Title: Comparative differences in musculoskeletal pain consultation and analgesic prescription for people with dementia: a UK wide matched cohort study

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Summary

This UK wide matched cohort study found that musculoskeletal pain experienced by people with dementia may be suboptimally managed compared to people without dementia.

ABSTRACT

Painful musculoskeletal conditions are common in older adults, however pain identification, assessment, and management are reported to be suboptimal for people with dementia. Adequate pain management is an integral aspect of care for people with dementia to prevent or delay negative outcomes, such as behavioural and psychological changes, emergency department attendance, and premature nursing home admission. This study aims to examine musculoskeletal consultations and analgesic prescriptions for people with dementia compared to people without dementia. A dementia cohort (*n*=36,582) and matched cohort were identified in the Clinical Practice Research Datalink (a UK wide primary care database). Period prevalence for musculoskeletal consultations and analgesic prescriptions were described and logistic regression applied to estimate associations between dementia and musculoskeletal consultation/analgesic prescription from time of dementia diagnosis to 5 years post diagnosis. People with dementia had a consistently (over time) lower prevalence and odds of musculoskeletal consultation and analgesic prescription compared to people without dementia. The evidence suggests that pain management may be suboptimal for people with dementia. These results highlight the need to increase awareness of pain and to employ better methods of pain assessment, evaluation of treatment response and acceptable and effective management for people with dementia, in primary care.

199/250 words

Introduction

Approximately half of community-dwelling (i.e. not within hospital or formal care) older adults with and without dementia have pain [49], with the most common cause of persistent pain being musculoskeletal based [45]. Musculoskeletal conditions are one of the most common reasons that people access healthcare services and confer a considerable burden to the individual and wider society [12].

Symptoms associated with dementia (e.g. diminished language capacity, memory impairment, and behavioural and psychology changes) may lead to difficulties articulating a pain experience or fulfilling their unmet need for pain relief [18]. Rather than verbally communicating their pain experience, people with dementia may express pain through nonverbal expressions and behavioural changes (e.g. poor sleep, decreased appetite, withdrawal from usual activities) [46]. Consequently, caregivers and clinicians may not recognise or interpret expressions of pain correctly; wrongly attributing expressions of pain (e.g. agitation) as a symptom of dementia, thus leading to the inadequate assessment and treatment of pain [27]. Research evidence predominately within formal care settings (i.e. care homes) has identified that people with dementia have significantly fewer pain assessments than older adults without dementia, and that pain identification becomes increasingly problematic aligned to dementia disease severity and level of cognitive impairment [40,43]. A similar picture exists with prescription of analgesics; with a recent systematic review and meta-analysis of cross-sectional data finding that people with dementia had a significantly lower analgesic prescription prevalence compared to people without dementia [49].

Clearly adequate pain identification and assessment is a prerequisite for optimal pain treatment generally [45], however there may be greater importance in those with dementia. Poorly managed pain has been associated with behavioural and psychological changes [21], increased emergency department attendance [29], and increased cognitive impairment [19], each of which is linked to poor outcomes for people with dementia such as premature care home admission [4] and death [11]. Adequate pain management is therefore an integral aspect of care to prevent or delay such outcomes, thereby supporting people with dementia to continue live independently, in accordance with key health policy agendas [2].

Much of the research evidence to date is focused on formal care populations (e.g. care home residents) [13], with research exploring pain management in community or primary care settings limited to cross-sectional, descriptive, and small sample designs [13]. Recent research has called for quantitative studies to examine pain assessment and analgesic prescribing for people with dementia within community settings such as primary care [30]. This study aimed to describe the longitudinal prevalence of musculoskeletal consultation and analgesic prescription for people with dementia compared to matched older adults without dementia in a UK primary care database.

Methods

1.1 Study setting and population

This study used data from the Clinical Practice Research Datalink (CPRD) GOLD to conduct a retrospective cohort study. CPRD is a UK primary care medical database containing high-quality and anonymised data on over 11 million patients [28], of which 2.8 million were active in 2017. In the UK, 98% of the population are registered with a general practice [28] making primary care electronic health record data an ideal representative sample. When compared to the UK 2011 census, CPRD patients were representative of the UK population in relation to age, gender, and ethnicity [28]. CPRD includes data on patients' clinical conditions, diagnoses, and symptoms that correspond to ICD classification codes, information on tests, referrals, and prescribed medications (corresponding to British National Formulary) as well as information on demographics and health behaviour [28]. Furthermore patient information from secondary care are also included in the CPRD, an example being medication prescribed from secondary care continued in primary care [3].

Data were retrieved from 1st January 1995 to 31st December 2017. For the purpose of this analysis, the general practices included were linked to the Office for National Statistics practice-level Index of Multiple Deprivation. Research indicates that practices with and without linked data are similar in regards to demographic data, years of follow-up, and prescribing of medication [22].

