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Sociodemographic inequalities in the management of depression in adults aged 55 and over: an analysis of English primary care data

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Abstract

Background: We do not know how primary care treatment of depression varies by age across both psychotropic medication and psychological therapies.

Methods: Cohort study including 19,710 people aged 55+ with GP recorded depression diagnoses and 26,276 people with recorded depression symptoms during the period 2009-2013, from 373 General Practices in The Health Improvement Network (THIN) database in England.

Main outcomes were initiation of treatment with anti-depressants, anxiolytics, hypnotics, anti-psychotic drugs, referrals to psychological therapies within six months of onset.

Results: Treatment rates with antidepressants are high for those recorded with new depression diagnoses (87.1%) or symptoms of depression (58.7%). Treatment in those with depression diagnoses varies little by age. In those with depressive symptoms there was a j-shaped pattern with reduced antidepressant treatment in those in their 60s and 70s followed by increased treatment in the oldest age groups (85+years), compared to those aged 55-59 years. Other psychotropic drug prescribing (hypnotics/anxiolytics, antipsychotics) all increase with increasing age. Recorded referrals for psychological therapies were low, and decreased steadily with increasing age, such that women aged 75-79 years with depression diagnoses had around six times lower odds of referral (OR 0.17, 95%CI 0.1 to 0.29) than those aged 55-59 years, and men aged 80-84 years had around seven times lower (OR 0.14, 95%CI 0.05 to 0.36).

Conclusions: The oldest age groups with new depression diagnoses and symptoms have fewer recorded referrals to psychological therapies, and higher psychotropic drug treatment rates in primary care. This suggests potential inequalities in access to psychological therapies.

Introduction

Depression is common in later life (Luppa *et al.*, 2010), is a major public health problem and one of the leading causes of disease burden worldwide (Whiteford *et al.*, 2013). Prevalence rates in people aged 75 years and over range from 4.6% to 9.3% for major depression defined using the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R or DSM-IV), and from 4.5% to 37.4% with a broader definition of depressive disorders using case definitions on depression symptom scales (Luppa *et al.*, 2010). Depressive symptoms, with or without major depressive disorder, impair functional ability and wellbeing as much as the most common chronic medical conditions such as diabetes, chronic lung disease and heart disease (Whiteford *et al.*, 2013). Late-life depression is associated with increased morbidity and all-cause mortality (Jeong *et al.*, 2013; Diniz *et al.* 2013; White *et al.* 2015) and similarly sub-clinical symptoms of depression have been associated with increased morbidity and mortality (White *et al.* 2015). This increased risk of mortality with depression in later life is largely explained by differences in physical activity, long-term conditions and impairments in physical and cognitive functioning (White *et al.* 2015).

There is evidence that late-life depression can be effectively treated with anti-depressants (Nelson *et al.* 2008; Kok *et al.* 2012; Thorlund *et al.* 2015) and psychological therapies such as Cognitive Behavioural Therapy (CBT) and Problem Solving Therapy (PST) (Gould *et al.*, 2012; Cuijpers *et al.*, 2014). Guidelines also suggest that GPs can consider (alongside other options) augmentation with antipsychotics when depression has not responded to initial anti-depressant treatment (National Institute for Health and Care Excellence (NICE), 2009). Hypnotics/benzodiazepines are not however recommended for treatment augmentation in depression (NICE, 2009). In Randomised Controlled Trials (RCTs) of treatment with anti-depressants in older people, there was significantly higher odds of improvement with anti-depressants compared to placebo (OR 1.78; 95% CI 1.42–2.24) with Numbers Needed to Treat (NNT) of 6.7 (95%CI 4.8-10), and no significant differences between type of anti-depressant (Kok *et al.*; 2012). In RCTs of psychological therapies compared to treatment as usual

in older people there are also significant improvement in symptoms for both CBT (14 trials, effect size -0.57; 95%CI -0.80 to -0.34) (Gould et al., 2012) and PST (3 trials, effect size 0.46; 95%CI 0.18-0.74) (Cuijpers et al., 2014). Combining all psychotherapies compared to treatment as usual in 44 trials, the effect size is 0.64 (95%CI 0.47-0.80), corresponding to a NNT of 3.

However evidence from the United Kingdom (UK) has suggested older people are less likely to attend psychological therapies (Royal College of Psychiatrists, 2013; de Lusignan *et al.*, 2012) and limited older evidence, mainly from North America, suggests they may be less likely to be treated in any modality (Unützer *et al.*, 2000; Crystal *et al.*, 2003; Harman *et al.*, 2004; Kessler *et al.*, 2005). It is not known if there are additional inequalities in treatment in older people living in more deprived or more rural areas, although there is some evidence that poorer older people may receive less treatment, in particular less psychotherapy (Crystal *et al.*, 2003). A greater understanding of the variation in treatment patterns for depression in primary care by age is required to identify whether there is evidence of inequitable access to care in contemporary practice. We have investigated the variation by age, gender, deprivation and neighbourhood in recorded primary care treatment for depression and symptoms of depression in older adults in England.

Methods

Study design: Population-based longitudinal cohort study.

Data source: We used data from The Health Improvement Network (THIN) UK primary care database (<http://www.csdmruk.imshealth.com/>), which contains the medical records of nearly 12 million patients from across the UK. This database is broadly representative of the UK population (Blak *et al.*, 2011) and includes information on consultations, symptoms, diagnoses, investigations, health measurements, demographics, prescriptions, surgical procedures and referrals. Information on medical conditions is entered using Read Codes (Booth, 1994), a hierarchical coding system including

diagnoses (which map into ICD-10 codes) and symptom codes. THIN data are linked to UK Census data using the individuals postal (zip) code, which provides measures of area deprivation, and the type of neighbourhood for example urban or rural. We restricted our sample to 373 practices from England, where we had available information on their linked Index of Multiple Deprivation (IMD) score (Department for Communities and Local Government, 2010) and where standard data quality criteria had been met (Horsfall *et al.*, 2013). THIN has been used extensively in epidemiological research, including depression (Rait *et al.*, 2009; Harris *et al.*, 2012) and the recorded prevalence of depression is broadly in line with large epidemiological studies of attendees to General Practice in Europe (King *et al.*, 2008). In the UK, General Practitioners are responsible for drug prescriptions issued in the community within the National Health Service (NHS), so information on anti-depressant and other psychotropic drug use is well recorded (Centre HaSCI, 2012).

Study population: We included all patients aged 55 years or older who were permanently registered for at least 18 months with a participating practice between 01/01/2009 and 31/12/2013, and had at least one diagnosis of depression or depression symptoms recorded in their GP medical record between 01/01/2009 and 30/06/2013. We extracted two cohorts, one with new depression diagnoses, and one with new depression symptoms. These were not mutually exclusive, as multiple episodes of depression diagnoses or symptoms were possible in the same individual, as long as they met criteria for separate episodes specified below.

