

Incidence and predictors of depression in non-demented primary care attenders aged 75 years and older: results from a 3-year follow-up study

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Abstract

Objective: to determine incidence and predictors of late-life depression.

Methods: this is a 3-year observational cohort study of 3,214 non-demented patients aged 75 and over completing three waves of assessment. The patients were recruited in 138 primary care practices in six urban areas in Germany. Depressive symptoms were measured at baseline, and 18 months and 36 months later using the GDS-15 Geriatric Depression Scale with a cut-off 0–5/6–15. Cox proportional hazard regression models were applied to examine predictors of incident depression, adjusting for sex, age, education, living situation, activities of daily living - and instrumental activities of daily living impairment, somatic comorbidity, alcohol consumption, smoking, mild cognitive impairment and apoE4 status.

Results: the incidence of depression was 36.8 (95% CI: 29.6–45.3) per 1,000 person-years in men and 46.0 (95% CI: 39.9–52.8) in women (sex difference $P = 0.069$). The incidence increased from 35.4 (95% CI: 29.7–41.9) per 1000 person-years between the ages of 75 and 79 to 75.2 (95% CI: 53.2–103.2) for subjects 85 years and older. After full adjustment for confounding variables, hazard ratios (HR) for incident depression were significantly higher for subjects 85 years and older (HR: 1.83, 95% CI: 1.24–2.70) and those with mobility impairment (HR: 2.53, 95% CI: 1.97–3.25), vision impairment (HR: 1.41, 95% CI: 1.04–1.91), mild cognitive impairment (HR: 1.52, 95% CI: 1.10–2.10), subjective memory impairment (HR: 1.33, 95% CI: 1.01–1.74) and current smoking (HR: 1.69, 95% CI: 1.13–2.53).

Conclusions: the incidence of depression increased significantly with age. In designing prevention programmes, it is important to call more attention on functional impairment, cognitive impairment and smoking.

Keywords: incident depression, predictors, prospective longitudinal study, older people

Introduction

Depression in old age occurs frequently, places a severe burden on patients and relatives and increases the utilisation of medical services and health care costs [1–2] (e.g. Cole and Dendukuri, 2003; Lippa *et al.*, 2008). Many studies indicate that not only Diagnostic and Statistic Manual of

Mental Disorders (DSM)-defined depressive disorders are associated with increased disability, but also depressive syndromes that do not fulfil the strict DSM criteria of major depressive disorder and dysthymia [3]. Although the association between age and depression received considerable attention, very little is known about the incidence of depression among those 75 years of age and older. Studies

that treat the group 65+ as one entity are often heavily weighted towards the age group 65–75. Therefore, the prediction of depression in the very old is uncertain, since many community-based studies lack adequate samples over the age of 75. To study the older old is also important, since some crucial risk factors such as bereavement, social isolation, somatic diseases and functional impairment become more common with increasing age. These factors may exert different effects in the younger old compared with the older old. Knowledge of risk factors is a prerequisite to designing tailored interventions, either to tackle the factors themselves or to define high-risk groups, since depression is treatable in most cases [4].

Based on a large sample of non-demented primary care attenders (age 75+), the objectives of this study are:

- to report age- and gender-specific incidence rates of depression, and
- to determine the impact of predictors at baseline (socio-demographic variables such as marital status, living situation and education; functional impairment and medical diagnoses, apoE4 status, lifestyle factors such as consumption of alcohol and nicotine, mild cognitive impairment) on incident depression.

Methods

Study population and design

Within the framework of the German Study on Ageing, Cognition, Dementia in Primary Care Patients (AgeCoDe Study), at baseline 3,327 patients recruited by 138 general practitioners in six study centres (Bonn, Düsseldorf, Hamburg, Leipzig, Mannheim and Munich) were assessed by means of structured clinical interviews conducted by trained physicians and psychologists during visits to the participants' homes. Inclusion criteria for GP patients were an age of 75 years and over, the absence of dementia in the GP's view [5], and at least one contact with the GP within the last 12 months. The follow-up I and II examinations were done, on average, 1.5, respectively, 3 years after the baseline interview. Information on sampling frame, eligible subjects and respondents is given in Figure 1.

