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# Quantifying the prevalence of frailty in English Hospitals

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 Title: Quantifying the prevalence of frailty in English Hospitals

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#### Abstract

Title: Quantifying the prevalence of frailty in English Hospitals

Objectives: Population ageing has been associated with an increase in co-morbid chronic disease, functional dependence, disability and associated higher health care costs. Frailty Syndromes have been proposed as a way to define this group within older persons. We explore whether frailty syndromes are a reliable methodology to quantify clinically significant frailty within hospital settings, and measure trends and geospatial variation using English secondary care dataset Hospital Episode Statistics (HES).

Setting: National English Secondary Care Administrative Data HES

Participants: All 50,540,141 patient spells for patients over 65 years admitted to acute provider hospitals in England (January 2005 - March 2013) within HES

Primary and secondary outcome measures: We explore the prevalence of Frailty Syndromes as coded by International Statistical Classification of Diseases, Injuries and Causes of Death (ICD-10) over time, and their geographic distribution across England. We examine national trends for admission spells, inpatient mortality and 30-Day readmission.

Results: A rising trend of admission spells was noted from January 2005 – March 2013(daily average admissions for month rising from over 2000 to over 4000). The overall prevalence of coded frailty is increasing (64559 spells in January 2005 to 150085 spells by Jan 2013). The majority of patients had a single frailty syndrome coded (10.2% vs total burden of 13.9%). Cognitive impairment and Falls (including significant fracture) are the most common frailty syndromes coded within HES. Geographic variation in frailty burden was in keeping with known distribution of prevalence of the English elderly population and location of NHS acute provider sites. Overtime, in-hospital mortality has decreased (>65yrs) whereas readmission rates have increased (esp.>85yrs)

Conclusions: This study provides a novel methodology to reliably quantify clinically significant frailty. Applications include evaluation of health service improvement over time, risk stratification and optimisation of services

Keywords: frailty, ageing, HES, Acute, England, Prevalence, Trends



# Article Summary:

- 1. The number of admissions to acute providers in those >65 years is rising, particularly in the very elderly (>85 years). Inpatient mortality is decreasing, but 30-Day non-elective readmission is increasing. The very elderly (>85 years) are more likely to be readmitted.
- 2. We defined frailty as the presence of at least one frailty syndrome: The overall prevalence of frailty for those over 65 years admitted to acute provider units is 13.9% as coded within HES
- 3. Cognitive impairment and Falls (including significant fracture) are the most common frailty syndromes coded within HES.
- There is an increase in coded admissions with anxiety and/or depression, especially from 2010. The 65-74 age-band exhibits a rising trend. Correlation with clinical datasets is warranted

Strengths and limitations of this study

- 1. This study is the first to attempt to use frailty syndromes as an operational definition within an English secondary care dataset.
- 2. The methodology uses whole population routinely collected data, with robust trend analysis examining coding reliability
- 3. This study is a retrospective analysis reliant on the accuracy, reliability and retrospective nature of coding within HES

# Introduction:

People are living longer. At present, it is estimated that 16.1% of the European population is over the age of 65 years(>65y), and this number is expected to rise to 22% by 2031 (1). In the developed world, the increase is greatest in those over 80 years, and this equates to approximately 3 million people in the UK(2). In health terms patients >65y now constitute two thirds of the general hospital population, account for 40% of all hospital bed days and 65% of NHS spend (3). Recent analysis suggests population ageing contributes directly to the increase in emergency admissions to hospitals(4).

Associated with this demographic shift there has been an increase in co-morbid chronic disease, functional dependence, disability, poorer quality of life and higher health care costs (5, 6). Patients in this category are often considered frail. Currently, there is no universally agreed operational definition for frailty (7). Frailty has been described as a clinical phenotype or a biophysical syndrome of accumulated deficit (frailty index). Phenotypic models describe frailty as specific clinical syndrome encompassing a cluster of characteristics, namely unintentional weight loss, exhaustion, weakness, slowness, and low physical activity (8). The frailty index is characterized by decreased resistance to stressors resulting from the accumulation of deficit across multiple physiological systems, culminating in an increased risk of adverse outcomes (9, 10). Methodologies to reliably identify the "frail" at-risk cohort within secondary care, both at patient and population level, are a current research priority (11-13).

In clinical practice the terms Geriatric Giants (14), Geriatric Syndromes (15, 16) or Frailty Syndromes (17) are often used to describe clinically vulnerable group within the elderly. They likely represent high order clinical manifestations of multi-factorial processes resultant from the accumulation and interaction of deficits and environmental factors. They include cognitive impairment, falls, mobility problems, pressure ulcers and incontinence. These syndromes, more prevalent in the elderly, confer a higher risk of death(8), institutionalization (18), disability and poor quality of life(15). They are arguably the consequences of frailty, or the manifestation of clinically significant frailty(19). Current National guidelines for the care of the older person in acute care recommend using frailty syndromes as a possible methodology to assess for frailty(17, 20).

In this study, we measure the trends for all hospital admissions, in-hospital death and re-admissions for those over 65 years. We describe Frailty Syndromes(17, 20) as an operational definition within the English secondary care dataset Hospital Episode Statistics (HES) in order to examine the frailty burden between 2005 and 2012. In addition we describe the geospatial variation of frailty in English secondary health care settings. We compare our results with the existing literature on frailty prevalence and discuss possible applications of this methodology.

# Methods:

# Data sources

HES is a national administrative database containing patient-level records of all admissions to NHS hospitals in England(21). It has high levels of data completeness and rigorous data cleaning processes to ensure data quality. Each record in HES corresponds to a finished consultant episode, during which a patient is under the care of an individual consultant. These episodes were aggregated into hospital spells covering a patient's total length of stay in a hospital (ie a hospital admission) using established methodology(22).

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HES contains 20 fields per record for diagnoses codes that are defined using the tenth revision of the International Statistical Classification of Diseases, Injuries and Causes of Death (ICD-10). The first of these is the primary diagnosis, with the rest available for coding of comorbidities or complications. HES does not contain present-on-admission flags. We reviewed HES for ICD-10 diagnostic codes that could be grouped for frailty syndromes (Appendix 1) in all 20 fields. We included only inpatients at acute non specialist hospital trusts, with elective and non-elective admissions for those 65 years and over>65yo. We excluded hyper-specialist hospitals and mental health units as they have a very different case-mix and data quality(23). Thus, we defined frailty as the presence of at least one frailty syndrome and within the cohort of patients greater than 65 years old.

Annual trend profiles were created for the grouped ICD-10 diagnostic codes from January 2005 to March 2013 to determine coding reliability and shifts (Appendix 2). The spells were aggregated both by age-band (65-74 years; 75-84 years; >85 years) and monthly. Monthly data are visualised as simple line plots in the first instance. Office of National Statistics (ONS) databases were queried for population size estimates or census data where available.

#### Study population

All hospital admissions for >65y to English acute trusts between January 2005 and March 2013 (N=50,540,141 patient spells) were available for analysis.

#### Temporal analysis:

To analyse the variation present in these time-series data, Statistical Process Control (SPC) is used to separate special cause variation (signal) from common cause variation, an inherent property of all systems. The XmR chart is used as it is a method that is not dependent on data distributions or underlying assumptions(24). When analysing count data, daily averages for months were calculated to correct for unequal "areas of opportunity"; for example, a count of February admissions will be lower by virtue of fewer days in February, and daily averages account for the difference in available days. For percentage data, such a correction is attained through division by the denominator – all spells and all spells with frailty. Adjustments for seasonal variation are made, and seasonalised reference lines are plotted, for more natural interpretation of the charts. In this work, a standard rule set for detection of signal is adopted, using Microsoft Excel to construct the charts(24).

## Spatial Analysis:

Geo-location is the identification of real-world geographic location of an object. Postcodes of provider sites were used to geo-locate sites, and map elements were derived from open source data provided by Office for National Statistics. Geo-locations aggregated to Primary Care Trust (PCT) level were attached to counts of frailty syndromes for patients >65y admitted to NHS acute providers in 2012 as this is the applicable unit for these data. Choropleths are thematic maps that shade or colour areas to represent classified values of specific phenomena. ESRI ArcMap 10.2 software was used to create a choropleth map. Annual trend profiles for inpatient mortality and non-elective readmission within 30 days were plotted. This temporal range of April 2006 to December 2012 was selected due to changes in structure of health geographies within England in 2006 (26), and to allow a sufficient follow up period to more accurately reflect the clinical outcomes listed above.

