham

3-2. Methods for analyses

3-2-1. Data extraction

The medical and therapy data were extracted and appended to the combined categorized dementia diagnostic codes for the analysis. The data of all ages were merged into the patient demographic file which contained 9,553,978 individuals. In the medical data, the identified cohort of patients who were recorded in a new way of GPs computer system (i.e., a user friendly inputting with a data recording window) were 46,030 (30/12/1899 - 18/01/2016), and in the conventional GP computer system, which involves GPs typing a keyword and choosing from the list of codes possibly with texts, were 300,029 (09/01/1960 - 18/01/2016). Patients who were prescribed dementia medications in the therapy data were 5,303 (09/05/1997 – 04/03/2016). In total, 204,414 (13.2%) of QOF, 388,084 (25%) of *Other diagnoses*, 331,370 (21.4%) of *Dementia symptoms*, 292,509 (18.9%) of *Vague indicators*, 4,566 (0.3%) of *Possible additional information*, 167,618 (10.8%) of *Likely MCI*, and 161,150 (10.4%) of the remained (not relevant or not sure) cases were in the interim data before analysis of incidence and preference rates, and selecting events by the categorized diagnosis category.

3-2-2. Dataset and the study population

The data for all the patients who had at least one of those codes, and the data showing which event had occurred were extracted. In terms of quality assurance, the start date of the events for each individual was selected at least one year after Acceptable Mortality Reporting (AMR, i.e., a quality indicator for person-time defines the earliest period of optimal mortality reporting for each practice [88]) date and at least one year after registration date. The events recorded within a year may be prevalent conditions [83]. Dementia is a syndrome generally appearing after the cognitive development stages, the 60+ age range was used for examination of the rates, and for comparisons with other studies (many of studies used the 65+ age range). Incidence and prevalence rates using the categorised dementia diagnostic codes were calculated.

3-2-3. Analyses strategy

Incidence rate calculation

The incidence rate was calculated for each year (as the number of new cases in each year divided by the person-years of follow-up for the year). To estimate incidence, it was necessary to identify the first of the events for each patient – i.e., the first occasion on which there was a dementia diagnosis (or prescription). The first dementia diagnosis per patient was selected and counted by event year for the categorized dementia diagnostic codes. To estimate the population incidence rate, person-years was calculated with the whole population contributing values (until the individual was observed in THIN database) by practice, country, gender, Townsend deprivation index and patient-age in that year.

Prevalence rate calculation

Prevalence is defined as the proportion of people in a year who have ever had a dementia diagnosis (or prescription) in this study. Prevalence is a single point in time measure whereas incidence is a rate over time. The numerator of prevalence used all those who have ever had a dementia diagnosis, made in the given year or at any time prior to that year. The first dementia diagnosis per patient in the given year was selected and counted by event year for the categorized dementia diagnostic codes. The denominator was calculated using all those in the dataset who registered on 1st July in that year by practice, country, gender, Townsend deprivation index and patient-age.

Diagnostic categories for incidence and prevalence rates

Initially, the incidence and prevalence rate figures were produced respectively using the following individual diagnostic codes: QOF, *Other diagnoses*, *Dementia symptoms*, *Vague indicators*, *Possible additional information*, *Likely MCI*, and *Prescribed medication*. The first diagnosis event by each diagnostic category, and the first *Prescribed medication* (regardless its diagnostic category) per individual were selected. Multiple diagnoses events per individual were allowed if the patient in the practice had more than one diagnosis at different time points. For instance, if a person had three diagnoses over time, e.g., QOF, *Other diagnoses* and *Dementia symptom*, each earliest diagnosis date was applied to the individual diagnostic category. That is to say, patients could be included in more than one diagnostic category.

As patients very likely have more than one diagnosis over time even in a short period time (e.g., within a year), this was examined via the population those who had any of the first dementia diagnosis codes (Section 4-1-1) among the individual diagnostic codes.
Following the examination, using of the combination of the diagnostic codes was decided for further analyses (instead of the individual diagnostic codes which an individual is duplicated in another code), excluding not informative codes, i.e., *Likely MCI* (which sharply increased in 2013, Table 4-2) and additionally, *Vague indicators* and *Possible additional information*.
The combination of the diagnostic codes were (1) QOF (default), (2) either of QOF and *Other diagnoses*, (3) either of QOF, *Other diagnoses* and *Prescribed medication*, (4) either of QOF, *Other diagnoses* and *Dementia symptoms*, and (5) either of QOF, *Other diagnoses, Dementia symptoms* and *Prescribed medication.*
The incidence and preference rates were calculated selecting events by the combination of the diagnostic codes, in addition to the estimations by each diagnostic code.

Subgroup analysis for incidence and prevalence rates

Subgroup analyses was performed using the multiple diagnoses events per individual by age group (60-69, 70-79, and 80+ years) and gender. Age was calculated using the dates of diagnosis (or prescription).

Chapter 4. Results on estimates of prevalence and incidence of dementia (1995-2015)

In this chapter, outcomes of the incidence and prevalence rates over time by the categorised dementia diagnostic codes will be presented. The dementia diagnostic codes which should be used to identify dementia will be discussed and decided with reference to the previously estimated rates from other studies.

4-1. Incidence rate of dementia

4-1-1. Frequencies of the first diagnosis (and prescription)

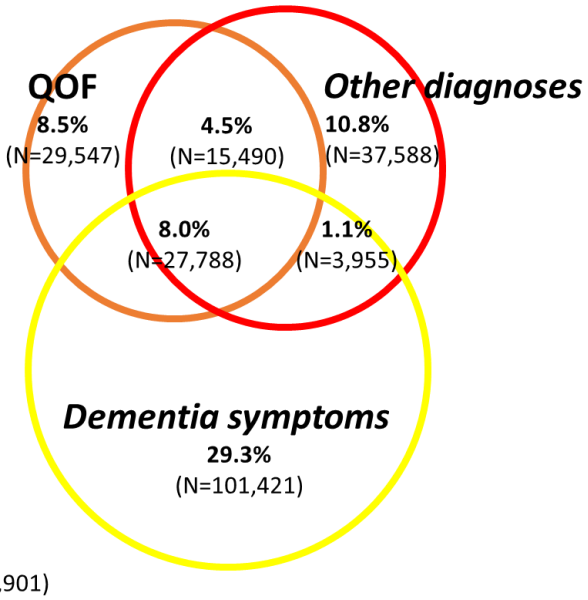
It was necessary to examine which categorised dementia diagnostic codes an individual fell into in the dataset, and whether those with the QOF based dementia diagnosis codes also had other categorized codes such as *Other diagnoses*, *Dementia symptoms*, or *Prescribed medication*. The combinations of the first dementia diagnosis codes an individual had ever had, and whether an individual had one or more of any of the dementia diagnostic codes (including medications) were examined.
More specifically, frequencies of the first diagnosis of each categorized code per person, and the overlap with the codes per person were examined for all ages, 1987-2016 (Figure 4-1). The total population (of the Venn diagram) was those who had any of the first dementia diagnosis codes among the QOF, *Other diagnoses*, *Dementia symptoms*, *Vague indicators*, *Possible additional information*, *Likely MCI* and *Prescribed medication* (N=346,690). The number of patients who had the first dementia diagnostic codes was QOF - 72,825 (21%), *Other diagnoses* - 84,821 (24.5%), *Dementia symptoms* - 133,164 (38.4%) and *Prescribed medication* - 29,626 (8.5%), respectively.

More than half of the people who had the first *Dementia symptoms* (N=101,421, 76.2%) were not overlapping with the people who either had the first QOF or *Other diagnoses*. This implies *Dementia symptoms* may contain more expansive codes (Figure 4-1 (1)). 12% (N=41,543) of those who had the first *Other diagnoses* and 30.4% (N=105,376) of those who had the first *Dementia symptoms* were uniquely identified respectively when they were combined with those who had the first QOF codes (Figure 4-1 (1)). There was a fairly large percentage of people who had the first *Other diagnoses*, *Dementia symptoms* and *Prescribed medication* other than the first QOF based codes.

Most of the patients (N=22,197, 74.9% of N=29,626) who had received the first *Prescribed medication* had either the first QOF or *Other diagnoses* (Figure 4-1 (2)). 2.1% (N=7,429) of people who had received the first *Prescribed medication* (N=29,626 for all ages) was uniquely identified among all the codes (i.e., QOF, *Other diagnoses, Dementia symptoms, Vague indicators, Possible additional information, Likely MCI* and *Prescribed medication*) (N=346,690) (Figure 4-1 (2)). Likewise, 2.1% (N=7,224) of people who had received the first *Prescribed medication* (N=28,960 for aged 60+ years) was uniquely identified among all the codes (Figure 4-1 (4)). 64.9% of the remaining patients (in the Venn diagram) indicate who had any of the first diagnoses among the *Dementia symptoms, Vague indicators, Possible additional information* and *Likely MCI* codes excluding the OQF, *Other diagnoses,* and *Prescribed medication* codes, Figure 4-1 (2). More than a half of the first prescriptions of the *Prescribed medication* were Donepezil 64.8% (N=19,185) and others (Galantamine (N=3,681, 12.4%), Rivastigmine (N=3,572, 12.1%) and Memantine (N=3,188, 10.8%), Table 3-1) [84].

Other than the QOF-based codes, the inclusion of these codes would appear to be important in identifying the exact population of people with dementia in primary care records.

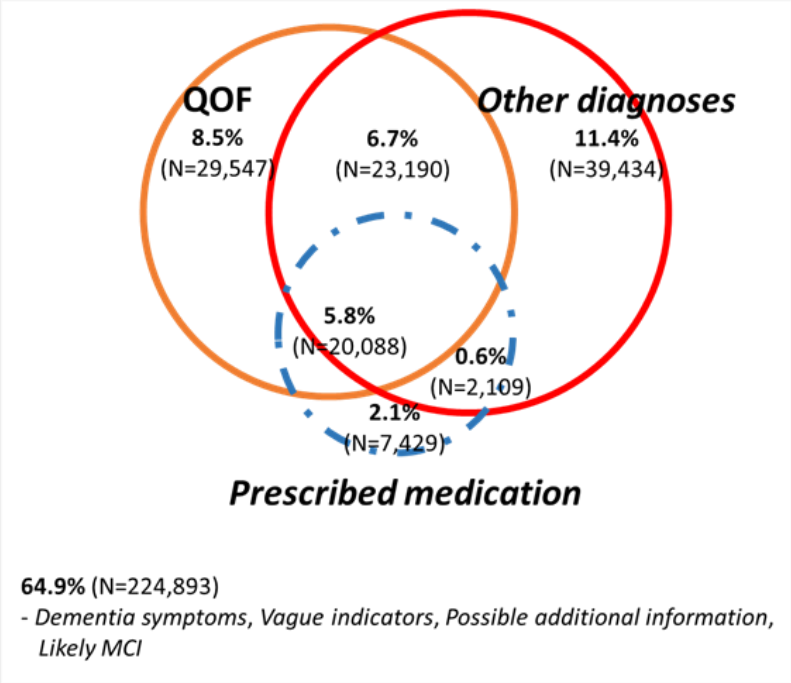
(1) Frequencies of the first diagnosis of QOF, *Other diagnoses* and *Dementia symptoms* (N=215,789 (62.2%)) among those who had any of the first individual diagnostic codes, without age restrictions



37.8% (N=130,901)
- Vague indicators, Possible additional information, Likely MCI, Prescribed medication

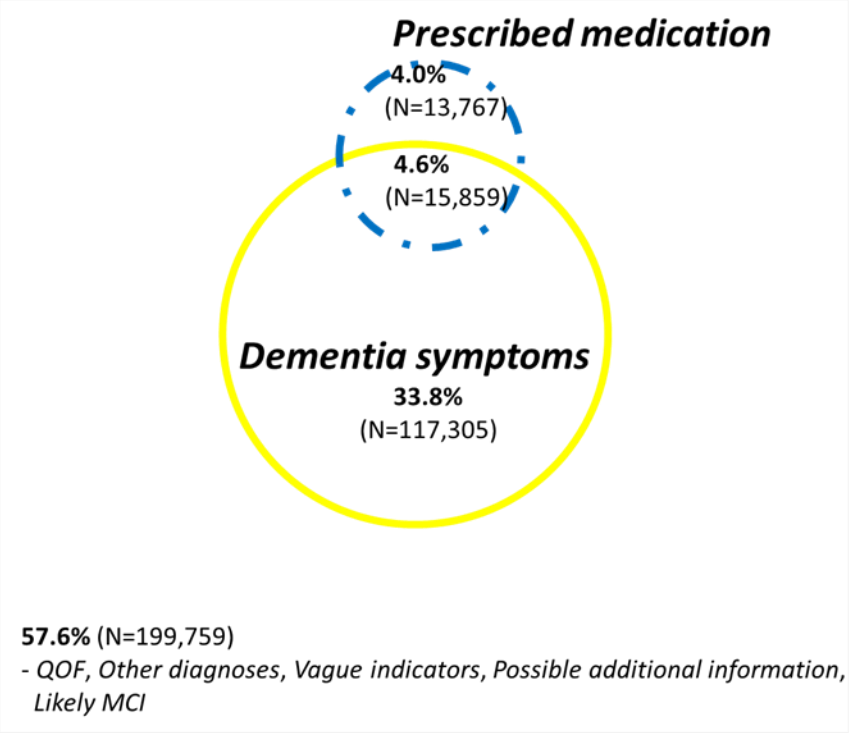
Note: 8.0% - OQF and *Dementia symptoms*

(2) Frequencies of the first diagnosis of QOF, *Other diagnoses* and *Prescribed medication* (N=121,797 (35.1%)) among those who had any of the first individual diagnostic codes, without age restrictions

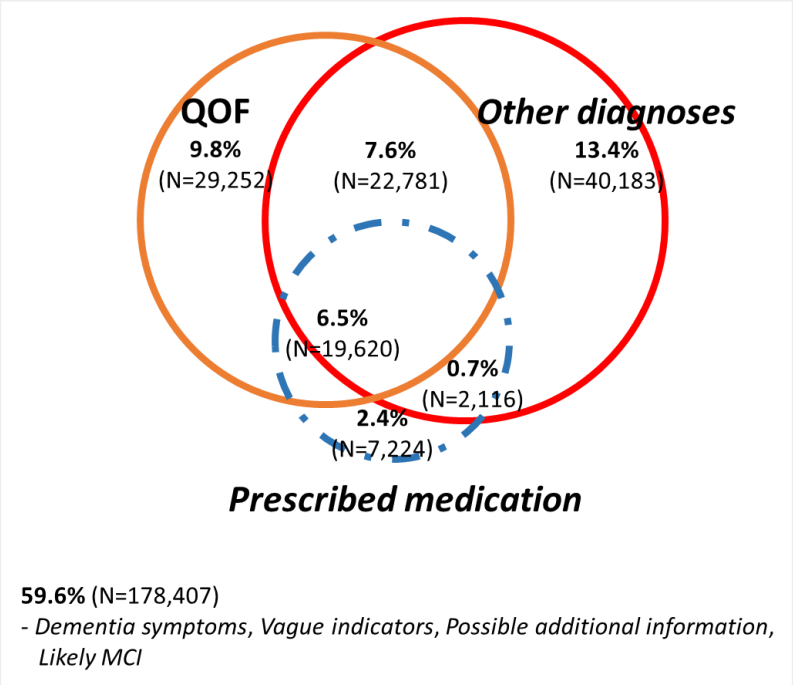


Note: 5.8% - OQF and *Prescribed medication*

(3) Frequencies of the first diagnosis of *Dementia symptoms* and *Prescribed medication* (N=146,931 (42.4%)) among those who had any of the first individual diagnostic codes, without age restrictions



(4) Frequencies of the first diagnosis of QOF, *Other diagnoses* and *Prescribed medication* (N=121,176 (40.4%)) among aged 60+ years who had any of the first individual diagnostic codes

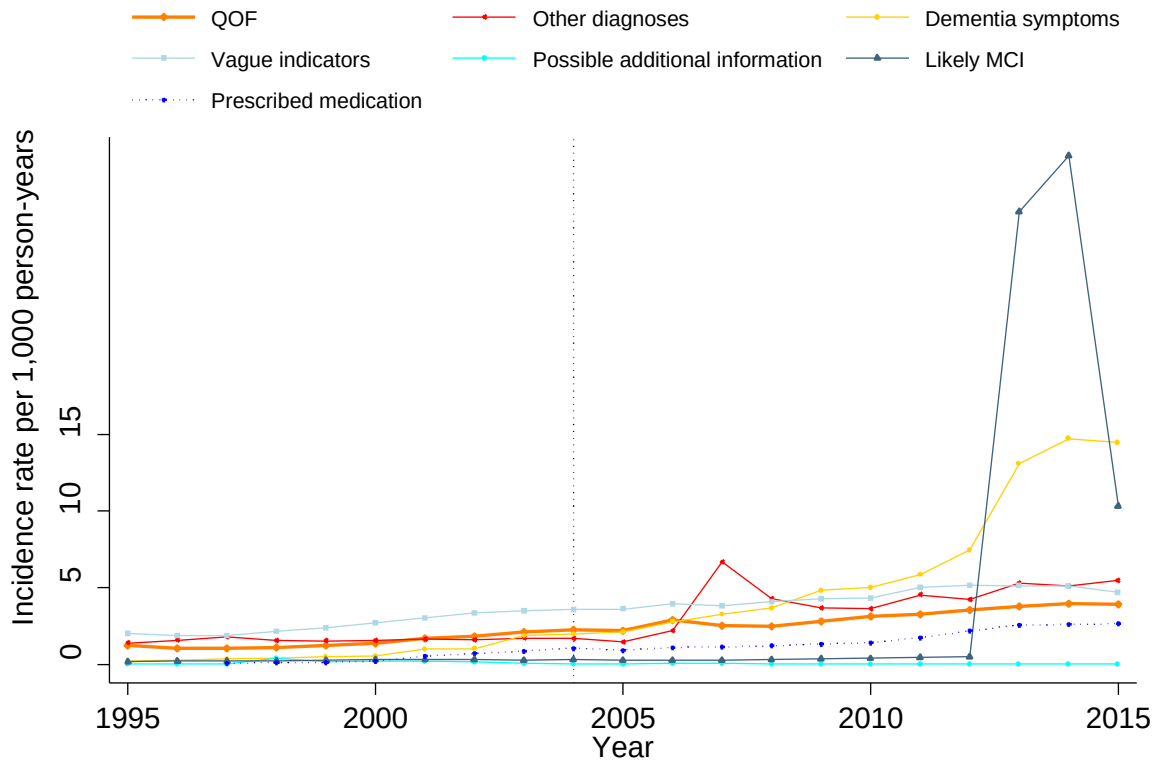


Note: 6.5% - OQF and *Prescribed medication*

Figure 4-1. Venn diagram of the first diagnosis and prescription

4-1-2. Exploration of the categories of codes over time

Incidence rates of the 60+ age group study population were presented by categorised dementia diagnostic codes (QOF, *Other diagnoses*, *Dementia symptoms*, *Vague indicators*, *Possible additional information*, *Likely MCI*) and the *Prescribed medication* (Figure 4-2 and Table 4-1). This is for the first event of the categorized diagnostic codes per person. The incidence rates were not mutually exclusive (as presented in the Venn diagrams, Figure 4-1).