Measures

Depressive symptoms

Depressive symptoms were ascertained using the 15-item version of the Geriatric Depression Scale (GDS) [6]. Owing to the simplified yes/no response format and the exclusion of questions on somatic symptoms, it is especially suitable for older people. This instrument has good psychometric properties also for German-speaking populations. For the German version of the GDS-15, a cut-off score of 6 yielded the best sensitivity (84.0%) and specificity (88.9%). Therefore, this cut-off was used in the present study as well

as in another recent longitudinal study on onset and persistence of depression in old age [7].

Mild Cognitive Impairment

Mild cognitive impairment (MCI) was diagnosed according to new consensus criteria proposed by the International Working Group on Mild Cognitive Impairment [8]. In this study, modified versions of the MCI were used [9]. *Subjective memory complaints* were assessed with the question: "Do you feel like your memory has become worse?"

Lifestyle factors

Lifestyle factors assessed include self-reported alcohol consumption and smoking, and it was differentiated between current consumers and non-consumers. With regard to alcohol consumption, current consumers were distinguished according to their average daily level of consumption: abstinent; <1 drink; 1–2 drinks; 2+ drinks. One drink is the equivalent of 10 g of pure alcohol.

The measurement of *functional impairment* (mobility, vision and hearing) was based on the SIDAM-ADL-Scale of the SIDAM instrument (Structured Interview for Diagnosis of Dementia of Alzheimer Type, Multiinfarct Dementia and Dementia of Other Etiology) [10]. To measure instrumental activities of daily living (IADL), we used an 8-item scale [11]. Subjects with an impairment in at least one of the eight items of the scale were regarded as impaired.

For each study participant his or her general practitioner filled out a questionnaire asking for *comorbidity*. Seventeen clinical diagnoses were predetermined by the questionnaire (answer: yes/no/I do not know). Based on this information somatic comorbidity was defined: no comorbidity/1–4 diagnoses/5+ diagnoses.

For DNA analysis, leucocyte DNA was isolated with the Quiagen blood isolation kit according to the instructions of the manufacturer (Quiagen, Hilden, Germany). *Apolipoprotein E (apoE) genotyping* was performed according to standard procedures [12]. In analyses subjects were divided into those with at least one 4 allele and those without an 4 allele.

Statistical analyses

The data were entered in the centres via an Internet-based Remote Data Entry System into a central ORACLE, version 9, database. The statistical analyses were performed with SPSS for Windows, version 15.0 and Statistical Analysis System (SAS), version 9.1.

In cohort studies, there are two methods to calculate incidence. An incidence risk is defined as the number of disease onsets divided by the number of persons at risk at baseline, whereas an incidence rate is the number of disease onsets divided by the person-years at risk. In our study, we were able to determine incidence rates which are more

