Depression is independently associated with increased length of stay and readmissions in multimorbid inpatients

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Abstract: Little is known about the impact of depression across a broad range of multimorbid patients hospitalized for reasons other than depression. The objective of the study was to investigate in a large sample of multimorbid inpatients whether ancillary depression is associated with increased length of stay (LOS) and readmissions, two important clinical outcomes with implications for healthcare utilization and costs. METHODS: We retrospectively analyzed a cohort of 253,009 multimorbid inpatients aged 18 at an academic medical center, 8/2009-8/2017. PRIMARY OUTCOME: LOS. SECONDARY OUTCOMES: LOS related to different main diagnoses, readmissions within 1, 3, 6, 12, and 24-months after discharge. RESULTS: Multivariable linear regression showed 24% longer LOS in patients with ancillary depression (1.24; 95% confidence interval [CI]: 1.22, 1.25). Females stayed 22% longer (1.22; 95% CI: 1.20, 1.25), males 24% (1.24; 95% CI: 1.22, 1.27). We identified 16 main diagnosis clusters in which ancillary depression was associated with significant LOS increases, with associations being strongest for "Failure and rejection of transplanted organs and tissues", "Other noninfective gastroenteritis and colitis", and "Other soft tissue disorders, not elsewhere classified". Multivariable logistic and Poisson regression showed independent associations of ancillary depression with increased readmission odds and frequencies at 1, 3, 6, 12, and 24 months. CONCLUSIONS: Ancillary depression was independently associated with increased LOS and more readmissions across a broad range of multimorbid inpatients.

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Abstract

Background: Little is known about the impact of depression across a broad range of multimorbid patients hospitalized for reasons other than depression. The objective of the study was to investigate in a large sample of multimorbid inpatients whether ancillary depression is associated with increased length of stay (LOS) and readmissions, two important clinical outcomes with implications for healthcare utilization and costs.

Methods: We retrospectively analyzed a cohort of 253,009 multimorbid inpatients aged ≥18 at an academic medical center, 8/2009-8/2017. Primary outcome: LOS. Secondary outcomes: LOS related to different main diagnoses, readmissions within 1, 3, 6, 12, and 24-months after discharge.

Results: Multivariable linear regression showed 24% longer LOS in patients with ancillary depression (1.24; 95% confidence interval [CI]: 1.22, 1.25). Females stayed 22% longer (1.22; 95% CI: 1.20, 1.25), males 24% (1.24; 95% CI: 1.22, 1.27). We identified 16 main diagnosis clusters in which ancillary depression was associated with significant LOS increases, with associations being strongest for “Failure and rejection of transplanted organs and tissues”, “Other noninfective gastroenteritis and colitis”, and “Other soft tissue disorders, not elsewhere classified”. Multivariable logistic and Poisson regression showed independent associations of ancillary depression with increased readmission odds and frequencies at 1, 3, 6, 12, and 24 months.

Conclusions: Ancillary depression was independently associated with increased LOS and more readmissions across a broad range of multimorbid inpatients.

Background

Depression is one of the largest contributors to global disease burden [1]. Its prevalence ranges between 3-10% in the general population, [2,3] 10% in primary care, [4,5] and 10-15% in hospitalized patients [6]. Depression often co-occurs with chronic physical diseases [7]. There is considerable variation in the rates of comorbid depression in specific diseases, with higher rates of prevalence of depression in a range of diseases including cancer (11%), [8] Parkinson's disease (17%), [9] acute coronary syndrome (19%), [10] arthritis (10-24%), [11] stroke (31%), [12] and diabetes (11-31%) [13].

The risk for depression is increased among multimorbid patients, [14] and the impact of depression on health is most severe when it co-occurs with physical disease [15,16]. Comorbid depression is associated with poorer physical functioning and quality of life, [17,18] greater disability, [19] and higher rates of mortality, [20,21] compared with those with depression only or physical disease only. The relationship between comorbid depression and physical disease is considered to be bidirectional, [22] with comorbid depression elevating the risk for physical diseases, such as diabetes, [23] stroke [24] and dementia, [25] and physical diseases elevating the risk of developing comorbid depression [14]. For example, the likelihood of depression increases threefold after a heart attack [26] and the risk of cardio-vascular disease increases by up to 90% in patients when there is comorbid depression [27].

The overall impact of comorbid depression with physical disease is reflected in higher resource utilization and healthcare costs [28]. A number of studies have reported the impact of comorbid depression on resource utilization and healthcare costs for specific populations, especially in high utilization populations such as diabetes, [29] pain [30] and cancer [31]. However, the impact on utilization and costs of comorbid depression as an ancillary condition

in multimorbid hospitalized patients with a primary diagnosis other than depression has received scant attention [32]. Nevertheless, this is of particular interest in the DRG era, since the primary diagnosis is usually the reason for hospital admission and is considered the most resource-intensive condition. If ancillary depression is evaluated as the less resource-intensive condition, it would be important to ascertain whether it systematically elevates resource utilization. Should this be that case, this would give impetus to further studies designed to establish the reasons for this and ways to improve patients and hospital outcomes.

The objective of this study was to investigate among a broad range of multimorbid hospitalized patients, whether depression as an ancillary diagnosis is associated with increased length of stay (LOS) and readmissions, two important clinical outcomes which also reflect healthcare utilization and costs [33].

Methods

Design and study period

We conducted a retrospective cohort study of all stays of patients discharged from our hospital between August 1st, 2009 and August 31st, 2017. Stays of patients who died during their stay were not considered. We derived our dataset from electronic health records, that is, we used routinely and prospectively collected data. The present investigation used completely anonymous data and conformed with the local law as well as the ethical review and research policies. Our study adhered to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [34].