The start of the follow-up was the latest of the following: 1st January 2009, 6 months after the patient's date of registration with the practice, the patient's 55th birthday and the date the practice achieved an acceptable level of data quality (Horsfall *et al.*, 2013). The end of the follow-up was the earliest of 31st December 2013, the patient's date of death, the patient's transfer out of the practice or the last date the practice contributed data to THIN. The records for the six months immediately following a

new registration with a GP were excluded to avoid pre-existing prevalent cases appearing to be new episodes of diagnosed depression or depressive symptoms (Lewis *et al.*, 2005).

Depression diagnoses & symptoms of depression definitions: GPs record depression in different ways, using both diagnostic codes and symptom codes (e.g. “low mood”) and these coding practices have changed over time (Rait *et al.*, 2009). Thus we included both groups in these analyses. Code lists were created for a) depression diagnoses and b) depression symptoms using standard methods (Davé & Petersen, 2009) and approved by a general practitioner and psychiatrist. Entries for depression symptoms were identified using Read codes related to depression but are too vague or uncertain to be classed as diagnoses, such as “low mood” or “C/O – feeling depressed”. As depression is often a recurrent disorder occurring over a lifetime we allowed patients to have multiple episodes of depression during follow-up. We defined a ‘new episode’ of depression diagnoses or symptoms as one where in the prior 12 months (“washout” period) the patient was not prescribed any anti-depressant drug nor had any entry in the database for symptoms or diagnoses of depression.

Study variables:

Outcomes: We determined the initiation of treatment recorded in GP records within 6 months from the onset of a new episode of diagnosed depression or depression symptoms in terms of:

- i. anti-depressant drugs
- ii. hypnotics and anxiolytics drugs
- iii. anti-psychotics drugs
- iv. referrals to psychological therapies including counselling

Records for drug treatment prescriptions were extracted using the British National Formulary (BNF) codes (Joint Formulary Committee, 2013). Prescriptions of amitriptyline for less than 50 mg per day were excluded as low doses of this drug are usually indicated for chronic pain rather than for treating

depression. Anti-depressant drugs include Tricyclic and related anti-depressants, Monoamine-oxidase inhibitors, Selective Serotonin Reuptake Inhibitors and other anti-depressant drugs. Hypnotics and anxiolytics include benzodiazepines, 'z-drugs' (zaleplon, zolpidem, zopiclone), clomethiazole, melatonin and buspirone. Anti-psychotics include both first and second generation oral anti-psychotics. Further details are reported in the BNF (Joint Formulary Committee, 2013).

Explanatory Variables: We estimated the effect of gender, age at onset of new episode of depression/symptoms, socio-economic status and type of neighbourhood on the treatment outcomes.

Age was initially treated as a continuous variable and handled via restricted cubic splines (Durrleman & Simon, 1989). Based on our preliminary exploratory analysis, and to facilitate practical interpretation, we then categorised age into 8 groups: 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89 and 90+ years.

Socio-economic status was defined using the Index of Multiple Deprivation (2010), a measure at the small area level including 38 separate indicators accounting for 7 types of deprivation – income, employment, health, education, barriers to housing and services, living environment and crime, classified into quintiles. Type of neighbourhood was measured at the small area level using the postcode linked to the Office of National Statistics (ONS) classification of areas in the UK population census, grouped into 3 categories: urban, town/fringe and rural (village, hamlet or isolated dwelling).

Analyses

We focussed on patients who had at least one new episode of diagnosed depression or depressive symptoms during the follow-up. For each of the new episodes we then determined whether or not treatment was initiated within six months from the onset. Since the data were clustered (multiple episodes are nested within patients, who in turn are clustered within practices), we used a generalized estimating equations approach with a logistic link function and a working independence correlation

structure (Zeger *et al.*, 1988). This consists of fitting logistic models as if the observations were independent but then accounting for the lack of independence by using a robust sandwich estimator for the standard errors (Huber, 1967; Royall, 1986).

All the models were adjusted for gender, age, deprivation quintile and type of neighbourhood. Since for a few of the treatment outcomes we observed significant interactions between gender and some of the other covariates, we stratified our analysis by gender. No important interactions between age groups and deprivation were found. Some patients, especially the older and frailer ones, did not survive or were not in the study long enough to be started on treatment. Patients who died within six months from episode onset without starting treatment were included in the analysis as not receiving the treatment. For patients who left the study alive (e.g. by moving GP practice) within six months from episode onset without starting treatment we carried out extensive sensitivity analyses to evaluate the robustness of our results to this type of loss to follow-up. In particular, we evaluated how our inferential conclusions were affected under alternative hypothetical scenarios, such as assuming that the treatment was always initiated (best case scenario) or never initiated (worst case scenario) when a patient had missing information on treatment initiation. Analysis was conducted using Stata version 13. Given multiple comparisons and the increased chance of a type I error, one should be cautious regarding interpretations of p-values between 0.01 to 0.05.

Results

Sample characteristics

There were 20,225 recorded new episodes of depression diagnoses in 19,710 registered patients aged 55 years and over within the period 01/01/2009 to 30/06/2013. There were 27,396 recorded new episodes of depressive symptoms from 26,276 patients in the same period. Just under two thirds of the study population were women, the median age at first episode was 64-69 years

(depending on diagnosis and gender) and the majority lived in urban neighbourhoods (Table 1). For most episodes of depression diagnoses (95.9%) and depression symptoms (93.9%) there was a complete six months follow-up.

Table 1: Characteristics of the study population with diagnoses and symptoms of depression

	Depression diagnosis		Depression symptoms	
	males	females	males	females
No. of patients (%)	7539 (38.2%)	12171 (61.8%)	9642 (36.7%)	16634 (63.3%)
Age at 1st recorded episode				
Median	64.1	65.7	66.8	68.9
IQR	[59.0,73.5]	[59.4,75.0]	[60.2,77.0]	[61.0,79.2]
Area deprivation (IMD)				
1 = Least deprived	1691 (22.4%)	2670 (21.9%)	2262 (23.5%)	3856 (23.2%)
2	1735 (23.0%)	2866 (23.6%)	2245 (23.3%)	3842 (23.1%)
3	1590 (21.1%)	2582 (21.2%)	1973 (20.5%)	3406 (20.5%)
4	1398 (18.5%)	2390 (19.6%)	1764 (18.3%)	3220 (19.4%)
5= Most deprived	985 (13.1%)	1442 (11.9%)	1248 (12.9%)	2046 (12.3%)
Missing	140 (1.9%)	221 (1.8%)	150 (1.6%)	264 (1.6%)
Type of neighbourhood				
Urban	5844 (77.5%)	9,394 (77.2%)	7269 (75.4%)	12590 (75.7%)
Town and fringe	910 (12.1%)	1,531 (12.6%)	1375 (14.3%)	2356 (14.2%)
Village, hamlet or isolated dwelling	616 (8.2%)	969 (7.9%)	807 (8.4%)	1337 (8.0%)
Missing	169 (2.2%)	277 (2.3%)	191 (2%)	351 (2.1%)

The majority of the study population only had a single episode of diagnosed depression (97.4%) or depression symptoms (95.9%) recorded during the study period. A few (2.6%) had two recorded episodes and six individuals had three episodes of diagnosed depression. Similarly 4.0% had two recorded episodes of depression symptoms and 31 individuals had three episodes of depression symptoms.