1.2 Study participants

Electronic health record data is principally collected in UK primary care using Read codes entered by members of primary care staff. Read codes are a standard, hierarchical vocabulary of clinical terms used to document various clinical information, including but not limited to symptoms, signs, diagnoses, and prescriptions [9].

A dementia cohort (exposed population) was identified with a dementia diagnostic Read code or a dementia-related drug between 1st January 1997 and 31st December 2017. Dementia index date was defined as the incident (first record) dementia diagnostic Read code or a dementia-related drug (whichever came first). A matched cohort (1:1) by year of birth, sex, and general practice was identified at baseline with no evidence of a dementia diagnostic Read code or a dementia-related drug between 1997 and 2017. Dementia index date was assigned for patients in the matched cohort

within their respective matched-pair for analysis. Read codes were identified from previously defined clinical codes lists [15,16] (available online at https://www.keele.ac.uk/mrr).

To be included in the dementia or matched cohort, all patients were 50 years old or older at index date, with no evidence of a Read code indicative of formal care residence during 1997 to 2017. All patients had at least a two-year period between their entry date and their index date, with no evidence of a Read code indicative of cancer diagnosis during this period. Additionally, patients were excluded 6 months before their first morbidity cancer Read code during follow up. Finally, all patients must have had evidence of a face-to-face, or telephone consultation with a GP or a nurse within a 90-day pre-and-post window of their assigned index date to ensure that they were active consulters.

1.3 Outcome measures

Musculoskeletal consultation

Musculoskeletal consultations were identified using previously validated Read codes documented in the patient's record (available online at www.keele.ac.uk/mrr) [31]. Previous research has documented musculoskeletal consultation as an appropriate marker to encapsulate pain identification and assessment for older adults in CPRD [5].

Analgesic prescription

Evidence of analgesic prescription was identified using a previously validated hierarchical classification [7] that categorised analgesics into six groups based on their potency, in line with the World Health Organisation analgesic ladder. At the bottom of the ladder are basic analgesic prescriptions (e.g. paracetamol). Opioid analgesic prescriptions were separated into four classifications based upon their potency; weak analgesics, moderate analgesics, strong analgesics (each containing increasingly strong opioids used alone or in combination with paracetamol), and very strong analgesics (very strong single opioids such as morphine), and NSAIDS [7]. An additional category included evidence of (any) analgesic prescription, irrespective of classification or potency.

1.4 Covariates

Covariates that could be associated with the outcomes of interest were identified from a systematic review conducted by the authors [13]. Covariates included:

- Evidence of specific comorbidities (cardiovascular-related conditions, diabetes, depression) during the two years before index date [52].
- A surrogate measure for comorbidity calculated using the total number of prescriptions during the two years before index date mapped to different British National Formulary sections [42,44].
- The frequency of consultations by each patient during the two years before index date defined as “any face-to-face or telephone consultation completed by a doctor or a nurse” [48].
- Length of follow up (the number of days from index date to exit date).
- The year of index date, as this may be at any time during the 20-year study period (1st January 1997 to 31st December 2017) to adjust for potential cohort effect over time.

1.5 Follow up

Follow up continued until five years after index date, or until the patient no longer contributed data, known as their ‘exit date’ (e.g. the date of the practice or patient left CPRD, patient death, 6 months prior to the patient’s first morbidity cancer Read code, or if the study end date (31st December 2017) was reached). All analysis was conducted for a maximum five-year period from index date, and each annual period from index date to five years after index date. Stratification into annual periods from index date allowed examination of any patterns in musculoskeletal consultation and analgesic prescription over time from index date in line with the expected progression of dementia and worsening of symptoms [24].

1.6 Statistical analysis

A matched cohort comparison was conducted. The baseline demographics were first described and compared using univariate statistical tests (e.g. t-test or chi-squared tests where appropriate).

To calculate period prevalence, patients contributed to the numerator of the equation if they had evidence of the outcome (musculoskeletal consultation or analgesic prescription) during the specified time period. If there was evidence of musculoskeletal consultation or analgesic prescription within the time period, additional consultations or analgesic prescriptions (of the same strength classification)

were ignored [31]. The denominator included patients eligible throughout the time period. Period prevalence was reported as a percentage.

Conditional logistic regression models examined the association between patient status (dementia cohort vs. matched cohort) and the outcome (evidence of musculoskeletal consultation or analgesic prescription during each time period). Conditional logistic regression models produced unadjusted and adjusted odds ratios (OR) and 95% Confidence Intervals (95% CI), accounting for matched variables (general practice, year of birth, and sex), and adjusting for previous recorded consultations for cardiovascular-related conditions, diabetes and depression, morbidity, length of follow up, year of index date, and consultation frequency. Model assumptions were checked, including the linearity of continuous covariates to the log of the outcome variable assumption. If the assumption was violated, continuous variables were categorised with homogeneity within each strata implicitly assumed.