## Results

Between January 2005 and March 2013, there was a rising trend with daily average admissions for month increasing from over 2000 to over 4000(Fig 1a). There has been an increase in all age bands over this period, 65-74 increasing from 161641 to 235756, 75-84 increasing from 162817 to 233870

 and >85 increasing from 71396-137991(Fig 1b ). The relative proportion of total admissions has remained constant each age band at 40%, 40% and 20% respectively. Examination of ONS data, (Appendix 4) finds that in the general UK population the number of >64 years old in the population increased from 8031000 in 2005, to 905179 in 2013. In 2005, the 65-74s represented 52% of those >65yr; in 2013 it was 54%; 75-84s were 36% and 33% 2005-2013; and >85s were 12% and 13%.

Analysis of trends shows that the coded overall frailty burden, based on the coding of at least one frailty syndrome, has increased from 12% to 14% between January 2005 and March 2013. There is evidence of seasonal peaks during winter, partly explained by similar patterns in admission spells (Fig 2)

The coding of the frailty syndromes has increased between 2005 and 2013. Most patients had one frailty syndrome coded (Figure 3) and the most common frailty syndromes described between 2005 and 2013 were cognitive impairment and falls ( including significant fracture) with cognitive impairment increasing to the same levels as falls representing approximately 10% of all spells in the those > 65y. Anxiety and/or depression has increased particularly from 2010(2.4%) to 2013(>4%)(Fig 4). There is a persistent and steady rise in coding for mobility problems.

Evaluating the frailty syndromes individually, the very elderly (>85 years) represent between 40-50% of the spells coded for that syndrome, with rising trend. The exception to this was anxiety and/or depression syndrome, which exhibited a rising trend in the 65-74s, and the 75-84s accounted for the largest group.(Appendix 3) Age-band stratification shows that cognitive impairment and falls in age-bands >85 years and 75-84 years account for a large majority of coded frailty syndromes within this cohort. These four groups accounted for 60.2% of frailty syndromes coded over this time period (N= 7399671)

Geographic variation in the frailty burden across admission spells in England was seen based on the 2012 HES data (Fig 5). For patients >65yr admitted to England Acute providers, the highest levels of frailty are seen in the Northeast, Central and South Coast. The top 5 PCTs for highest admissions numbers are Nottingham City, Halton & St Helens, Warrington, Waltham Forrest and Wolverhampton city.

Between April 2006 to December 2012, 1,160,299 (3.4%) spells were associated with inpatient mortality, though a decreasing trend is observed e.g. April 2006 (N=15042) to April 2012(N=14437) (Fig 6a). Non-elective re-admission rates within 30days of discharge have increased for all admissions > 65y from approximately 11% to 12 %. (Fig 6b). The rates of readmission increased across the age bands > 65yrs (10%), 75-84 (12%) and >85 (14%). Though the overall number of very elderly (>85 years) with non-elective 30-Day readmission is lower than the other two age-bands, they have more readmissions (Fig 7).

## Discussion:

Frailty is often defined as a clinical state in which there is an increase in an individual's vulnerability for adverse events and harm when exposed to a stressor(25). It is distinct but related to disability and co-morbidity(26, 27). Some approaches to the measurement of frailty have been characteristically biophysical with emphasis on detection of the consequences of sarcopaenia and chronic inflammation-malnutrition(8). Another approach is to measure frailty in relation to the clinical consequences of accumulated loss and insufficiency in ageing individuals(ie the relationship to mortality and adverse outcomes)(28). Both approaches appear complementary(29) and overlap, though not completely(30). Frailty measurement is problematic in the acute care setting. High levels

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of disease acuity on top of chronic multi-morbidity, multidimensional complexity and diagnostic uncertainty are challenging for healthcare systems, with increasing evidence and concern for compromised patient safety, quality of care and experience (31-34).

We have examined the prevalence of frailty syndromes within English HES data from both a temporal and geospatial point of view. Temporal analysis, it allows us to observe shifts in diagnostic coding, and observe trend in signal changes over time. Spatial analysis allows us to explore geographic heterogeneity of frailty syndrome prevalence, with consequent implications for service provision and equity of care.

Comparison with ONS data, the corresponding admissions to English acute providers for patients with frailty syndromes is larger than might be expected by demographic shift associated with ageing. Additionally, 75-84s make up approximately one-third of the population of those over 65 years, but have 40% of the admissions, and >85s are approximately 13% of the population of those over 65 years but have 20% of the admissions

This study has focussed on patients admitted to hospital >65y in England to better understand the impact of frailty syndromes. To the authors knowledge, this is the first study to examine the prevalence of frailty syndromes for patients >65y across England. This study confirms increasing number of > 65y admitted to hospital (elective and non-elective). The relative burden of coded frailty syndromes has increased over this period with cognitive impairment increasing to similar levels to falls. Anxiety and/or depression is also increasing in this group.

When complex systems fail (biological or otherwise), high-order functions can be first disrupted (35). Frailty syndromes represent the clinical manifestation of high-order disruption, providing a useful clinical marker of multi-dimensional deficit accumulation. The overall prevalence rate of frailty syndromes found in this study is 13.9%. Between 2005-2013, though there has been an increase in the numbers of patients admitted >65y, the percentage by age band has remained stable, thus not suggesting major drift towards older age groups within the older population. However, within the >65y group, frailty syndromes are more prevalent with the older age bands.

Prevalence rates of frailty vary depending on population and operational definition used in reported studies. Reported prevalence in community dwelling adults varies tremendously (from 4.0% to 59.1%)(36). A recent systematic review reported pooled frailty prevalence across *21 community dwelling study cohorts* as 10.7% (N=61,500)(36). The recent Survey of Health, Ageing and Retirement in Europe (SHARE) study reported frailty prevalence as 4.1% in *community dwelling adults > 50 years*(N=16,584) in 10 European countries (prevalence of 17% in those over 65 years)(37). In the UK, the Hertfordshire Cohort Study(38) reported an overall prevalence of 6.3% for 638 *community dwelling 64-74 year olds*, while the English Longitudinal study of ageing(39) reported a prevalence of 8% and 13% for 3055 *community dwelling over 65 year olds* (using the Phenotype(8) and Frailty Index(10) definitions respectively).

The prevalence of inpatient frailty in our study was lower than expected from smaller reported clinical studies within secondary care (range 24.7% - 80%): (n=220 >70 years admitted to acute geriatric ward from Emergency department(40), (n=6701)40% [Phenotype] and 32.5%[SOF(41)]; (n=1388 >70 years admitted to cardiology service(42), (n=9008 27%[Phenotype] and 63%[Frailty Scale(43)]); (n=298 >75 years admitted to 5 different specialist wards, 50%-80%[Groningen Frailty Index(44, 45]]); (n=307 > 75 years with diagnosed non-ST elevation myocardial infarction(46), 48.5%[n=2305 >65 years Clinical Frailty Scale(47)); (n=752 medical inpatients > 75 years(48),. In the UK, 2 recent studies (12, 13) reported frailty prevalence for n=667 patients >70 years admitted to Acute Medical Units(AMU) at 69%[ISAR(49)], 17.9%[Phenotype], 66.4%[SOF], 24.9%[Avila-Funes],

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 24.1%[Rothman] and 30.9%[Frailty index]. Importantly, these studies mainly consisted of nonelective admissions, while our study cohort comprised of both elective and non-elective admissions to hospital. However, it may be that this methodology truly underestimates the prevalence of frailty within HES.

Not all frailty syndromes are observed, within HES, to be equally prevalent, nor do they appear to be increasing at the same rate. The observed differences and increase in frailty syndromes in this study (Figure 4) may reflect improvements in coding practice within HES due to the introduction of Healthcare Resource Group (HRG version 4 introduced in April 2007) and Payment by Results (since April 2009). The national dementia strategy was also published in 2009. However, this observed rising trend may also reflect a genuine increase in number of diagnosis. Correlation with clinical datasets for comparison is consequently a necessary research priority.

The frailty syndromes are more prevalent in the very elderly (>85), with a rising trend. The exception to this is anxiety and/or depression, where the most prevalent age-band is 75-84 years, which exhibits a declining trend, while the increase in this anxiety and/or depression from 2010 appears to mainly be in the 65-74 age-band, a pattern noted independently by the HSCIC(50). Correlation with clinical datasets is warranted to ensure accuracy.

This analysis suggests that coexistence of multiple frailty syndromes is uncommonly coded within HES; even though we used coded frailty syndromes within all 20 of HES diagnostic domains, incomplete coding may still be a cause, as not all morbidities will be acknowledged and coded for each admission, only those deemed relevant to care at that time. However, it has been noted that accumulation of deficit beyond a certain level is incompatible with survival (51), and thus multi-morbidity would have a ceiling effect. Further investigation on multiple frailty syndromes could be profitable.

Inpatient mortality trends in this population exhibit seasonality with peaks during winter, which persist after adjustment for number of admissions (spells). These peaks, coupled with rising 30-Day readmissions (particularly in the very elderly) suggest differences in service provision over the year. A question arises here: is this seasonality appropriate for the UK population and the provision of care?

