# Incidence of filled antidepressant prescriptions among people with newly diagnosed diabetes and its interaction with occupational status within the working population of Denmark 1996-2010

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# Abstract

**Aims**: People with diabetes have heightened levels of depressive symptoms, but less is known about the development of these symptoms in relation to diabetes duration. In this study, we examined the use of prescribed antidepressants in the first five years after diagnosis of diabetes among the working-age population in Denmark.

**Methods**: All Danish adults aged 18-54 years, diagnosed with diabetes in the study period were included. Diabetes status and purchase of prescription antidepressants were obtained from validated population registers. Data analysis focused on filled antidepressant prescriptions at ≤ 1 and ≤ 5 years from diagnosis with diabetes.

**Results**: 35,677 people diagnosed with diabetes were included in the study. At ≤ 1 year post-diagnosis, 2.6% had filled antidepressant prescriptions. At ≤ 5 years, this figure rose to 10.4%. Overall, both female gender and lower socioeconomic status were associated with higher incidence of filled antidepressant prescriptions. Diabetes duration modified the degree of differences between men and women and socioeconomic strata.

**Conclusion:** Diagnosis with diabetes immediately impacts mental wellbeing, with higher rates of filled antidepressant prescriptions in the first year after diagnosis. People of working age diagnosed with diabetes face specific challenges and addressing such challenges would enhance patient experiences. Focus on mental health in the clinical encounter with people newly diagnosed with diabetes is warranted and important.

**Keywords**: Diabetes Mellitus; Diagnosis; Antidepressants; Socioeconomic status.

## Introduction

The link between diabetes and depressive symptoms is well established [[1](#_ENREF_1)]. The exact nature of the depressive symptoms experienced by people with diabetes (PWD) and what they signify, however, still generates controversy [[2](#_ENREF_2)]. Often this controversy revolves around the question of whether or not PWD are more prone to clinical depression [[1](#_ENREF_1)] and, if so, what mechanisms link the two conditions [[3](#_ENREF_3)]. Hard evidence concerning the onset of depressive symptoms in temporal relation to a diagnosis of diabetes remains scant [[4](#_ENREF_4)] and research conducted in this area has produced results with conflicting conclusions [[5](#_ENREF_5), [6](#_ENREF_6)]. What is clear, however, is that the presence of depressive symptoms, even at levels below the threshold for clinical depression, impact on behaviours pertinent to diabetes self-management [[7](#_ENREF_7), [8](#_ENREF_8)]. In this light it is important to establish evidence regarding the onset of depressive symptoms in temporal relation to a diagnosis of diabetes. In order to assess the psychological impact following a diagnosis of diabetes, we examined cases of incident diabetes in Denmark from 1996 onwards and determined what proportion filled antidepressant prescriptions within five years of a diagnosis of diabetes.

The analysis undertaken in this study is focussed on the working-age population (< 60 years). The deleterious effects of diabetes on employment and ability to work are well established [[9](#_ENREF_9)], but recent research has clearly underlined how poor mental health compounds these effects [[10-12](#_ENREF_10)]. We believe it is important, therefore, to generate evidence which encourages the development of support in the workplace for PWD, not least when both diabetes of both types, and poor mental health are often associated with stigma and discrimination in the context of work [[13-15](#_ENREF_13)]. Highlighting the stresses and strains to which people diagnosed with diabetes may be subject serves to underline the need for workplace support, which is proven to protect people with diabetes against premature exit from paid employment [[16](#_ENREF_16)].

## Methods

Using population registers we established a cohort including all Danish adults aged 18 - 54 years, free of diabetes and no history of antidepressant use. No history of antidepressant use was operationalised as individuals having no record of a filled antidepressant prescription in the twelve months prior to their diagnosis with diabetes. This exclusion was undertaken to ensure the likelihood that the cases of filled antidepressant prescriptions captured in our analyses were related to diagnosis with diabetes rather than reflecting a previous history of antidepressant use, which aside from being a predictor for subsequent use of antidepressants has also been associated with an increased risk of developing type 2 diabetes [[17](#_ENREF_17)]. Diabetes status was determined by using the Danish National Diabetes Register (DNDR), a comprehensive and validated register [[18](#_ENREF_18), [19](#_ENREF_19)]. We identified filled antidepressant prescriptions in the Register of Medicinal Product Statistics [[20](#_ENREF_20)] by using all medications with the ATC- classification NO6A.