Results

Baseline demographics

The study cohort included 73,164 participants (36,582 dementia cohort, and 36,582 matched cohort) at baseline. Table 1 shows the baseline characteristics of the two cohorts. The dementia cohort and matched cohort were 59.8% female, with a mean age of 79.9 (standard deviation, 8.3) at the index date. The dementia cohort had significantly shorter median follow up (in days) than the matched cohort (621 vs 1225 days). During the two years before index date, the dementia cohort had a higher count of codes indicating comorbidity, and in specific were more likely to have records of cardiovascular-related conditions, depression and diabetes, compared to the matched cohort.

Musculoskeletal consultations

5-year prevalence of musculoskeletal consultations

During the five-year period following index date, the dementia cohort had a significantly lower prevalence (12.3%) of musculoskeletal consultation than the matched cohort (58.5% vs 70.8%). Multivariable conditional logistic regression found that during the five-year period from index date, the dementia cohort had a lower odds of musculoskeletal consultation than the matched cohort (adjusted OR = 0.83, 95% CI 0.78 to 0.89) (see Table 2).

Annual prevalence of musculoskeletal consultations

The prevalence of musculoskeletal consultation for the dementia cohort gradually decreased in each annual period from index date to five years after index date (24.5% to 19.5% p<.001). In contrast, the prevalence of musculoskeletal consultation for the matched cohort remained relatively stable throughout follow up, with a slight increase in consultation prevalence during the latter annual periods. Multivariable conditional logistic regression models found the difference between the dementia cohort and matched cohort increased with the increase of disease duration of dementia (see Table 2) (first year: adjusted OR = 0.82, 95% CI 0.78 to 0.85; final year: adjusted OR = 0.61, 95% CI 0.54 to 0.68).

Analgesic prescription

5-year prevalence analgesic prescription

The five-year prevalence of evidence of any analgesic prescription was similar for the dementia cohort compared to the matched cohort (76.7% vs. 79.0%, respectively; adjusted OR = 0.97 (0.91 to 1.03) (see Table 3).

When stratified into analgesic classifications, the five-year prevalence of basic analgesics was highest for the dementia cohort and matched cohort (63.5%, 62.1%, respectively), followed by weak analgesics, strong analgesics, NSAIDs, moderate analgesics, and lastly, very strong opioids (2.9%, 3.0%, respectively). The dementia cohort and matched cohort had a similar five-year prevalence of basic analgesic prescription. However, the dementia cohort had a lower five-year prevalence and odds of being prescribed a weak analgesic, moderate analgesic, strong analgesic or NSAID compared to the matched cohort (see Table 3).

Annual prevalence of analgesic prescription

The annual prevalence of analgesic prescription remained relatively stable for the dementia cohort and matched cohort from index date to 5 years (see Table 4). This reflected the multivariable logistic regression models (first year of follow up: adjusted OR 0.96, 95% CI 0.93 to 0.99; final year of follow up: adjusted OR 0.89, 95% CI 0.83 to 0.97).

The annual prevalence of analgesic prescription was also stratified into analgesic classifications. The dementia cohort and matched cohort had a similar prevalence and odds of basic analgesic prescription, irrespective of annual period (see Table 4). Similarly, the annual prevalence of very strong analgesic prescription was similar for the dementia cohort and matched cohort throughout follow up, with the wide confidence intervals indicating no significant difference (year 1 adjusted OR 0.78, 95% CI, 0.63 to 0.97; year 5 adjusted OR 1.03, 95% CI 0.55 to 1.94).

Conversely, the dementia cohort had a lower annual prevalence and odds of weak analgesic, moderate analgesic, strong analgesic, and NSAID prescription compared to the matched cohort. Importantly, the prevalence of these analgesic prescriptions steadily lowered from index date throughout follow up for the dementia cohort.

Discussion

This study of over 70,000 patients in primary care found that people with dementia had a consistently lower prevalence of musculoskeletal consultation than older adults without dementia and this

discrepancy increased over time. This study also found people with dementia were recorded to lower evidence of weak, moderate, strong, and NSAID prescriptions compared to older adults without dementia, again with the discrepancy increasing throughout follow up. The following sections will explore these findings further, with reflection upon previous literature.

Our findings add to the literature by demonstrating that people with dementia had a lower prevalence of recorded musculoskeletal consultation than older adults without dementia and this is consistent with research conducted within care home settings [40]. Furthermore, the longitudinal perspective of this study enabled investigation into the prevalence of musculoskeletal consultations over time, with findings showing a decreased prevalence throughout follow up for people with dementia. This finding complements previous research that found that pain identification and assessment decreased with increased cognitive impairment [43], and decreased ability to provide a self-report of pain [35], using an assumption that the 5 year time period in this study would represent a sufficient period to represent dementia disease progression.