Note: The dotted vertical lines indicate a year (2004) the OQF was introduced by NHS England

Figure 4-2. Incidence rates per 1,000 person-years, 60+ years by individual diagnostic codes (QOF, *Other diagnoses, Dementia symptoms, Vague indicators, Possible additional information, Likely MCI, Prescribed medication)*

Table 4-1. Incidence rates per 1,000 person-years, 60+ years by individual diagnostic codes

Year	QOF	*Other diagnoses*	*Dementia symptoms*	*Prescribed medication*
1995	1.2	1.4	0.2	-
1996	1.0	1.6	0.3	-
1997	1.0	1.8	0.3	0.1
1998	1.1	1.6	0.4	0.1
1999	1.2	1.5	0.5	0.1
2000	1.4	1.5	0.5	0.2
2001	1.7	1.6	1.0	0.5
2002	1.8	1.6	1.0	0.7
2003	2.1	1.7	1.9	0.9
2004	2.2	1.7	2.0	1.1
2005	2.2	1.5	2.1	0.9
2006	2.9	2.2	2.8	1.1
2007	2.5	6.7	3.2	1.1
2008	2.5	4.3	3.7	1.2
2009	2.8	3.7	4.8	1.3
2010	3.1	3.6	5.0	1.4
2011	3.3	4.5	5.8	1.7
2012	3.5	4.2	7.5	2.2
2013	3.8	5.3	13.1	2.6
2014	4.0	5.1	14.7	2.6
2015	3.9	5.5	14.5	2.7

Incidence rates by the QOF defined dementia codes, aged 60+ years

The incidence rate of dementia as defined using the QOF codes gradually and slowly increased (1.2, 2.2 and 3.9 per 1,000 person-years in 1995, 2004 and 2015 respectively, aged 60+ years, Table 4-1). [X] Dementia in Alzheimer's disease (Eu00.00) and [X] Vascular dementia (Eu01.00) were increased continuously (Appendix Table 4). The dementia indicators of ongoing management with relatively large points (15 for 'DEM002' in 2013 and 39 for 'DEM004' in 2015) have been added over time. These are indicators of 'the percentage of patients diagnosed with dementia whose care has been reviewed in a face-to-face review in the preceding 12 months' (Appendix Table 3).

Incidence rates by the *Other diagnoses* codes, aged 60+ years

The incidence rates of the *Other diagnoses* also increased over time, but it showed a sharp increase in 2007 (1.4, 1.7, and 5.5 per 1,000 person-years in 1995, 2004, and 2015 respectively, aged 60+ years, Table 4-1). Regarding the sharply increasing pattern of the *Other diagnoses* in 2007, frequencies of the *Other diagnoses* (N= 84,821, all ages) codes were examined (Appendix Table 5). There was a high frequency of Dementia annual review (6AB..00, N=657 in 2006 and N=7,208 in 2007). After launching QOF (in 2004), the revision of DEM 2 indicator in which the percentage of patients diagnosed with dementia whose care has been reviewed in the previous 15 months (15 points) was released in 2006 [18, 89-95]. A slightly updated version of DEM002 indicator (a face-to-face review in the preceding 12 months with the same point) was released in 2013 [18, 89-95] (Appendix Table 3). This might explain the phenomenon of the dementia annual review increasing in 2007. On the other hand, senile/presenile dementia (E00..12, N=1,003) noticeably decreased in 2006 (N=7,698 in 1995-2005). Besides, there were newly appeared codes categorized as *Other diagnoses* in 2006 such as Dementia care plan related (8CMZ.00, 8CMZ000, 8CMZ200), Dementia advance care plan related (8CMZ300, 8CMe000, 8CSA.00), Referral to dementia care related (8Hla.00, 8IAe000, 8IAe200) and Dementia monitoring related (9Ou1.00-9Ou5.00).

Incidence rates by codes suggest *Dementia symptoms*, aged 60+ years

The *Dementia symptoms* showed a slight and steady increasing pattern up to the final date (0.2, 2.0 and 14.5 per 1,000 person-years in 1995, 2004 and 2015 respectively, aged 60+ years, Table 4-1). The six item cognitive impairment test (3AD3.00) and GPCOG - general practitioner assessment of cognition (38Dv.00) increased sharply from 2013 (among the codes categorised as *Dementia symptoms*). The GPCOG, which was introduced in 2002 (by Brodaty *et al*. [96], is designed to assist GPs in detecting dementia). Dementia ES (2013/14) may have influenced this increase and further

investigation seems required. Memory assessment (3A...11) increased in 2013 (Appendix Table 6). One of the plausible reasons might be changes in policies regarding the points (i.e., incentives) (Appendix Table 3). Elderly at risk rating scale (388m.00), the six item cognitive impairment test (3AD3.00) and referral to atrial fibrillation clinic (8HTY.00) showed the highest frequencies over time (Appendix Table 6).

Incidence rates by *Likely MCI*, aged 60+ years

The codes that were categorised as *Likely MCI* sharply increased in 2013. A high frequency of 'at risk of dementia' (14Od.00, N=42,252 in 2013 and N=20 in 2012) was found in 2013 (Table 4-2). The Read code 14Od (read v2) was indicated that it must to be used to record to assist in identifying any patient in an at risk group in the NHS DES specification, 2013 [16]. Regarding the cause of the phenomenon, further investigation seems required. The code (14Od.00) was categorised as 'Additional Read terms compatible with, but not defining, dementia' in the literature [32]. As this suggests that an individual did not have dementia yet in this category, *Likely MCI* was omitted from further analysis. The final version of the graph is presented in Figure 4-3 (without *Likely MCI*).

Table 4-2. Frequencies of *Likely MCI* codes, all ages

Code (N=6)	Description	2005-2009	2010	2011	2012	2013	2014	2015	Total
14Od.00	At risk of dementia	4	11	16	20	42252	46306	11778	100387
E2A1000	Mild memory disturbance	3858	343	391	405	385	266	171	5819
Eu05700	[X]Mild cognitive disorder	1155	256	282	352	346	155	145	2691
28E0.00	Mild cognitive impairment	4	4	5	11	98	301	357	780
3AE2.00	GDS level 3 - mild cognitive decline	16		6	1	7	5	5	40
3AE1.00	GDS level 2 - very mild cognitive decline	2	2	1	1	2	1		9

The prescribed rate of the *Prescribed medication* dementia also increased gradually and slowly (0.1, 1.1 and 2.7 per 1,000 person-years in 1997, 2004, and 2015 respectively, aged 60+ years, Table 4-1).

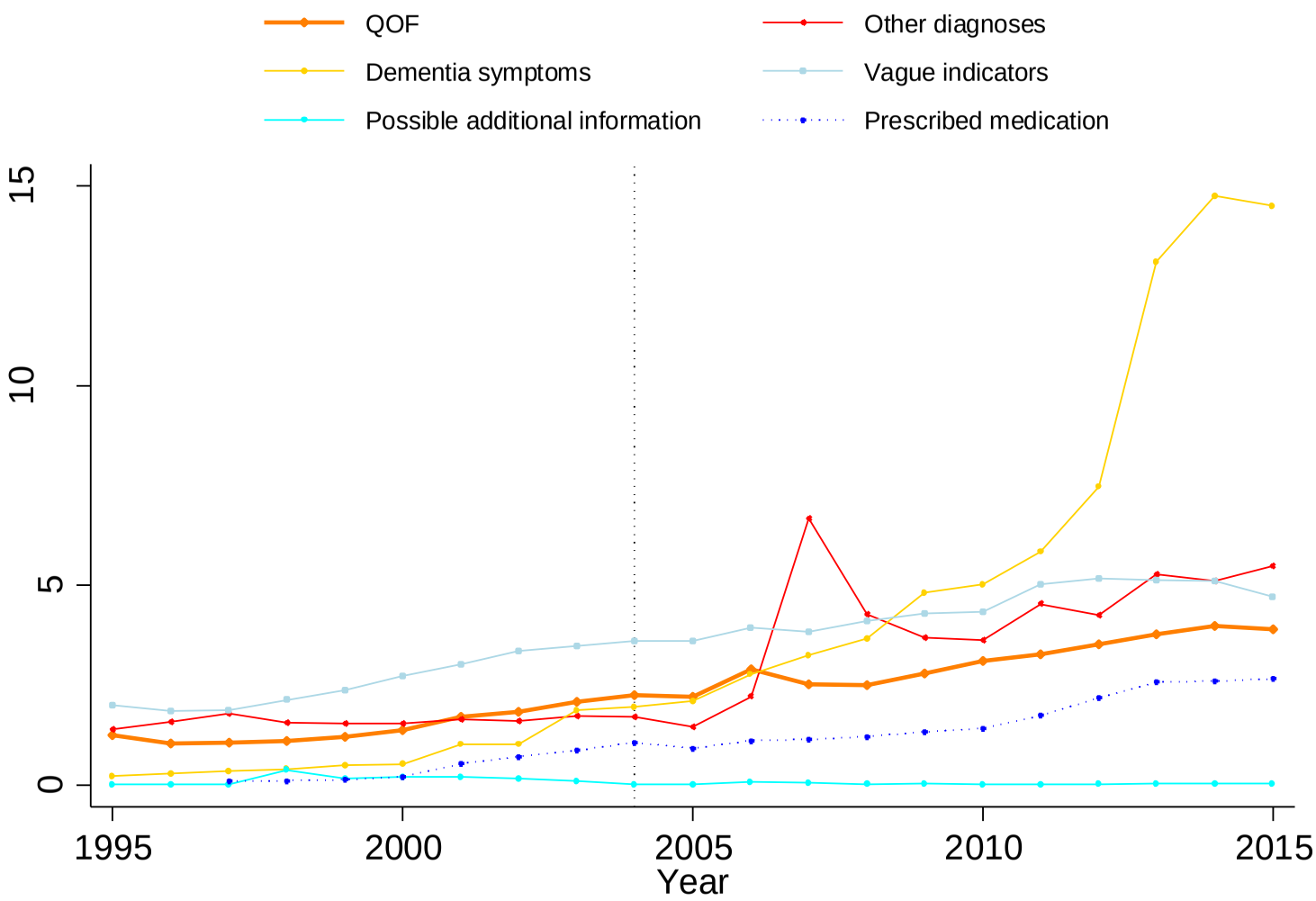


Figure 4-3. Incidence rates per 1,000 person-years, 60+ years by individual diagnostic codes excludcing *Likely MCI* (QOF, *Other diagnoses*, *Dementia symptoms*, *Vague indicators*, *Possible additional information*, *Prescribed medication*)

4-1-3. Incidence rates of dementia, aged 60+ years

Incidence rates by multiple diagnostic codes

The incidence rates of the first diagnosis with the combination of the diagnostic codes were calculated (Figure 4-4 and Table 4-3). Individuals may receive more than one diagnostic code, and looking at which combination of codes will provide a picture of incidence seems sensible or consistent with evidence from elsewhere. The incidence rates of the QOF/*Other diagnoses/Prescribed medication* (2.4, 3.6, and 5.5 per 1,000 person-years in 1995, 2004, and 2015 respectively, aged 60+ years) and without the *Prescribed medication* showed similar figures (Table 4-3). These rates were slightly higher than the incidence rates with the individual *Other diagnoses* as year goes, but the patterns look similar to it (Table 4-3). The incidence rates of the QOF/*Other diagnoses*/*Dementia symptoms/Prescribed medication* (2.5, 4.7, and 15.9 per 1,000 person-years in 1995, 2004, and 2015 respectively, aged 60+ years) and without the *Prescribed medication* showed similar figures as well. These rates were slightly higher as the year went on compared to the incidence rates with the individual *Dementia symptoms*, but the patterns look similar (Table 4-3).

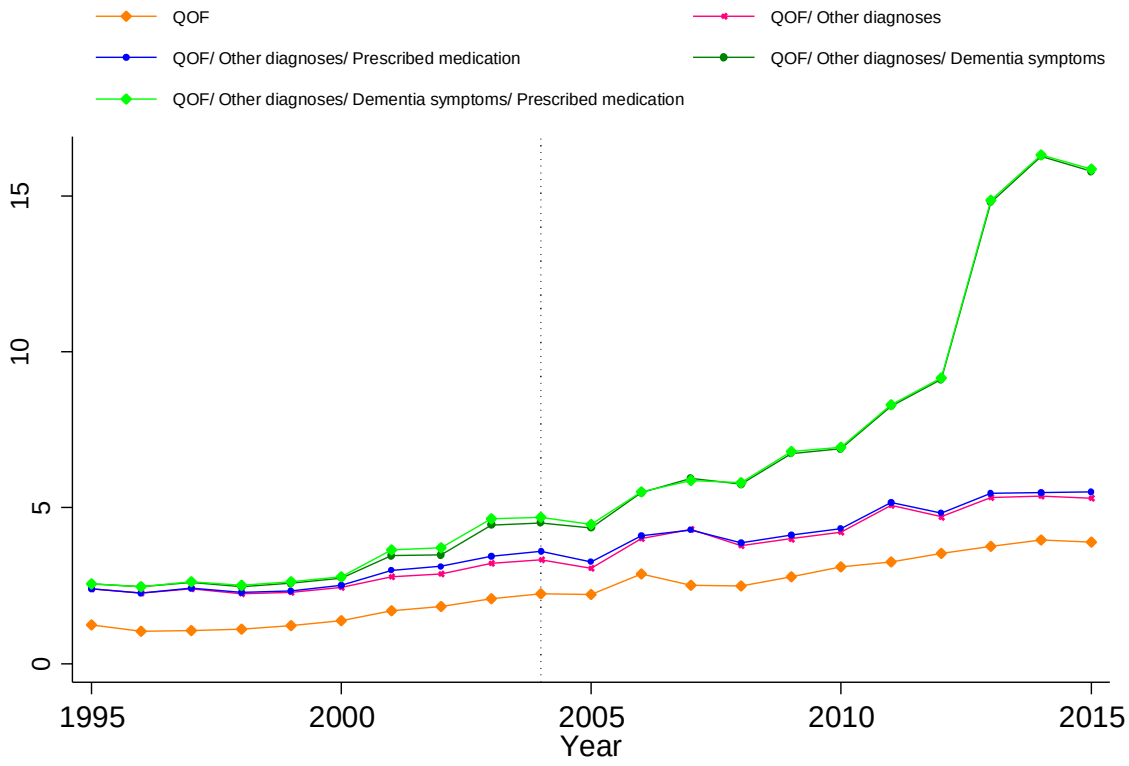


Figure 4-4. Incidence rates per 1,000 person-years, 60+ years by multiple diagnostic codes (QOF, QOF/*Other diagnoses*, QOF/*Other diagnoses/Prescribed medication*, QOF/*Other diagnoses/Dementia symptoms*, QOF/*Other diagnoses/Dementia symptoms/Prescribed medication*)

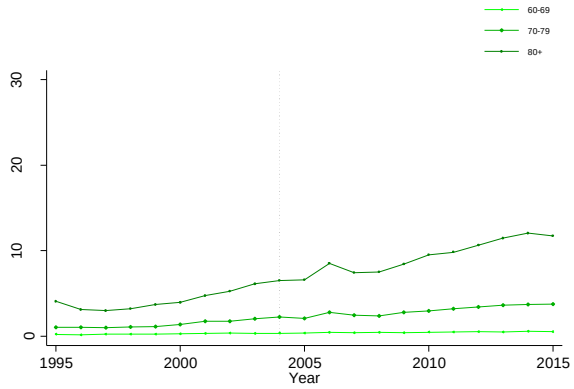
Table 4-3. Incidence rates per 1,000 person-years, 60+ years by multiple diagnostic codes

Year	QOF	QOF/ *Other diagnoses*	QOF/ *Other diagnoses/ Prescribed medication*	QOF/ *Other diagnoses/ Dementia symptoms*	QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*
1995	1.2	2.4	2.4	2.5	2.5
1996	1.0	2.3	2.3	2.5	2.5
1997	1.0	2.4	2.4	2.6	2.6
1998	1.1	2.3	2.3	2.5	2.5
1999	1.2	2.3	2.3	2.6	2.6
2000	1.4	2.4	2.5	2.7	2.8
2001	1.7	2.8	3.0	3.5	3.6
2002	1.8	2.9	3.1	3.5	3.7
2003	2.1	3.2	3.5	4.5	4.7
2004	2.2	3.3	3.6	4.5	4.7
2005	2.2	3.1	3.3	4.3	4.5
2006	2.9	4.0	4.1	5.5	5.5
2007	2.5	4.3	4.3	5.9	5.9
2008	2.5	3.8	3.9	5.8	5.8
2009	2.8	4.0	4.1	6.7	6.8
2010	3.1	4.2	4.3	6.9	7.0
2011	3.3	5.1	5.2	8.3	8.3
2012	3.5	4.7	4.8	9.1	9.2
2013	3.8	5.3	5.5	14.8	14.9
2014	4.0	5.4	5.5	16.3	16.3
2015	3.9	5.3	5.5	15.8	15.9

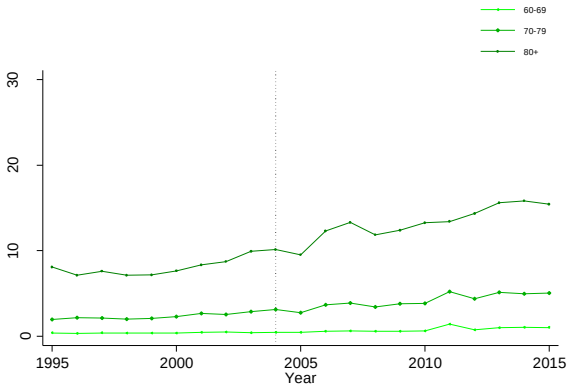
4-1-4. Age-specific incidence rates of dementia: aged 60-69, 70-79, and 80+ years

The incidence rates of the multiple dementia diagnostic codes for the 80+ age group were more than doubled over time in comparison with the rates of the 60-69 and 70-79 age groups (Figure 4-5).