Geographic variation in frailty burden appears to be in keeping with known distribution of prevalence of the English elderly population and location of NHS acute provider sites, particularly within urban areas. Healthcare providers and commissioners should consider their local populations when planning services, where frailty may be a larger consideration than other locations. Further study into environmental factors in relation to frailty is a necessary next step.

#### Limitations:

This study is a retrospective analysis reliant on data coded from hospital data warehouses, and subsequently cleaned into HES. As such, its validity is dependent on accuracy of data coding. Including all 20 diagnostic coding fields may help to mitigate this, but correlation with clinical datasets may be warranted for local investigations. Resultant prevalence rates described may underestimate frailty syndromes in this population.

Anxiety and/or depression was only recently recognised as a geriatric syndrome by the Education Committee Writing Group of the American Geriatrics Society(16). It appears to fulfil several criteria that makes it an attractive putative candidate for a frailty syndrome(51): poor mental health is often associated with chronic physical deficits(52), it appears to increase with age(Fig 4), it is associated

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with adverse outcome(53), it is neither to rare or too common(Fig 4) Recent study has linked it to frailty (52, 54) in older persons, though comprehensive study of its relationship to adverse outcomes with relation to frailty is still lacking. Further study, including correlation with clinical datasets, is warranted.

#### Conclusion:

To our knowledge this study is the first to attempt to use frailty syndromes as an operational definition within an English secondary care dataset. While the study is dependent on the accuracy, reliability and retrospective nature of coding within HES, its strengths include being a whole population analysis, with robust trend analysis examining coding reliability. It utilizes routinely collected data and is comprehensive in its coding of frailty within all of the diagnostic coding positions in the HES dataset. Future studies to correlate with clinical datasets are needed to further investigate the phenomena discovered in this study.

This study provides a methodology to reliably quantify frailty. Applications include the ability to evaluate the effect of interventions over time allowing for health service quality improvement. Geographic analysis allows both providers and payers to highlight areas of need, unmet or otherwise for more intelligent targeting of resources, from a public health or clinical perspective. A reliable and quantifiable metric for frailty enables the development of risk-prediction models and clinical scoring systems that will aid targeted interventions to vulnerable populations that will benefit most.

#### Ethics

As per Governance Arrangements for Research Ethics Committees (GAfREC), Research limited to secondary use of information previously collected in the course of normal care (without an intention to use it for research at the time of collection), provided that the patients or service users are not identifiable to the research team in carrying out the research.

## Disclaimer:

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

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## Contributorship:

JS conceived study, designed analysis, interpreted results and wrote first draft AJP designed analysis, interpreted results, contributed to ongoing writing SS and KD designed analysis TW designed SPC analysis DL designed GIS analysis DB conceived study, designed analysis, interpreted results and contributed to ongoing writing

# Data sharing:

No additional data

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## Figure Legend

Figure 1a: Daily average admission spells for month and percentage total frailty burden for England NHS acute trusts and Figure 1b: The number and percentage of spells for patients > 65 years by ageband admitted to English acute providers

Figure 2: The percentage of admissions to English acute providers coded with at least one frailty syndrome

Figure 3: Trends for the prevalence of count of frailty syndromes and total frailty burden for patients >65 years admitted to NHS acute provider hospitals between April 2006 to December 2012

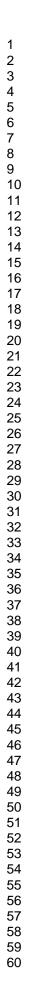
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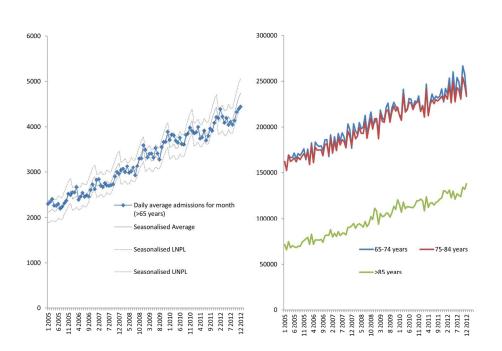
Figure 4: Trends for the prevalence of frailty syndromes for patients > 65 years admitted to NHS acute provider hospitals between January 2005 and March 2013

Figure 5: Percentage of spells for patients >65 years with admission to NHS acute Trusts with at least one frailty syndrome by PCT by quintiles (Numerator=admission spells with at least one frailty syndrome; Denominator=total admission spells to NHS acute Trusts within English PCT)

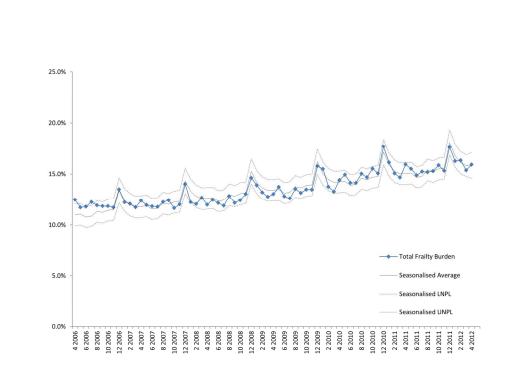
Figure 6a: Percentage of spells with inpatient mortality admitted to English providers and Fig 6b: non-elective 30D readmission in patients > 65 years admitted to English acute providers

Figure 7: Number and Percentage non-elective readmissions in patient > 65 years admitted to NHS acute providers by age-band

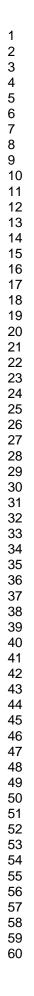


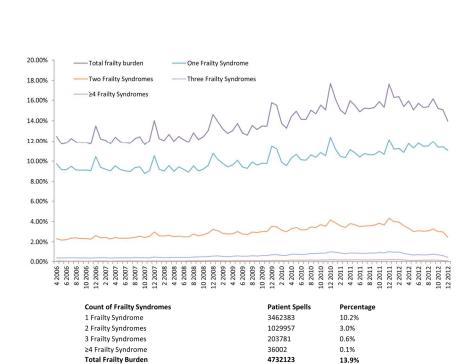


190x142mm (300 x 300 DPI)



190x142mm (300 x 300 DPI)





190x142mm (300 x 300 DPI)

13.9%

-Anxiety / Depression

Cognitive Impairment

- Dependence

Incontinence

Mobility Problems

Pressure Ulcers

Falls

1 2012 4 2012 7 2012 10 2012

2.4%

1.0%

8.7%

1.1%

2.0%

1.1%

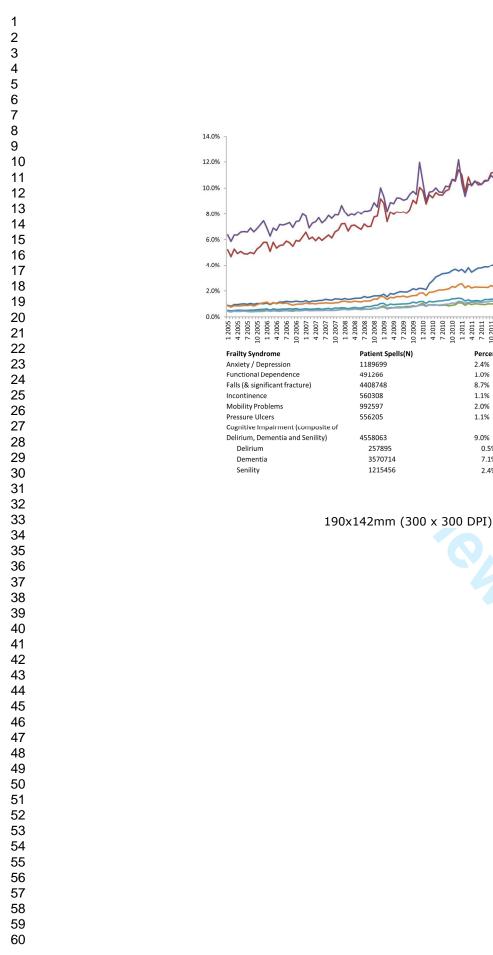
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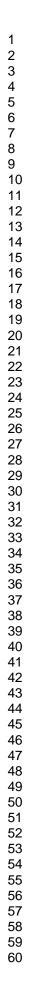
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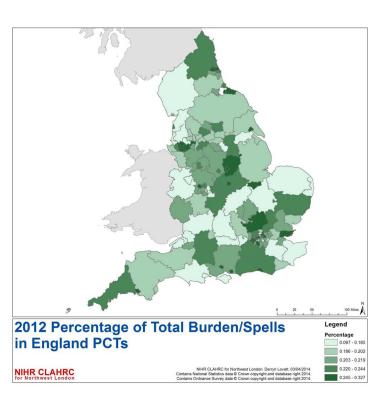
7.1%