Similarly, for analgesics, patterns were found that differed between people with and without dementia that concur with previous literature. For example this study found that the prevalence of basic analgesic prescription was similar for people with dementia and older adults complementing findings of other studies that found people with dementia were prescribed similar [6,51], or higher rates [26,34,50] of paracetamol use than older adults without dementia [13]. Such findings may reflect the recommendation that paracetamol should be used as the first-line treatment for persistent pain due to the good side effect profile [1]. These recommendations are, however, in discordance with NICE Chronic pain: assessment and management guidelines (currently in development) that recommend paracetamol should not be given for chronic pain management [41]. This study found that prevalence of weak, moderate, and strong analgesic prescription was lower for people with dementia. This reflects the findings of a recent meta-analysis that reports people with cognitive impairment may use less opioids than people without cognitive impairment [25] and also evidence on the limitations of opioids to treat persistent pain in older adults [1,39] and particularly concerns associated with opioid use in people with dementia [17,23,37]. Whilst the patterns of weak to strong analgesic prescription were generally lower for people with dementia, the findings on very strong analgesic were less reliable with wider confidence intervals (adjusted OR 0.83, 95% CI 0.57 to 1.22). This may be reflective of the rarity of very strong analgesic prescription in primary care that may have reduced the

precision of the estimates but also may be because very strong opioid prescriptions (such as for morphine or Oxycodone) would be warranted when the pain source is perhaps more severe and more easily identifiable (e.g. an acute injury). Finally, the five-year prevalence of NSAID prescription was 9% lower for people with dementia than older adults without dementia (19.2% vs. 28.3%, respectively), reflecting previous literature [47,51]. Additionally, this study found a steadily lowering prevalence of NSAID prescription throughout follow up. This finding is supported by a number of studies that also found a decreasing prevalence of NSAID use throughout the course of dementia [6,24] all of which reflect numerous guidelines recommending that NSAIDs should be considered rarely for older adults, and only if safer therapies (e.g. paracetamol) have failed to relieve pain due to potential side effects [1,39].

Strengths and limitations

A key strength of this study is the use CPRD, as this database is broadly representative of the UK primary care population [28] with demonstrated validity in coding practice [33]. Furthermore, this study has utilised established and validated Read code and prescription lists to identify the cohort (dementia), outcome and covariates [8,16,38]. Use of electronic health records such as CPRD confers additional advantages as they record actual events and are not subject to selection or reporting bias associated with survey-based designs which can have added issues when applied to the collection of data from people with dementia [53]. In addition, results were adjusted for overall consultation frequency for each participant which accounts for increased likelihood of coding due to increased presentation (as consultations may be elevated due to dementia).

There are, however, several limitations associated with this study. Advances have been made to improve the detection of dementia within primary care, however there may have been patients within the matched cohort with undiagnosed dementia [32] and this potential misclassification may mean the strength of the associations with pain outcomes are underestimated. Furthermore, whilst electronic health data captures a wealth of information it cannot capture unrecorded health related information, for example self-managed pain and use of over-the-counter analgesics, therefore prevalence estimates of analgesic prescriptions (especially basic analgesics) in this study are likely to underestimated. Similarly, this study did not directly examine the association between dementia severity and pain outcomes, as cognitive evaluations (e.g. General Practitioner Assessment of

Cognition (GPCOG) score) are inconsistently recorded in electronic health record data [20]. This is an important limitation as people with moderate or severe dementia are less likely than people with mild dementia to report their pain or have their pain identified by others [43]. This limitation was mitigated by the 5-year follow up to reflect expected progression of dementia and worsening of symptoms [24].

In terms of the longitudinal analysis, this research aimed to describe the prevalence of musculoskeletal consultation and analgesic prescriptions over time from index date, in line with expected dementia progression. However, research and UK policy have highlighted the untimely coding of a dementia diagnosis in primary care records, with a small number of patients only receiving a recording of dementia during the latter, and more severe stages [10]. The untimely diagnosis of dementia in primary care may implicate the accuracy of longitudinal temporal analysis starting from an index date representing dementia diagnosis.

This study conducted a descriptive comparison of analgesic prescription between a dementia cohort and matched cohort by examining evidence of analgesic prescription in each time period. By identifying 'evidence of' analgesic prescription, rather than examining analgesic count may have underestimated the difference in analgesic prescription between people with and without dementia. Future studies should build upon this evidence by examining the number of pain prescriptions for people with dementia compared to a matched cohort.