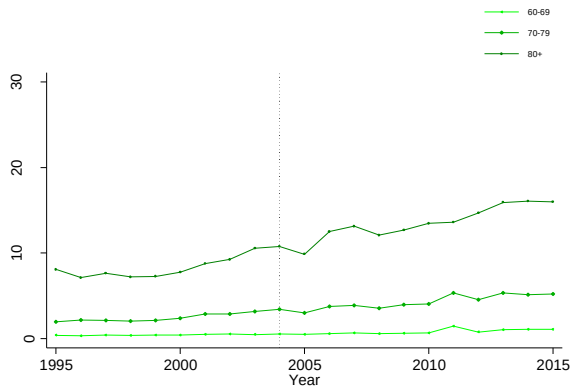
(1) QOF



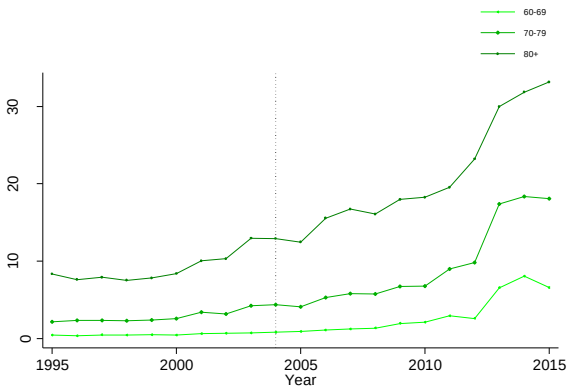
(2) QOF/*Other diagnoses*



(3) QOF/*Other diagnoses/Prescribed medication*



(4) QOF/*Other diagnoses/Dementia symptoms*



(5) QOF/*Other diagnoses/Dementia symptoms/Prescribed medication*

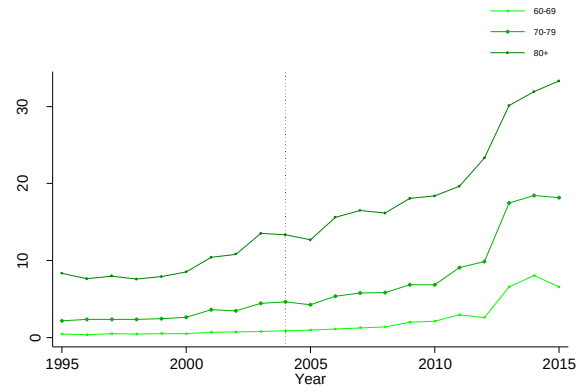


Figure 4-5. Age-specific incidence rates per 1,000 person-years by multiple diagnostic codes

The age-specific incidence rates per 1,000 person-years of the QOF/*Other diagnoses/Dementia symptoms/Prescribed medication* for the 60-69, 70-79 and 80+ age brackets were 0.5, 2.1, 8.3, in 1995, 0.9, 4.6,13,3 in 2004, and 6.6, 18.2, 33.3 in 2015 respectively (Table 4-4).

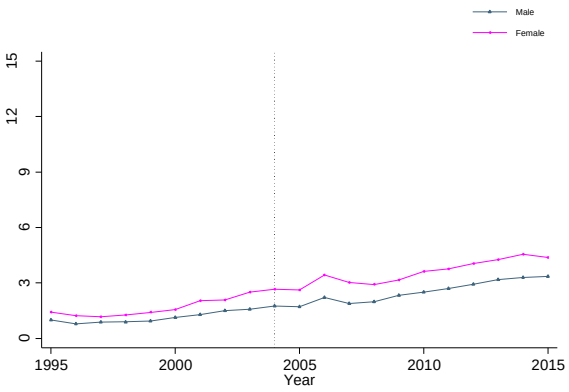
Table 4-4. Age-specific incidence rates per 1,000 person-years by multiple diagnostic codes

Year	QOF			QOF/ *Other diagnoses*			QOF/ *Other diagnoses/ Prescribed medication*			QOF/ *Other diagnoses/ Dementia symptoms*			QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*		
	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+
1995	0.2	1.0	4.1	0.4	1.9	8.1	0.4	1.9	8.1	0.5	2.1	8.3	0.5	2.1	8.3
1996	0.2	1.0	3.1	0.3	2.2	7.1	0.3	2.2	7.1	0.4	2.3	7.6	0.4	2.3	7.6
1997	0.2	1.0	3.0	0.4	2.1	7.6	0.4	2.1	7.6	0.5	2.3	7.9	0.5	2.4	8.0
1998	0.2	1.1	3.2	0.3	2.0	7.1	0.4	2.0	7.2	0.4	2.3	7.5	0.4	2.3	7.6
1999	0.2	1.1	3.7	0.4	2.1	7.2	0.4	2.1	7.3	0.5	2.4	7.8	0.5	2.4	7.9
2000	0.3	1.4	3.9	0.4	2.3	7.6	0.4	2.4	7.7	0.5	2.6	8.4	0.5	2.6	8.5
2001	0.3	1.8	4.7	0.4	2.6	8.3	0.5	2.9	8.8	0.6	3.4	10.0	0.7	3.6	10.4
2002	0.3	1.7	5.2	0.5	2.6	8.7	0.5	2.9	9.2	0.7	3.2	10.3	0.7	3.4	10.8
2003	0.3	2.0	6.1	0.4	2.9	9.9	0.5	3.1	10.5	0.7	4.2	13.0	0.8	4.4	13.5
2004	0.3	2.2	6.5	0.5	3.1	10.1	0.5	3.4	10.8	0.8	4.4	12.9	0.9	4.6	13.3
2005	0.3	2.1	6.6	0.4	2.7	9.5	0.5	3.0	9.9	0.9	4.1	12.5	0.9	4.3	12.7
2006	0.4	2.8	8.5	0.6	3.6	12.3	0.6	3.8	12.5	1.1	5.3	15.6	1.1	5.4	15.6
2007	0.4	2.4	7.4	0.6	3.9	13.3	0.6	3.9	13.1	1.2	5.8	16.7	1.3	5.8	16.5
2008	0.4	2.4	7.5	0.6	3.4	11.8	0.6	3.5	12.1	1.3	5.8	16.1	1.4	5.8	16.2
2009	0.4	2.8	8.4	0.6	3.8	12.4	0.6	4.0	12.7	1.9	6.7	18.0	2.0	6.8	18.1
2010	0.5	3.0	9.5	0.6	3.8	13.3	0.6	4.0	13.5	2.1	6.8	18.3	2.1	6.9	18.4
2011	0.5	3.2	9.8	1.4	5.2	13.4	1.4	5.3	13.6	2.9	9.0	19.6	2.9	9.1	19.6
2012	0.5	3.4	10.6	0.7	4.4	14.4	0.8	4.5	14.7	2.6	9.8	23.2	2.6	9.9	23.3
2013	0.5	3.6	11.5	1.0	5.1	15.6	1.0	5.3	15.9	6.6	17.4	30.0	6.6	17.5	30.1
2014	0.6	3.7	12.0	1.0	4.9	15.8	1.1	5.1	16.1	8.0	18.3	31.9	8.1	18.4	31.9
2015	0.5	3.8	11.7	1.0	5.0	15.4	1.1	5.2	16.0	6.6	18.1	33.2	6.6	18.2	33.3

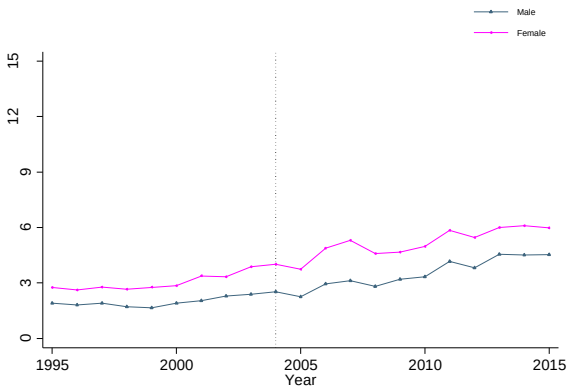
4-1-5. Gender-specific incidence rates of dementia, aged 60+ years

The incidence rates of the categorised dementia diagnostic codes were slightly higher in females over time (in comparison to males) (Figure 4-6). Interestingly, the incidence rates of males, both (4) QOF/*Other diagnoses/Dementia symptoms* and (5) QOF/*Other diagnoses/Dementia symptoms/Prescribed medication*, were instantly higher than the rates of females in 2013-14.

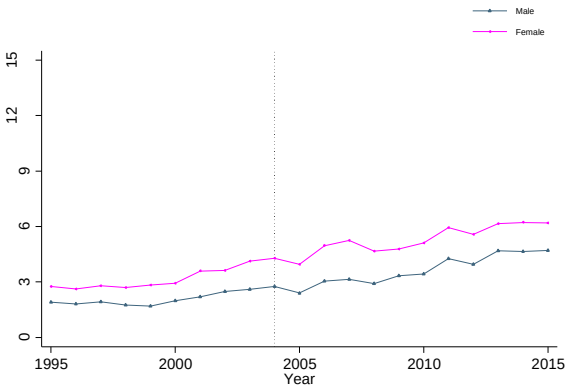
(1) QOF



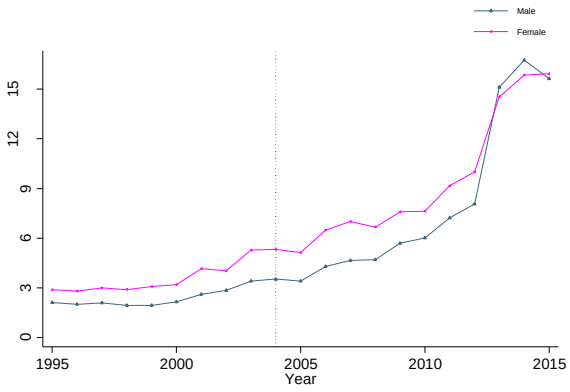
(2) QOF/*Other diagnoses*



(3) QOF/*Other diagnoses/Prescribed medication*



(4) QOF/*Other diagnoses/Dementia symptoms*



(5) QOF/*Other diagnoses/Dementia symptoms/Prescribed medication*

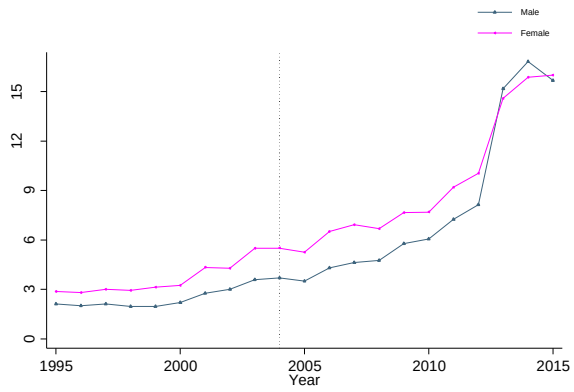


Figure 4-6. Gender-specific incidence rates per 1,000 person-years, 60+ years by multiple diagnostic codes

The gender-specific incidence rates per 1,000 person-years of the QOF/*Other diagnoses/Dementia symptoms/Prescribed medication* for males and females were 2.1, 2.9 in 1995, 3.7, 5.5 in 2004, and 15.7, 16.0 in 2015 respectively for aged 60+ years (Table 4-5).

Table 4-5. Gender-specific incidence rates per 1,000 person-years, 60+ years by multiple diagnostic codes

Year	QOF		QOF/ *Other diagnoses*		QOF/ *Other diagnoses/ Prescribed medication*		QOF/ *Other diagnoses/ Dementia symptoms*		QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
1995	1.0	1.4	1.9	2.8	1.9	2.8	2.1	2.9	2.1	2.9
1996	0.8	1.2	1.8	2.6	1.8	2.6	2.0	2.8	2.0	2.8
1997	0.9	1.2	1.9	2.8	1.9	2.8	2.1	3.0	2.1	3.0
1998	0.9	1.3	1.7	2.7	1.8	2.7	1.9	2.9	2.0	2.9
1999	0.9	1.4	1.6	2.8	1.7	2.8	1.9	3.1	2.0	3.1
2000	1.1	1.6	1.9	2.9	2.0	2.9	2.1	3.2	2.2	3.2
2001	1.3	2.0	2.0	3.4	2.2	3.6	2.6	4.1	2.8	4.3
2002	1.5	2.1	2.3	3.3	2.5	3.6	2.8	4.0	3.0	4.3
2003	1.6	2.5	2.4	3.9	2.6	4.1	3.4	5.3	3.6	5.5
2004	1.8	2.7	2.5	4.0	2.7	4.3	3.5	5.3	3.7	5.5
2005	1.7	2.6	2.2	3.7	2.4	4.0	3.4	5.1	3.5	5.3
2006	2.2	3.4	3.0	4.9	3.0	5.0	4.3	6.5	4.3	6.5
2007	1.9	3.0	3.1	5.3	3.1	5.2	4.6	7.0	4.6	6.9
2008	2.0	2.9	2.8	4.6	2.9	4.7	4.7	6.7	4.8	6.7
2009	2.3	3.2	3.2	4.7	3.3	4.8	5.7	7.6	5.8	7.7
2010	2.5	3.6	3.3	5.0	3.4	5.1	6.0	7.6	6.1	7.7
2011	2.7	3.8	4.2	5.9	4.3	5.9	7.2	9.2	7.3	9.2
2012	2.9	4.0	3.8	5.5	4.0	5.6	8.1	10.0	8.1	10.0
2013	3.2	4.3	4.5	6.0	4.7	6.1	15.1	14.5	15.2	14.6
2014	3.3	4.5	4.5	6.1	4.7	6.2	16.8	15.8	16.8	15.9
2015	3.4	4.4	4.5	6.0	4.7	6.2	15.6	15.9	15.7	16.0

4-2. Prevalence rate of dementia

4-2-1. Prevalence rates of dementia, aged 60+ years

Prevalence rates by each diagnostic code

The prevalence rates per 1,000 persons by individual dementia diagnostic codes showed overall similar patterns with the incidence rates by them (Figure 4-7 and Figure 4-3). However, the *Dementia symptoms* showed a more steadily increasing pattern than the incidence rate although it leapt somewhat in 2003. The prevalence rates by the QOF diagnosis showed a somewhat stable pattern up to recently whereas the *Other diagnoses* showed a sharp increase in 2007 as the incidence rate by the codes. (A table of the prevalence rates per 1,000 persons by individual diagnostic codes is presented in Appendix Table 7).

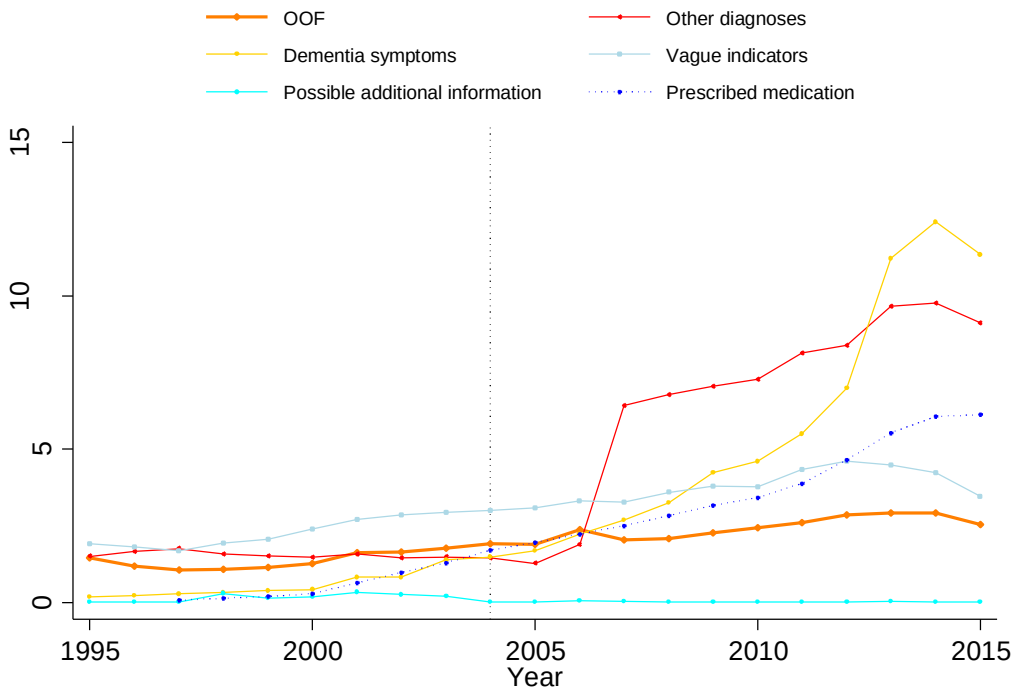


Figure 4-7. Prevalence rates per 1,000 persons, 60+ years by individual diagnostic codes excluding *Likely MCI* (with six categories)

Prevalence rates by multiple diagnostic codes

The prevalence rates of the first diagnosis using the combination of the diagnostic codes were estimated (Figure 4-8 and Table 4-6). The prevalence rates per 1,000 persons for those aged 60+, who had any one of the first diagnoses among the QOF/*Other diagnoses*/*Prescribed medication* were 2.8, 3.2 and 10.2 per 1,000 persons in 1995, 2004, and 2015 respectively. The prevalence rates with those codes including the *Dementia symptoms were* 3.0, 4.3 and 19.4 in 1995, 2004, and 2015 respectively (Table 4-6).