Treatment initiation (all ages)

Anti-depressants were the most common treatment initiated in the six months following a newly recorded episode of depression or depression symptoms. For each new recorded episode of depression in GP records, the majority (87.1%) were treated with an anti-depressant within six months (Supplementary Table 1), and the majority of these (89.8%) were initiated on the same day as the diagnosis was first recorded. For each new recorded episode of symptoms of depression in GP records, more than half (58.7%) were treated with an anti-depressant within six months, and the majority of these (77.4%) were initiated on the same day as the symptom was first recorded. All other treatment modalities were much less common. For those with a new recorded diagnosis of depression 14.2% were initiated on an hypnotic drug, 9.2% on an anxiolytic, and 2.7% on an anti-psychotic drug. Similarly for newly recorded symptoms of depression 13.4% were initiated on a hypnotic, 8.4% on an anxiolytic, and 2.7% on an anti-psychotic drug. For both diagnosis and symptoms of depression, anxiolytics and antipsychotics were initiated more often between one to six months after the first episode. With overall high prescribing of antidepressants, co-prescribing rates were very high, such that for depression diagnoses 90.6% of people prescribed hypnotics and anxiolytics were also prescribed an anti-depressant, and 87.2% of these prescribed anti-psychotics were also prescribed an anti-depressant. For symptoms 68.5% of those prescribed hypnotics and anxiolytics and 68.4% of those prescribed an anti-psychotic were also prescribed an anti-depressant.

Recorded referrals to psychological therapies including counselling were low; only 3.5% of new episodes of depression diagnoses and 3.4% new episodes of depression symptoms had a code indicating a referral had been made within six months of presentation (Supplementary table 1).

Variation in treatment by age, gender, deprivation and type of neighbourhood

Depression diagnoses

Pharmacological treatments

Among patients with a diagnosis of depression there were no significant differences in the odds of being prescribed an anti-depressant by age group (Table 2). Similarly there were no differences in prescribing in older people by area deprivation, or by neighbourhood for men. There were some differences in anti-depressant prescribing by neighbourhood for women, with an increase in anti-depressant prescribing in women living in town and fringe (suburban areas in outskirts of cities) neighbourhoods (OR 1.32, 95%CI 1.01 to 1.74) in comparison to those living in urban neighbourhoods.

There was no significant difference by age in anxiolytic and hypnotic prescribing for men, however for women prescribing increased with increasing age, with the highest prescribing at age 85-89 (OR 1.61, 95%CI 1.29 to 2.02). There were no differences in anxiolytic or hypnotic prescribing by deprivation or neighbourhood. Anti-psychotic prescribing in people with depression increased with age for both men and women, particularly in the oldest age group aged 90 and over, in both men (OR 4.09, 95%CI 1.85 to 9.05) and women (OR 7.14, 95%CI 3.83 to 13.30) in comparison to those aged 55-59 years (Table 3). There were no differences in anti-psychotic prescribing by either deprivation or type of neighbourhood.

Table 2: Odds ratios of drug treatment for recorded new episodes of depression diagnoses in men and women by age, deprivation and neighbourhood

	Anti-depressant prescription				Anxiolytic or hypnotic prescription			
	Men		Women		Men		Women	
	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*
Age group		0.53		0.41		0.29		<0.001
55-59 years	1		1		1		1	
60-64 years	0.88 (0.74, 1.05)		1.12 (0.95, 1.32)		1.00 (0.87, 1.16)		1.22 (1.07, 1.39)	
65-69 years	0.93 (0.74, 1.18)		1.20 (1.00, 1.43)		1.05 (0.88, 1.26)		1.30 (1.12, 1.5)	
70-74 years	0.86 (0.69, 1.07)		0.99 (0.81, 1.21)		1.28 (1.05, 1.55)		1.40 (1.22, 1.62)	
75-79 years	1.02 (0.79, 1.33)		0.97 (0.79, 1.18)		1.13 (0.91, 1.41)		1.26 (1.08, 1.47)	
80-84 years	0.89 (0.66, 1.22)		1.01 (0.80, 1.27)		1.14 (0.91, 1.43)		1.38 (1.14, 1.68)	
85-89 years	0.90 (0.61, 1.31)		1.08 (0.79, 1.47)		1.02 (0.74, 1.39)		1.61 (1.29, 2.02)	
90+ years	1.64 (0.78, 3.44)		0.89 (0.60, 1.31)		1.16 (0.70, 1.91)		1.49 (1.09, 2.05)	
Deprivation		0.91		0.56		0.14		0.18
1 (lowest)	1		1		1		1	
2	0.89 (0.70, 1.13)		0.85 (0.69, 1.04)		1.02 (0.86, 1.21)		0.93 (0.81, 1.08)	
3	0.91 (0.71, 1.17)		0.84 (0.67, 1.05)		1.04 (0.88, 1.24)		0.91 (0.78, 1.07)	
4	0.93 (0.72, 1.19)		0.89 (0.72, 1.12)		0.9 (0.73, 1.09)		0.86 (0.72, 1.02)	
5 (highest)	0.93 (0.68, 1.25)		0.86 (0.63, 1.18)		0.82 (0.66, 1.02)		0.79 (0.66, 0.96)	
Neighbourhood		0.92		0.02		0.13		0.15
Urban	1		1		1		1	
Town and fringe	1.01 (0.74, 1.37)		1.32 (1.01, 1.74)		1.23 (1.01, 1.49)		1.19 (1, 1.43)	
Village, hamlet, isolated dwelling	0.95 (0.72, 1.27)		0.98 (0.72, 1.33)		1.10 (0.85, 1.41)		1.10 (0.92, 1.31)	

* From Wald test for heterogeneity

Table 3: Odds ratios of drug treatment and referrals for recorded new episodes of depression diagnoses in men and women by age, deprivation and neighbourhood