Finally, differences in the reported effects between cohorts may in part be influenced by immortal time bias. In essence 'unhealthier' patients in the dementia cohort may have left the study (e.g. due to death, transfer to a care home), leaving a healthier cohort of people with dementia (i.e. less likely to have pain). Inspection of the median time in study showed significant differences between the cohorts (much less time for the dementia cohort), and this would be expected because selection of people with dementia will invariably include a higher level of mortality. However, checks in data show that the dementia cohort and the matched cohort that remained in the study during the last annual time period from index date (year four to five) were similar in regard to a range of baseline characteristics as people included in the first year after index date (see appendix A). Additionally, multivariable analyses adjusted for 'length of follow up' to negate the impact of immortal time bias on the results. To fully understand this issue future studies should include time-to-event regression techniques (e.g. survival analysis with matched censoring) to give estimation of the potential for immortal time bias.

There are potential clinical implications from these findings. Although analgesics may be over prescribed relative to other forms of treatment in older people [36], such prescribing is another marker (just as musculoskeletal consultation is) of the level of consideration and awareness of attending clinicians to the problem of pain [41]. Taking this to be the case, then this study provides further evidence that less consideration may be paid to pain in people with dementia, and so it seems even less attention as dementia progresses. Clearly symptoms of dementia create additional challenges for clinicians in the assessment and treatment of pain [13,14], however there is also evidence of tangible benefits of effective management of pain such as tackling potential unmet needs directly related to pain [53] as well as conferring benefits beyond pain [21].

Conclusion

This study is the first to examine potential differences in pain assessment and treatment prevalence in people with and without dementia at a primary care population level. The results confirm findings of previous studies focused on care home settings that show similar trends of lower rates of pain assessment and treatment. The evidence suggests a need to understand more about practical methods to increase awareness of pain and to employ better methods of pain assessment, evaluation of treatment response and acceptable and effective management for people with dementia, in primary care.

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Conflict of interest

Dr Laurna Bullock, Dr John Bedson, Dr Ying Chen, Professor Carolyn A. Chew-Graham and Dr Paul Campbell have nothing to disclose.

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Table 1. Characteristics of study participants in the dementia cohort (*n*=36,582) and the matched cohort (*n*=36,582) at baseline

	Dementia cohort *n*=36,582	**Matched cohort** *n*=36,582	***p value***
Gender, female % (n)	59.8 (21,860)	59.8 (21,860)	matched
Year of index date Mean (SD)	2008.67 (4.91)	2008.67 (4.91)	matched
Age at index date Mean (SD)	79.9 (8.3)	79.9 (8.3)	matched
Follow up (days) Median (IQR)	621 (250, 1192)	1225 (551, 2246)	<.001
Practice IMD			matched
1 – Least deprived	16.3 (5958)	16.3 (5958)	
2	19.2 (7010)	19.2 (7010)	
3	19.8 (7259)	19.8 (7259)	
4	21.2 (7743)	21.2 (7743)	
5 – Most deprived	23.5 (8612)	23.5 (8612)	
Morbidity count Median (IQR)*	11 (6, 16)	10 (6, 15)	<.001
Consultation freq Median (IQR)*	34 (19, 55)	28 (15, 47)	<.001
CVD yes % (n)*	7.4 (2705)	6.0 (2194)	<.001
Depression/Bipolar yes % (n)*	8.1 (2962)	2.6 (965)	<.001
Diabetes yes % (n)*	16.7 (6115)	14.9 (5459)	<.001

SD Standard Deviation, CVD cardiovascular disease, IMD practice-level Indices of Multiple Deprivation, IQR Interquartile Range

*Recorded during the 2 years before index date

Table 2. Period prevalence and odds of musculoskeletal consultation for the dementia cohort and matched cohort

Years	**Dementia cohort**	**Matched cohort**		
	Prevalence % (95% CI)		**OR** (95% CI)	**Adjusted* OR** (95% CI)
0 to 5 (the overall 5-year period)	58.54 (56.99 to 60.08)	70.76 (69.95 to 71.56)	0.84 (0.79 to 0.90)	0.83 (0.78 to 0.89)
0 to 1	24.46 (23.92 to 25.00)	30.79 (30.27 to 31.31)	0.80 (0.77 to 0.83)	0.82 (0.78 to 0.85)
1 to 2	22.26 (21.62 to 22.90)	30.55 (29.98 to 31.12)	0.73 (0.70 to 0.77)	0.73 (0.70 to 0.77)
2 to 3	19.94 (19.18 to 20.73)	30.56 (29.92 to 31.21)	0.65 (0.61 to 0.69)	0.66 (0.62 to 0.71)
3 to 4	19.27 (18.33 to 20.25)	31.71 (30.99 to 32.44)	0.60 (0.56 to 0.65)	0.62 (0.56 to 0.67)
4 to 5	19.52 (18.29 to 20.80)	31.04 (30.23 to 31.87)	0.63 (0.57 to 0.70)	0.61 (0.54 to 0.68)