In order to follow PWD for five years after their diagnosis, inclusion of incident diabetes cases was suspended at 31 December 2005.

#### 2.1 Occupational Status

For each individual in the cohort, we identified their highest occupational status category in the study period according to the Register-based Labour Force Statistics [[21](#_ENREF_21)]. We adopted the International Labour Organisation hierarchical categorization of occupational status, which is built into the categorisations applied by Statistics Denmark: 1) High-skilled employment, 2) Executive Management, 3) Medium-skilled employment, 4) Basic-skilled employment, 5) Self-employed, 6) Unskilled employment, and 7) Unemployed.

**2.2 Statistical Analysis**

We analysed people whom we could follow for ≥5 years. The results indicate the number of people with newly diagnosed diabetes who started antidepressants within five years of their diabetes diagnosis. We stratified our analyses by occupational status and gender. In both cases, these stratifications were considered important, as both occupational status (low) and gender (female) are known risk factors for use of antidepressants.

The determination of statistical significance focussed on two distinct outcomes. First, we were interested in determining whether antidepressant use was evenly distributed throughout the follow-up period e.g. ~20% of cases in each year for the first five years after diagnosis with diabetes. Statistical significance was determined by using two-sided Fisher’s exact tests. In addition, using the highest ranked socioeconomic category in the different groups as the reference group and employing a two-sided Fisher’s exact test again, we examined differences in the proportion of all cases of filled antidepressant prescriptions observed during the follow-up period, which occurred in the first year after diagnosis with diabetes. Finally, we undertook interaction analyses to compare differences in the results between men and women using chi-squared testing.

## Results

From a potential study-population of 37,790 participants, 2,113 (5.6%) individuals were excluded because they had filled a prescription for antidepressants within one year prior to their diagnosis with diabetes. This resulted in a total study population comprising 35,677 participants; 20,158 (56.5%) men and 15,519 (43.5%) women. Mean age at entry was 43.2 years. 6,340 participants (17.8%) filled an antidepressant prescription during the study period. 3,742 of these participants could be followed for five years after their diagnosis with diabetes (Table 1).

The distribution of cases throughout the five year follow-up period indicates that filled prescriptions were proportionally higher in the first year after diagnosis of diabetes. For both men and women the distribution of cases throughout the five year follow-up period is significantly non-random for the first year after diagnosis (Figure 1).

In the analysis stratified by occupational class (Table 2) the proportion of individuals who fill antidepressant prescriptions ≤ 1 year after diagnosis with diabetes was similar for all occupational groups. However, at ≤ 5 years individuals in the occupational groups of lower socioeconomic status were more likely to have filled an antidepressant prescription. Conversely, when looking to the proportion of all individuals that had filled an antidepressant prescription ≤ 5 years after diagnosis, it was those from the occupational groups with higher socioeconomic status who were more likely to have done so at ≤ 1 year after diagnosis with diabetes.

Although the distribution of filled antidepressants prescriptions is significantly skewed toward ≤ 1 year overall, this was not the case for participants in the sub-groups ‘Executive management’, ‘Unskilled employment’ and ‘Unemployed’ indicating that they filled antidepressant prescriptions at a relatively consistent level throughout the five year period post-diagnosis with diabetes.

Using high-skilled employment as reference, we also sought to examine whether occupational class influenced the likelihood of filling a prescription for antidepressants at ≤ 5 years after diagnosis. The analysis revealed that participants in basic-skilled employment, unskilled employment and the unemployed were significantly more likely to have filled a prescription for antidepressants than those in high-skilled employment. In the case of men, those in basic-skilled employment who filled an antidepressant prescription ≤ 5 years after diagnosis with diabetes were significantly less likely to have done so after one year than those in high-skilled employment. For women significant differences were seen for unskilled employment and among the unemployed.

Overall, women were significantly more likely to fill antidepressant prescriptions than men within 5 years of a diagnosis with diabetes (p=<0.0001) (Table 3). Likewise, women were more likely to fill an antidepressant prescription in the first year after diagnosis with diabetes (p=0.005). Yet while women had significantly higher rates of filled antidepressants prescriptions throughout the follow-up period as a whole, of those who filled antidepressant prescriptions in the follow-up period, men were significantly more likely to do so in the first year after diagnosis with diabetes (p=0.013).