2.4%

Percentage







190x142mm (300 x 300 DPI)

Seasonalised LNPL

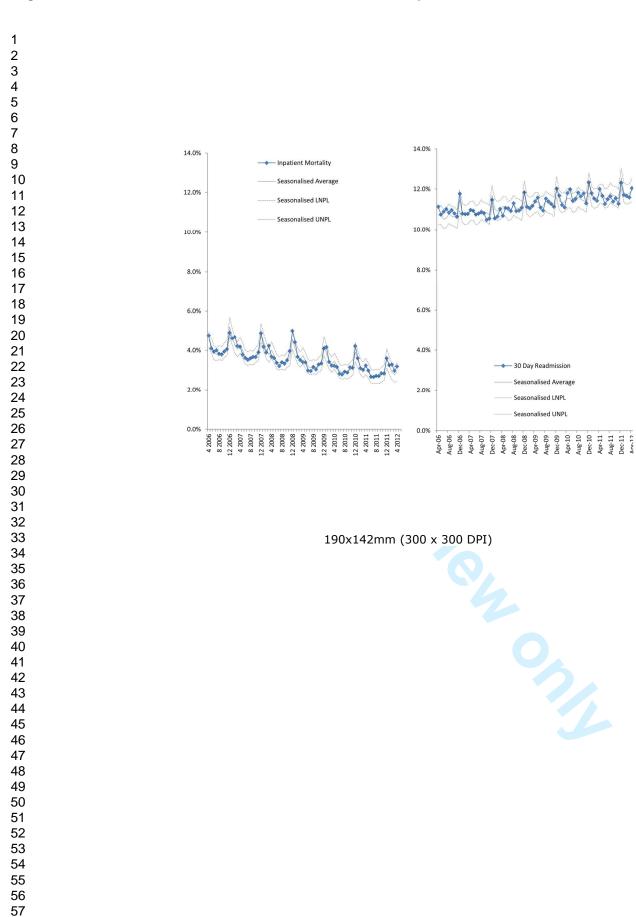
Seasonalised UNPL

Dec-08

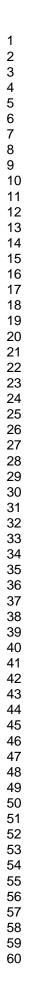
Apr-09 Aug-09 Apr-10 -

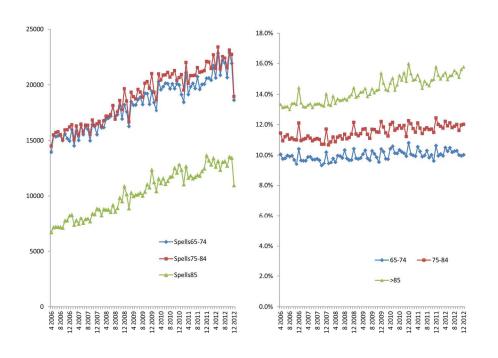
Aug-10 Dec-10 Apr-11 Aug-11 Dec-11

Dec-09



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190x142mm (300 x 300 DPI)

# Appendix 1

Frailty Syndrome	ICD-10	Diagnos	tic Code						
Anxiety and Depression	F320	F320-	F320	F320-D	F3200	F3200-	F3200A	F3200D	F3201
		F3201A	F3201D	F3207	F320X	F321	F321 1	F321-	F321-
		F321-D	F3210	F3210-	F3210A	F3210D	F3211	F3211-	F3211
		F32111	F3211A	F3211D	F3219	F322	F322 D	F322-	F322-
		F32211	F3229	F322X	F323	F323 D	F323-	F323	F323-
		F3230	F3231	F3239	F324	F325	F326	F327	F328
					F328A			F329 D	
				F329-D		F329/			
						F329A			
		F329Q		F32X-		F330		F330-D	
		-			F3301D			F331-	
						F3311			
						F3320			F333-
					F3333			F335	F336
		F337	F338			F3380		F339 A	
				F3396		F380		F3800	
		F3800D				F3810A			F388-
		F38X	F410			F4100			
		F411	F411-	F411-D		F412-		F4122	
		F413			F418-	F419		F419	
			F419X					F4300	
		F4302			F431			F432 2	
						F4320			
						F4320			
						F4325			
						F4323		F4325A	F4323
		F4326 F439-	F43Z6A	F440	F440-	F441	F441-	F436-	F439
		F4422			F444		F445	F445-	F446
		F446-					F4480	F4481	F4481
~				F4488		F449-			
Delirium	F050	F050 A		F051		F051 D			
			F051D	F058	F058-	F058	F059	F059 D	F059-
		F059							
Dementia	F000				F000+			F000-D	
				F0000A		F00010			
				F00032		F00040			
				F000a		F001 0			
						F001-D			
						F0011A			
						F0014			
					F001D			F002 D	
						F002-D			
						F0024			
		F009				F009*			F009-
		F009-D	F009 A	F0090	F00901	F0090A	F0091	F00912	F0091

	50002	F00024	50002	F0002A	F0004	F00044	F000A	F000 A)
							F009A	-
							FOOX	
								F0100A
								F0102D
		F0104						
							F01101	
							F01120	
								F0114A
		F0117					F012 A	
							F01232	
							F013-D	
							F0133	F01330
	F0134	F01340	F01341	F01342	F018	F018 A	F018-	F018-A
	F0180	F0181	F0182	F0183	F0184	F018D	F019	F019 *
	F019 A	F019 D	F019*	F019-	F019	F019-A	F019-D	F0190
	F0191	F01910	F0192	F01921	F0192A	F0193	F0194	F01941
	F01942	F0197	F0199	F019A	F019D	F019N	F019Z8	F01X
	F01X-	F02.	F020	F020 A	F020 D	F020*	F020-	F020-A
	F020-D	F0200	F02001	F0200A	F0201	F02012	F0202	F0203
	F0203A	F0204	F0204A	F020A	F020D	F021	F021 A	F021*
	F021-	F021-A	F0210	F0211	F0214	F021A	F022	F022 A
	F022 D	F022*	F022-	F022-A	F0220	F0220A	F0222	F0223
	F0224	F022A	F023	F023 A	F023 D	F023*	F023+	F023-
	F023-A	F023-D	F0230	F02301	F0230A	F0231	F0231A	F0232
	F02320	F02321	F0232A	F0233	F02331	F0233A	F0234	F02341
	F02342	F0234A	F023A	F023AG	F023D	F023X	F023XA	F024
	F024 A	F024*	F024-A	F0240	F0241	F02412	F0242A	F0243
							F028 D	
							F0280A	
								F0284A
		F028D				F03-		F0300
							F03X*	
							F03X00	
							F03X20	
		F03X3					F03X9	
	F03XG				F03742		R410	R410 D
							R410 R410L	
	R410- R411		R4100 R411X		R4109 R412-	R410D		R410X R413
		R411- R418 D				r\413	ñ413-	N413
	R418			R418		7740	7740	7740
•		Z742			Z743	Z743-		Z748-
	Z749		Z74X	Z750				Z751-
		Z751-D			Z752	Z752-	Z7520	
					Z755	Z755-	Z755-D	27555
	Z758		Z759		Z75X			
			R55X+	R227	R55X	R55X-D	R55X7	R55XA
	R55X D							
	R55XD	R55XX	S320	S320 0	S320-	S320-D	S3200	S3200D
	R55XD	R55XX S3202	S320 S3205		S320- S3209		S3200 S321	