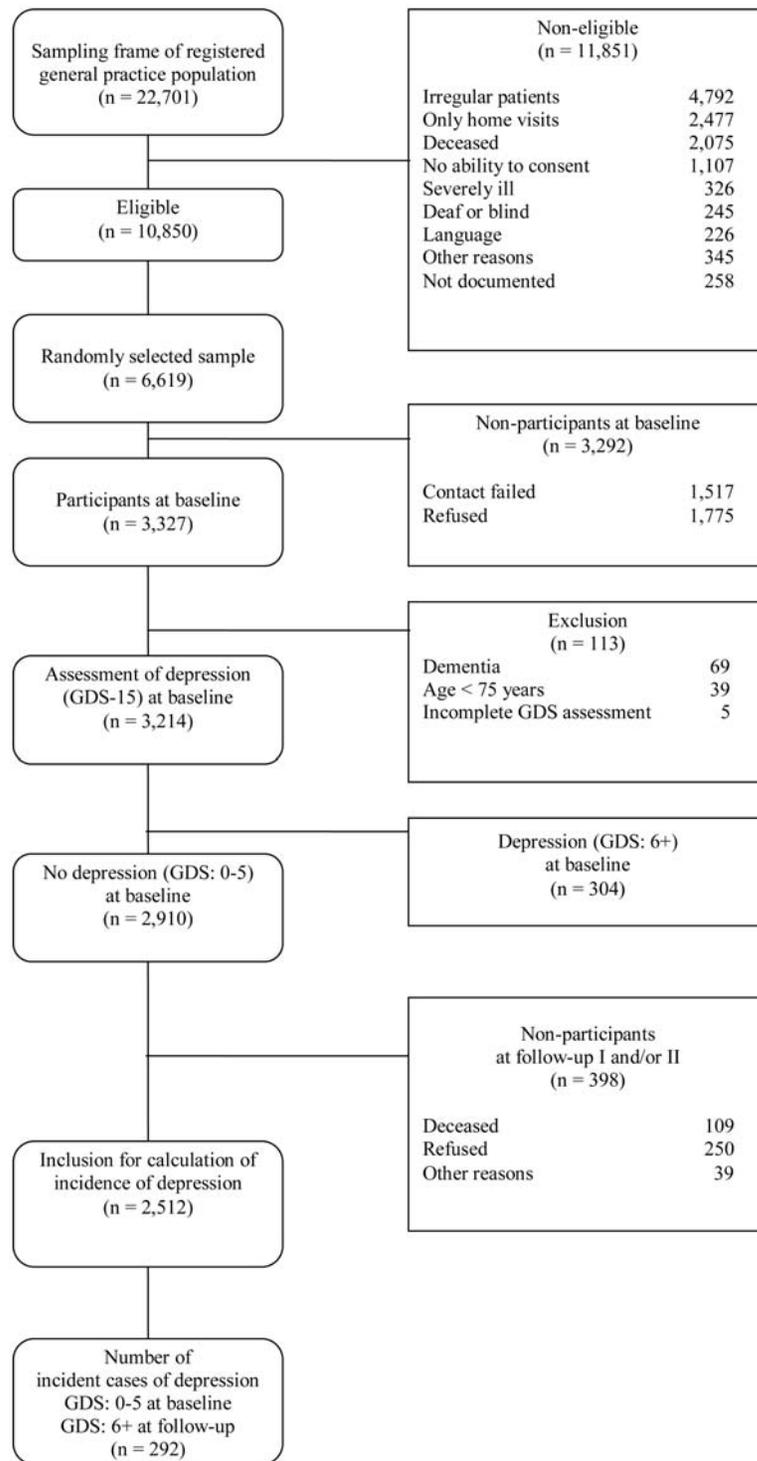


Figure 1. Flow chart describing sample of a 3-year follow-up study.

precise than incidence risks. Furthermore, incidence can be distinguished into first incidence and total incidence. First incidence is defined as the first disorder in a person's lifetime, hence the population at risk includes all subjects at the beginning of the study who have never had any previous episode of the disorder [13]. Since particularly among older persons recall of remote events such as a depressive

episode is of questionable accuracy, in this study incidence rates of depression are presented as total incidence [13]: It is based on respondents who were not depressed at baseline (GDS-15 score: 0–5) but who may have had a previous history of the disorder. Incident depression was considered to be present when the GDS-15 increased to 6 and more points during the follow-up measurements. The incidence

rates were obtained by dividing the number of new onset depressive episodes by the number of person-years at risk. Participants were censored when one of the following events occurred: dementia, death, loss during the interim or end of follow-up II (3 years after baseline). The 95% confidence intervals (CIs) were based on the Poisson distribution.

Cox proportional hazard regression models (bivariate and multivariate) were applied to examine the relationship between risk factors and incident depression. In all analyses, a *P*-value of <0.05 was considered statistically significant.

Results

Response rates

At baseline, the study population consisted of 2,910 participants without depression (Figure 1). During the 3-year follow-up period, the attrition rate was 13.7%: 3.8% died, 8.6% refused to be interviewed and 1.3% could not be interviewed for other reasons (including dementia). Of the original sample, 2,512 subjects (86.3%) completed the GDS-15 at the follow-up.

Demographic characteristics

Of the 2,512 patients interviewed, 896 were men (35.7%) and 1,616 women (64.3%). The mean age was 79.6 years (SD = 3.5; range: 75–99). The baseline sample included only persons living in private households, whereby 50.6% were living alone. The majority of the patients was widowed (44.9%) or married (43.8%); only 6.0% of the subjects were never married and 5.3% were divorced. Based on the revised CASMIN classification [14], 60.4% of the subjects exhibited a low level of education (in general, elementary school), 27.7% a middle level of education and 11.9% a high level of education.