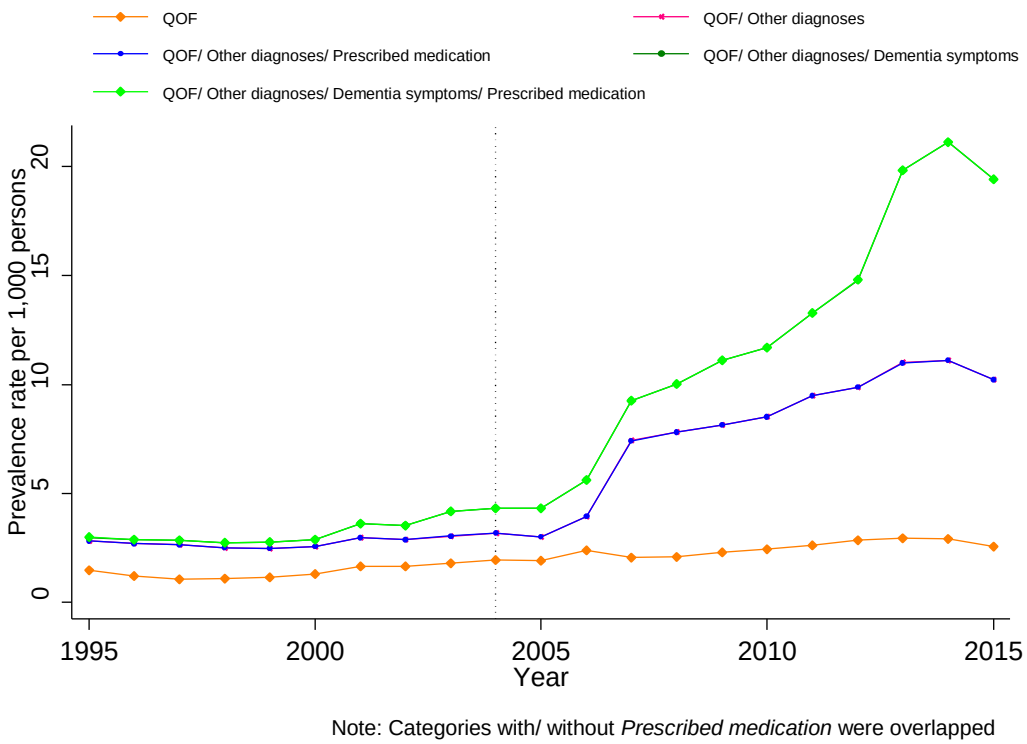


Figure 4-8. Prevalence rates per 1,000 persons, 60+ years by multiple diagnostic codes (uses five different combinations of four categories)

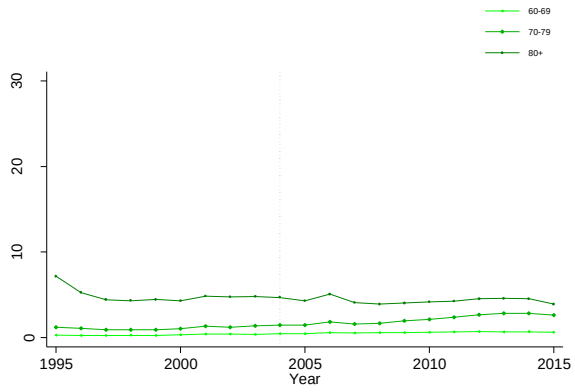
Table 4-6. Prevalence rates per 1,000 persons, 60+ years by multiple diagnostic codes

Year	QOF	QOF/ *Other diagnoses*	QOF/ *Other diagnoses/ Prescribed medication*	QOF/ *Other diagnoses/ Dementia symptoms*	QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*
1995	1.4	2.8	2.8	3.0	3.0
1996	1.2	2.7	2.7	2.9	2.9
1997	1.1	2.6	2.6	2.8	2.8
1998	1.1	2.5	2.5	2.7	2.7
1999	1.1	2.5	2.5	2.8	2.8
2000	1.3	2.5	2.5	2.9	2.9
2001	1.6	3.0	3.0	3.6	3.6
2002	1.6	2.9	2.9	3.5	3.5
2003	1.8	3.0	3.0	4.2	4.2
2004	1.9	3.2	3.2	4.3	4.3
2005	1.9	3.0	3.0	4.3	4.3
2006	2.4	3.9	3.9	5.6	5.6
2007	2.0	7.4	7.4	9.2	9.2
2008	2.1	7.8	7.8	10.0	10.0
2009	2.3	8.1	8.1	11.1	11.1
2010	2.4	8.5	8.5	11.7	11.7
2011	2.6	9.5	9.5	13.3	13.3
2012	2.8	9.9	9.9	14.8	14.8
2013	2.9	11.0	11.0	19.8	19.8
2014	2.9	11.1	11.1	21.1	21.1
2015	2.5	10.2	10.2	19.4	19.4

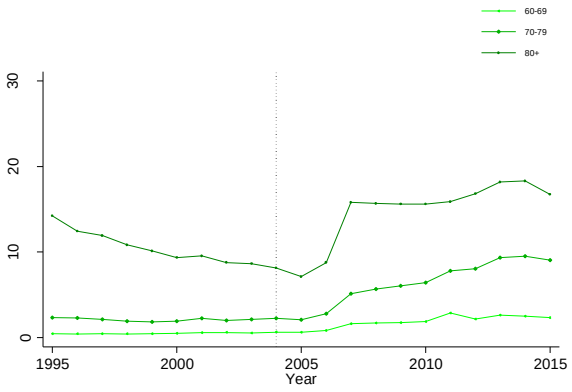
4-2-2. Age-specific prevalence rates of dementia: aged 60-69, 70-79, and 80+ years

The prevalence rates of the multiple dementia diagnostic codes for the 80+ age range more than doubled over time in comparison with the rates of the 60-69 and 70-79 age groups (Figure 4-9). The age-specific prevalence rates with and without the *Prescribed medication* (Figure 4-9 (2) and (3)) for those who had QOF/Other diagnoses were very similar. This may be imply the study population who were diagnosed by either the QOF or *Other diagnoses* mostly received medication. This interpretation could be applied to the similar pattern for those who either had QOF or *Other diagnoses* or *Dementia symptoms* (Figure 4-9 (4) and (5)). The age-specific prevalence rates per 1,000 persons of the QOF/*Other diagnoses /Prescribed medication* for the 60-69, 70-79 and 80+ age groups were 0.4, 2.3, 14.2 in 1995, 0.6, 2.3, 8.1 in 2004, and 2.3, 9.0, 16.7 in 2015 respectively. The age-specific prevalence rates per 1,000 persons with those codes including the *Dementia symptoms* for the 60-69, 70-79 and 80+ age groups were 0.5, 2.5, 14.6 in 1995, 1.1, 3.2, 10.5 in 2004, and 9.2, 21.1, 25.7 in 2015 respectively (Table 4-7).

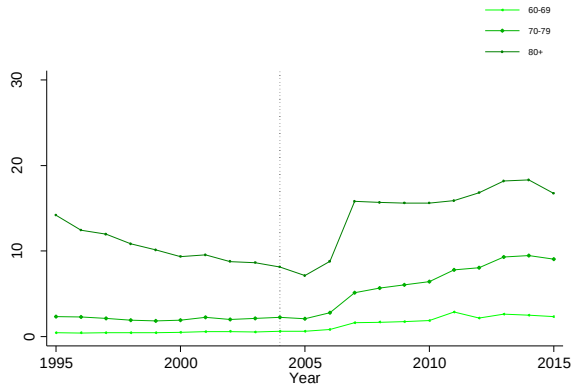
(1) QOF



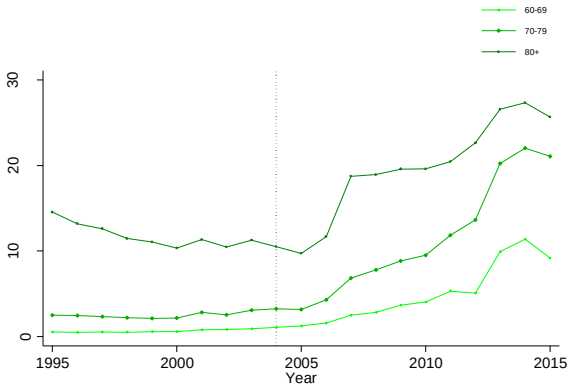
(2) QOF/*Other diagnoses*



(3) QOF/*Other diagnoses/Prescribed medication*



(4) QOF/*Other diagnoses/Dementia symptoms*



(5) QOF/*Other diagnoses/Dementia symptoms/Prescribed medication*

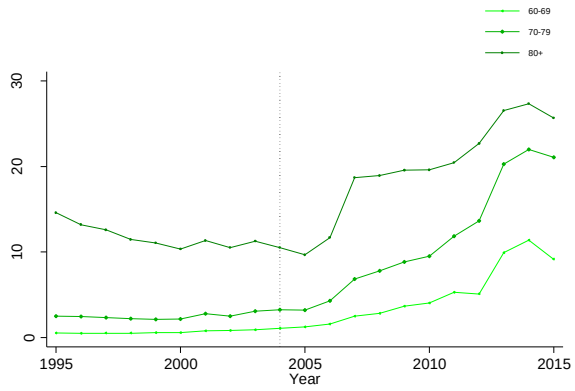


Figure 4-9. Age-specific prevalence rates per 1,000 persons by multiple diagnostic codes

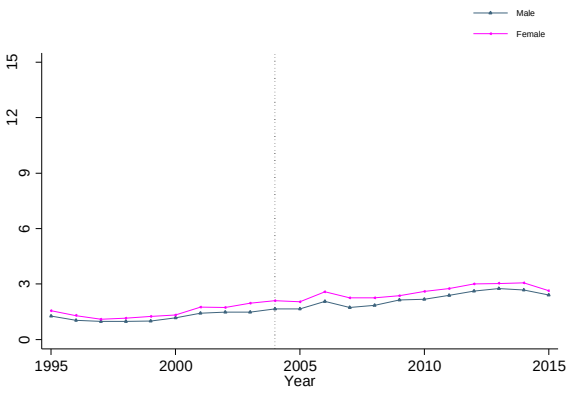
Table 4-7. Age-specific prevalence rates per 1,000 persons by multiple diagnostic codes

Year	QOF			QOF/ *Other diagnoses*			QOF/ *Other diagnoses/ Prescribed medication*			QOF/ *Other diagnoses/ Dementia symptoms*			QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*		
	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+
1995	0.3	1.2	7.2	0.4	2.3	14.2	0.4	2.3	14.2	0.5	2.5	14.6	0.5	2.5	14.6
1996	0.2	1.1	5.3	0.4	2.3	12.4	0.4	2.3	12.4	0.5	2.5	13.2	0.5	2.5	13.2
1997	0.2	0.9	4.4	0.4	2.1	11.9	0.4	2.1	12.0	0.5	2.3	12.6	0.5	2.3	12.6
1998	0.3	0.9	4.3	0.4	1.9	10.8	0.4	1.9	10.8	0.5	2.2	11.5	0.5	2.2	11.5
1999	0.2	0.9	4.4	0.4	1.8	10.1	0.4	1.8	10.1	0.6	2.1	11.1	0.6	2.1	11.1
2000	0.3	1.0	4.3	0.5	1.9	9.3	0.5	1.9	9.3	0.6	2.2	10.3	0.6	2.2	10.3
2001	0.4	1.3	4.8	0.6	2.2	9.6	0.6	2.2	9.5	0.8	2.8	11.3	0.8	2.8	11.3
2002	0.4	1.2	4.8	0.6	2.0	8.8	0.6	2.0	8.8	0.8	2.5	10.5	0.8	2.5	10.5
2003	0.3	1.3	4.8	0.5	2.1	8.6	0.5	2.1	8.6	0.9	3.1	11.3	0.9	3.1	11.3
2004	0.4	1.5	4.7	0.6	2.2	8.1	0.6	2.3	8.1	1.1	3.2	10.5	1.1	3.2	10.5
2005	0.4	1.4	4.3	0.6	2.1	7.1	0.6	2.1	7.1	1.2	3.2	9.7	1.2	3.2	9.7
2006	0.6	1.8	5.1	0.8	2.8	8.8	0.8	2.8	8.8	1.6	4.3	11.7	1.6	4.3	11.7
2007	0.5	1.6	4.1	1.6	5.1	15.8	1.6	5.1	15.8	2.5	6.8	18.7	2.5	6.8	18.7
2008	0.6	1.6	3.9	1.7	5.6	15.7	1.7	5.7	15.7	2.8	7.8	18.9	2.8	7.8	18.9
2009	0.6	2.0	4.0	1.7	6.0	15.6	1.7	6.0	15.6	3.7	8.8	19.6	3.6	8.9	19.6
2010	0.6	2.1	4.1	1.9	6.4	15.6	1.9	6.4	15.6	4.0	9.5	19.6	4.0	9.5	19.6
2011	0.6	2.4	4.2	2.9	7.8	15.9	2.9	7.8	15.9	5.3	11.9	20.4	5.3	11.8	20.5
2012	0.7	2.7	4.5	2.2	8.1	16.8	2.2	8.1	16.8	5.1	13.6	22.7	5.1	13.6	22.7
2013	0.6	2.8	4.6	2.6	9.3	18.2	2.6	9.3	18.2	9.9	20.3	26.6	9.9	20.3	26.5
2014	0.7	2.8	4.5	2.5	9.5	18.3	2.5	9.5	18.3	11.4	22.0	27.4	11.4	22.0	27.4
2015	0.6	2.6	3.9	2.3	9.0	16.7	2.3	9.0	16.7	9.2	21.1	25.7	9.2	21.1	25.7

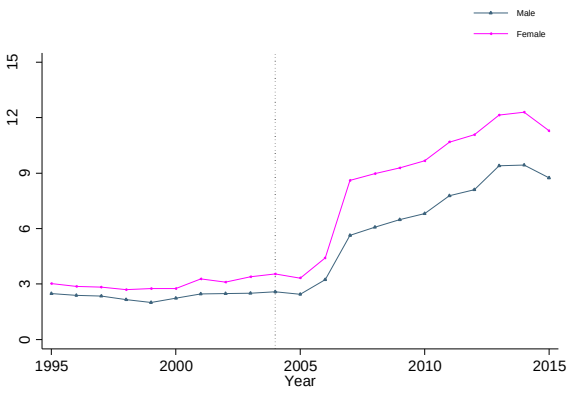
4-2-3. Gender-specific prevalence rates of dementia, aged 60+ years

The prevalence rates of the categorised dementia diagnostic codes were slightly higher in females over time (in comparison to males) (Figure 3-6). However, the incidence rates of males with (4) or (5) QOF/*Other diagnoses/Dementia symptoms* (/*Prescribed medication)* were similar to the rates of females in 2013-15. The gender-specific prevalence rates per 1,000 people of the QOF/*Other diagnoses*/*Prescribed medication* for males and females were 2.5, 3.0 in 1995, 2.6, 3.5 in 2004, and 8.7, 11.3 in 2015 respectively for aged 60+ years. The gender-specific prevalence rates with those codes including the *Dementia symptoms* were 2.7, 3.1 in 1995, 3.7, 4.7 in 2004, and 19.2, 19.6 in 2015 respectively for the 60+ age group (Table 4-8).

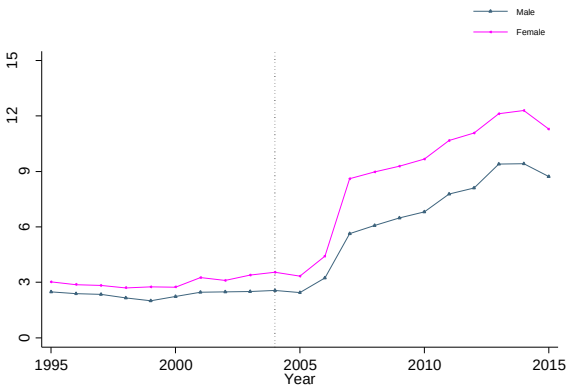
(1) QOF



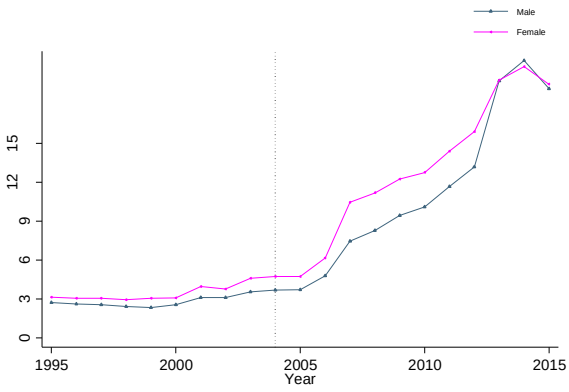
(2) QOF/*Other diagnoses*



(3) QOF/*Other diagnoses/Prescribed medication*



(4) QOF/*Other diagnoses/Dementia symptoms*



(5) QOF/*Other diagnoses/Dementia symptoms/Prescribed medication*

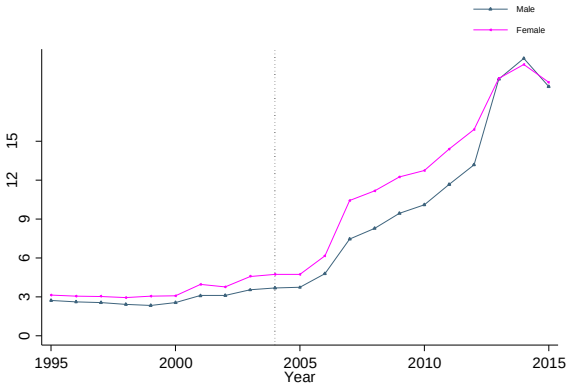


Figure 4-10. Gender-specific prevalence rates per 1,000 persons, 60+ years by multiple diagnostic codes

Table 4-8. Gender-specific prevalence rates per 1,000 persons, 60+ years by multiple diagnostic codes

Year	QOF		QOF/ *Other diagnoses*		QOF/ *Other diagnoses/ Prescribed medication*		QOF/ *Other diagnoses/ Dementia symptoms*		QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
1995	1.3	1.6	2.5	3.0	2.5	3.0	2.7	3.1	2.7	3.1
1996	1.0	1.3	2.4	2.9	2.4	2.9	2.6	3.1	2.6	3.0
1997	1.0	1.1	2.3	2.8	2.4	2.8	2.6	3.0	2.6	3.0
1998	1.0	1.1	2.2	2.7	2.2	2.7	2.4	2.9	2.4	2.9
1999	1.0	1.2	2.0	2.8	2.0	2.8	2.3	3.0	2.3	3.0
2000	1.2	1.3	2.2	2.7	2.2	2.7	2.5	3.1	2.5	3.1
2001	1.4	1.8	2.5	3.3	2.5	3.3	3.1	4.0	3.1	3.9
2002	1.5	1.7	2.5	3.1	2.5	3.1	3.1	3.8	3.1	3.8
2003	1.5	2.0	2.5	3.4	2.5	3.4	3.5	4.6	3.5	4.6
2004	1.6	2.1	2.6	3.5	2.6	3.5	3.7	4.7	3.7	4.7
2005	1.7	2.0	2.5	3.3	2.5	3.3	3.7	4.7	3.7	4.7
2006	2.1	2.6	3.2	4.4	3.2	4.4	4.8	6.2	4.8	6.2
2007	1.7	2.3	5.6	8.6	5.6	8.6	7.4	10.5	7.4	10.4
2008	1.9	2.2	6.1	9.0	6.1	9.0	8.3	11.2	8.3	11.2
2009	2.1	2.4	6.5	9.3	6.5	9.3	9.4	12.2	9.4	12.2
2010	2.2	2.6	6.8	9.7	6.8	9.7	10.1	12.8	10.1	12.7
2011	2.4	2.7	7.8	10.7	7.8	10.7	11.7	14.4	11.7	14.4
2012	2.6	3.0	8.1	11.1	8.1	11.1	13.2	15.9	13.2	15.9
2013	2.7	3.0	9.4	12.1	9.4	12.1	19.8	19.9	19.8	19.9
2014	2.7	3.1	9.4	12.3	9.4	12.3	21.4	20.9	21.4	20.9
2015	2.4	2.6	8.7	11.3	8.7	11.3	19.2	19.6	19.2	19.6

4-3. Main findings

4-3-1. Codes need to be used for identification of dementia

Age-specific incidence rates of dementia per 1,000 women-years

The age-specific incidence rates of dementia per 1,000 women was calculated and compared to the figures from previous studies. The references about the age-specific incidence rates of dementia per 1,000 men were not available, although there was the age-specific incidence rates for the small US cohorts (i.e., Late-Onset Alzheimer Disease/National Cell Repository for Alzheimer Disease (NIA-LOAD/NCRAD) and Estudio Familiar de Influencia Genetica en Alzheimer (EFIGA) families) [97]. The incidence rates for the 65-69 and 70-79 age groups using another primary care database, CPRD (1990-2012) [32] showed similar figures to the estimated incidence rates using the QOF/*Other diagnoses/Dementia symptoms* (/*Prescribed medication*) in this study. The incidence rates for the 65-69, 70-79 and 80+ age groups from the longitudinal cohort study, CFAS II (2011-2013) [28], revealed

similar figures to the estimated incidence rates using the QOF/*Other diagnoses/Dementia symptoms* (/*Prescribed medication*) (Table 1-2 and Table 4-9). (The incidence rates with and without the *Prescribed medication* were similar.)