	Antipsychotic prescription				Referral for psychological therapies			
	Men		Women		Men		Women	
	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*
Age group		<0.001		<0.001		<0.001		<0.001
55-59 years	1		1		1		1	
60-64 years	0.94 (0.61, 1.45)		1.43 (0.90, 2.27)		0.69 (0.52, 0.91)		0.71 (0.55, 0.92)	
65-69 years	1.97 (1.29, 3.00)		1.68 (1.00, 2.85)		0.53 (0.36, 0.79)		0.58 (0.43, 0.78)	
70-74 years	1.42 (0.83, 2.44)		2.12 (1.35, 3.34)		0.41 (0.27, 0.63)		0.45 (0.3, 0.67)	
75-79 years	1.95 (1.25, 3.03)		2.43 (1.56, 3.78)		0.43 (0.26, 0.72)		0.17 (0.1, 0.29)	
80-84 years	2.08 (1.19, 3.63)		2.33 (1.40, 3.88)		0.14 (0.05, 0.36)		0.19 (0.1, 0.36)	
85-89 years	1.31 (0.61, 2.82)		4.65 (2.98, 7.26)		0.24 (0.09, 0.65)		0.34 (0.19, 0.62)	
90+ years	4.09 (1.85, 9.05)		7.14 (3.83, 13.3)		— ^a		0.16 (0.04, 0.63)	
Deprivation		0.71		0.43		0.44		0.46
1 (lowest)	1		1		1		1	
2	1.04 (0.69, 1.56)		1.10 (0.78, 1.55)		1.03 (0.72, 1.47)		0.93 (0.64, 1.36)	
3	1.13 (0.74, 1.73)		1.24 (0.86, 1.77)		0.78 (0.53, 1.16)		0.74 (0.47, 1.15)	
4	1.28 (0.83, 1.96)		0.86 (0.58, 1.27)		1.03 (0.67, 1.58)		0.97 (0.63, 1.48)	
5 (highest)	0.93 (0.56, 1.54)		1.14 (0.76, 1.70)		0.84 (0.53, 1.34)		1.01 (0.64, 1.60)	
Neighbourhood		0.67		0.998		0.39		0.27
Urban	1		1		1		1	
Town and fringe	1.22 (0.77, 1.92)		1.01 (0.69, 1.47)		1.42 (0.85, 2.38)		1.39 (0.84, 2.28)	
Village, hamlet, isolated dwelling	1.18 (0.68, 2.07)		0.99 (0.65, 1.50)		1.22 (0.74, 2.01)		0.93 (0.56, 1.54)	

* From Wald test for heterogeneity

^a The regression coefficient could not be estimated.

Non-pharmacological treatments

The odds of recorded referral for psychological therapies including counselling reduced steadily with increasing age for both men and women (see Table 3). For example women aged 75-79 years were around six times less likely (OR 0.17, 95%CI 0.1 to 0.29) to be referred than those aged 55-59 years, and men aged 80-84 years were around seven times less likely (OR 0.14, 95%CI 0.05 to 0.36) to be referred than men aged 55-59 years. There was no differences in recorded referrals for psychological therapies by either deprivation or type of neighbourhood.

Depression symptoms

Pharmacological treatments

There was a J-shaped pattern for prescribing of anti-depressants for older people with new recording of depression symptoms by age group, with a reduction in prescribing for those in their 60s and 70s followed by an increase in those over 85 years (see Table 4). There were no significant differences in prescribing of anti-depressants by deprivation or type of neighbourhood.

Anxiolytic and hypnotic prescribing increased with increasing age (Table 4) . There was a significant difference in prescribing of anxiolytics and hypnotics by deprivation for women but not men, with lower rates of prescribing for women living in the most deprived neighbourhoods (OR 0.80, 95%CI 0.67 to 0.96). There were significant increases in prescribing of anti-psychotics with increasing age, rising to a more than three-fold increase in prescribing for those aged 90 or more in both men (OR 3.22, 95%CI 1.74 to 5.95) and women (OR 3.02, 95%CI 1.96 to 4.65) compared to those 55-59 years (Table 5). There was higher prescribing of anti-psychotics in those living in the most deprived neighbourhoods in men but not women. There were no significant differences by type of neighbourhood.

Table 4: Odds ratios of drug treatment for newly recorded depression symptoms in men and women by age, deprivation and type of neighbourhood

	Anti-depressant prescription				Anxiolytic or hypnotic prescription			
	Men		Women		Men		Women	
	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*
Age group		<0.001		<0.001		<0.001		0.002
55-59 years	1		1		1		1	
60-64 years	0.92 (0.82, 1.03)		0.94 (0.85, 1.03)		0.97 (0.83, 1.13)		1.1 (0.98, 1.25)	
65-69 years	0.77 (0.67, 0.89)		0.86 (0.76, 0.96)		1.03 (0.86, 1.22)		1.29 (1.13, 1.48)	
70-74 years	0.82 (0.71, 0.95)		0.96 (0.85, 1.08)		1.25 (1.04, 1.49)		1.28 (1.11, 1.47)	
75-79 years	0.97 (0.84, 1.12)		0.91 (0.81, 1.01)		1.17 (0.98, 1.40)		1.22 (1.07, 1.4)	
80-84 years	1.06 (0.9, 1.25)		1.03 (0.91, 1.17)		1.37 (1.14, 1.64)		1.25 (1.08, 1.45)	
85-89 years	1.33 (1.11, 1.6)		1.12 (0.96, 1.29)		1.44 (1.14, 1.82)		1.28 (1.1, 1.49)	
90+ years	1.23 (0.9, 1.67)		1.29 (1.08, 1.55)		1.35 (0.98, 1.87)		1.15 (0.95, 1.39)	
Deprivation		0.20		0.24		0.26		0.04
1 (lowest)	1		1		1		1	
2	1.13 (0.98, 1.3)		1.09 (0.96, 1.25)		1.02 (0.86, 1.20)		0.97 (0.85, 1.09)	
3	1.14 (0.95, 1.36)		1.03 (0.90, 1.18)		0.99 (0.83, 1.17)		0.85 (0.75, 0.98)	
4	1.12 (0.93, 1.36)		1.12 (0.96, 1.31)		0.91 (0.75, 1.10)		0.94 (0.81, 1.08)	
5 (highest)	1.28 (1.03, 1.59)		1.18 (1, 1.39)		0.80 (0.64, 1.01)		0.80 (0.67, 0.96)	
Neighbourhood		0.63		0.99		0.93		0.25
Urban	1		1		1		1	
Town and fringe	0.94 (0.77, 1.14)		1.0 (0.86, 1.17)		1.03 (0.87, 1.23)		1.1 (0.95, 1.27)	
Village, hamlet, isolated dwelling	0.91 (0.73, 1.13)		0.99 (0.82, 1.19)		1.02 (0.83, 1.24)		0.95 (0.82, 1.1)	