CI confidence intervals, OR odds ratio

*Adjusted for previous recorded consultations for cardiovascular-related conditions, diabetes and depression, comorbidity count, length of follow up, year of index date, consultation frequency

Time point 0 = index date

Table 3. Five year period prevalence and odds of analgesic prescriptions for the dementia cohort and matched cohort

	Dementia cohort prevalence % (95% CI)	**Matched cohort prevalence % (95% CI)**	**OR (95% CI)**	**Adjusted* OR (95% CI)**
Any analgesic	76.73 (75.37 to 78.03)	78.99 (78.26 to 79.70)	0.98 (0.93 to 1.05)	0.97 (0.91 to 1.03)
Basic analgesic	63.45 (61.92 to 64.95)	62.13 (61.27 to 62.98)	1.05 (0.99 to 1.13)	1.03 (0.96 to 1.11)
Weak analgesic	31.34 (29.90 to 32.81)	36.49 (35.64 to 37.34)	0.88 (0.81 to 0.97)	0.86 (0.78 to 0.95)
Moderate analgesic	17.98 (16.81 to 19.22)	22.15 (21.42 to 22.89)	0.79 (0.70 to 0.89)	0.74 (0.65 to 0.85)
Strong analgesic	22.86 (21.57 to 24.21)	28.36 (27.57 to 29.17)	0.77 (0.70 to 0.86)	0.70 (0.62 to 0.78)
Very strong analgesic	2.90 (2.42 to 3.48)	3.01 (2.72 to 3.32)	0.84 (0.63 to 1.13)	0.83 (0.57 to 1.22)
NSAID	19.21 (18.01 to 20.48)	28.26 (27.47 to 29.06)	0.68 (0.61 to 0.76)	0.68 (0.61 to 0.76)

CI Confidence Interval, OR Odds Ratio, NSAID Nonsteroidal Anti-Inflammatory Drugs

*Adjusted for previous recorded consultations for cardiovascular-related conditions, diabetes and depression, comorbidity count, length of follow up, year of index date, consultation frequency

Table 4. Annual prevalence and odds of analgesic prescriptions for the dementia cohort and matched cohort

	0 to 1	**1 to 2**	**2 to 3**	**3 to 4**	**4 to 5**
Any analgesic					
Dementia cohort prevalence % (95% CI)	51.73 (51.10 to 52.36)	50.55 (49.78 to 51.32)	49.20 (48.23 to 50.16)	48.64 (47.42 to 49.86)	49.58 (48.01 to 51.15)
Matched cohort prevalence % (95% CI)	54.18 (53.62 to 54.74)	54.41 (53.79 to 55.03)	54.55 (53.85 to 55.24)	55.14 (54.36 to 55.91)	55.73 (54.85 to 56.61)
OR (95% CI)	0.97 (0.94 to 0.99)	0.94 (0.92 to 0.98)	0.94 (0.90 to 0.98)	0.91 (0.86 to 0.96)	0.91 (0.85 to 0.98)
Adj OR* (95% CI)	0.96 (0.93 to 0.99)	0.93 (0.90 to 0.97)	0.92 (0.88 to 0.96)	0.90 (0.85 to 0.96)	0.89 (0.83 to 0.97)
Basic analgesic					
Dementia cohort prevalence % (95% CI)	37.30 (36.69 to 37.91)	36.86 (36.12 to 37.61)	36.64 (35.71 to 37.57)	36.22 (35.06 to 37.40)	36.58 (35.08 to 38.10)
Matched cohort prevalence % (95% CI)	35.78 (35.24 to 36.32)	36.19 (35.60 to 36.79)	36.82 (36.15 to 37.50)	37.57 (36.81 to 38.33)	38.91 (38.05 to 39.78)
OR (95% CI)	1.06 (1.03 to 1.09)	1.05 (1.01 to 1.09)	1.05 (1.00 to 1.11)	1.03 (0.96 to 1.10)	0.97 (0.89 to 1.05)
Adj OR* (95% CI)	1.05 (1.02 to 1.09)	1.03 (0.98 to 1.08)	1.04 (0.98 to 1.11)	1.01 (0.93 to 1.09)	0.95 (0.87 to 1.05)
Weak analgesic					
Dementia cohort prevalence % (95% CI)	13.61 (13.18 to 14.05)	12.68 (12.17 to 13.20)	12.19 (11.57 to 12.83)	11.28 (10.53 to 12.07)	10.97 (10.03 to 11.99)