Table 4-9. Age-specific incidence rates per 1,000 women-year, 60+ years by multiple diagnostic codes

Year	QOF			QOF/ *Other diagnoses*			QOF/ *Other diagnoses/ Prescribed medication*			QOF/ *Other diagnoses/ Dementia symptoms*			QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*		
	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+	60-69	70-79	80+
1995	0.2	1.0	4.3	0.3	1.9	8.5	0.3	1.9	8.5	0.4	2.1	8.7	0.4	2.1	8.7
1996	0.2	1.2	3.2	0.3	2.2	7.3	0.3	2.2	7.3	0.4	2.4	7.8	0.4	2.4	7.8
1997	0.2	1.1	3.0	0.4	2.3	7.7	0.4	2.3	7.7	0.5	2.5	8.1	0.5	2.5	8.1
1998	0.2	1.1	3.3	0.3	2.1	7.5	0.3	2.2	7.6	0.4	2.4	8.0	0.4	2.5	8.0
1999	0.2	1.2	3.9	0.4	2.4	7.6	0.4	2.4	7.7	0.5	2.6	8.3	0.5	2.7	8.5
2000	0.2	1.4	4.2	0.3	2.4	8.1	0.3	2.5	8.2	0.4	2.7	8.9	0.4	2.8	9.0
2001	0.4	1.9	5.2	0.5	2.9	9.0	0.6	3.2	9.4	0.7	3.6	10.8	0.7	3.9	11.2
2002	0.3	1.9	5.3	0.5	2.7	9.0	0.5	3.1	9.6	0.6	3.5	10.5	0.7	3.8	11.1
2003	0.3	2.2	6.6	0.5	3.1	10.7	0.5	3.4	11.3	0.8	4.5	13.8	0.9	4.7	14.4
2004	0.3	2.4	6.9	0.4	3.3	11.0	0.5	3.6	11.6	0.8	4.7	13.8	0.8	4.9	14.2
2005	0.4	2.2	7.1	0.5	2.9	10.5	0.5	3.2	10.9	0.9	4.3	13.4	1.0	4.5	13.7
2006	0.4	3.0	9.1	0.5	4.0	13.5	0.5	4.1	13.7	1.0	5.7	16.9	1.1	5.7	16.9
2007	0.4	2.7	8.1	0.6	4.2	14.9	0.6	4.3	14.6	1.2	6.1	18.4	1.2	6.1	18.0
2008	0.4	2.6	8.0	0.5	3.8	13.1	0.5	3.8	13.4	1.2	6.0	17.5	1.2	6.0	17.6
2009	0.4	2.7	8.8	0.6	3.9	13.3	0.6	4.0	13.5	1.9	6.8	19.2	1.9	6.9	19.2
2010	0.5	3.1	10.1	0.6	4.1	14.3	0.6	4.3	14.5	1.9	6.8	19.4	1.9	6.9	19.5
2011	0.5	3.2	10.6	1.4	5.4	14.6	1.5	5.6	14.8	2.8	9.3	20.8	2.8	9.4	20.8
2012	0.5	3.5	11.3	0.8	4.5	15.4	0.8	4.7	15.7	2.5	9.8	24.3	2.5	9.9	24.4
2013	0.5	3.7	12.1	0.9	5.1	16.6	0.9	5.3	17.0	5.5	16.0	29.7	5.5	16.1	29.8
2014	0.5	3.8	12.9	1.0	5.0	17.0	1.0	5.2	17.2	6.8	17.0	31.3	6.8	17.1	31.3
2015	0.5	3.7	12.4	0.9	5.1	16.5	1.0	5.4	17.0	5.9	17.5	32.6	5.9	17.6	32.8

Table 4-10. Age-specific incidence rates per 1,000 women-years (Table 1-2 and Table 4-9)

Age in years		CPRD (Brown *et al*., 2016 [32])	QOF/ *Other diagnoses/ Dementia symptoms*	QOF/ *Other diagnoses/ Dementia symptoms* (/*Prescribed medication*)	CFAS II (Matthews *et al*., 2016 [27])	QOF/ *Other diagnoses/ Dementia symptoms*	QOF/ *Other diagnoses/ Dementia symptoms* (/*Prescribed medication*)
		1990-2012	1995-2012		2011-2013		
		Table 1-2.	Table 4-9.		Table 1-2.	Table 4-9.	
60-69	65-69	1.18	0.4 - 2.8	0.4 - 2.8	4.6	2.8 - 5.5	2.5 - 5.5
70-79	70-74	8.06	2.1 - 9.8	2.1 - 9.9	6.4	9.3 - 16.0	9.4 - 16.1
	75-79				16.1		
80+	80-84	-	7.8 - 24.3	7.8 - 24.4	39.6	20.8 - 29.7	20.8 - 29.8
	85+				55.3		

Age-specific prevalence of dementia per 1,000 persons

Although a direct comparison of the figures was not possible as the prevalence rate does not have the same numerator-denominator relationship as the prevalence percentage (%) reported in other studies (Table 1-1), the age-specific prevalence rates per 1,000 persons using the codes of QOF/*Other diagnoses*(/*Prescribed medication*) (Table 4-6) showed similar figures to the consensus estimates. Prevalence rates additionally with the *Dementia symptoms* showed somewhat higher (i.e., over-estimated) figures to the consensus estimates, but the rates were similar to the figure for the 90+ age group (Table 4-11).

Table 4-11. Age-specific prevalence (%) (Table 1-1) and Age-specific prevalence rates per 1,000 persons (Table 4-6)

Age in years		2014			2011-2013		
		Dementia UK 2014 report (Prince *et al.* [6])	QOF/ *Other diagnoses* (/*Prescribed medication*)	QOF/ *Other diagnoses/ Dementia symptoms* (/*Prescribed medication*)	CFAS II (Matthews *et al*., 2016 [27])	QOF/ *Other diagnoses* (/*Prescribed medication*)	QOF/ *Other diagnoses/ Dementia symptoms* (/*Prescribed medication*)
		Table 1-1	Table 4-6		Table 1-1	Table 4-6	
60-69	60-64	0.9	2.5	11.4	-	2.2 - 2.9	5.1 - 9.9
	65-69	1.7			1.5		
70-79	70-74	3.0	9.5	22.0	2.7	7.8 - 9.3	11.8 - 20.3
	75-79	6.0			5.7		
80+	80-84	11.1	18.3	27.4	10	15.9 - 18.2	20.5 - 26.5
	85-89	18.3			16.1		
	90-94	29.9			30.1		
	95+	41.1			-		

In summary, the age-specific incidence rates of dementia for women with the QOF/*Other diagnoses/Dementia symptoms* (/*Prescribed medication*) codes were at similar levels to other studies (Table 4-10). A direct comparison between the prevalence rate and the prevalence percentage (%) was not possible, taking into account the age-specific prevalence of dementia with the QOF/*Other diagnoses* (/*Prescribed medication*), i.e., the codes without *Dementia symptoms,* were at a similar level to the consensus estimates. The codes additionally with the *Dementia symptoms* showed similar prevalence estimates for the 90+ population (Table 4-11).

Table 4-12-1. Summary table of the incidence rates per 1,000 person-years, 60+ years (2013-15)

Codes	Year	Total	60-69	70-79	80+	Male	Female
QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*	2013	14.9	6.6	17.5	30.1	15.2	14.6
	2014	16.3	8.1	18.4	31.9	16.8	15.9
	2015	15.9	6.6	18.2	33.3	15.7	16.0

Table 4-12-2. Summary table of the prevalence rates per 1,000 persons, 60+ years (2013-15)

Codes	Year	Total	60-69	70-79	80+	Male	Female
QOF/ *Other diagnoses/ Prescribed medication*	2013	11.0	2.6	9.3	18.2	9.4	12.1
	2014	11.1	2.5	9.5	18.3	9.4	12.3
	2015	10.2	2.3	9.0	16.7	8.7	11.3
QOF/ *Other diagnoses/ Dementia symptoms/ Prescribed medication*	2013	19.8	9.9	20.3	26.5	19.8	19.9
	2014	21.1	11.4	22.0	27.4	21.4	20.9
	2015	19.4	9.2	21.1	25.7	19.2	19.6

Codes to be considered other than the QOF defined codes

The highest frequencies of the codes in *Other diagnoses* include the codes related to dementia annual review (6AB..00, N=35,798) and dementia monitoring (9Ou1.00, n=3256 and 66h..00, N=1,901) since 2006-07 (Appendix Table 5). These codes seem to be considered to include the identification of dementia that those defined in the QOF could not cover. Although the categorised *Dementia symptoms* codes contain expansive diagnostic codes (including the codes rarely used such as Memory: present time (3A2..00, N=1) and Memory: present year (3A4..00, N=1), the *Dementia symptoms* may cover related information or missed cases of dementia in a primary care database. In order to cover the limitations of clinical records in primary care databases, the *Dementia symptoms* seems to be appropriate for use in a study design with a primary care database. The highest frequencies of the codes in the *Dementia symptoms* were Mini-mental state examination (388m.00, N=20,316) and the six item cognitive impairment test (3AD3.00, N=20,211), Referral to memory clinic (8HTY.00, N=11,178) and Behaviour assessment (3AB..00, N=9,326) (Appendix Table 6).

Chapter 5. Discussion and recommendations

How dementia should be identified from primary care records in the UK was explored using the estimated incidence and prevalence of dementia in THIN database. In total, 894 Read codes (with some of ICD-10) were extracted from a systematic review of the previous studies which used primary care databases in the UK to identify people with dementia. There were a number of inconsistencies in the codes across the studies. Some studies only used the QOF defined codes whereas some studies used other codes other than the QOF defined codes to identify dementia (Table 2-2 to Table 2-7). In total, 949 additional codes from a THIN data dictionary were extracted, which had not been previously included but may be of importance. All of these codes were collated and categorized to identify people with dementia in THIN dataset. As a supplementary marker of dementia, people on medications to treat Alzheimer's disease were identified. Individuals were on the first *Prescribed medication* were 29,626 (1987-2016, Table 3-1). Those comprehensively collected codes were examined for whether they are definitive markers of dementia, possible dementia or symptoms, overlaps of the first diagnosis among the categorized codes were looked at. The results showed that there are a number of people who were doubted to have dementia with other codes, but they did not have QOF based codes so it may well be important to include other dementia diagnostic codes. Using other codes additionally with the QOF defined codes, i.e., the QOF/*Other diagnoses/Dementia symptoms (/Prescribed medication)* showed were similar to the incidence rates in women of 60+ years to other studies which used the UK's primary care database (Table 4-10). Therefore, all of these additional markers of dementia might be important. The estimated incidence rates per 1,000 person-years for those aged 60+ who had any of the first diagnosis among the QOF, *Other diagnoses, Dementia symptoms* and *Prescribed medication* were 14.9 to 15.9 in 2013-15. The estimated prevalence rates per 1,000 persons for the 60+ age group who had any of the first diagnoses among the QOF, *Other diagnoses* and *Prescribed medication* were 11.0 to 10.2 in 2013-15 (Table 4-12). Since the QOF was introduced in 2004, there were slight and steady increasing trends in both incidence and prevalence rates (when they were compared between 2004 and 2013-15, Table 4-3 and Table 4-6). The trends of the incidence and prevalence rates with only the QOF based codes are 2.2, 3.8- 3.9 in 2004 and 2013-15, and 1.9, 2.9- 2.5 in 2004 and 2013-15 respectively (Table 4-3 and Table 4-6).

Randomised controlled trials (RCTs) are probably not feasible to answer complicated research questions related to dementia as people with dementia are often excluded from RCTs. This type of study design is likely to be underpowered and the quality of the results obtained is highly influenced by several components. This type of study also requires consent from the participants although diagnosis of dementia for the study population would be more firmly verified. A large observational

study design (using propensity score matching and appropriate confounding controlling analyses such as multivariate regression) using the population in a primary care database will control the limitations that a study design of a RCT has. Nevertheless, this type of study design in dementia related studies also has limitations and one of the greatest challenges would be to accurately identify people with dementia. In order to achieve this, firstly it was important to grasp the correct codes which define dementia in the primary care records. In fact, it would be problematic to miss out or incorrectly categorize people with dementia in the related research (even though this aspect could be overcome somewhat by enough power in the large routine data sources). Diagnosis of dementia is often is not easy; many factors could disrupt the formal diagnosis process of an individual (as discussed in section 1-1-3). One of the difficulties is that the codes for recording dementia are not very systematically organized, and the usage of codes not very accurate in general.

5-1. Strength and limitations

In terms of identifying accurate codes to identify dementia in the primary care database, the main strengths of this study are: (1) use of systematic literature sources for the dementia diagnostic codes in the UK primary care databases; (2) inclusion of other available sources of dementia diagnostic codes as a supplement or a verification process; (3) use of systematically categorized dementia diagnostic codes which were comprehensively collected for the calculation of incidence and prevalence rates over time (up to a recent date) in the electronic primary care dataset; (4) comparisons of the estimated rates with other literature figures and consensus estimates to examine the coverage of the rates by each code, and to identify the codes needed to be used. It will be important to use adequate diagnostic codes, considering the difficulty in identifying the clinical syndrome in primary care records; (5) although high-quality coding of clinical data is not yet universal [98], a code system of a primary care database in the UK has been updated continuously as policies and education for health professionals have been changed or improved. Even though research has been performed traditionally in the UK, dementia has received considerable attention recently. There has been constant pressure and effort for high quality primary care in the UK imposing more conditions on the QOF [13] and improving data quality[11].

[11] Volunteered clinicians have been part of data quality schemes and received feed-back on the quality of their coding. However, there is no clear evidence reported so far about whether it can improve data quality (de Lusignan, S., et al., 2002).

The study has a number of limitations. Potential sources of bias or limitations in the methodologies are: (1) Synthesis and categorization of the codes to identify dementia could be biased by researchers' opinions. In terms of the internal validity, more than one researcher has confirmed; (2) incidence and prevalence rates from literature or consensus estimates are not exactly possible for a direct comparison as study designs, populations and measures (e.g., percentage versus rate) are not exactly identical. In addition, different definitions and calculations of the denominator for the rates might be used in the studies. In this study, the population incidence rates were estimated instead of incidence rates at risk of the event which an individual will be censored at dementia diagnosis. More restricted definitions of the denominator could be further applied. However since the denominator is not a cohort level, the differences are not expected not to be very big; (3) it seems difficult to use the incidence or prevalence rate itself as a pure gold standard to decide on the codes which identify dementia. It will be influenced by many factors including the design and the population of a study. A sudden change of the rate for a specific code could be due to changes in policy or a system related to the syndrome or the codes. In addition, determinants of the incidence or prevalence rate are not known. Further research about the characteristics of the population will be also required to figure out determinants; (4) estimated incidence and prevalence rates could have confidence intervals (or reference ranges) where the standard deviation of the rates are applied after modelling using a Poisson distribution for instance. The arithmetic proportion estimation was presented in this study.

5-2. Recommendations

Codes needs to be used in primary care records

To identify people with dementia in the observational routine data sources such as primary care records, instead of using a designed RCT, it will be important to carefully identify the study population. Alternative or additional methods to identify dementia will be needed in primary care records. The method of comparison for the incidence and prevalence of dementia with the other estimates (using the comprehensive range of codes) suggested to use the codes containing *Other diagnoses* (Table 2-3) (or *Prescribed medication* for treatments of Alzheimer's disease or various other memory impairments, Table 3-1) at least in addition to the QOF defined codes (without missing out a number of people with dementia). Additional use of the *Dementia symptoms* codes seem to identify the very elderly population with dementia, implying the codes may cover important cases or the related information of dementia in primary care records. Individuals with dementia tends to be

have more than a single code over the time frames. Nevertheless, in some cases, only limited evidence could be accessible in the records for people with dementia (e.g., referral to memory clinic or a cognitive related decline/impairment test without outcomes). The codes suggest *Dementia symptoms* (Table 2-4) consist of those tests or screenings. Nonetheless, codes about non-specific symptoms may need to be used carefully as it is possible memory or cognitive function could be influenced by other factors such as individual's stress or medications.