* From Wald test for heterogeneity

Table 5: Odds ratios of drug treatment and referrals for newly recorded depression symptoms in men and women by age, deprivation and type of neighbourhood

	Antipsychotic prescription				Referral for psychological therapies			
	Men		Women		Men		Women	
	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*	OR (95%CI)	p-value*
Age group								
55-59 years	1	<0.001	1	<0.001	1	<0.001	1	<0.001
60-64 years	0.94 (0.61, 1.45)		1.3 (0.91, 1.86)		0.92 (0.72, 1.18)		0.84 (0.67, 1.06)	
65-69 years	1.59 (1.04, 2.42)		1.83 (1.33, 2.52)		0.51 (0.36, 0.74)		0.66 (0.52, 0.84)	
70-74 years	1.49 (0.97, 2.3)		1.42 (0.95, 2.14)		0.24 (0.15, 0.40)		0.36 (0.25, 0.53)	
75-79 years	1.82 (1.24, 2.68)		2.08 (1.41, 3.06)		0.35 (0.23, 0.52)		0.33 (0.23, 0.49)	
80-84 years	2.27 (1.48, 3.46)		1.55 (1, 2.41)		0.16 (0.08, 0.33)		0.25 (0.18, 0.36)	
85-89 years	1.94 (1.2, 3.13)		2.86 (1.92, 4.25)		0.16 (0.07, 0.36)		0.17 (0.1, 0.29)	
90+ years	3.22 (1.74, 5.95)		3.02 (1.96, 4.65)		0.21 (0.06, 0.67)		0.10 (0.04, 0.27)	
Deprivation		0.004		0.69		0.94		0.53
1 (lowest)	1		1		1		1	
2	1.03 (0.68, 1.55)		1.06 (0.79, 1.41)		0.97 (0.66, 1.43)		0.79 (0.57, 1.09)	
3	1.48 (1.01, 2.16)		1.12 (0.82, 1.53)		1.01 (0.68, 1.50)		0.88 (0.62, 1.26)	
4	1.75 (1.21, 2.54)		1.21 (0.92, 1.58)		1.01 (0.62, 1.66)		0.92 (0.60, 1.42)	
5 (highest)	1.70 (1.12, 2.59)		1.16 (0.83, 1.62)		0.87 (0.52, 1.46)		0.78 (0.49, 1.23)	
Neighbourhood		0.28		0.50		0.15		0.96
Urban	1		1		1		1	
Town and fringe	0.99 (0.67, 1.45)		0.84 (0.63, 1.13)		1.11 (0.66, 1.86)		1.07 (0.68, 1.68)	
Village, hamlet, isolated dwelling	0.63 (0.35, 1.12)		1.02 (0.72, 1.45)		0.66 (0.39, 1.10)		1.03 (0.69, 1.55)	

* From Wald test

for heterogeneity

Supplementary Table 1: Treatment initiations and time to treatment for depression diagnoses and symptoms

Treatment	Overall no. (%) treatment initiations	Time of treatment initiation in those started on each treatment. N(%)			
		0 days	1-14 days	15-30 days	1-6 months
Depression diagnoses (N=20225)					
Anti-depressant drugs	17619 (87.1%)	15819 (89.8%)	754 (4.3%)	421 (2.4%)	625 (3.5%)
Hypnotics	2879 (14.2%)	1002 (34.8%)	579 (20.1%)	467 (16.2%)	831 (28.9%)
Anxiolytics	1864 (9.2%)	517 (27.7%)	407 (21.8%)	270 (14.5%)	670 (36%)
Antipsychotics	554 (2.7%)	91 (16.4%)	91 (16.4%)	92 (16.6%)	280 (50.6%)
Psychological therapies	712 (3.5%)	224 (31.5%)	195 (27.4%)	70 (9.8%)	223 (31.3%)
Depression Symptoms (N=27396)					
Anti-depressant drugs	16072 (58.7%)	12437 (77.4%)	1495 (9.3%)	711 (4.4%)	1429 (8.9%)
Hypnotics	3666 (13.4%)	1272 (34.7%)	770 (21.0%)	613 (16.7%)	1011 (27.6%)
Anxiolytics	2303 (8.4%)	531 (23.1%)	461 (20.0%)	339 (14.7%)	972 (42.2%)
Antipsychotics	752 (2.7%)	113 (15.0%)	165 (21.9%)	118 (15.7%)	356 (47.4%)
Psychological therapies	933 (3.4%)	328 (35.2%)	300 (32.1%)	83 (8.9%)	222 (23.8%)

Non-pharmacological treatments

As with those with depression diagnoses, recorded referrals for psychological therapies for older people with depression symptoms decreased steadily with increasing age (Table 5). For example, men aged 80-84 had six times lower odds of a referral recorded than men aged 55-59 years (OR 0.16, 95%CI 0.08 to 0.33) and women aged 80-84 years had four times lower odds of a recorded referral than women aged 55-59 years (OR 0.25, 95%CI 0.18 to 0.36). There were no significant differences in referrals for psychological therapies by either deprivation or type of neighbourhood.

Sensitivity analysis

We explored the impact of differential drop-out by age, as more people left the dataset without six months follow-up in the oldest age groups. This showed that using the best (all people who leave the practice are treated) and worst (no people are treated) case scenarios had little impact on the findings for most outcomes, with overlapping confidence intervals. The exception was referrals to psychological therapies for those aged 80 or more, where our observed findings were close to the worst case scenario (those leaving the practice within six months are not referred), and significantly lower than the best case scenario (that all people who leave the practice with depression are referred for psychological therapies within six months from the onset of their depression/symptom recording), however this scenario is very unlikely in practice.

Discussion

Treatment rates with anti-depressants are high across all ages for older adults recorded with a new episode of both depression diagnoses and symptoms, and with the majority treatment is initiated on the same day as the diagnosis or symptom is first recorded. There is little variation in initiation of anti-depressant drugs by age for those with a new recorded depression diagnosis – the majority of people are started on an anti-depressant regardless of age, gender, deprivation or neighbourhood. A J-shaped variation in treatment with anti-depressants by age is seen, however, for those with recorded new symptoms of depression (e.g. 'low mood'), with lowest prescribing in those 65-69 years and higher rates in age 85+ years in both men and women. Prescribing of anxiolytics, hypnotics and antipsychotics all increased with increasing age, particularly for anti-psychotics, where prescribing was much higher in the oldest age groups. Overall recorded referrals for psychological therapies including counselling were low, and steadily decreased

with increasing age, for those with both new recorded episodes of depression diagnoses and symptoms, and those in the older age groups (e.g. 80 years or more) were much less likely to have a recorded referral.