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S330       S330       S331       S331       S331       S331       S331       S333       S333         S332       S333       S334       S4210       S4210       S4210       S4210       S4210       S4210       S4210       S422       S4220       S422       S422       S424       S425       S420       S421       S431       S431       S431       S431 <th>S3259</th> <th>S327</th> <th>S327 0</th> <th>S327-</th> <th>S3270</th> <th>S3270D</th> <th>S3271</th> <th>S328</th>	S3259	S327	S327 0	S327-	S3270	S3270D	S3271	S328
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S4240D S4241       S4241D S4244       S4248       S4249       S427       S427-         S4270       S4270D S4271       S428       S428-       S4280       S4281       S429         S4290       S430       S4300       S4310       S4310       S4310       S4310       S4310       S4310       S4341       S4340       S4341       S4340       S4341       S4340       S4341       S4341       S4340       S4315       S435       S4260       S6220       S6220       S6230       S6230       S6231       S6231       S6231       S6231								
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S429 0       S429 0       S4290       S4290       S4291       S4299       S4300         S430-       S430-       S430-       S4300       S4302       S4309       S4300       S431       S431-         S4310       S4316       S4310       S432       S432-       S4320       S433       S433-         S4330       S434       S434-       S4340       S4434       S444       S6200       S6200       S6200       S6200       S6200       S6220       S622       S622       S622       S622       S6220       S6220       S6220       S622       S6230       S623       S6230       S623       S6230       S6244       S6240       S6240       S6240       S6240       S6240       S6240       S6240       S6240       S6280	S4240D	S4241	S4241D	S4244	S4248	S4249	S427	S427-
S430-       S430-       S430-       S4300       S4310       S431-       S431-         S4310       S4316       S4310       S432       S432-       S4320       S433       S433-         S4330       S434       S434-       S434-       S434-       S434-       S434-       S434-       S437-       S620       S6200-       S6200-       S6200-       S6200-       S6210-       S6210-       S6210-       S6210-       S6210-       S6210-       S6220-       S621	S4270	S4270D	S4271	S428	S428-	S4280	S4281	S429
S4310       S4310       S432       S432       S4320       S433       S433         S4330       S434       S434       S4340       S4341       S4340       S4341       S4340       S435       S435         S436       S436       S436       S4360       S437       S437       S437       S620       S6200       S6200       S6201       S6201       S6208       S621       S6210       S6210       S6210       S6220       S622       S6220       S622       S6220       S6220       S622       S6220       S6220       S622       S6230       S6230       S6230       S6231       S6231       S6231       S6236       S6230       S6236       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S7200       S7210       S	S429 0	S429-	S4290	S4290D	S4291	S4299	S430	S430 0
S4330S434S4340S4341S4340S4341S4340S435S435-S436S436S4360S437S437-S620S6200S6200S6200S6200S6211S6211S6214S6218S622S6220S622-S6220S6200S6211S6211S6211S6213S6231S6236S6230S6231S6231S6236S6230S6231S6231S6234S6241S6241S6241S6241S6241S6241S6241S6241S6241S6280S6280S6280S6280S6280S6280S6280S6280S6280S6280S6280S6280S6280S7200S7200S7200S7200S7200S7200S7200S7200S7200S7200S7200S7210S7230S7230S7230 </th <th>S430-</th> <th>S430</th> <th>S4300</th> <th>S4302</th> <th>S4309</th> <th>S430D</th> <th>S431</th> <th>S431-</th>	S430-	S430	S4300	S4302	S4309	S430D	S431	S431-
S436       S436       S436       S437       S437       S620       S6200       S6201         S6200       S6200       S6201       S6204       S6208       S621       S6210       S621-         S6210       S6211       S6211       S6211       S6218       S622       S6230       S623-       S623-         S6230       S6230       S6231       S6231       S6234       S6236       S6239       S624-         S6240       S6240       S6240       S6240       S6240       S6240       S6280       S6280       S6280         S6260       S6280       S6280       S6281       S6285       S6280       S6280       S6280       S6280       S6280       S7200       S7201       S7201       S7200       S7200       S7200       S7210	S4310	S4316	S431D	S432	S432-	S4320	S433	S433-
S6200       S6200       S6201       S6204       S6208       S621       S6210       S6210         S6210       S6211       S6211       S6218       S622       S6220       S6230       S6230       S6231       S62310       S6234       S6236       S6239       S624         S6230       S6230       S6231       S62310       S6234       S6234       S6236       S6239       S624         S6240       S6240       S6247       S6270       S6271       S6274       S628       S6280       S7200       S7200       S7200       S7200       S7200       S7200       S7200       S7210       S7210 </th <th>S4330</th> <th>S434</th> <th>S434-</th> <th>S4340</th> <th>S4341</th> <th>S434D</th> <th>S435</th> <th>S435-</th>	S4330	S434	S434-	S4340	S4341	S434D	S435	S435-
S6210       S6211       S6211       S6211       S6220       S6220       S6220       S6230       S6230       S6230       S6230       S6230       S6231       S6231       S6231       S6231       S6234       S6234       S6234       S6230       S6230       S6231       S6231       S6234       S6240       S6280       S7200       S7210       S7210 <t< th=""><th>S436</th><th>S436-</th><th>S436D</th><th>S437</th><th>S437-</th><th>s620</th><th>S620 0</th><th>S620-</th></t<>	S436	S436-	S436D	S437	S437-	s620	S620 0	S620-
S6220D S6221       S6221D S6228       S623       S6230       S623-       S623-         S6230       S6230D S6231       S6231D S6234       S6236       S6239       S624         S6240       S624-       S6240       S6240D S6241       S6241D S6244       S625         S626-       S627       S6270       S6271       S6288       S6280       S6280         S6280       S6280-       S6280D S6281       S6288       S6280       S629         S7200       S7200-       S7200-       S7200       S7200-       S7200       S7200-       S7210-       S7210-       S7210-       S7210-       S7210-       S721-       S7210       S7210-	S6200	S6200D	S6201	S6204	S6208	S621	S621 0	S621-
S6230       S6230       S6231       S6231       S6234       S6236       S6239       S624         S6240       S6240       S6240       S6240       S6241       S6241       S6241       S6241       S6241       S6244       S625         S626-       S627       S6270       S6271       S628       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S7200       S7210       S7230       S7230<	S6210	S6211	S6211D	S6218	S622	S622 0	S622-	S6220
S6240       S6240       S6240       S62410       S62410       S62441       S6244       S625         S626-       S627       S6270       S6271       S628       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S6280       S7200       S7210	S6220D	S6221	S6221D	S6228	S623	S623 0	S623-	S623
S626-       S627       S6270       S6271       S6274       S628       S6280       S6280         S6280       S6280-       S6280       S6280       S6281       S6288       S6289       S6280       S6280         S7200       S7210       S7230       S7230       S72	S6230	S6230D	S6231	S6231D	S6234	S6236	S6239	S624