Designs of dementia related studies

There are a number of comorbidities in people with dementia, and hypertension (high blood pressure) is one of the most frequent (alongside diabetes) [12][99]; it has been reported that it is associated with increasing cognitive impairment and vascular dementia [100]. In addition, there is limited evidence on the treatment of hypertension, using antihypertensive treatments (AHTs), in people with dementia. It is unlikely that it will be possible to conduct sufficiently powered research on dementia with complicated questions using a RCT study[13]. Findings from RCTs may not be generalizable to elderly people with frailty[14], even limiting the applicability of the findings to more severely frail or demented people [101-103]. This means that alternative methods of research need to be used to examine the questions. One potential method would be using a large observational database of routine primary care to fulfil those research questions. Previous evidence on the topics are based on small or not to be of high quality trial data [104]. The quality of the results obtained from RCTs is highly influenced by several components - the collected data, the method used for adjustment of potential confounders (including selection of the confounders), and the interpretation of the results and the potential limitations [105]. RCTs may be affected by a selection and recall bias (i.e., a systematic error of events or experiences from the past by study participants) [104]. Faraoni *et al*., (2016) addressed the fact that "Large observational trials using propensity score matching (to balance the covariates in the two groups [106], and therefore account for observable confounding factors) and appropriate multivariate regression analyses might better reflect the 'real clinical world' than a RCT performed in a homogenous subgroup of patients" [105]. Research with a well-designed large population database to address these deficiencies (dealing with potential bias, chance or confounding) will be meaningful. Primary care datasets have huge potentials enable to study incidence of dementia and related symptoms, causes and outcomes of dementia, management of dementia and comorbidities such as

[12] Scrutton *et al.*, 2016 underlined that people with dementia were less likely to be diagnosed with hypertension with some other comorbidities.
[13] The Hypertension IN Dementia (HIND) of blood pressure lowering in people with dementia (Welsh, 2016)
[14] HYVET (HYpertension in the Very Elderly Trial) and SPRINT (Systolic Blood Pressure Intervention Trial) excluded patients from care homes and those with an established diagnosis of dementia.

hypertension. An in-depth understanding of the definition of dementia and how it is recorded in a primary care database will be important to design a comorbidity related study, especially critical to evaluate precisely the effect of a comorbidity. It is highly likely miss out a number of people have dementia using narrow definition of dementia diagnostic codes that is critical in the study design. For instance, a study of hypertension management would only inform about the management in those with more advanced dementia if the people included were those with more advanced dementia and/or relevantly young (as the outcomes suggested, Table 4-11). It would be reasonable to use broad definition of dementia codes to design for the management of hypertension among people with dementia, especially for prevention interventions. The strict inclusion of study population with narrowly defined dementia diagnostic codes is likely to provide limited outcomes, i.e., measures that quantify disease like incidence rates will be underestimated, and it would make difficult to generalize the findings. That is to say, management will not be generalisable to the wider dementia population [107] and the findings will not inform us about management of hypertension in those with no diagnosis but with symptoms. On the other hand, it is likely to affect the validity of the outcomes if a study use excessively broad definition of diagnostic codes, without series of specific symptoms or single/temporary diagnostic codes, and include people actually without a disease. If a study includes those with only symptoms but not diagnosis, then the incidence estimates will be too high. Therefore, performing sensitivity analysis to examine the outcomes with a narrow and a broad definition of a disease would be ideal. Identifying people with comorbidities besides hypertension in those with dementia is also important. A greater depth of understanding of pathology of a disease will be important to correctly define and management of a disease.

5-3. Further research

Usages of dementia diagnostic codes in primary care

A sudden changed pattern of the incidence rate (after the QOF scheme launched on 1st April 2004) of some codes could be due to several plausible reasons: (1) Target patients may be changed; (2) encouraging usage of specific dementia diagnosis codes (other than QOF based codes) which may not be sufficient to get before the QOF scheme launched; (3) level of the payments/incentives were increased (for a specific codes related); (4) Improved GP's education on monitoring, diagnosis or prompt onward referral on dementia; and (5) the technical documentations (e.g. the NICE menu for dementia indicators), which help the scheme can be applied practically, might have developed and circulated after the QOF scheme launched; and (6) software a GP use to record might have updated; Further research into dementia diagnostic codes, investigating their usages including GPs' usage

behaviours, and strategies to improve a quality of coding in a UK primary care database seems to be required. There are inferences, and a study reported that detailed feedback to GPs (using data quality markers) had a significant effect on data quality [98].

Global trends in the prevalence, incidence and mortality of dementia

Recent global trends showed moderately consistent evidence and declining prevalence rates of dementia in high-income countries in Western Europe (e.g., Spain, 1988-95 [38], UK, 1993-2011 [51]) and Germany, 2007-09 [33]) and US, 1993-2002 [108]). However, there is some contrary evidence to suggest increasing prevalence (in Sweden, 2001-06 [39] and Japan, 1985-2005 [36]) [109]. Evidence of these trends was inconsistent across studies. This was examined by changes in the prevalence rates within the study period (e.g., 1993 versus 2011 in the CFAS, UK [51]) [109]. (The adjusted odds ratios for the relative changes (%) were presented using the 'metan' package in STATA/SE (version 15.0, StataCorp LLC) in Appendix Figure 1-1). Relative change (%) in prevalence per year was -1.7% decrease in the CFAS, UK [51], -3.6% in Zaragoza, Spain [38] with independent sampling over time, −1.2 % (women aged 75-84 years) in Germany which used the insurance claims data [33] and -3.2% in the HRS, US [108]. Other studies from Stockholm, Sweden [49], Goteborg, Sweden [52] and Indianapolis, IN, US, African Americans [53] did not show trends. On the other hand, the Umea study, Sweden [39] (with aged 85+ years) showed +8.0% of increase and in Hisayama, Japan [36] (with aged 65+ years) showed +1.9% of increase in dementia and +12.8 % increase in Alzheimer's disease (Appendix Table 1) [109].

The incidence of dementia also showed a decline in western European countries, relative change (%) per year of −3.5 % in Bordeaux, France, 1988-2010 [50], −2.5 % in the Rotterdam, Netherlands, 1990-2000 [37], −3.0 % in Germany, 2004-10 [34]. In addition, incidence of dementia were also in decline in North America; such as -5.5% (−4.4 % for Alzheimer's disease) in Indianapolis, IN, US for African Americans, 1991-2002 [48], −1.7 % in Framingham, US, 1980-2006 [45] for dementia (−2.1 % for vascular dementia and −1.2 % for Alzheimer's disease), and −0.6 % in the Ontario, Canada, 2002-13 [35] (Appendix Table 2-2) [109].

Research of dementia prevalence or incidence will be highly influenced by diagnostic factors including diagnostic criteria and policies in public health of the country. Declining incidence trends may be balanced by a trend of longer survival with dementia [109] although the mortality of dementia has been reported little so far globally. As discussed in the second paragraph of Chapter 5, most of the studies estimated the incidence and prevalence of dementia based on the selective cohorts of the populations with short and long intervals (3-20 years) between waves, and they are probably cannot feasibly to answer complicated research questions. This study showed the incidence and prevalence rates of dementia as defined with only the QOF codes increased little by little over time (1995-2015).

These findings were obtained from the real-world cohorts (i.e., large observational study design using a primary care database (THIN) for the UK population). This will control the limitations of those epidemiological cohort databases (e.g., CFAS and UK biobank), some other research cohorts (such as TRACK HD, i.e., a prospective observational biomarker study [110] and the NIMROD (Neuroimaging of Inflammation in MemoRy and Other Disorders) study [111]), or RCT design studies, despite its limitation of accurate identification of people in dementia that has been addressed and examined in this study. Further in-depth investigation with a robust design, enough power and accuracy (controlling comprehensive related factors and understanding dementia diagnosis systems of a country) to examine prevalence and incidence rates of dementia is required; so that generalizable rates and an overall effect of global trends could be derived. This could be performed using a well-managed and systematically structured primary care database of the country. Identification of the dementia population using the proper codes will be essential in this process.

Further study regarding dementia comorbidity and treatments

Up to now, there has been no clear evidence based guidelines in terms of the management of hypertension, i.e., one of the most frequent comorbidities, in people with established dementia [112]. For instance, there is no evidence that a risk of polypharmacy in a frail or cognitively impaired person (or person who has dementia) is great enough to outweigh the benefits of AHTs [103]. The NICE (National Institute for Health and Care Excellence) guidance (2011) on AHTs mentions 'comorbidities' when prescribing. For instance, it says to "offer people aged 80+ years the same antihypertensive drug treatment as people aged 55–80 years, taking into account any comorbidities [113]". However, the guideline does not provide either enough evidence or advice about how to take account of comorbidities, nor advice about how to take account of dementia. Most people with high blood pressure and dementia are usually treated in the same way as those who do not have dementia although the relationship between blood pressure and dementia is complex and it may not be best to do so. For example, blood pressure tends to fall before and during the onset of dementia. Furthermore, the regulation of brain perfusion is impaired in people with established dementia (for example, there is an increased prevalence of orthostatic hypotension) and people with dementia are additionally particularly prone to drug-associated orthostatic hypotension. Impaired perfusion of the brain can increase brain damage, and orthostatic hypotension can cause falls and injuries. This means that lowering blood pressure in people with established dementia could potentially harm them, by making their dementia worse or harming them in other ways [114]. An evidence based dementia-specific guideline for the management of hypertension with AHTs is required which contains in-depth information about risks (such as falls and related fractures, and cardiovascular related adverse

events[15]) and benefits, and population most likely to have risks and benefits. Understanding the potential risks and benefits of AHTs in dementia including comorbidity, polypharmacy, and use of a specific medication will eventually be beneficial to patients, carers and health professionals on management of hypertension.

The alternative ways of identifying people with dementia were examined with the prevalence and incidence of dementia in the UK, using The Health Improvement Network (THIN) database. Further study may need to focus on the examination of associations between exposure to AHTs, and outcomes in patients with dementia (in comparison to patients without dementia) with a large observational study design, using a UK primary care dataset. This study suggested using of the codes containing *Other diagnoses* (or *Prescribed medication* for treatments) at least, in addition to the QOF defined codes for study design, in order not to miss out a number of people with dementia in primary care records. This study showed additional use of the *Dementia symptoms* codes seem to identify the very elderly population with dementia, implying the codes may cover important cases or the related information of dementia in primary care records.

[15] A systematic review paper of pharmacotherapy for hypertension in the elderly underlined that a person who is at high immediate risk of suffering a cardiovascular event but without other comorbidities, may have a higher benefit to-risk ratio than the average trial participant (Musini *et al*, 2009). Long term higher levels of blood pressure are associated with eventual damage to blood vessels and the organs served by them – the heart, kidney, eyes and brain are all organs particularly prone to such damage. In general, lowering blood pressure in those in whom it is elevated reduces the risk of adverse outcomes.

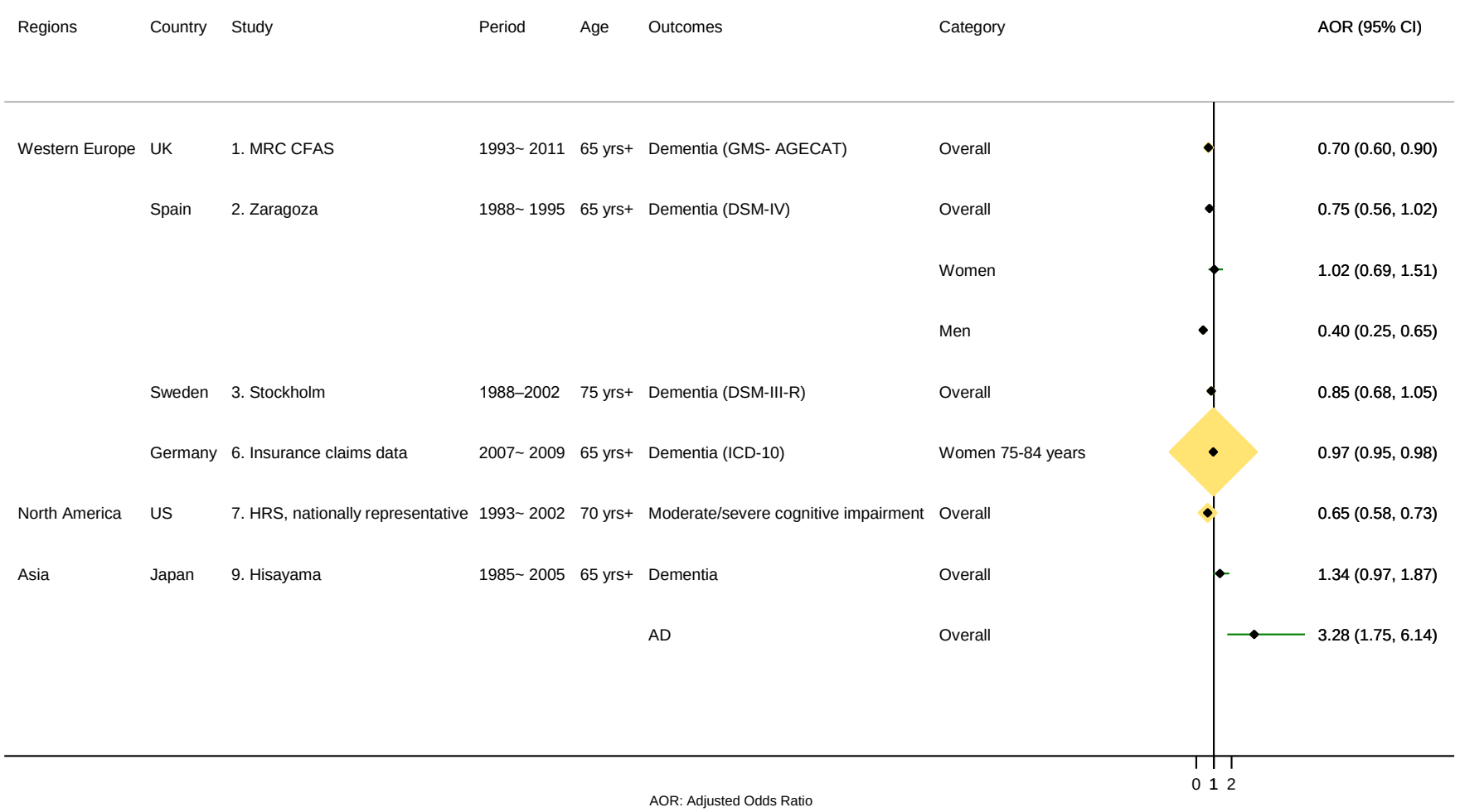
Appendix

Appendix Table 1. Relative change (%) per year - estimated changes in prevalence of dementia or Alzheimer's disease over time [109]

Regions	Country	Study	Period	Age range	Outcomes	OR (95% CIs)	Relative change (%) per year
Western Europe	UK	1. MRC CFAS [51]	1993–2011	65+ years	Dementia (GMS- AGECAT)	0.70 (0.60-0.90)	−1.7 %
	Spain	2. Zaragoza, Spain [38]	1988–1995	65+ years	Dementia (DSM-IV)	0.75 (0.56-1.02)	−3.6 %
	Sweden	3. Stockholm, Sweden [49]	1988–2002	75+ years	Dementia (DSM-III-R)		No trend
	Sweden	4. Goteborg, Sweden [52]	1976–2000 (70 years), 1976–2005 (75 years)	70 years, 75 years	Dementia historical criteria		No trend
	Sweden	5. Umea, Sweden [39]	2001–2006	85+ years	Dementia (DSM-IV)		+8.0%
	Germany	6. Germany, insurance claims data [33]	2007–2009	65+ years	Dementia (ICD-10)	0.97 (0.95-0.98)	−1.2 % (women aged 75-84 years)
North America	US	7. HRS, nationally representative, US [108]	1993–2002	70+ years	Moderate/severe cognitive impairment (probable dementia)	0.65 (0.58-0.73)	−3.2 %
	US	8. Indianapolis, IN, US, African Americans [53]	1991–2002	65+ years	Dementia (DSM-III-R), AD		No trend
Asia	Japan	9. Japan, Hisayama [36]	1985–2005	65+ years	Dementia, AD	1.34 (0.97-1.87) 3.28 (1.75-6.14)	+1.9 % (Dementia) + 12.8 % (AD)

*AD: Alzheimer's disease

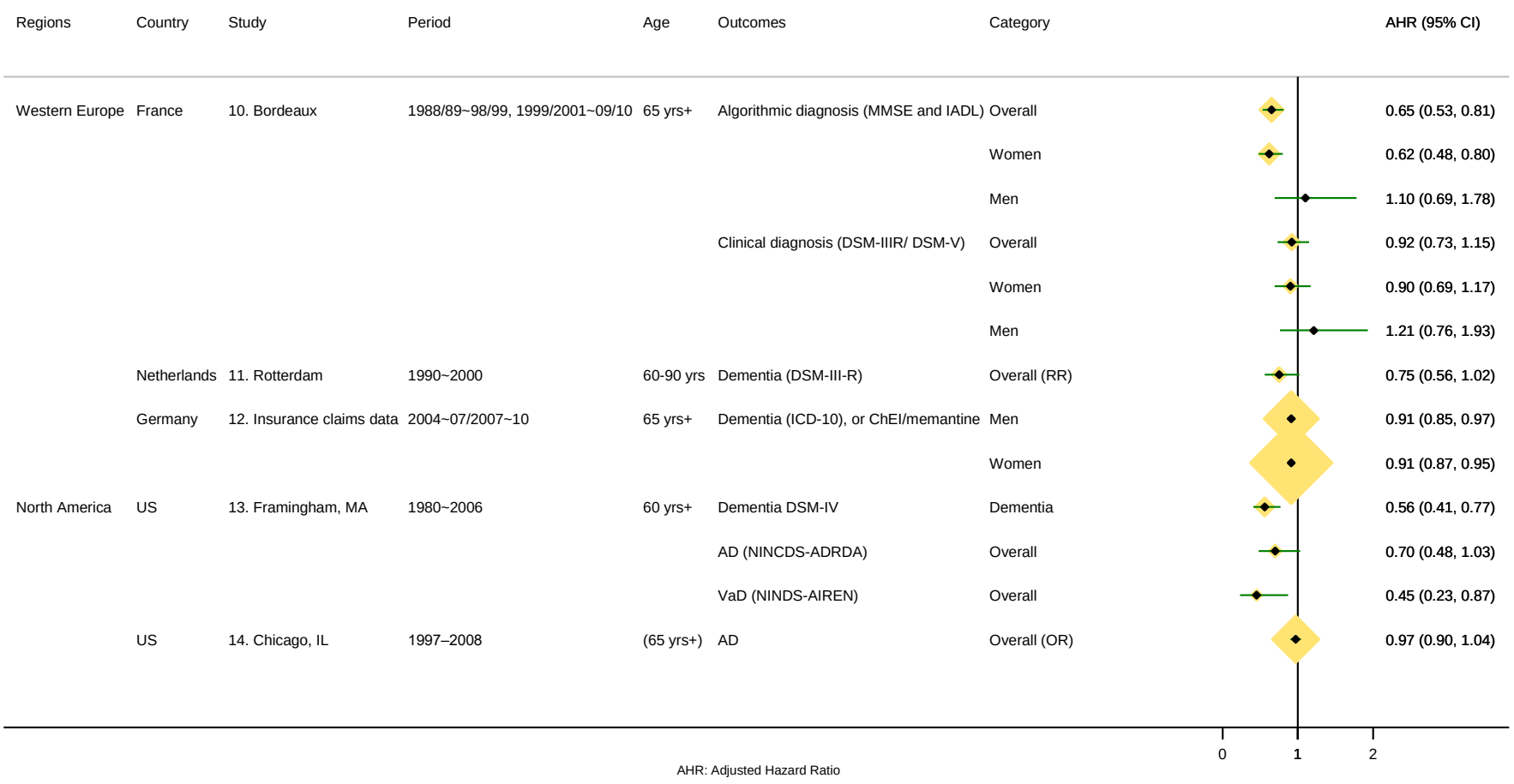
Appendix Figure 1-1. Estimated changes in prevalence of dementia or Alzheimer's disease over time [109]