Age- and gender-specific incidence rates of depressive disorders

Among the 2,512 participants who completed the GDS-15 during the follow-up, 292 subjects fulfilled the criteria for incident depression (GDS-15: 6+ points). The overall incidence of depression was 42.7 (95% CI: 38.0–47.9) per 1,000 person-years (Table 1). The incidence rate was 36.8 (95% CI: 29.6–45.3) in men and 46.0 (95% CI: 39.9–52.89) in women (sex difference *P* = 0.038). The incidence rate increased with age: from 35.4 (95% CI: 29.7–41.9) between the ages of 75 and 79 to 75.2 (95% CI: 53.2–103.2) for subjects 85 years and older. Among those over 85 years of age and older incidence rates were highest for both genders.

Predictors of incident depression

Table 2 contains the hazard ratios (HR) for each potential risk factor, first in a bivariate model and then fully adjusted for all the variables studied. Even in the fully adjusted model the risk for incident depression was significantly higher among subjects 85 years and older compared with the youngest age group (75–79). In none of the analyses were living situation, marital status and level of education significantly associated with incident depression.

In both models, no significant HRs were found for hearing impairment, somatic comorbidity, current alcohol consumption and apoE4 status.

Bivariate analysis revealed a significant correlation between functional impairment (IADL) and incident depression. However, after adjustment for all variables this association was no longer statistically significant.

It could be demonstrated in bivariate and multivariate models that mobility impairment, vision impairment, mild cognitive impairment, subjective memory impairment and smoking increased the risk of incident depression significantly.

Table 1. Incidence of depression (GDS-15: 0–5 points at baseline and 6+ points at follow-up I and/or follow-up II)

No depression at baseline (GDS-15: 0–5 points)	<i>n</i>	Number of new cases	Sum of risk years	Incidence per 1,000 person-years (95% CI)	<i>P</i> -value
Total	2,512	292	6,832	42.7 (38.0–47.9)	0.069
Men	896	90	2,444	36.8 (29.6–45.3)	
Women	1,616	202	4,388	46.0 (39.9–52.8)	
Total					
75–79	1,379	136	3,842	35.4 (29.7–41.9)	
80–84	928	118	2,485	47.5 (39.3–56.9)	0.010 (versus 75–79)
85+	205	38	505	75.2 (53.2–103.2)	0.000 (versus 75–79)
Men					
75–79	535	55	1,479	37.2 (28.0–48.4)	
80–84	301	24	822	29.2 (18.7–43.5)	0.163 (versus 75–79)
85+	60	11	143	76.7 (38.3–137.3)	0.021 (versus 75–79)
Women					
75–79	844	81	2,363	34.3 (27.2–42.6)	
80–84	627	94	1,663	56.5 (45.7–69.2)	0.000 (versus 75–79)
85+	145	27	362	74.6 (49.1–108.5)	0.000 (versus 75–79)

Table 2. Bivariate and fully adjusted associations to predict incident depression (GDS-15: at baseline: 0–5 points; at follow-up I and/or II: 6+ points)