S6280       S6280-       S6280-       S6281       S6288       S6289       S6280       S6280         S7200       S7200       S7200-       S7210-       S7240-       S7240-       S7240-       S7240-       S7240-       S7240-       S7240-       S7240-       S7240-       S	S624 0	S624-	S6240	S6240D	S6241	S6241D	S6244	S625
S720       S720 0       S720 0       S720 0       S7200 0       S7201 0       S7201 0       S7201 0       S7201 0       S7201 0       S7210 0	S626-	S627	S627 0	S6271	S6274	S628	S628 0	S628-
S72009       S7200A       S7200D       S7201       S7201D       S7203       S7204       S7205         S7208       S7209       S720A       S720D       S721       S7210       S7211       S7230       S7240       <	S6280	S6280-	S6280D	S6281	S6288	S6289	S628O	S629
S7208S7209S720AS720DS721S7210S721-S7210S72100S7210DS7210S7210S7210S7210S7210S7210S7210S7220S7220S7220S7220S7220S7221S7210S7210S7210S7210S723S7230S7231S7230S7231S7230S7230S7230S7230S7230S7230S7240	S720	S720 0	S720-	S720-D	S720.0	S7200	S7200-	S72000
S72100 S7210D S7211       S7215       S7219       S721D S7210 S7221       S7210 S7210 S7221         S7220 S722 S7220 S7221       S7230D S7231 S7230       S7230D S7231 S7230       S7230D S7231 S7230         S7230 S7230 S7230 S7231 S7230 S7240 S	S72009	S7200A	S7200D	S7201	S7201D	S7203	S7204	S7205
S722 0       S723 0       S724 0	S7208	S7209	S720A	S720D	S721	S721 0	S721-	S7210
S723       S723 0       S723 1       S723 0       S7230 0       S7240 0       S7280 0       S7280 0       S7280 0       S7290 0       S729 0       S730 0       S730 0       S731 0       S7	S72100	S7210D	S7211	S7215	S7219	S721D	S7210	S722
S723D       S724       S7240       S724-       S7240       S7280       S7280       S7280       S7290       S7290       S7290       S7290       S7290       S7290       S7290       S7290       S7300       S731       S7310       S7310       S7315       S7310       S7333       W0033       W0022       W0022       W0024       W003       W0033       W0033       W0034       W0042       W0040       W0044       W0044       W0044       W0044       W0044       W0044       W0044       W0045       W005       W0055       W0050       W0050       W00	S722 0	S722-	S7220	S7220D	S7221	S72210	S7221D	S7222
S7246       S727       S727-       S7270       S7271       S728       S7280       S7280         S7280       S72800       S7280       S7281       S7280       S7290       S7290       S7290       S7290       S7290       S7290       S7290       S7290       S7290       S7300       S7300       S7300       S7310       S7310       S7310       S7315       S7310       S7331       S7315       S7310       S7325       S7325       S7325       S7325       S7326       S7326       S7326       S7326       S7310       S7315       S7310       S7315       S7310       S7315       S7310       S7315       S7310       S7315       S7	S723	S723 0	S723 1	S723-	S7230	S7230D	S7231	S7236
S7280       S7280D S7281       S728D       S729       S7290       S729-       S7290         S7290D S7291       S7295       S7299       S729D       S72X       S730       S730-         S730-D       S7300       S730D       S731       S731-       S7310       S7315       S731D         S73X       S73X-       W000       W000-       W009       W00A       W001-         W0010       W0012       W0019       W002       W002-       W002A       W003       W003-         W0033       W003A       W004       W004-       W0040       W0049       W004A       W004D         W005       W005-       W006       W006-       W007-       W008       W008-         W0080       W008A       W009       W009-       W0099       W009A       W010         W010       W010       W010-       W010-A       W0100       W0103       W0103         W0104       W0108       W0109       W010A       W011-       W0111       W0113	S723D	S724	S724 0	S724-	S7240	S7240A	S7240D	S7241
S7290D S7291       S7295       S7299       S729D       S72X       S730       S730-         S730-D       S7300       S730D       S731       S731-       S7310       S7315       S731D         S73X       S73X-       W000       W000-       W0009       W000A       W001-         W0010       W0012       W0019       W002       W002-       W002A       W003       W003-         W0033       W003A       W004       W004-       W0040       W0049       W004A       W004D         W005       W005-       W006       W007-       W007-       W008       W008-         W0080       W008A       W009       W009-       W0099       W009A       W010         W010       W010       W010-       W010-A       W0100-A       W010-A       <	S7246	S727	S727-	S7270	S7271	S728	S728 0	S728-
S730-D       S7300       S7310       S731-       S7310       S7315       S731D         S73X       S73X-       W000       W000-       W0009       W000A       W001-         W0010       W0012       W0019       W002       W002-       W002A       W003-         W0033       W003A       W004-       W004-       W0049       W004A       W004D         W005       W005-       W006-       W007-       W008       W008-         W0080       W008A       W009-       W0090       W0099       W009A       W010         W010       W010       DW010-       W010-A       W0100       W0103       W0103         W0104       W0108       W0109       W010A       W011-       W0111       W0111	S7280	S7280D	S7281	S728D	S729	S729 0	S729-	S7290
S73X       S73X-       W000       W000-       W0009       W000A       W001-         W0010       W0012       W0019       W002       W002-       W002A       W003       W003-         W0033       W003A       W004-       W0040       W0049       W004A       W004D         W005       W005-       W006       W006-       W007-       W008       W008-         W0080       W008A       W009       W009-       W0090       W009A       W010         W010       W010       DW010-       W010-A       W0100       W0103         W0104       W0108       W0109       W010A       W011-       W0111       W0118	S7290D	S7291	S7295	S7299	S729D	S72X	S730	S730-
W0010 W0012 W0019 W002 W002- W002A W003 W003-         W0033 W003A W004 W004- W0040 W0049 W004A W004D         W005 W005- W006 W006- W007 W007- W008 W008-         W0080 W008A W009 W009- W0090 W0099 W009A W010         W010 AW010 DW010- W010-A W0100 W0101 W0103         W0104 W0108 W0109 W010A W011	S730-D	S7300	S730D	S731	S731-	S7310	S7315	S731D
W0033 W003A W004W004- W0040 W0049 W004A W004DW005 W005- W006W006- W007 W007- W008 W008-W0080 W008A W009W009- W0090 W0099 W009A W010W010 AW010 DW010-W010-AW0100 W0104 W0108 W0109 W010A W011W011- W0111 W0118	S73X	S73X-	W000	W000-	W0009	W000A	W001	W001-
W005W005-W006-W007-W008W008-W0080W0090W009-W0090W0094W010W010AW010DW010-W010-AW0100W0101W0104W0108W0109W010AW011-W0111W0114W0108W0109W010AW011-W0111	W0010	W0012	W0019	W002	W002-	W002A	W003	W003-
W0080 W008A W009W009- W0090 W0099 W009A W010W010 AW010 DW010-W010-AW0100 W0101 W0103W0104 W0108 W0109 W010A W011W011- W0111 W0118	W0033	W003A	W004	W004-	W0040	W0049	W004A	W004D
W0080 W008A W009W009- W0090 W0099 W009A W010W010 AW010 DW010-W010-AW0100 W0101 W0103W0104 W0108 W0109 W010A W011W011- W0111 W0118								
W010 AW010 DW010-W0100 W0101 W0103W0104 W0108 W0109 W010A W011W011-W0111 W0118								
W0104 W0108 W0109 W010A W011 W011- W0111 W0118								