Appendix Table 2. Relative change (%) per year - estimated changes in incidence of dementia or Alzheimer's disease over time [109]

Regions	Country	Study	Period	Age range	Outcomes	AHR (95% CIs)	Relative change (%) per year
Western Europe	France	10. Bordeaux, France [50]	1988/1989–1998/ 1999 and 1999/ 2001– 2009/2010	65+ years	Algorithmic diagnosis (using MMSE and IADL)	0.65 (0.53-0.81)	−3.5 % (Overall)
					Clinical diagnosis (DSM-IIIR/DSM-V)	0.62 (0.48-0.8)	−3.8 % (Women)
	Netherlands	11. Rotterdam, Netherlands [37]	1990–2000	60-90 years	Dementia (DSM-III-R)	0.75 (0.56-1.02) (RR)	−2.5 %
	Germany	12. Germany, insurance claims data [34]	2004-2007/2007-2010	65+ years	Dementia (ICD-10), or cholinesterase inhibitors/memantine	0.91 (0.85-0.97) (Man)	−3.0 %
						0.91 (0.87-0.95) (Woman)	
	Sweden	3. Stockholm, Sweden [49]	1988–2002	75+ years	Dementia (DSM-III-R)		Not reported
North America	US	8. Indianapolis, IN, US, African Americans [115]	1991–2002	65+ years	Dementia (DSM-III-R) AD		−5.5 % (Dementia) −4.4 % (AD)
	US	13. Framingham, MA, US [45]	1980–2006	60+ years	Dementia DSM-IV AD (NINCDS-ADRDA) VaD (NINDS-AIREN)	0.56 (0.41-0.77)	−1.7 % (Dementia)
						0.70 (0.48-1.03)	−1.2 % (AD)
						0.45 (0.23-0.87)	−2.1 % (VaD)
	US	14. Chicago, IL, US [53]	1997–2008	65+ years	AD		No trend
	Canada	15. Ontario, Canada; health insurance plan, hospital discharge and ambulatory care register [35]	2002–2013	Not reported	Dementia diagnosis (ICD-9 or ICD-10) or cholinesterase inhibitor prescription		−0.6 %
Africa	Nigeria	16. Ibadan, Nigeria [48]	1991–2002	Not reported (possibly 65+ years)	Dementia (DSM-III-R) AD		No trend

Appendix Figure 2-1. Estimated changes in incidence of dementia or Alzheimer's disease over time [109]



Appendix Table 3. The QOF indicator codes, points and payment stage changed over time [18, 89-95]

	Indicator	Points	Payment stages	Achievement thresholds	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Records	DEM 1: The practice can produce a register of patients diagnosed with dementia	5													
	DEM001. The contractor establishes and maintains a register of patients diagnosed with dementia	5													
On-going management	DEM 2: The percentage of patients diagnosed with dementia whose care has been reviewed in the previous 15 months	15	25-60% 35-70%												
	DEM002. The percentage of patients diagnosed with dementia whose care has been reviewed in a face-to-face review in the preceding 12 months	15		35-70%											
	DEM004. The percentage of patients diagnosed with dementia whose care plan has been reviewed in a face-to-face review in the preceding 12 months	39		35–70%											
	DEM 3. The percentage of patients with a new diagnosis of dementia (from 1 April 2011) with a record of FBC, calcium, glucose, renal and liver function, thyroid function tests, serum vitamin B12 and folate levels recorded 6 months before or after entering on to the register, Based on NICE 2010 menu ID: NM09	6	40-80%												
	DEM 4. The percentage of patients with a new diagnosis of dementia recorded between the preceding 1 April to 31 March with a record of FBC, calcium, glucose, renal and liver function, thyroid function tests, serum vitamin B12 and folate levels recorded 6 months before or after entering on to the register, Based on NICE 2010 menu ID: NM09	6	45-80%												
	DEM003. The percentage of patients with a new diagnosis of dementia recorded in the preceding 1 April to 31 March with a record of FBC, calcium, glucose, renal and liver function, thyroid function tests, serum vitamin B12 and folate levels recorded between 6 months before or after entering on to the register, Based on NICE 2010 menu ID: NM09	6		45-80%											
	DEM005. The percentage of patients with a new diagnosis of dementia recorded in the preceding 1 April to 31 March with a record of FBC, calcium, glucose, renal and liver function, thyroid function tests, serum vitamin B12 and folate levels recorded between 12 months before or 6 months after entering on to the register, Based on NICE 2010 menu ID: NM09	6		45–80%											

Appendix Table 4. Frequencies of QOF Read codes, all ages

Code (N=54)	Description	1995-2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
Eu01.00	[X]Vascular dementia	1313	584	641	964	995	1063	1222	1406	1452	1517	1495	1477	1211	15340
F110.00	Alzheimer's disease	3060	740	756	898	739	863	951	1028	1000	1085	1061	1019	749	13949
Eu02z00	[X] Unspecified dementia	1824	592	614	885	736	700	777	883	902	916	956	902	795	11482
Eu00.00	[X]Dementia in Alzheimer's disease	673	237	240	379	340	355	445	515	631	711	802	769	666	6763
E000.00	Uncomplicated senile dementia	1149	151	137	141	109	115	113	96	115	130	105	84	69	2514
E00z.00	Senile or presenile psychoses NOS	887	47	37	33	32	18	16	27	18	17	15	10	6	1163
Eu00200	[X]Dementia in Alzheimer's dis, atypical or mixed type	5	6	8	6	23	23	38	43	71	86	117	150	163	739
Eu02500	[X]Lewy body dementia	1	2	6	42	58	76	70	87	77	84	85	82	62	732
Eu02300	[X]Dementia in Parkinson's disease	179	20	31	30	29	39	49	48	41	57	60	73	53	709
E00..00	Senile and presenile organic psychotic conditions	372	53	49	50	32	13	5	7	5	13	10	12	13	634
E041.00	Dementia in conditions EC	43	13	16	78	44	36	29	40	45	51	53	59	42	549
E004.00	Arteriosclerotic dementia	213	37	33	26	43	25	30	25	34	26	20	15	14	541
F116.00	Lewy body disease	111	43	48	19	33	30	16	19	26	29	28	23	24	449
Eu01z00	[X]Vascular dementia, unspecified	27	7	16	17	16	24	47	37	39	45	50	58	36	419
Eu00z00	[X]Dementia in Alzheimer's disease, unspecified	53	12	12	13	14	16	27	26	26	44	43	46	45	377
Eu02.00	[X]Dementia in other diseases classified elsewhere	16	11	4	28	11	44	39	29	39	33	34	37	38	363
Eu01100	[X]Multi-infarct dementia	123	19	23	32	24	15	16	16	16	16	13	13	15	341
Eu01300	[X]Mixed cortical and subcortical vascular dementia	6		8	6	8	13	15	21	29	48	56	58	61	329
E001.00	Presenile dementia	94	20	13	20	19	15	19	17	17	23	20	16	12	305
Eu00100	[X]Dementia in Alzheimer's disease with late onset	6	4	4	6	10	8	10	12	26	38	55	39	40	258
F110100	Alzheimer's disease with late onset	34	8	14	7	3	8	13	12	15	22	29	46	33	244
F110000	Alzheimer's disease with early onset	36	16	9	15	10	12	18	20	16	24	22	13	16	227
E002000	Senile dementia with paranoia	78	14	9	14	13	4	10	4	5	4	7	3	2	167
E002100	Senile dementia with depression	92	19	8	6	3	2	5	4	6	2	5	6	4	162
F112.00	Senile degeneration of brain	25	1	3	21	12	4	6	2	9	11	16	25	12	147
E00y.00	Other senile and presenile organic psychoses	130	1	1	3	1		3			1	3	1	2	146
Eu00000	[X]Dementia in Alzheimer's disease with early onset	4		3	8	11	4	6	12	10	16	13	25	15	127
E004z00	Arteriosclerotic dementia NOS	29	3	9	7	6	5	6	4	5	12	5	12	6	109
Eu01y00	[X]Other vascular dementia	4	1	2	3	4	3	10	6	14	11	16	7	17	98
Eu01200	[X]Subcortical vascular dementia	8	1	6	2	3	2	4	9	11	13	18	9	10	96
E003.00	Senile dementia with delirium	16	2	2	2	7	8	6	4	7	7	4	11	4	80
E001z00	Presenile dementia NOS	21	5	7	3	7	3	4	7	7	4	3	3	1	75
E001200	Presenile dementia with paranoia	22	8	2		3	3	4	2	1	2		2	1	50
E012.00	Other alcoholic dementia		2	3	6	5	4	2	4	7	3	3	2	8	49
E002.00	Senile dementia with depressive or paranoid features	21	4	3	5	1		3	1	2	2	1		1	44
F111.00	Pick's disease	14	1	4	4		2	4	2	2	3	4	3	1	44
Eu02200	[X]Dementia in Huntington's disease	9	1	3	2	3	1	1	2	6	3	4	4	2	41
E001300	Presenile dementia with depression	15	1		2	1	1		2	1	1		3		27
E004000	Uncomplicated arteriosclerotic dementia	16		1	1	2	1	1		1	1		1	1	26

Eu01000	[X]Vascular dementia of acute onset	1			2	2		2		6	3	3	6		25
Eu02000	[X]Dementia in Pick's disease	1	1	2	4	1	3	3		1	3		3	3	25
Eu04100	[X]Delirium superimposed on dementia	4			2			1	1	2	3	2	4	6	25
Eu02y00	[X]Dementia in other specified diseases class if elsewhere	1				1	3	4	1	2	4	5	3		24
E004300	Arteriosclerotic dementia with depression	14	4	3				1		1					23
E001100	Presenile dementia with delirium	4	1		1	2	2	2	1	3	2	1	1	2	22
E004200	Arteriosclerotic dementia with paranoia	8	1			1		1				1			12
E012000	Chronic alcoholic brain syndrome	1	1	1	1	1			1		1		3	2	12
Eu02100	[X]Dementia in Creutzfeldt-Jakob disease	2	1	1	1	1				3		1	2		12
E001000	Uncomplicated presenile dementia	3				2	1	1	1				1		9
E002z00	Senile dementia with depressive or paranoid features NOS	1			5		1				1		1		9
E02y100	Drug-induced dementia	1			1			1	1			1	1		6
E004100	Arteriosclerotic dementia with delirium	2					2					1			5
A411000	Sporadic Creutzfeldt-Jakob disease												1	2	3
Eu02400	[X]Dementia in human immunodef virus [HIV] disease	2		1											3

Appendix Table 5. Frequencies of *Other diagnoses* codes, all ages

Code (N=48)	Description	1995-2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
6AB..00	Dementia annual review	18	657	7208	4525	3567	3426	3547	3980	4652	4218	35798
E00..12	Senile/presenile dementia	7698	1003	721	646	618	647	616	611	533	461	13554
E00..11	Senile dementia	2391	390	305	221	270	269	273	302	328	276	5025
9Ou1.00	Dementia monitoring first letter	-	26	149	97	208	156	1240	398	549	433	3256
1461	-	1977	285	164	129	140	146	145	162	140	106	3394
Eu02z14	[X] Senile dementia NOS	1680	237	184	138	169	181	173	172	156	111	3201
Eu00z11	[X]Alzheimer's dementia unspec	421	128	116	144	173	173	203	206	212	241	2017
66h..00	Dementia monitoring	2	13	81	65	95	125	168	191	624	537	1901
E004.11	Multi infarct dementia	669	74	66	57	52	49	49	39	34	34	1123
Eu01.11	[X]Arteriosclerotic dementia	185	25	22	15	10	14	11	4	10	3	299
9Ou4.00	Dementia monitoring verbal invite	-	-	1	1		3	21	2	144	116	288
Eu00112	[X]Senile dementia,Alzheimer's type	96	31	31	21	22	13	24	19	17	14	288
8CMZ.00	Dementia care plan	-	-	-	-	-	-	1	1	81	94	177
E012.11	Alcoholic dementia NOS	77	12	8	9	7	13	10	13	19	7	175
8Hla.00	Referral to dementia care advisor	-	-	-	-	-	-	4	35	61	50	150
9Ou..00	Dementia monitoring administration	1	-	2	8	7	2	7	13	74	11	125
Eu10711	[X]Alcoholic dementia NOS	44	9	7	4	7	5	15	6	8	6	111
8CSA.00	Dementia advance care plan agreed	-	-	-	-	-	-	-	-	-	101	101
9Ou5.00	Dementia monitoring telephone invite	-	-	5	11	10	2	7	9	6	20	70
Z59..00	Reminiscence therapy	-	-	-	-	1	8	26	18	5	1	59
Eu02z16	[X] Senile dementia, depressed or paranoid type	38	1	3	1	-	2	-	1	-	-	46
9Ou2.00	Dementia monitoring second letter	-	-	1	-	2	5	3	3	6	12	32
28E1.00	Moderate cognitive impairment	-	-	-	-	-	-	-	-	6	17	23
Eu00113	[X]Primary degen dementia of Alzheimer's type, senile onset	2	1	2	-	-	1	4	3	3	5	21
Eu02z13	[X] Primary degenerative dementia NOS	13	1	1	2	2	1	-	-	-	-	20
Eu00011	[X]Presenile dementia,Alzheimer's type	2	2	1	2	3	1	3	-	2	2	18
3AE3.00	GDS level 4 - moderate cognitive decline	3	-	4	2	2	1	1	1	1	2	17
Eu02z11	[X] Presenile dementia NOS	2	-	1	-	4	2	2	2	1	3	17
F118.00	Frontotemporal degeneration	1	-	-	-	-	-	-	6	6	4	17
8CMZ000	Dementia care plan agreed	-	-	-	-	-	1	-	-	4	9	14
Eu00111	[X]Alzheimer's disease type 1	1	1	1	1	1	-	2	2	3	2	14
28E2.00	Severe cognitive impairment	-	-	-	-	-	-	-	-		11	11
Eu01111	[X]Predominantly cortical dementia	2	2	-	-	2	1	1	1	-	-	9
3AE4.00	GDS level 5 - moderately severe cognitive decline	2	-	4	-	1	-	-	-	1	-	8
8IAe000	Dementia advance care plan declined	-	-	-	-	-	-	-	-	-	7	7
9Ou3.00	Dementia monitoring third letter	-	-	-	-	3	2	-	-	1	1	7
Eu00012	[X]Primary degen dementia, Alzheimer's type, presenile onset	2	1	-	-	1	-	1	-	1	-	6
3AE5.00	GDS level 6 - severe cognitive decline	1	-	1	-	1	-	1	-	-	-	4
Fyu3000	[X]Other Alzheimer's disease	-	-	1	-	1	-	-	-	1	-	3

ZS7C500	Language disorder of dementia	1	1	-	-	-	-	-	-	1	-	3
Eu00013	[X]Alzheimer's disease type 2	1	-	-	-	1	-	-	-	-	-	2
8CMZ100	Dementia care plan reviewed	1	-	-	-	-	-	-	-	-	-	1
E00y.11	Presbyophrenic psychosis	1	-	-	-	-	-	-	-	-	-	1
8BM0200	Dementia medication review	-	-	-	-	-	-	-	-	-	-	0
8CMZ200	Dementia care plan declined	-	-	-	-	-	-	-	-	-	-	0
8CMZ300	Dementia care plan review declined	-	-	-	-	-	-	-	-	-	-	0
8CMe000	Dementia advance care plan	-	-	-	-	-	-	-	-	-	-	0
8IAe200	Dementia advance care plan review declined	-	-	-	-	-	-	-	-	-	-	0

Appendix Table 6. Frequencies of *Dementia symptoms* codes, all ages

Code (N=135)	Description	1995-2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
388m.00	Mini-mental state examination	159	17	23	23	973	1762	2322	2258	2953	3152	2497	2509	1668	20316
3AD3.00	Six item cognitive impairment test	1	12	29	65	94	168	691	679	538	1112	4487	6648	5687	20211
8HTY.00	Referral to memory clinic	2	1	194	316	374	531	823	940	1137	1516	1869	1926	1549	11178
3AB..00	Behaviour assessment	804	87	83	92	96	91	851	2199	1426	990	1134	819	654	9326
ZRaA.11	MMSE - Mini-mental state examination	645	527	504	925	609	289	305	406	544	624	605	508	445	6936
3A...11	Memory assessment	533	172	141	179	127	131	155	160	167	243	2168	610	1184	5970
38Dv.00	GPCOG - general practitioner assessment of cognition								10	89	221	1166	1455	1308	4249
388V.00	Mini mental state score	2	5	169	362	404	362	358	375	506	666	500	303	199	4211
3A...12	Dementia assessment	1178	214	187	265	231	222	265	324	183	141	417	278	101	4006
28E..00	Cognitive decline	539	195	213	257	269	290	249	285	303	321	288	345	268	3822
28G..00	Forgetful	665	268	291	279	234	251	232	229	227	234	223	155	114	3402
Z7CEH15	Poor memory	106	133	152	183	223	266	285	284	348	330	329	275	295	3209
8IEu.00	Dementia screening declined									1		183	1261	1111	2556
F11z.11	Cerebral atrophy	872	156	165	159	150	174	171	135	133	128	121	102	73	2539
38Dv000	GPCOG (GP assessment of cognition) patient examination									2	12	625	1029	850	2518
Z7CEH14	Memory problem	80	82	95	116	128	171	218	223	255	287	294	262	253	2464
3AD..00	Dementia test	73	20	16	20	51	45	54	34	222	802	625	130	31	2123
388m.11	MMSE score			1	3	98	158	202	287	324	332	220	173	130	1928
ZRaA.00	Mini-mental state examination	101	131	134	193	178	187	228	148	150	158	108	79	67	1862
9Nk1.00	Seen in memory clinic	2	1			1	50	130	197	220	294	309	348	294	1846
Z7CEH00	Memory impairment	87	100	108	121	91	98	88	75	97	93	112	99	99	1268
311B.00	Cognitive assessment	2		2	1		10	183	118	119	121	256	186	114	1112
Z7CEJ00	Memory lapses	2	20	29	54	60	78	87	71	101	100	102	128	95	927
Z7CF800	Poor short-term memory	72	93	96	86	99	76	71	73	66	41	33	41	30	877
1JA2.00	Suspected dementia							1	2	4	116	199	211	210	743
Z7CF811	Short-term memory loss	73	122	94	96	66	54	54	50	41	25	26	22	17	740
R00z011	[D]Memory deficit	317	35	34	48	49	47	40	29	32	23	24	11	6	695
E2A1100	Organic memory impairment	240	41	47	29	31	27	31	33	43	41	41	40	23	667
ZR16.11	AMT - Abbreviated mental test	5	23	16	31	39	37	49	49	59	99	98	74	85	664
ZR3b.00	Cognitive failures questionnaire							1		1		90	393	138	623
ZRBg.00	Everyday memory questionnaire											584	1	10	595
3AD1.00	Ten item dementia test	78	66	56	52	53	62	36	17	26	89	26	19	6	586
28H..00	Mentally vague	53	35	56	47	49	41	42	36	39	28	25	29	14	494
ZR16.00	Abbreviated mental test	23	22	29	33	28	44	42	26	34	77	43	16	11	428
8IEn.00	Referral to memory clinic declined											130	169	76	375
38Dv100	GPCOG (GP assessment of cognition) informant interview								1	1	5	102	154	93	356
F11z.00	Cerebral degeneration NOS	244	16	16	15	9	16	5	9	4	7	2	2	3	348
3AF..00	Addenbrooke's cognitive examination revised		1						16	39	48	87	80	73	344
ZRa2.00	Microcog - assessment of cognitive function	3	3	5	2	2	2	56	19	9	28	126	23		278
Z7CE615	Loss of memory	26	18	27	20	29	25	30	16	26	19	12	11	12	271
2JR..00	Lack mental capacity make decision Mental Capacity Act 2005									2	32	46	79	56	215
9OqE.00	Dementia screening questionnaire completed											52	108	53	213
Z7CEA00	Impairment of registration	2				1	2	21	58	42	12	31	31	9	209