Treatment rates with anti-depressants for older people in our study are much higher than previous research on primary care prescribing (Harman *et al.*, 2006) and the fact that treatment was commonly initiated on the same day the depression diagnosis was first entered, suggests that formal coding for depression diagnoses in GP records may be driven in part by decisions to prescribe anti-depressants. It was also striking that anti-depressant treatment rates, while lower than for depression diagnoses, are still high for those coded with symptoms only (e.g. 'low mood'), suggesting that GPs are either opting to use less specific codes for people they feel have significant depression, or that they are prescribing anti-depressants for people with milder symptoms who may not meet criteria for a major depressive episode. Anti-depressant prescribing for this potentially milder group with a recorded depression symptom increases in the oldest age groups (e.g. 85+ years), despite some evidence suggesting that in older people efficacy of anti-depressants declines with increasing age, and with lower severity (Calati *et al.*, 2013). Most trials of the effectiveness of anti-depressants in older people have been conducted with a 'younger old' population, with a mean age of around 71 years, and thus our knowledge of efficacy for the oldest age groups is limited (Benraad *et al.*, 2016). The different patterns of prescribing with age for those with depression diagnoses and symptoms suggests that where symptoms are severe enough to record a depression diagnosis GPs prescribe anti-depressants regardless of age, but for potentially milder episodes recorded only as symptoms of low mood, age, and contextual factors related to age (e.g. employment, or frailty with increasing age) may influence decisions to prescribe.

Our findings are also consistent with other work demonstrating that prescribing of hypnotics increases with increasing age (Olfson *et al.*, 2015) and anti-psychotic prescribing in people without documented severe mental illness is high and rises with age (Marston *et al.*, 2014). We did not exclude those with co-morbid psychosis, and so some prescribing may be appropriate for this indication. Some of this might be explained by prescribing of anti-psychotics for co-morbid conditions such as agitation in dementia, however due to the risk of adverse side effects such as stroke in older people (Douglas & Smeeth, 2008) anti-psychotic prescribing is rarely indicated for this group. Similarly hypnotics have been associated with increased risk of adverse effects including cognitive impairment (Tannenbaum *et al.*, 2012), fractures (Xing *et al.*, 2014) and death (Parsaik *et al.*, 2016) and so continued increased use in this older age group is concerning.

The decline in referrals for psychological therapies including counselling with increasing age is consistent with other evidence, which has demonstrated low treatment rates in older age groups (Unützer et al., 2000; Crystal et al., 2003; Harman et al., 2004; Kessler et al., 2005; de Lusignan *et al.*, 2012), and low self-reported use of psychological therapies in older people in the general population in the recent Adult Psychiatric Morbidity Survey in England (Lubian *et al.*, 2016). This is despite evidence suggesting that CBT has similar effectiveness in later life (Gould *et al.*, 2012), and that once in therapy older people have high levels of adherence (Serfaty *et al.*, 2009). Our study demonstrated a particularly steep decline in recorded referrals for psychological therapies with increasing age, suggesting that some of the low self-reported use of psychological therapies by older people is explained by low referrals from their GP.

This is the first study to our knowledge to explore variations in primary care treatment for new depression diagnoses/depression symptoms by age across all modalities, in a large nationally representative dataset. There are several potential limitations with this work. Depression is under-recognised at all ages in primary care settings, with a sensitivity of 50% for unassisted diagnoses of depression by GPs (Mitchell *et al.*, 2009). This may be slightly worse for older age groups (Mitchell *et al.*, 2010). Our analysis therefore only represents the treatment for those with diagnoses and symptoms recorded in their medical records, and is therefore not generalizable to all depression in the community, including those who may benefit from treatment but are not or mis-diagnosed. The accuracy of GP recorded depression diagnoses is higher, with a specificity of 81% against diagnostic instruments (Mitchell *et al.*, 2009). We do not know the accuracy or validity of GP recorded depression symptoms. We defined new episodes of depression as having no entry for any depression diagnosis or symptom codes or prescriptions for anti-depressant treatment in the previous 12 months. GPs do not consistently enter data on when a patient has recovered from their depression, and it is possible that some people may have continuing depression while having no recorded contact with their GP for this problem. However the majority (97.4%) only had a single recorded episode during follow-up, so this is unlikely to have affected our findings.

Common to all studies on primary care data, there will be some missing data. Prescription data are well recorded (Bourke *et al.*, 2004; Lewis *et al.*, 2007), and the psychotropic drugs of interest are not available without a prescription. These data represent a record of medicines issued, and the patient may not be taking the medication as prescribed, however it does represent the doctor's treatment strategy, our key measurement of interest. There were low recorded

rates of referrals for psychological therapies in comparison to evidence from other countries such as the USA (Harman et al., 2006), however our data is consistent with other UK data from local pilot sites of the Increasing Access to Psychological Therapies (IAPT) programme (de Lusignan *et al.*, 2012). Nonetheless recorded referrals are likely to reflect an under-recording of true rates, as not all referrals will be formally coded on GP systems. GP records would not include self-referrals to psychological therapies, though as evidence suggests that uptake of IAPT services is low in older people (Royal College of Psychiatrists, 2013), this is unlikely to explain the lower recorded GP referral rates. We do not know whether any such under-recording systematically varies by age, so our results may be consistent with, under or over-estimated the true differences. There were fewer people in our sample in the oldest age category of 90 years or more (340 people with new recorded depression and 964 people with new symptoms), affecting the precision of our estimates for this group. A small proportion of people had less than six months of follow-up data due to death (2% of those with depression diagnoses, 3.6% of those with symptoms) or leaving the practice (2% of those with depression diagnoses, 2.5% if those with symptoms), however this attrition was higher in the oldest age groups. Our sensitivity analysis suggested that this is unlikely to have had a significant impact on our results.