W0128	W0129	W012A	W012X	W013	W013-	W0130	W0131
W0139	W013A	W014	W014-	W0140	W0141	W0148	W0149
W014A	W015	W015-	W0150	W0152	W0158	W0159	W015A
W016	W016-	W0160	W016A	W017	W017-	W018	W018-
W0180	W0181	W0182	W0185	W0188	W0189	W018A	W019
W019-	W0190	W0191	W0192	W0195	W0198	W0199	W019A
W020	W020-	W020A	W021	W021-	W022	W022-	W023
W023-	W0230	W0239	W023A	W024	W024-	W024A	W025
W025-	W026	W026-	W027	W028	W028-	W0280	W0281
W0282	W028A	W029	W029-	W0290	W0291	W0293	W0299
W029A	W030	W030-	W0300	W0301	W0309	W030A	W031
W031-	W0319	W031A	W032	W032-	W0320	W0329	W032A
W033	W033-	W0330	W0331	W0333	W0339	W033A	W034
W034-	W0349	W035	W035-	W036	W036-	W037	W037-
W038	W038-	W0380	W0383	W038A	W039	W039-	W0390
W0398	W0399	W039A	W040	W040-	W0409	W040A	W041
W041-	W0410	W0419	W042	W042-	W0429	W043	W043-
W044	W044-	W045	W045-	W046	W0460	W0469	W047
	W048-						
W050-	W0504	W0509	W050A	W051	W051-	W0519	W051A
	W052-						
	W0549						
	W058						
	W0599						
	W0609						W0611
	W061A						
	W063						
	W066-						W069-
						W070-	W0700
W0690	W0691						
				W070A	W071	W071-	W0711
W0701	W0706	W0708	W0709				
W0701 W0718	W0706 W0719	W0708 W071A	W0709 W072	W072-	W0720	W0728	W0729
W0701 W0718 W072A	W0706 W0719 W073	W0708 W071A W073-	W0709 W072 W074	W072- W074-	W0720 W075	W0728 W075-	W0729 W0752
W0701 W0718 W072A W0759	W0706 W0719 W073 W076	W0708 W071A W073- W076-	W0709 W072 W074 W077	W072- W074- W077-	W0720 W075 W078	W0728 W075- W078-	W0729 W0752 W0782
W0701 W0718 W072A W0759 W079	W0706 W0719 W073 W076 W079-	W0708 W071A W073- W076- W0790	W0709 W072 W074 W077 W0798	W072- W074- W077- W0799	W0720 W075 W078 W079A	W0728 W075- W078- W080	W0729 W0752 W0782 W080-
W0701 W0718 W072A W0759 W079 W0808	W0706 W0719 W073 W076 W079- W0809	W0708 W071A W073- W076- W0790 W080A	W0709 W072 W074 W077 W0798 W081	W072- W074- W077- W0799 W081-	W0720 W075 W078 W079A W0810	W0728 W075- W078- W080 W0819	W0729 W0752 W0782 W080- W082
W0701 W0718 W072A W0759 W079 W0808 W082 A	W0706 W0719 W073 W076 W079- W0809 W082-	W0708 W071A W073- W076- W0790 W080A W0829	W0709 W072 W074 W077 W0798 W081 W082A	W072- W074- W077- W0799 W081- W083	W0720 W075 W078 W079A W0810 W083-	W0728 W075- W078- W080 W0819 W0830	W0729 W0752 W0782 W080- W082 W084
W0701 W0718 W072A W0759 W079 W0808 W082 A W084-	W0706 W0719 W073 W076 W079- W0809 W082- W085	W0708 W071A W073- W076- W0790 W080A W0829 W085-	W0709 W072 W074 W077 W0798 W081 W082A W0850	W072- W074- W077- W0799 W081- W083 W085A	W0720 W075 W078 W079A W0810 W083- W086	W0728 W075- W078- W080 W0819 W0830 W086-	W0729 W0752 W0782 W080- W082 W084 W0860
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W0701 W0718 W072A W0759 W079 W0808 W082 W0884- W087 W089A	W0706 W0719 W073 W076 W079- W0809 W082- W082- W085 W087- W090	W0708 W071A W073- W076- W0790 W080A W0829 W085- W088 W090 A	W0709 W072 W074 W077 W0798 W081 W082A W082A W0850 W088- W090-	W072- W074- W077- W081- W083 W085A W085A W085A	W0720 W075 W078 W079A W0810 W083- W086 W089 W0901	W0728 W075- W078- W080 W0819 W0830 W086- W089- W0909	W0729 W0752 W0782 W080- W082 W084 W0860 W0899 W090A
W0701 W0718 W072A W0759 W079 W0808 W082 W0882 W084- W087 W089A W089A	W0706 W0719 W073 W076 W079- W0809 W082- W085 W085 W087- W090 W091-	W0708 W071A W073- W076- W0790 W080A W0829 W085- W085- W088 W090 A W092	W0709 W072 W074 W077 W0798 W081 W082A W0850 W088- W090- W092-	W072- W074- W0799 W081- W083 W085A W085A W0889 W0900 W0920	W0720 W075 W078 W079A W0810 W083- W086 W089 W0901 W0901	W0728 W075- W080 W0819 W0830 W086- W089- W0909 W092A	W0729 W0752 W0782 W080- W082 W084 W0860 W0899 W090A W093
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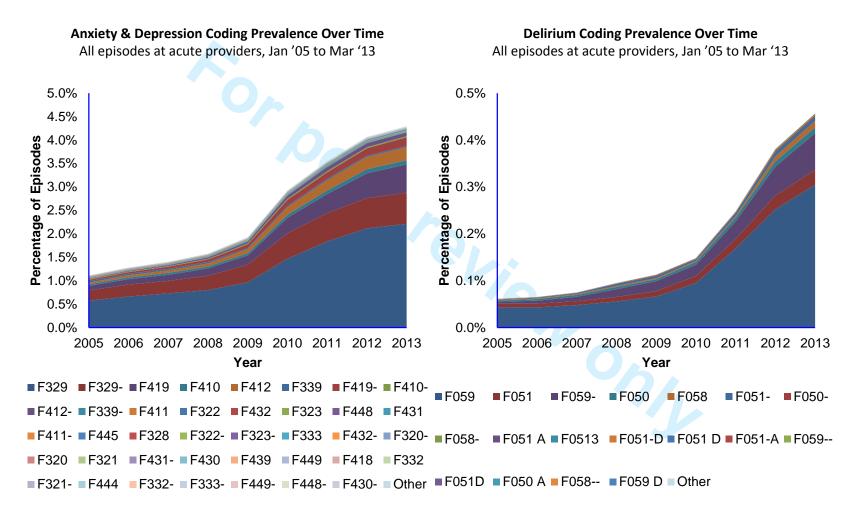
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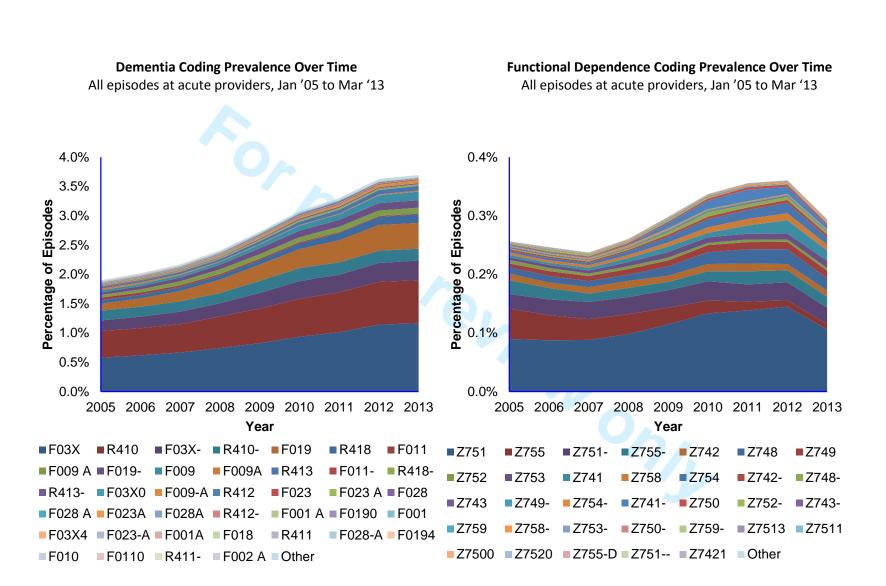
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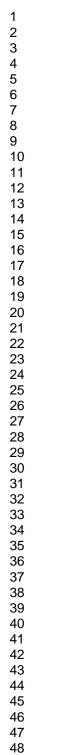
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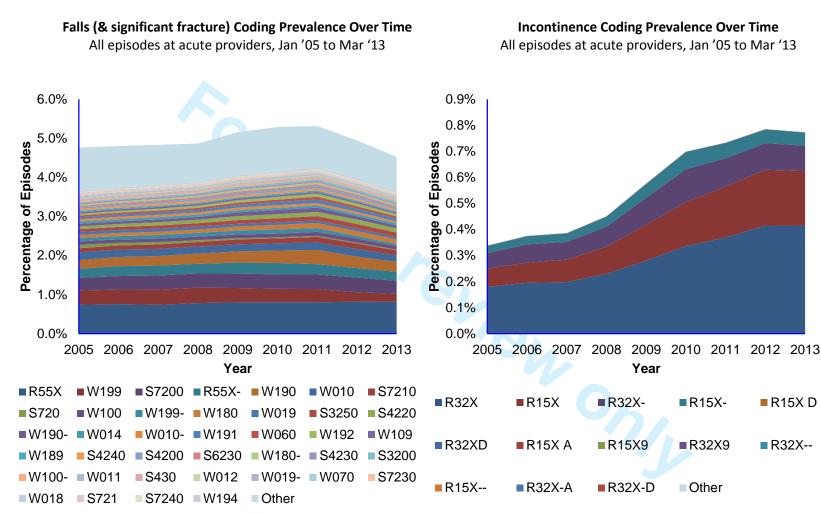
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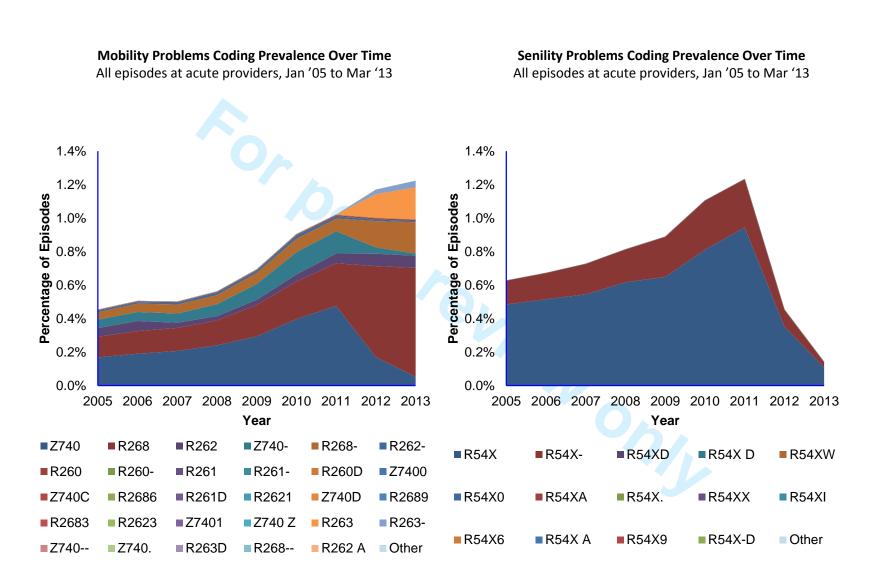
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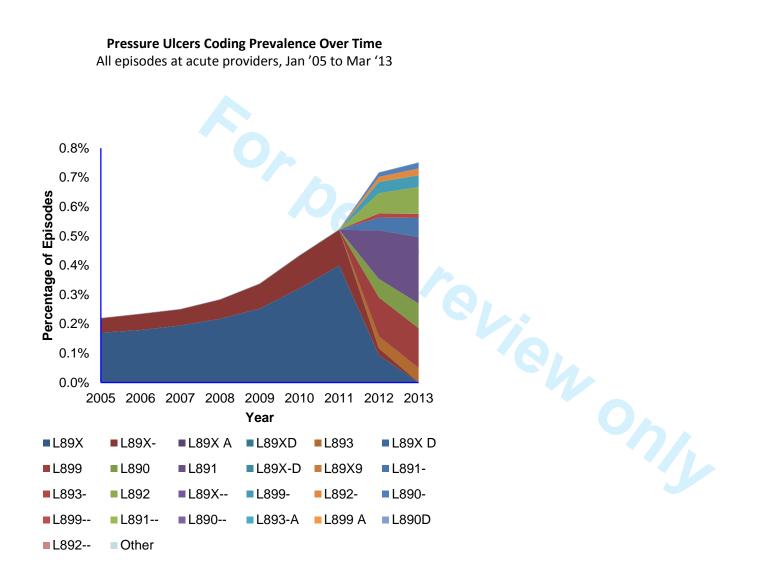