Although women had a significantly higher incidence of filled antidepressant prescriptions within the first year after a diagnosis of diabetes (p=0.005), this was only observed among basic-skilled employment (p=0.004). After five years of follow-up, there were significant differences between men and women in high-skilled employment, medium-skilled employment, basic-skilled employment and unskilled employment. In each case women were significantly more likely to have filled an antidepressant prescription.

## Discussion

Our results indicate that, within five years of a diagnosis of diabetes, around 1 in 10 people subsequently fills a prescription for antidepressants, with the highest risk being in the first year post-diagnosis. These findings accord with results presented elsewhere [[4](#_ENREF_4), [22](#_ENREF_22)]. The fact that we have restricted our analyses to the first five years after diagnosis is significant as the risk for developing late-stage complications of diabetes should be relatively low in this period and, for many with longer diabetes duration, it is treatment intensity [[23](#_ENREF_23)], complications [[24](#_ENREF_24)] and functional disability [[25](#_ENREF_25)] which drive the relationship between diabetes and the manifestation of depressive symptoms. It is important to emphasise, however, that we do not have data about the presence or otherwise of complications and comorbid conditions at the point of diagnosis with diabetes.

The fact that we have delimited our analyses to the working-age population is also of importance. In general, diabetes debut among women is significantly later than for men [[18](#_ENREF_18)] and thus proportionally more women than men will first develop diabetes after they have exited the labour market. Likewise, use of antidepressants in the population as a whole increases with age [[26](#_ENREF_26)], so an analysis investigating all adults with diabetes would, in all likelihood, identify even higher rates of filled antidepressant prescriptions in the first five years after diagnosis. Recognizing this limitation, we believe that there are important reasons for specifically investigating the use of antidepressants among people of working age recently diagnosed with diabetes.

It has previously been shown that, among those who articulate psychosocial problems at diagnosis, work-related concerns figure prominently [[27](#_ENREF_27)]. In this view, distress and anxiety about the anticipated impact of diabetes on work ability and income influence the development of depressive symptoms observed in the aftermath of diagnosis. Likewise, previous research has indicated that balancing the demands of work with the demands of managing diabetes can also be a source of psychological distress [[28](#_ENREF_28)]. The manifestation of depressive symptoms among people with newly diagnosed diabetes is, whatever the underlying cause, particularly concerning in view of the fact that both work disability [[29](#_ENREF_29)] and disability retirement [[30](#_ENREF_30)] among people with diabetes are significantly increased by mental health issues.

The incidence of filled antidepressant prescriptions in the first year following a diagnosis of diabetes was roughly equivalent across occupational classes. Occupational status thus had little apparent impact on antidepressant prescriptions at ≤ 1 year post diagnosis. It is noteworthy, however, that at five years after diagnosis there are significant differences according to occupational status, where we observe a social gradient familiar to studies of depression in the population as a whole [[31](#_ENREF_31)]. This suggests that diagnosis with a chronic disease such as diabetes may have a levelling effect in terms of a more general propensity towards the development of depression/depressive symptoms, but that this effect becomes attenuated with time.

In interpreting the results, it is necessary to acknowledge that they may reflect detection bias [[4](#_ENREF_4)], as people will be in more regular contact with their primary healthcare provider in the first year after diagnosis [[32](#_ENREF_32)]. It may be questioned, for example, to what extent the relative vulnerability of men in the first year after diagnosis is driven by detection bias, or whether they actually struggle more to come to terms with the acute stresses associated with diagnosis of chronic disease while still of working age. Likewise, it is impossible to determine if the use of antidepressants in the first year after diagnosis with diabetes can be ascribed to processes of adjustment or maladjustment. It has, for example, been proposed that some degree of negative arousal may be necessary in the process of coming to terms with a diagnosis of diabetes [[33](#_ENREF_33)] and actively addressing this with healthcare providers may lead to the prescription of antidepressants. Previous research has also shown that people of higher socioeconomic status will seek specialist care when confronted with health threats significantly more than others [[34](#_ENREF_34)].