Our findings suggest that there are opportunities to improve how GPs in the UK may treat depression in older adults. Hypnotics/anxiolytics and anti-psychotics appear to be over-utilised and prescribing rates rise with increasing age. Recording of referrals for psychological therapies was low and decreased substantially with increasing age. The differences in choice of therapy in older adults across all ages are stark; for depression 87% are prescribed anti-depressants, and only 3.5% referred to psychological therapies within six months. This is despite evidence of the benefit of psychological therapies in older people with a lower NNT (3 vs. 6.7 for antidepressants). There was no evidence that GPs were more reluctant to initiate antidepressants in the oldest age groups with more complex co-morbidities; prescribing of antidepressants was slightly higher in the oldest age groups for those with new depression symptoms. The prevalence of co-morbidities, frailty and disability increase greatly in the very old (Collard *et al.*, 2012), and that this may limit accessibility of psychological therapies, which may be driving the reduced referrals and compensatory increases in drug prescribing in depression. In addition this age group has a lower use of information technology, limiting access to low intensity computer-based psychological therapies that are now widely available for milder depression. GPs may therefore use antidepressants and other drugs more often due to a perceived or real lack of alternative options to manage low mood in the oldest age groups. Other possible

explanations for lower referrals to psychological therapies may include the prioritisation of physical over mental health needs (Murray et al 2006) and a view that feeling low is a natural consequence of ageing and loneliness that does not need treatment (Murray *et al.*, 2006; Corcoran *et al.*, 2013). These would not however explain the high rates of anti-depressant prescribing in older age groups. Commissioners should consider how they can ensure that those with low mood in this group have access to non-drug treatment. Further research should understand why older people are referred less often for psychological therapies, and evaluate the cost-effectiveness of alternatives for psychological support of the oldest age groups.

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Details of contributors: KW and YBS conceived the study, all authors designed the study and developed the protocol, MF extracted and analysed the data, all authors contributed to interpretation of the findings, KW drafted the paper, all authors made significant contributions to drafts of the paper and approved the final draft. KW is the guarantor for the study.

Ethical review: The National Health Service (NHS) South-East Multicentre Research Ethics Committee approved THIN's provision of anonymous patient data to researchers in 2002. We obtained scientific approval for this study from CSD Medical Research's Scientific Review Committee in Nov 2014.

Data sharing: Statistical code is available from the corresponding author at k.walters@ucl.ac.uk

No additional data available due to the nature of the dataset (healthcare records).

References

- Benraad CE, Kamerman-Celie F, Munster BC, Oude Voshaar RC, Spijker J, Rikkert O, Marcel GM.** (2016) Geriatric characteristics in randomised controlled trials on antidepressant drugs for older adults: a systematic review. *International Journal of Geriatric Psychiatry*. 31:990–1003. doi: 10.1002/gps.4443
- Blak BT, Thompson M, Dattani H, Bourke A.** (2011). Generalisability of The Health Improvement Network (THIN) database: demographics, chronic disease prevalence and mortality rates. *Informatics in Primary Care* 19(4), 251-255.
- Booth N.** (1994) What are the Read Codes? *Health Libraries Rev.* 11:177-82.
- Bourke A, Dattani H, Robinson M.** (2004) Feasibility study and methodology to create a quality-evaluated database of primary care data. *Informatics in Primary Care* 12:171-177.
- Calati R, Signorelli MS, Balestri M, Marsano A, De Ronchi D, Aguglia E, Serretti A.** (2013) Antidepressants in elderly: metaregression of double-blind, randomized clinical trials. *Journal of Affective Disorders*. 147(1):1-8.
- Centre HaSCI.** (2012) *Prescriptions Dispensed in the Community, Statistics for England - 2001-2011.*
- Collard RM, Boter H, Schoevers RA, Oude Voshaar RC.** (2012) Prevalence of Frailty in Community-Dwelling Older Persons: A Systematic Review. *Journal of the American Geriatrics Society*. 60(8):1487-92.
- Corcoran J, Brown E, Davis M, Pineda M, Kadolph J, Bell H.** (2013) Depression in older adults: A meta-synthesis. *Journal of Gerontological Social Work*. 56(6):509-34.
- Crystal S, Sambamoorthi U, Walkup JT, Akincigil A.** (2003) Diagnosis and treatment of depression in the elderly medicare population: predictors, disparities, and trends. *Journal of the American Geriatrics Society*. 51(12):1718-28.
<http://www.csdmruk.imshealth.com/> Last accessed 02.09.16
- Cuijpers P, Karyotaki E, Pot AM, Park M, Reynolds CF.** (2014) Managing depression in older age: psychological interventions. *Maturitas*. 79(2):160-9.
- Davé S, Petersen I.** (2009) Creating medical and drug code lists to identify cases in primary care databases. *Pharmacoepidemiology and Drug Safety* 18(8):704-707.
- de Lusignan S, Chan T, Parry G, Dent-Brown K, Kendrick T.** (2012) Referral to a new psychological therapy service is associated with reduced utilisation of healthcare and sickness absence by people with common mental health problems: a before and after comparison. *Journal of Epidemiology & Community Health* 66(6):e10.
- Department for Communities and Local Government.** (2010) The English indices of deprivation 2010.
<http://www.communities.gov.uk/publications/corporate/statistics/indices2010> Last accessed 02.09.16
- Diniz BS, Butters MA, Albert SM, Dew MA, Reynolds CF.** (2013) Late-life depression and risk of vascular dementia and Alzheimer's disease: systematic review and meta-analysis of community-based cohort studies. *British Journal of Psychiatry* 202(5):329-35.
- Douglas IJ, Smeeth L.** (2008) Exposure to antipsychotics and risk of stroke: self-controlled case series study. *British Medical Journal* 337:a1227.

- Durrleman S, Simon R.** (1989). Flexible regression models with cubic splines. *Statistics in Medicine* 8: 551-561.
- Gould RL, Coulson MC, Howard RJ.** (2012). Cognitive behavioral therapy for depression in older people: a meta-analysis and meta-regression of randomized controlled trials. *Journal of the American Geriatrics Society* 60(10):1817-1830.
- Harman JS, Edlund MJ, Fortney JC.** (2004) Disparities in the adequacy of depression treatment in the United States. *Psychiatric Services* 55(12), 1379-1385.
- Harman JS, Veazie PJ, Lyness JM.** (2006) Primary care physician office visits for depression by older Americans. *Journal of General Internal Medicine* 21(9):926-30.
- Harris T, Carey IM, Shah SM, DeWilde S, Cook DG.** (2012). Antidepressant prescribing in older primary care patients in community and care home settings in England and Wales. *Journal of the American Medical Directors Association* 13(1), pp.41-47.
- Horsfall L, Walters K, Petersen I** (2013). Identifying periods of acceptable computer usage in primary care research databases. *Pharmacoepidemiology and Drug Safety* 22(1):64-69.
- Huber PJ.** (1967) The behaviour of maximum likelihood estimators under non-standard conditions. In *Proceedings of the fifth Berkeley Symposium on Mathematical Statistics and Probability*. University of California Press: Berkeley, USA, pp. 221-233.
- Jeong HG, Lee JJ, Lee SB, Park JH, Huh Y, Han JW, Kim TH, Chin HJ, Kim KW.** (2013) Role of severity and gender in the association between late-life depression and all-cause mortality. *International Psychogeriatrics*. 25(04):677-84.
- Joint Formulary Committee.** (2013) *British National Formulary* (66th edition). London: BMJ Group and Pharmaceutical Press.
- Kessler RC, Demler O, Frank RG, Olfson M, Pincus HA, Walters EE, Wang P, Wells KB, Zaslavsky AM.** (2005) Prevalence and treatment of mental disorders, 1990 to 2003. *New England Journal of Medicine*. 352(24):2515-23.
- King M, Nazareth I, Levy G, Walker C, Morris R, Weich S, Bellón-Saameño JÁ, Moreno B, Švab I, Rotar D, Rifel J.** (2008) Prevalence of common mental disorders in general practice attendees across Europe. *The British Journal of Psychiatry*. 192(5):362-7.
- Kok RM, Nolen WA, Heeren TJ.** (2012) Efficacy of treatment in older depressed patients: a systematic review and meta-analysis of double-blind randomized controlled trials with antidepressants. *Journal of Affective Disorders*. 41(2):103-15.
- Lewis JD, Bilker WB, Weinstein RB, Strom BL.** (2005) The relationship between time since registration and measured incidence rates in the General Practice Research Database. *Pharmacoepidemiology and Drug Safety*. 14(7):443-51.
- Lewis JD, Schinnar R, Bilker WB, Wang X, Strom BL.** (2007) Validation studies of the health improvement network (THIN) database for pharmacoepidemiology research. *Pharmacoepidemiology and Drug Safety*. 16(4):393-401.