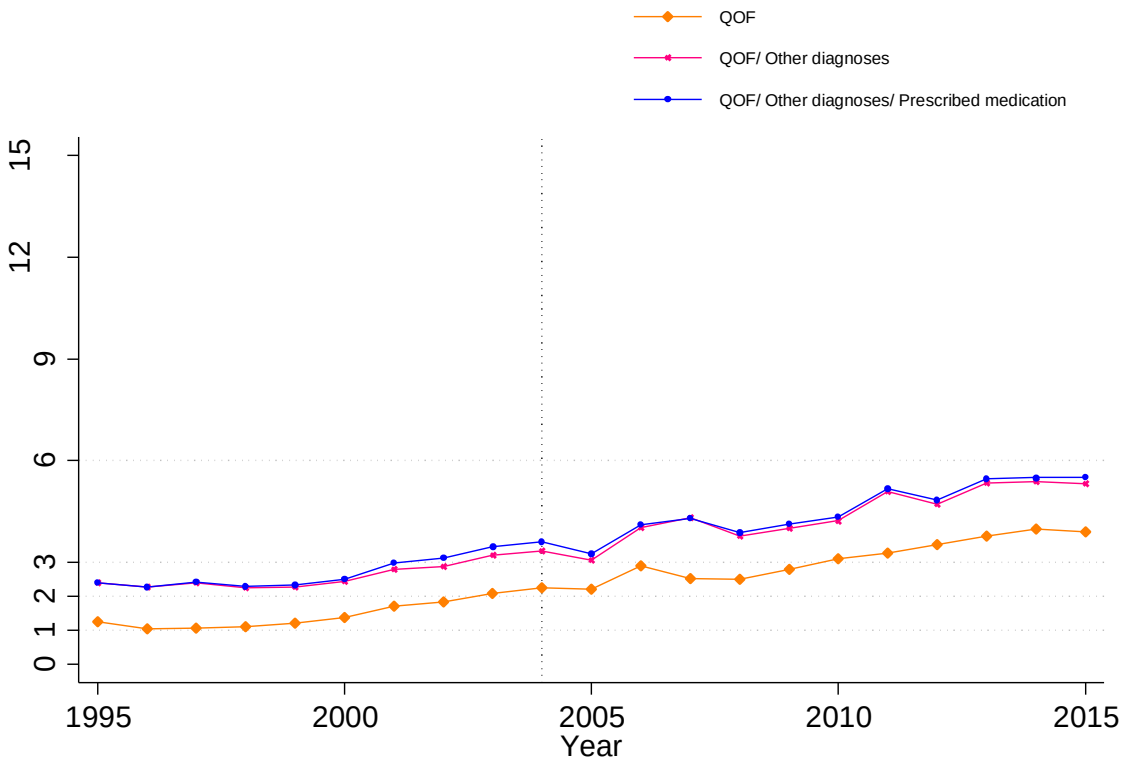
ZR3V.00	Clinical dementia rating scale	1	1			1	1	1	4	13	49	26	29	41	167
1B1Y.00	Poor visual sequential memory			12	10	7	7	12	7	17	21	8	11	4	116
Z7CEA11	Impairment of working memory	4	6	2	6	10	7	7	10	10	12	14	12	5	105
3AA1.00	Memory: address recall unsucc.	86	6	4		2	1	2				1			102
1B1A100	Short-term memory loss									6	39	24	23	8	100
7P10400	Neuropsychology test of memory					10	2	5	10	30	9	13	7		86
ZR2X.11	Memory concentration test	9	12	11	8	4	2	6	1	4	9	9	1	3	79
ZR3a.00	Cognitions questionnaire	2	3	2	5	5	3	4	5	2	8	11	16	10	76
Z7CEH13	Bad memory	2	4	5	5	2	3	7	6	6	4	17	7	6	74
8CET.00	Dementia leaflet given												1	71	72
28E3.00	Cognitive impairment												25	44	69
3AE..00	Global deterioration scale: assessment of prim deg dementia		1	2	4	2	1	3	1		36	6	8	4	68
Z7CEH11	Memory dysfunction	4	1	3		1	4	2	1	2	2	33	2	2	57
ZRaY.00	Neurobehavioural cognitive status examination	7	1	5	5	3	2	2	11	3	7	4	3	4	57
Z7CE616	LOM - Loss of memory	2	3	6	4	5	7	6	6	3	5	5	1	1	54
F11..00	Other cerebral degenerations	29	1	2	4	2	1	2			2	3	3	2	51
3AD2.00	Thirty seven item dementia test	7			1	2	5	6	1	5	7	4	3	7	48
3A91.00	Memory: count down unsuccess.	9	2	2	5	6	5	2	2				6	1	40
ZRaA200	Modified mini-mental state examination		3	4	7	5	3	3		1	1	7	2	4	40
3A40.00	Memory: present year not known	9		1	6	8	2	1			6		2	2	37
8IBB000	Dementia assessment not indicated												17	15	32
ZR3V.13	Dementia rating scale	4	1	1	2	1	4	3	2	2	2	5			27
3A80.00	Memory: import.person not knwn	8		2	2	3	6	2	1			1			25
3A30.00	Memory: present place not knwn	10	2	3	3	4									22
F11x700	Cerebral degeneration due to Jakob - Creutzfeldt disease	5	2			2	5	1	1	1	2	2			21
1B1a.00	Memory loss - amnesia			3	4	2	1	1	1	3		1		1	17
3A60.00	Memory: present month not knwn	8	1	1	2	1	2	1							16
3A70.00	Memory: important event not kn	7	2	1	1	2	2								15
F11x900	Cerebral degeneration in Parkinson's disease							2	3	4	3		3		15
Z7CEH12	Memory deficit	1	1	2		1	1	3			1	3	1	1	15
ZR1I.00	Allen cognitive performance test		2				3	3	1			2	2	2	15
3A20.00	Memory: present time not known	7	1	1	1	3	1								14
ZRa3.11	MEAMS - Middlesex elderly assessment of mental state			1	4	3	1	4		1					14
8IEu000	Dementia screening questionnaire declined												5	8	13
F11x200	Cerebral degeneration due to cerebrovascular disease	7	1	2	1				1						12
F11yz00	Other cerebral degeneration NOS	3		1	1		1		2		1	1	1	1	12
Z7CFO00	Poor long-term memory				1				3	4		1		3	12
ZR1K.00	Alzheimer's disease assessment scale		2	2	2	1	2			1	2				12
ZRVa.00	Lowenstein OT cognitive assessment	2	1	5	1		2								11
Z7CFz00	Memory aided by use of lists		1		2	1	2	3					1		10
3A10.00	Memory: own age not known	6				1									7
F11x600	Cerebral degeneration due to vitamin B12 deficiency	5		1					1						7
Z7CFw00	Unable to remember today's date				1				1	1	1			3	7
F11y.00	Other cerebral degeneration	2				1	1			2					6
Z7CFH00	Forgets recent activities	2	1		1	1			1						6
ZRV9.11	Kendrick cognitive tests for the elderly		1	1	1		1		1				1		6
9OqD.00	Dementia screening questionnaire sent to patient											1	2	2	5
Z7CFJ00	Forgets what has just said		1			1		2	1						5
Z7CFi00	Forgets what has just done			2		1			1		1				5

ZR1H.00	Allen cognitive level screening tool							1		1		2	1	5
ZR3T.00	Clifton assessment procedures for the elderly					2	1				1		1	5
ZR3V.12	CDR - Clinical dementia rating scale				1	1			1	1	1			5
ZRa3.00	Middlesex elderly assessment of mental state	1		2		1				1				5
ZRaA100	Modified mini-mental state 3MS examination	1	1		3									5
3A1..00	Memory: own age	3											1	4
Z7A1.00	Cognitive skills training	3								1				4
Z7A1300	Memory skills training	3										1		4
Z7CEA12	Impairment of immediate recall						1	1			1		1	4
Z7CFM00	Forgets what has just heard	1		2	1									4
Z7CFO11	Long-term memory loss			1			1	2						4
ZR1n.12	AMI - Autobiographical memory interview					1	1		1				1	4
ZR3V.11	DRS - Clinical dementia rating scale		1		2			1						4
1S21.00	Disturbance of memory for order of events			1	1	1								3
3A9..00	Memory: count down	2					1							3
Z7CFq00	Unable to remember own date of birth					1		2						3
ZR1K.11	ADAS - Alzheimer's disease assessment scale	1	2											3
ZR2X.12	BDRS - Blessed dementia rating scale					1				2				3
ZR2X.13	Information-memory-concentration test			1							1	1		3
3A50.00	Memory: own DOB not known	1										1		2
9OqF.00	No response to dementia screening invitation											1	1	2
Z7CEA13	Impairment of primary memory	1						1						2
Z7CFU00	Unable to remember day of the week				1			1						2
Z7CFx00	Memory aided by use of labels		1						1					2
ZD11300	Auditory memory therapy	1						1						2
3A2..00	Memory: present time	1												1
3A4..00	Memory: present year					1								1
3AA..00	Memory: address recall		1											1
F11x400	Cerebral degeneration due to neoplastic disease	1												1
F11x500	Cerebral degeneration due to myxoedema										1			1
F11xz00	Cerebral degeneration other disease NOS										1			1
Z59..11	RT - Reminiscence therapy				1									1
Z7CE612	Memory gone							1						1
Z7CEI00	Mixes past with present	1												1
Z7CFK00	Forgets what has just read		1											1
Z7CFQ00	Unable to remember own date of birth							1						1
Z7CFS00	Unable to remember own age								1					1
Z7CFS11	Cannot remember own age							1						1
Z7CFe00	Unable to reproduce geometric figure at five minutes		1											1
ZR1N.00	Anomalous sentences repetition test										1			1
ZR1n.00	Anomalous sentences repetition test	1												1
ZR3k.00	Consonant trigrams test				1									1
ZRVa.11	LOTCA - Lowenstein OT cognitive assessment							1						1

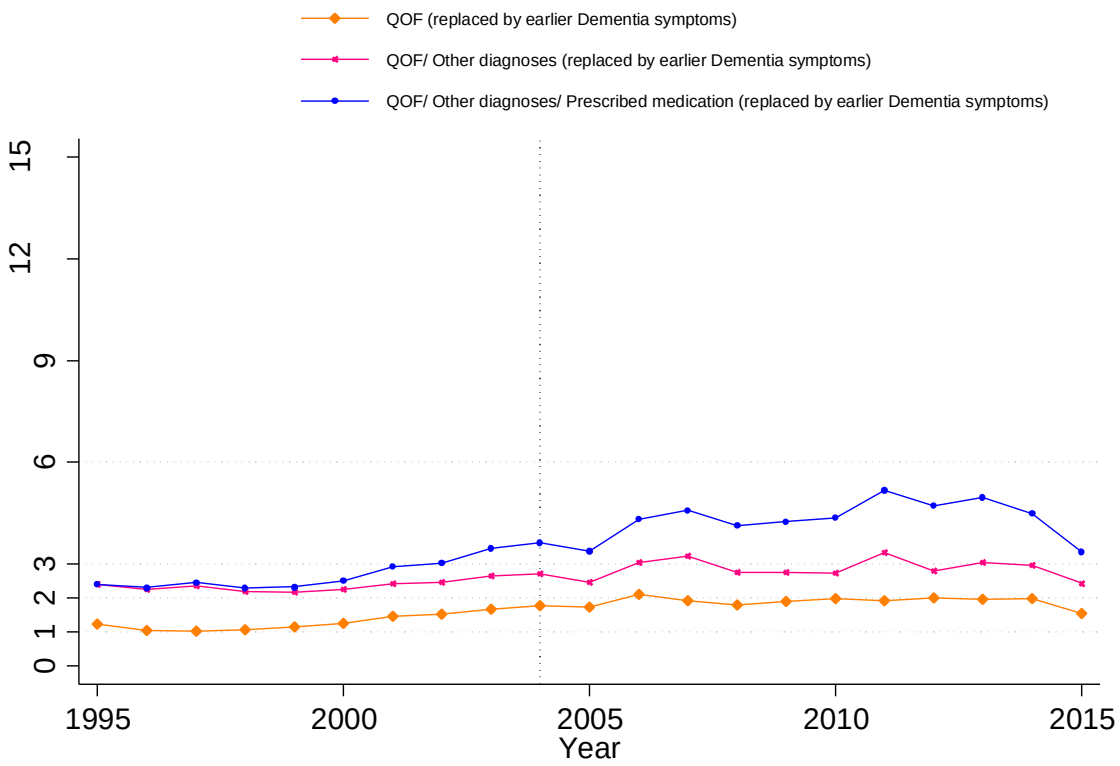
Appendix Table 7. Prevalence rates per 1,000 persons, 60+ years by individual diagnostic codes

Year	QOF	*Other diagnoses*	*Dementia symptoms*	*Prescribed medication*
1995	1.4	1.5	0.2	-
1996	1.2	1.7	0.2	-
1997	1.1	1.8	0.3	0.1
1998	1.1	1.6	0.3	0.1
1999	1.1	1.5	0.4	0.2
2000	1.3	1.5	0.4	0.3
2001	1.6	1.6	0.8	0.6
2002	1.6	1.5	0.8	1.0
2003	1.8	1.5	1.4	1.3
2004	1.9	1.5	1.5	1.7
2005	1.9	1.3	1.7	2.0
2006	2.4	1.9	2.2	2.2
2007	2.0	6.4	2.7	2.5
2008	2.1	6.8	3.3	2.8
2009	2.3	7.0	4.2	3.2
2010	2.4	7.3	4.6	3.4
2011	2.6	8.1	5.5	3.9
2012	2.8	8.4	7.0	4.6
2013	2.9	9.7	11.2	5.5
2014	2.9	9.8	12.4	6.1
2015	2.5	9.1	11.4	6.1

Appendix Figure 3-1. Incidence rates per 1,000 person-years, 60+ years

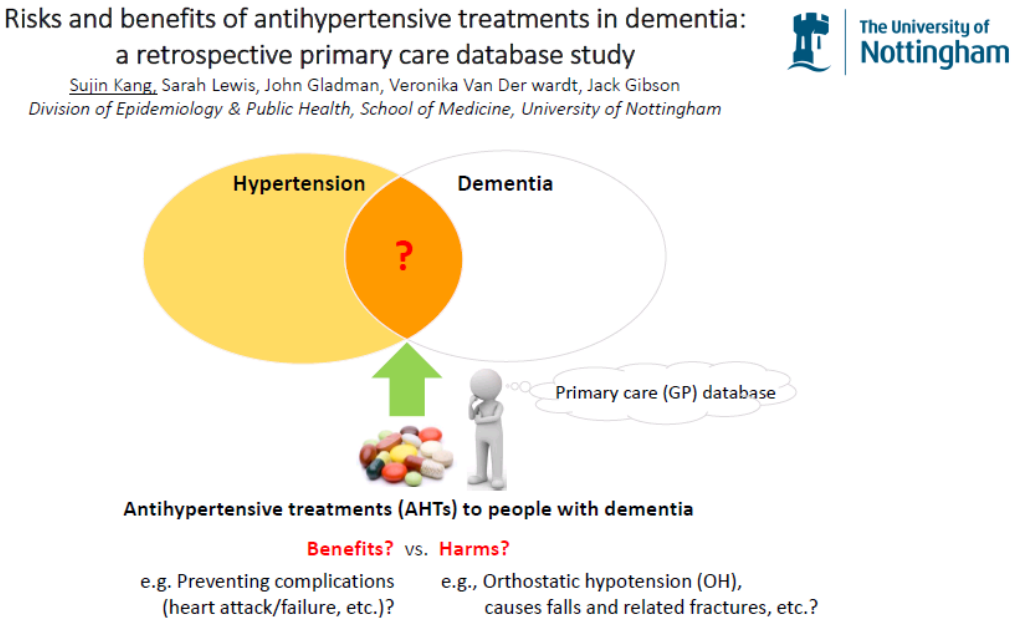


Appendix Figure 3-2. Incidence rates per 1,000 person-years, 60+ years - each date was replaced with the date of the fist *Dementia symptoms* if it is earlier.



The incident rates of (1) QOF, (2) QOF/*Other diagnoses* and (3) QOF/*Other diagnoses/Prescribed medication* decreased compares to Appendix Figure 3-1 (as each diagnosis date was replaced by the first *Dementia symptoms* if it is earlier).

Appendix Figure 4. 2 minute presentation for M&HS Forum, 2017



Appendix Figure 5. e-Poster for M&HS Forum, 2017



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