Matched cohort prevalence % (95% CI)	15.49 (15.09 to 15.90)	15.58 (15.13 to 16.04)	15.46 (14.96 to 15.97)	16.18 (15.61 to 16.76)	16.49 (15.84 to 17.15)
OR (95% CI)	0.91 (0.86 to 0.95)	0.87 (0.81 to 0.92)	0.85 (0.78 to 0.92)	0.72 (0.64 to 0.80)	0.72 (0.63 to 0.84)
Adj OR* (95% CI)	0.90 (0.85 to 0.96)	0.87 (0.80 to 0.93)	0.85 (0.77 to 0.93)	0.77 (0.68 to 0.88)	0.73 (0.62 to 0.85)
Moderate analgesic					
Dementia cohort prevalence % (95% CI)	7.04 (6.73 to 7.37)	6.32 (5.95 to 6.71)	6.22 (5.77 to 6.71)	6.38 (5.81 to 7.00	6.40 (5.67 to 7.21)
Matched cohort prevalence % (95% CI)	8.52 (8.21 to 8.84)	8.48 (8.14 to 8.83)	8.29 (7.91 to 8.68)	8.03 (7.61 to 8.46)	7.83 (7.37 to 8.32)
OR (95% CI)	0.86 (0.80 to 0.92)	0.81 (0.74 to 89)	0.84 (0.74 to 0.94)	0.73 (0.63 to 0.85)	0.84 (0.69 to 1.03)
Adj OR* (95% CI)	0.86 (0.80 to 0.94)	0.78 (0.70 to 0.87)	0.82 (0.71 to 0.94)	0.72 (0.60 to 0.85)	0.77 (0.61 to 0.97)
Strong analgesic					
Dementia cohort prevalence % (95% CI)	11.12 (10.73 to 11.52)	10.42 (9.95 to 10.90)	9.71 (9.16 to 10.30)	9.86 (9.16 to 10.61)	9.84 (8.94 to 10.81)
Matched cohort prevalence % (95% CI)	13.06 (12.68 to 13.44)	13.31 (12.90 to 13.74)	13.28 (12.81 to 13.75)	13.55 (13.02 to 14.09)	13.69 (13.09 to 14.30)
OR (95% CI)	0.84 (0.80 to 0.89)	0.76 (0.71 to 0.81)	0.73 (0.67 to 0.80)	0.72 (0.64 to 0.81)	0.71 (0.61 to 83)
Adj OR* (95% CI)	0.77 (0.72 to 0.82)	0.71 (0.65 to 0.77)	0.64 (0.58 to 0.72)	0.65 (0.57 to 0.74)	0.61 (0.51 to 0.73)

Very strong analgesic					
Dementia cohort prevalence % (95% CI)	1.35 (1.21 to 1.50)	1.40 (1.23 to 1.59)	1.41 (1.20 to 1.65)	1.17 (0.94 to 1.47)	1.54 (1.20 to 1.98)
Matched cohort prevalence % (95% CI)	1.30 (1.18 to 1.43)	1.42 (1.28 to 1.57)	1.39 (1.23 to 1.56)	1.33 (1.17 to 1.53)	1.40 (1.21 to 1.63)
OR (95% CI)	1.00 (0.85 to 1.17)	1.03 (0.84 to 1.26)	1.14 (0.88 to 1.47)	0.83 (0.60 to 1.16)	0.93 (0.61 to 1.43)
Adj OR* (95% CI)	0.78 (0.63 to 0.97)	0.91 (0.70 to 1.18)	0.94 (0.66 to 1.34)	0.75 (0.49 to 1.13)	1.03 (0.55 to 1.94)
NSAID					
Dementia cohort prevalence % (95% CI)	6.97 (6.66 to 7.30)	6.29 (5.92 to 6.67)	5.51 (5.08 to 5.96)	5.08 (4.57 to 5.65)	5.68 (4.99 to 6.45)
Matched cohort prevalence % (95% CI)	11.09 (10.74 to 11.44)	10.62 (10.24 to 11.01)	10.17 (9.76 to 10.60)	9.75 (9.29 to 10.22)	9.53 (9.02 to 10.06)
OR (95% CI)	0.64 (0.60 to 0.68)	0.56 (0.54 to 0.64)	0.54 (0.48 to 0.60)	0.54 (0.46 to 0.62)	0.64 (0.53 to 0.78)
Adj OR* (95% CI)	0.66 (0.62 to 0.71)	0.59 (0.54 to 0.65)	0.54 (0.48 to 0.61)	0.57 (0.48 to 0.67)	0.61 (0.80 to 0.76)

*Adjusted for previous recorded consultations for cardiovascular-related conditions, diabetes and depression, comorbidity count, length of follow up, year of index date, consultation frequency

CI Confidence Interval, OR Odds Ratio, NSAID Nonsteroidal Anti-Inflammatory Drugs

Time point 0 = index date

Appendix A. Descriptive characteristics of the dementia cohort and matched cohort during each annual period