- Lubian K, Weich S, Stansfeld S, Bebbington P, Brugha T, Spiers N, McManus S, Cooper C.** (2016) *Adult Psychiatric Morbidity Survey: Survey of Mental Health and Wellbeing, England, 2014. Chapter 3: Mental Health Treatment and Service Use.* Published September 29, 2016 <http://content.digital.nhs.uk/catalogue/PUB21748> Last accessed 11.11.16
- Luppa M, Sikorski C, Luck T, Ehreke L, Konnopka A, Wiese B, Weyerer S, König HH, Riedel-Heller SG** (2010). Age- and gender-specific prevalence of depression in latest-life – Systematic review and meta-analysis. *Journal of Affective Disorders* 136, 212-221.
- Marston L, Nazareth I, Petersen I, Walters K, Osborn DP.** (2014) Prescribing of antipsychotics in UK primary care: a cohort study. *BMJ Open*.4(12):e006135.
- Mitchell AJ, Vaze A, Rao S.** (2009) Clinical diagnosis of depression in primary care: a meta-analysis. *The Lancet* 374:609-619.
- Mitchell AJ, Rao S, Vaze A.** (2010) Do primary care physicians have particular difficulty identifying late-life depression? A meta-analysis stratified by age. *Psychotherapy and Psychosomatics* 79:285-294.
- Murray J, Banerjee S, Byng R, Tylee A, Bhugra D, Macdonald A.** (2006) Primary care professionals' perceptions of depression in older people: a qualitative study. *Social Science & Medicine*. 63(5):1363-73.
- National Institute for Health and Care Excellence (NICE).** (2009, updated April 2016) *Clinical Guideline 90, Depression in adults : recognition and management.* <https://www.nice.org.uk/guidance/cg90/chapter/1-Guidance>. Last accessed 08.06.17
- Nelson JC, Delucchi K, Schneider LS.** (2008) Efficacy of second generation antidepressants in late-life depression: a meta analysis of the evidence. *American Journal of Geriatric Psychiatry* 16:558-567.
- Olfson M, King M, Schoenbaum M.** (2015) Benzodiazepine use in the United States. *JAMA Psychiatry* 72: 136–142
- Parsaik AK, Mascarenhas SS, Khosh-Chashm D, Hashmi A, John V, Okusaga O, Singh B.** (2016) Mortality associated with anxiolytic and hypnotic drugs—A systematic review and meta-analysis. *Australian and New Zealand Journal of Psychiatry*. 50(6):520-533.
- Rait G, Walters K, Griffin M, Buszewicz M, Petersen I, Nazareth I.** (2009) Recent trends in the incidence of recorded depression in primary care. *British Journal of Psychiatry*. 195(6):520-4.
- Royal College of Psychiatrists** (2013). Report of the Second Round of the National Audit of Psychological Therapies (NAPT) 2013. London: Healthcare Quality Improvement Partnership.
<http://www.rcpsych.ac.uk/workinpsychiatry/qualityimprovement/nationalclinicalaudits/psychologicaltherapies/psychologicaltherapies.aspx> Last accessed 02.09.16
- Royall RM.** (1986) Model robust confidence intervals using maximum likelihood estimators. *International Statistical Reviews* 54:221-226.

- Serfaty MA, Haworth D, Blanchard M, Buszewicz M, Murad S, King M.** (2009) Clinical effectiveness of individual cognitive behavioral therapy for depressed older people in primary care: a randomized controlled trial. *Archives of General Psychiatry.* 66(12):1332-40.
- Tannenbaum C, Paquette A, Hilmer S, Holroyd-Leduc J, Carnahan R.** (2012) A systematic review of amnestic and non-amnestic mild cognitive impairment induced by anticholinergic, antihistamine, GABAergic and opioid drugs. *Drugs and Aging.* 29(8):639-58.
- Thorlund K, Druyts E, Wu P, Balijepalli C, Keohane D, Mills E.** (2015) Comparative Efficacy and Safety of Selective Serotonin Reuptake Inhibitors and Serotonin-Norepinephrine Reuptake Inhibitors in Older Adults: A Network Meta-Analysis. *Journal of the American Geriatrics Society.* 63(5):1002-9.
- Unützer J, Simon G, Belin TR, Datt M, Katon W, Patrick D.** (2000) Care for depression in HMO patients aged 65 and older. *Journal of the American Geriatrics Society.* 48(8):871-8.
- White J, Zaninotto P, Walters K, Kivimäki M, Demakakos P, Shankar A, Kumari M, Gallacher J, Batty GD.** (2015) Severity of depressive symptoms as a predictor of mortality: the English longitudinal study of ageing. *Psychological Medicine.* 45(13):2771-9.
- Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, Charlson FJ, Norman RE, Flaxman AD, Johns N, Burstein R.** (2013) Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet* 382(9904): 1575-1586.
- Xing D, Ma XL, Ma JX, Wang J, Yang Y, Chen Y.** (2014) Association between use of benzodiazepines and risk of fractures: a meta-analysis. *Osteoporosis International.* 25(1):105-20.
- Zeger SL, Liang K-Y, Albert PS.** (1988) Models for longitudinal data: a generalized estimating equation approach. *Biometrics* 44:1049-1060.