It is also necessary to recognise the limitation of not being able to distinguish between type 1 and type 2 diabetes. Our inclusion criteria entail that the majority of cases of incident diabetes will be type 2, but some cases of type 1 diabetes will also be included in our results. Yet while we do not believe that cases of type 1 diabetes will impact on our overall findings, there is no doubt that, were such data available, it would be useful to undertake a separate analysis on cases of type 1 diabetes. At present, there is some evidence concerning the psychosocial challenges connected to the transition to work life among people with type 1 diabetes diagnosed in childhood, but to the best of our knowledge there is currently no evidence available indicating the extent to which people diagnosed with type 1 diabetes in adulthood are prone to depressive symptoms.

Finally, it must also be recognised that antidepressants have acquired a wider range of indications in recent years [[35](#_ENREF_35)], some of which are related to the treatment of somatic symptoms associated with diabetes, such as diabetes related polyneuropathy[[36](#_ENREF_36)]. However, we determined that excluding the antidepressants used to treat symptoms of neuropathy was not necessary in light of the fact that such symptoms would not be very prevalent in a population of people with relatively short duration of diabetes. Nonetheless, it cannot be discounted that some of the filled antidepressant prescriptions captured in our analysis were not indicated for the treatment of depressive symptoms. Acknowledging these limitations, we believe that the data we present makes an important contribution to this far from fully understood aspect of diabetes treatment.

Our findings support the view that the affective impact of diagnosis with a chronic illness is challenging [[37](#_ENREF_37), [38](#_ENREF_38)]. This points to a specific risk for the development of depressive symptoms among PWD that concerns the impact of the diagnosis itself and is independent from the risk for depressive symptoms driven by the wear and tear of living with the condition over time. Given what we now know of the deleterious effects that poor mental health has among PWD in the labour market, our findings support the view that a focus on an individual’s working situation and prospects in the clinical encounter, at or around the point at which they are diagnosed, could contribute to PWD being better able to achieve and maintain fulfilling and productive work lives.

The study suggests a complexity in pathways from diagnosis with diabetes to use of antidepressants. It seems important in a clinical context to establish supplementary information about the person with diabetes, to understand the psychosocial processes involved in their adjustment to life with the disease. Allowing for the fact that some degree of negative arousal may actually produce positive self-management behaviours, the extent to which people with diabetes are prescribed antidepressants still gives cause for concern. For while prescription of antidepressants among people with diabetes is common practice, the evidence for how to best manage medical and psychological outcomes simultaneously is not robust [[39](#_ENREF_39)]. More rigour with regard to generating relevant depression profiles [[40](#_ENREF_40)] and associating these with prescription practices would enhance quality of care in this regard. Early interventions addressing the mental wellbeing of people recently diagnosed with diabetes may serve to facilitate a process of adjustment and coping with the challenges posed by a life with the disease.