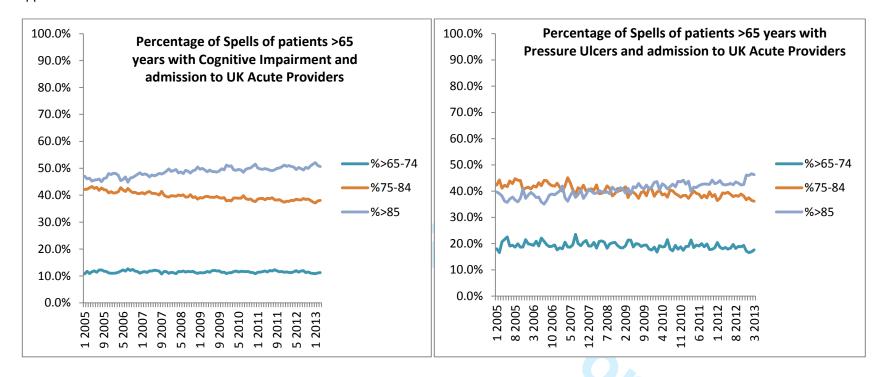


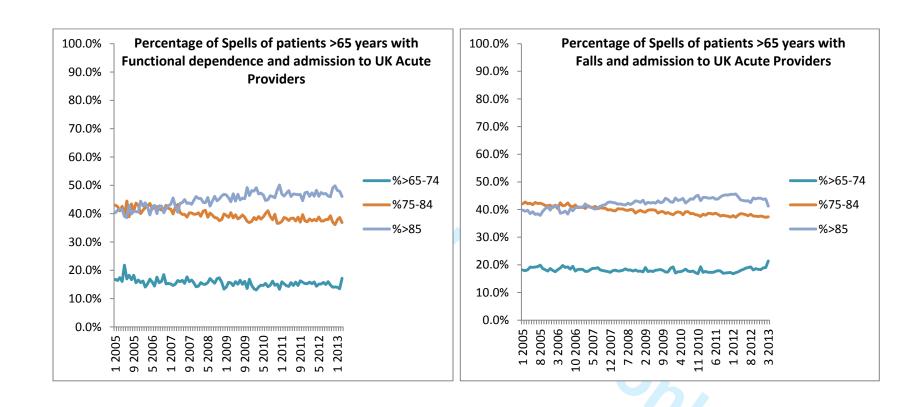


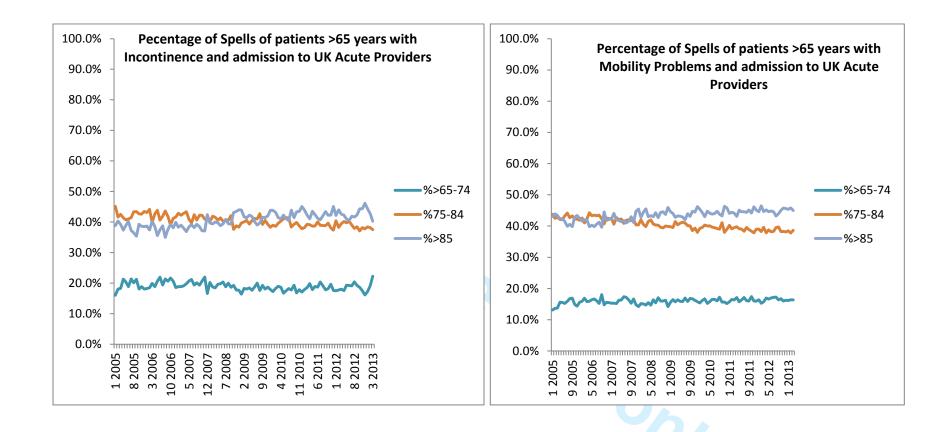
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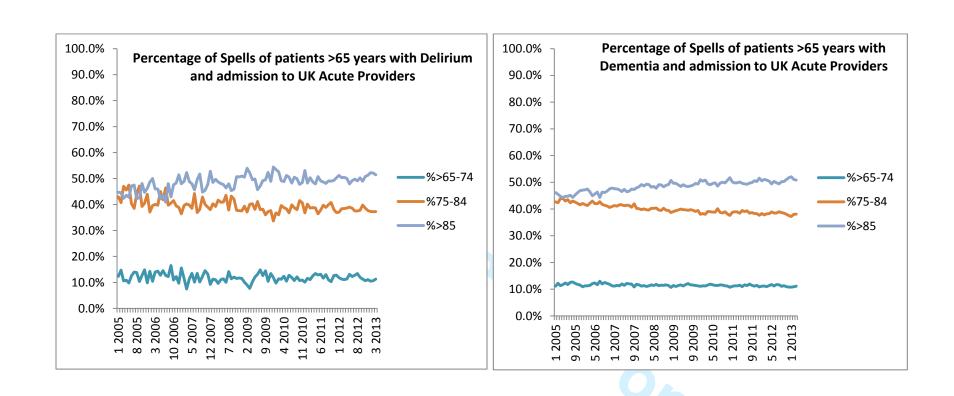


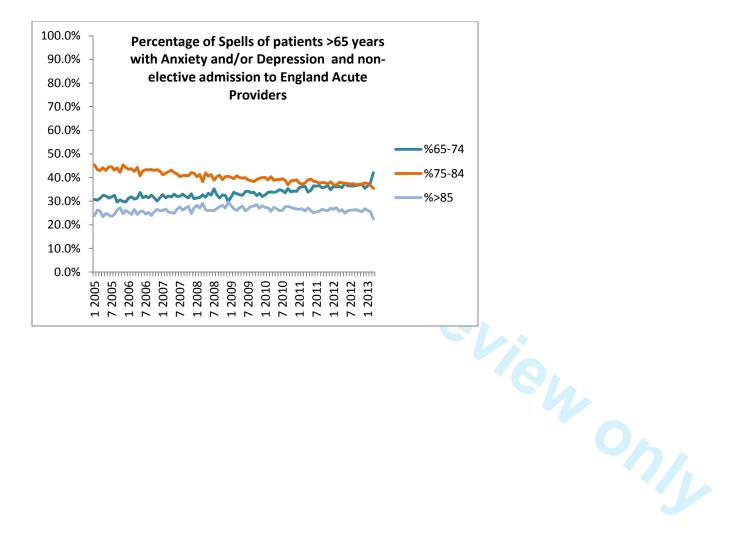
## Appendix 3











# Appendix 4

http://www.ons.gov.uk/ons/taxonomy/index.html?nscl=Population+Estimates

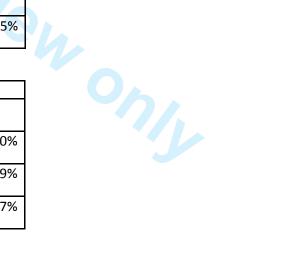
ENGLAND	2005	2013	% change
All ages	50606000	53865817	6.44%
65-74	4189100	5023573	19.92%
75-84	2855100	3043739	6.61%
85+	986800	1237867	25.44%

# % of population

ENGLAND	2005	2013	% change
Denominator, all ages	50606000	53865817	6.44%
65-74	8.28%	9.33%	12.66%
75-84	5.64%	5.65%	0.16%
85+	1.95%	2.30%	17.85%

# % of >65yo population

ENGLAND	2005	2013	% change
Denominator, o65s	8031000	9305179	15.87%
65-74	52%	54%	3.50%
75-84	36%	33%	-7.99%
85+	12%	13%	8.27%



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## STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\* Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 3
Methods			
Study design	4	Present key elements of study design early in the paper	Page 3-4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 3-4
Participants	6	<ul> <li>(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</li> <li>Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</li> <li>Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants</li> </ul>	Page 4
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	Page 4, Appendix 2
Study size	10	0 Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 3-4, Appendix 1
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 4
		(b) Describe any methods used to examine subgroups and interactions	Page 4
		(c) Explain how missing data were addressed	Page 4
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed	Page 4

Page	39	of	39	
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	(	Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
	(	e) Describe any sensitivity analyses	N/A
Results			
Participants		a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 4
	(	b) Give reasons for non-participation at each stage	N/A
	(	c) Consider use of a flow diagram	N/A
Descriptive data		a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 4
	(	b) Indicate number of participants with missing data for each variable of interest	N/A
	(	c) Cohort study—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15* 0	Cohort study—Report numbers of outcome events or summary measures over time	N/A
	0	Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
	0	Cross-sectional study—Report numbers of outcome events or summary measures	Page 4-5
Main results		a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
	(	b) Report category boundaries when continuous variables were categorized	N/A
	(	c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17 F	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 4-5
Discussion			
Key results	18 5	Summarise key results with reference to study objectives	Page 5-7
Limitations		Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 7
Interpretation		Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 5-7
Generalisability	21 [	Discuss the generalisability (external validity) of the study results	Page 5-7
Other information			
Funding		Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 8

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies. **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.