Annual Time period	**0 to 1**	**1 to 2**	**2 to 3**	**3 to 4**	**4 to 5**
			Dementia cohort		
n	**24,247**	**16,110**	**10,314**	**6471**	**3893**
Gender, female % (n)	59.7 (14473)	60.0 (9671)	60.7 (6259)	61.1 (3953)	61.7 (2403)
Age at index Mean (SD)	79.0 (8.2)	82.07 (6.6)	82.5 (6.0)	83.3 (5.6)	84.1 (5.4)
Year of index date Mean (SD)	2008.1 (4.7)	2007.5 (4.5)	2007.3 (4.2)	2006.6 (3.9)	2005.9 (3.6)
Morbidity count Median (IQR)[£]	10 (6, 15)	10 (6, 15)	9 (5, 14)	9 (5, 13)	9 (5, 14)
Consultation freq Median (IQR)[£]	30 (16, 51)	31 (16, 51)	31 (16, 51)	32 (17, 51)	31 (16, 51)
Follow up (days) Median (IQR)	966 (626, 1503)	1289 (968, 1801)	1614 (1322, 2142.3)	2463 (1889, 3319)	2346 (2046, 2833)
Practice IMD % (n)					
1 – Least deprived	16.0 (3869)	15.8 (4083)	15.8 (1632)	15.9 (1030)	16.0 (624)
2	19.4 (4713)	19.2 (4737)	19.3 (1988)	19.5 (1259)	18.7 (729)
3	19.9 (4814)	19.6 (4793)	19.4 (2006)	19.3 (2146)	19.6 (764)
4	20.8 (5052)	20.9 (5184)	20.9 (2155)	21.1 (1366)	21.3 (828)
5 – Most deprived	23.9 (5799)	24.4 (5935)	24.6 (2533)	24.3 (1571)	24.4 (948)
CVD yes % (n)*	7 (1698)	6.9 (1106)	6.8 (705)	6.6 (430)	6.4 (784)
Depression yes % (n)*	8.4 (2035)	8.8 (1423)	9.3 (961)	9.8 (637)	10.6 (411)
Diabetes yes % (n)*	15.9 (3844)	15.0 (2421)	14.2 (1466)	13.4 (869)	12.4 (484)

Appendix A. Descriptive characteristics of the dementia cohort and older adult cohort during each annual period

Annual Time period	**0 to 1**	**1 to 2**	**2 to 3**	**3 to 4**	**4 to 5**
			Matched cohort		
n	**30,316**	**24,732**	**19,849**	**15,663**	**12,276**
Gender, female % (n)	60.1 (18,230)	60.4 (14946)	60.7 (12056)	61.2 (9582)	61.2 (7515)
Age at index Mean (SD)	79.6 (8.1)	81.68 (6.5)	83.0 (6.0)	83.8 (5.7)	84.5 (5.4)
Year of index Mean (SD)	2008.4 (4.6)	2007.9 (4.4)	2006.8 (4.3)	2006.2 (4.0)	2005.5 (3.8)
Morbidity count Median (IQR)*	10 (6, 15)	9 (5, 14)	9 (5, 14)	9 (5, 13)	8 (5, 13)
Consultation freq Median (IQR)*	31 (17, 51)	31 (17, 51)	31 (17, 51)	32 (17, 51)	32 (17, 52)
Follow up (days) Median (IQR)	1507 (872, 2506)	1813 (1202, 2764)	2132 (1533, 3039)	2463 (1889, 3319)	2774 (2236.3, 3572)
Practice IMD % (n)					
1 – Least deprived	16.5 (4989)	16.5 (2551)	16.6 (3298)	16.9 (2641)	16.9 (2080)
2	19.2 (5811)	19.2 (3091)	19.2 (3816)	19.1 (2989)	19.2 (2353)
3	19.6 (5949)	19.4 (3165)	19.0 (3778)	18.8 (2946)	18.8 (2304)
4	20.9 (6328)	21.0 (3370)	21.0 (4176)	21.4 (3346)	21.2 (2597)
5 – Most deprived	23.9 (7239)	24.0 (3933)	24.1 (4781)	23.9 (3741)	24.0 (2942)
CVD yes % (n)*	6 (1825)	6.1 (1506)	5.1 (1214)	6.1 (951)	6.7 (262)
Depression yes % (n)*	2.6 (796)	2.7 (657)	2.7 (545)	2.8 (437)	2.7 (335)
Diabetes yes % (n)*	14.3 (4332)	13.8 (3402)	13.0 (2571)	12.1 (1889)	11.5 (1407)

CVD cardiovascular disease, SD Standard Deviation, IQR interquartile range, BNF British National Formulary, IMD Indices of Multiple Deprivation

*Recorded during the 2 years before index date