Variable (at baseline)	Incident cases GDS-15: 6+n/N \	Bivariate HR (95% CI)	P-value	HR fully adjusted (95% CI)	P-value
Sex					
Male	90/896	1		1	
Female	202/1,616	1.25 (0.97–1.60)	0.075	1.28 (0.93–1.78)	0.126
Age					
75–79	136/1,379	1		1	
80–84	118/928	1.33 (1.04–1.71)	0.021	1.19 (0.92–1.55)	0.178
85+	38/205	2.11 (1.47–3.03)	0.000	1.83 (1.24–2.70)	0.002
Living alone					
Yes	155/1,272	1.10 (0.88–1.39)	0.348	0.93 (0.62–1.39)	0.728
No	137/1240	1		1	
Marital status					
Single	20/151	1		1	
Married	119/1,099	0.81 (0.50–1.30)	0.386	0.89 (0.49–1.62)	0.720
Divorced	19/133	1.09 (0.58–2.04)	0.788	1.05 (0.55–2.02)	0.865
Widowed	134/1,129	0.89 (0.56–1.43)	0.899	0.81 (0.50–1.33)	0.419
Level of education (CASMIN)					
Low	189/1,519	1		1	
Middle	71/695	0.80 (0.61–1.05)	0.120	0.69 (0.51–0.92)	0.013
High	32/298	0.83 (0.57–1.22)	0.360	0.88 (0.59–1.31)	0.549
Mobility impairment					
Yes	160/798	2.91 (2.31–3.66)	0.000	2.53 (1.97–3.25)	0.000
No	132/1,714	1		1	
Vision impairment					
Yes	56/326	1.65 (1.23–2.21)	0.001	1.41 (1.04–1.91)	
No	236/2,186	1		1	0.025
Hearing impairment					
Yes	94/748	1.12 (0.88–1.43)	0.344	1.00 (0.77–1.29)	0.998
No	198/1,764	1		1	
Functional impairment (IADL)					
Yes	31/144	2.17 (1.50–3.16)	0.000	1.48 (0.99–2.21)	0.052
No	261/2,368	1		1	
Somatic comorbidity*					
No	23/191	1		1	
1–4 diagnoses	182/1,769	0.85 (0.55–1.31)	0.477	0.90 (0.56–1.43)	0.661
5+ diagnoses	84/537	1.34 (0.84–2.12)	0.213	1.20 (0.73–1.98)	0.455
Mild cognitive impairment**					
Yes	56/331	1.68 (1.25–2.24)	0.000	1.52 (1.10–2.10)	0.011
No	235/2,179	1		1	
Subjective memory impairment					
Yes	196/1,444	1.54 (1.20–1.96)	0.001	1.33 (1.01–1.74)	0.039
No	96/1,068	1		1	
Current alcohol consumption***					
Abstinent	155/1,191	1		1	
<1 drink	66/654	0.75 (0.56–1.00)	0.055	0.84 (0.62–1.14)	0.271
1–2 drinks	31/328	0.70 (0.47–1.03)	0.073	0.90 (0.60–1.35)	0.638
2+ drinks	40/324	0.75 (0.66–1.34)	0.757	1.18 (0.79–1.76)	0.405
Current smoking					
Yes	29/175	1.52 (1.04–2.24)	0.031	1.69 (1.13–2.53)	
No	263/2,337	1		1	0.010
apoE4****					
Yes	63/506	1.11 (0.84–1.47)	0.460	1.07 (0.81–1.43)	0.603
No	215/1,919	1		1	

No information available: * n = 15; ** n = 2; *** n = 15; **** n = 87.

Discussion

Incidence studies on late-life depression are rare. A recent review [15] focusing on persons 70 years of age and older reported 22 incidence studies: 15 studies (categorical

diagnostics) were based on classification systems such as DSM or ICD (International Classification of Diseases) and 7 studies (dimensional diagnostics) were based on depression scales such as the GDS. The current study is the largest prospective longitudinal study to date to determine

the incidence of depression to be carried out among subjects 75 years of age and older. We found that the incidence of late-life depression in Germany is substantial: Based on 2,512 patients recruited in 138 general practices, the overall incidence of depression was 42.7 (95% CI: 38.0–47.9) per 1,000 person-years. A direct comparison with other studies is difficult, however, due to the varying operationalisation of depressive disorders, heterogeneous age groups and different ways to calculate incidence [16]. Different follow-up periods in incidence studies on late-life depression are reported ranging from 6 months [17] to 7 years [18] in cohort studies using dimensional diagnostics. It is well-documented that the incidence rate of Major Depression ranging between 2 and 11 per 1,000 person-years is much lower than the incidence of clinically relevant depressive symptoms [15]. Among the two studies that have estimated incidence rates of DSM-defined depressive disorders in non-demented elderly cohorts, rates ranged between 8 per 1,000 person-years in the USA [19] and 23 per 1,000 person-years in Sweden [16]. Compared with this, the incidence of depression in the present study is much higher.

Unfortunately only one out of seven incidence studies reported in the systematic review [15] is—such as our study—based on incidence rates: The Leiden 85-plus study [20] in which depression was also assessed with the GDS-15 reported an incidence rate of 68 (95% CI: 50–85), which is similar to the rate of 75.2 (53.2–103.2) found in our study for subjects 85 years and older.