**Conflict of interest**: None declared

**Table 1: Descriptive Statistics**

|  |  |  |  |
| --- | --- | --- | --- |
| **No. of unique individuals in the dataset** | | | |
|  | **N cases of incident diabetes in study period** | **N filled antidepressant prescription ≤ 1 year post diabetes diagnosis** | **N filled antidepressant prescription ≤ 5 year post diabetes diagnosis** |
| All | 88,802 | 9,819 | - |
| Those who appear in dataset for at least 5 years | 35,677 | 6,340 | 3,742 |
| **Job status categorization** | **N** | **N with depression within 1 year** | **N with depression within 5 years** |
| High-skilled employee | 6,595 | 178 | 599 |
| Executive management | 1,708 | 36 | 127 |
| Medium-skilled employee | 5,450 | 139 | 542 |
| Low-skilled employee | 16,136 | 429 | 1,771 |
| Self-employed | 2,220 | 65 | 226 |
| Unskilled Employee | 3,051 | 80 | 372 |
| Unemployed | 517 | 15 | 91 |
| **Means** | | | |
| Men/Women | | 56.5% / 43.5% | |
| Age at Entry | | 43.2 | |
| Years in dataset | | 8.6 | |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table 2: Occupational status stratified analysis of filled antidepressant prescriptions for people with diabetes in the first five years after diagnosis with diabetes.** | **Filled antidepressant prescription ≤ 1 year (%)** | **Filled antidepressant prescription ≤ 5 years (%)** | **Share of filled antidepressant prescriptions at ≤ 5 years, which were filled at ≤ 1 year (%)** | **Different from random distribution of cases in each year after diagnosis, p-value** | **Different from high-skilled employment at ≤ 5 years, p-value** | **N** |
| **(a) Both men and women** | | | | | | |
| **All** | 2.6% | 10.4% | 25.3% | <0.001 | - | 35,677 |
| **1: High-skilled employment** | 2.7% | 9.1% | 29.7% | <0.001 | - | 6,595 |
| **2: Executive management** | 2.1% | 7.4% | 28.3% | 0.142 | 0.831 | 1,708 |
| **3: Medium-skilled employment** | 2.6% | 9.9% | 25.6% | 0.030 | 0.129 | 5,450 |
| **4: Basic skilled-employment** | 2.7% | 11.0% | 24.2% | 0.003 | 0.009 | 16,136 |
| **5: Self-employed** | 2.9% | 10.2% | 28.8% | 0.037 | 0.864 | 2,220 |
| **6: Unskilled employment** | 2.6% | 12.2% | 21.5% | 0.651 | 0.006 | 3,051 |
| **7: Unemployed** | 2.9% | 17.6% | 16.5% | 0.701 | 0.008 | 517 |
| **(b) Men** | | | | | | |
| **All** | 2.4% | 9.0% | 27.1% | <0.001 | - | 20,158 |
| **1: High-skilled employment** | 2.5% | 7.8% | 32.0% | 0.002 | - | 3,498 |
| **2: Executive management** | 2.2% | 7.0% | 31.9% | 0.096 | 1.000 | 1,352 |
| **3: Medium-skilled employment** | 2.3% | 8.1% | 28.2% | 0.058 | 0.376 | 2,713 |
| **4: Basic skilled-employment** | 2.3% | 9.4% | 24.8% | 0.019 | 0.023 | 9,363 |
| **5: Self-employed** | 2.9% | 9.7% | 29.9% | 0.042 | 0.673 | 1,726 |
| **6: Unskilled employment** | 2.7% | 10.8% | 24.8% | 0.412 | 0.149 | 1,419 |
| **7: Unemployed** | 4.6% | 20.7% | 22.2% | 1.000 | 0.446 | 87 |
| **(c) Women** | | | | | | |
| **All** | 2.9% | 12.4% | 23.5% | 0.009 | - | 15,519 |
| **1: High-skilled employment** | 2.9% | 10.6% | 27.8% | 0.022 | - | 3,097 |
| **2: Executive management** | 1.7% | 9.3% | 18.2% | 1.000 | 0.305 | 356 |
| **3: Medium-skilled employment** | 2.8% | 11.8% | 23.9% | 0.253 | 0.282 | 2,737 |
| **4: Basic skilled-employment** | 3.1% | 13.1% | 23.6% | 0.075 | 0.135 | 6,773 |
| **5: Self-employed** | 3.0% | 11.9% | 25.4% | 0.662 | 0.754 | 494 |
| **6: Unskilled employment** | 2.6% | 13.4% | 19.2% | 0.904 | 0.025 | 1,632 |
| **7: Unemployed** | 2.6% | 17.0% | 15.1% | 0.517 | 0.026 | 430 |

Table 3: Interaction Analysis of differences between men and women

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Filled antidepressant prescription ≤ 1 year (%)**  **Men vs. Women, p-value** | **Filled antidepressant prescription ≤ 5 years (%)**  **Men vs Women,**  **p-value** | **Share of filled antidepressant prescriptions at ≤ 5 years, which were filled at ≤ 1 year (%)**  **Men vs. Women,**  **p-value** |
| **All** | 0.005 | <0.0001 | 0.013 |
| **1. High-skilled employee** | 0.293 | 0.0001 | 0.282 |
| **2. Executive management** | 0.677 | 0.171 | 0.179 |
| **3. Medium-skilled employee** | 0.250 | <0.0001 | 0.272 |
| **4. Low-skilled employee** | 0.004 | <0.0001 | 0.580 |
| **5. Self-employed** | 0.991 | 0.166 | 0.616 |
| **6. Unskilled Employee** | 0.947 | 0.030 | 0.201 |
| **7. Unemployed** | 0.494 | 0.499 | 0.486 |

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