In agreement with most studies that report gender-specific incidences, we also found that women had a somewhat higher risk of becoming depressed than men did. We could not confirm the results of Palsson *et al.* [16] that at all ages the incidence of depression was higher in women than in men. In our study, substantial sex-specific differences in the incidence per 1,000 person-years were found only in the 80–84 year olds (men: 29.2; women: 65.5), whereas in age groups 75–79 (men: 37.2; women: 34.3) and 85+ (men: 76.7; women: 75.6) rates were very similar for both genders.

In their review, Büchtemann *et al.* [15] conclude that among subjects 70 years and older the relationship between age and incident depression is inconsistent between studies. Some studies [7, 21–22], but not all [17, 23–26], have found that the incidence of depression steadily increases with age. In the present study incidence rates for men and women were particularly high among those beyond the age of 85.

This investigation confirms the results of a meta-analysis [1] that neither educational level, marital status, living situation nor the presence of chronic diseases contributed to the incidence of depression. Our results indicate that impairments of mobility and vision are much stronger predictors of incident depression than are individual somatic illnesses, respectively, the number of medical diagnoses. This also corroborates results from a meta-analysis [1]

where poor daily functioning was significantly associated with the development of depression.

There is general agreement on the cross-sectional correlation between depressive and cognitive symptoms [4, 27]. Longitudinal studies suggest that depression is a risk factor for cognitive impairment. In our study we could also demonstrate in multivariate analysis that mild cognitive impairment and subjective memory impairment increase the risk of incident depression.

With regard to the relationship between lifestyle factors (consumption of nicotine and alcohol) and incident depression, our results supported the findings of cross-sectional studies [4, 28]; no significant correlations between consumption of alcohol and depressive symptoms were found in either study; however, the correlations between current smoking and depressive symptoms were highly significant, even after controlling for potential risk factors.

In several studies the relationship between the ApoE4 allele and late-life depression was examined, but the results are inconsistent. A recent review [29] reported nine studies that found ApoE4 to be a significant risk factor for depression. However, in agreement with our findings, in 12 studies such a relationship could not be confirmed.

A number of factors may have influenced the findings and should be considered when interpreting the results: cases were defined according to scores on the Geriatric Depression Scale (GDS-15), not according to clinical diagnostic criteria. However, this widely used instrument has shown good psychometric properties and allows comparisons with epidemiological studies in different countries.

Although we included numerous statistical controls, there may be other potential confounders that we omitted as they were unavailable. The survey excluded institutionalised older people, subjects who were unable to attend a primary care physician's practice, and those who suffered from dementia. Since these factors increase the incidence of depressive disorders, incidence rates in our study are probably underestimated. Finally, in our study, similar to that of other authors [e.g. 30], only currently depressed individuals were excluded at baseline, but not those with a previous depression. Some of those individuals who were defined as not depressed at baseline might have had a previous depression. Since persons with a previous depression are at increased risk for a new episode and were included in our study, our incidence rates may be overestimated. However, it has to be noted that retrospective information from the interviewees may underrate depression: Some persons might not remember previous depressive episodes or may conceal them from the interviewer. Recall bias may be particularly high among older people. A 13.7% attrition rate between baseline and the 36-month follow-up period might have influenced the estimate of incidence rates. In the case of deceased participants interviews were made with family and caregivers only to assess dementia, but not

depression. Therefore, our incidence rates may be underestimated.

Key points

- Among a large sample of non-demented individuals (75 years of age and older) living in private households in Germany, depression (GDS-15 Geriatric Depression Scale: cut-off score: 0–5/6+) was assessed at baseline, and 1.5 and 3 years later.
- The incidence of depression was substantial: 36.8 per 1,000 person-years in men and 46.0 in women.
- The incidence increased from 35.4 per 1000 person-years between the ages of 75 and 79 to 75.2 for subjects 85 years and older. This should alert general practitioners to look for signs and symptoms of depression particularly among the oldest old.
- After full adjustment for confounding variables, HRs for incident depression were significantly higher for subjects 85 years and older and for those with mobility impairment, vision impairment, mild cognitive impairment, subjective memory impairment and current smoking.
- To prevent late-life depression, it is important to call more attention to the impact of functional and cognitive impairment.

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Conflicts of interest

None declared.

Ethical approval

The ethics committees of the participating centres approved the study. Written informed consent was obtained from all participants.

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