Setting

The University Hospital Zurich is a tertiary care academic medical center in Switzerland with approximately 850 beds and 35,000 admissions per year. It covers all clinical specialties except orthopedic surgery and pediatrics.

The University Hospital Zurich has a consultation-liaison psychiatric service which is also in charge of the center for eating disorders. This center provides 12 beds in proximity to the University Hospital Zurich. That setting was not considered as a clinical inpatient unit in the present study and these patients were therefore excluded. Thus, a total of 31 clinical units cared for the analyzed patients.

Participants

We included all multimorbid inpatients aged ≥18. Multimorbidity was defined as the presence of two or more diagnoses [35]. Patients with only one diagnosis, patients who

were multimorbid due to one main diagnosis plus ancillary depression, and patients with depression as their main diagnosis were excluded. Overall, only 9% (n=25,011) of patients normally discharged from the considered inpatient units were excluded from our analyses (cf. Supplementary Figure SF1).

Main outcomes and measures

The primary end point was the impact of ancillary depression on LOS. An additional subgroup analysis provided a more detailed examination of this outcome. We stratified the subgroup analysis by sex (further data on patient characteristics stratified by sex is presented in Supplementary Table ST1 as recommended [36]). Regarding that subgroup analysis, we stratified the continuous variable age into five groups.

Of note, we used the natural logarithm to transform the outcome variable due to the skewed distribution of LOS, thereby generating a normal distribution, as described elsewhere [37]. This transformation allowed the application of linear regression models to investigate the association of ancillary depression with our main outcome. The resulting estimated coefficients from the log-transformed outcome were back-transformed by raising *e* to the power of the coefficients. The back-transformed coefficients could then be interpreted as percentage increases or decreases (e.g. a back-transformed coefficient resulting in a value of 1.24 for ancillary depression would indicate a 24% longer stay).

Secondary end points included the effect of ancillary depression on LOS in patients among main diagnosis groups, and, the association with readmissions within 1 month (30 days), 3 months, 6 months, 12 months and 24 months after discharge of the patients.

We report main diagnosis groups as ICD-10 categories according to the first three digits of the ICD-10 codes (International Classification of Diseases, WHO, Geneva, Switzerland). We considered each main diagnosis group if at least 25 stays of patients with ancillary depression were in the group (resulting in 135 [11%] groups of a total of 1275 distinct main diagnosis groups). Those main diagnosis categories were further analyzed for the secondary end point of the effect of ancillary depression on LOS in patients with specific main diagnoses.

The number of patients considered in the readmission analyses varied depending on the time frames considered for the following reasons: If a patient was admitted on 3rd of August 2017, no complete information was available as to whether the patient was readmitted within 30 days. Similarly, we were unable to calculate the number of previous admissions in the past two years if a patient was admitted in 2010. For the readmission analyses, we therefore excluded patients with incomplete data.

Exposure

The exposure of interest was depression as an ancillary diagnosis and not as the main diagnosis. The first diagnosis in the diagnosis list as defined by the providers was usually the main diagnosis, which was additionally flagged as such in the available dataset.

Depression was defined by the ICD-10 diagnosis codes F20.4, F31.3-F31.5, F32*, F33*, F34.1, F41.2, and F43.2* (asterisk means zero or more digits) [38].

Co-variables

Co-variables were included in the regression models according to *a priori* knowledge and literature [39–42]. We controlled for multimorbidity severity by adjusting for diagnosis count [43].

Multivariable linear regression modelling of the association of ancillary depression with a longer LOS adjusted for age, sex, marital status, diagnosis count (excluding depression), year discharged, and six chronic diseases (alcohol misuse [44], metastatic cancer [45,46], chronic heart failure [47], chronic pain [48], diabetes, [49] all defined by [50], and COPD [51] defined by ICD-10 codes J43* or J44*). For the secondary analysis related to LOS, that is depending on main diagnoses, the models were adjusted for the same co-variables where appropriate.

Multivariable logistic regression and Poisson regression modelling of the association of ancillary depression with a readmission as a single event, and further with higher numbers of readmissions, respectively, were all adjusted for age, sex, marital status, LOS, diagnosis count (excluding depression), year discharged, the number of previous stays (past two years), and the same six chronic diseases as listed above.

Statistical analysis

Descriptive statistics for baseline characteristics included medians and interquartile ranges for variables with a non-normal distribution. Numbers and percentages of the total were given for categorical variables. We performed comparative statistical analysis to describe patients without versus with ancillary depression. We used unpaired Wilcoxon tests to compare the distributions of continuous variables between patients without versus with ancillary depression, and chi-square tests to compare categorical variables between groups.

We considered a p-value of ≤0.05 as indicating statistical significance for the primary end point. However, we conservatively controlled for multiple testing in all secondary end point analyses by using the Bonferroni correction. For instance, the respective value for the analyses of main diagnosis categories had to be ≤0.00037 (0.05/135), since we ran 135 regression models to test 135 distinct main diagnoses.

We performed statistical analyses using the software R, version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 278,020 inpatients were normally discharged during the study period. Of those, 25,011 patients were excluded, leaving 91% of the total number of considered inpatient stays for further analysis (Supplementary Figure SF1). The baseline characteristics are presented in Table 1.

Primary end point

The unadjusted linear regression model resulted in an increased LOS by 56% (1.56; 95% confidence interval [CI]: 1.53, 1.58) associated with ancillary depression in multimorbid hospitalized patients. After adjusting for co-variables, the multivariable linear regression model showed that ancillary depression was independently associated with a 24% increase of the LOS (Table 2). Of note, each diagnosis in this model resulted in an additional 10% increase of the LOS.

Overall, the adjusted model for the female patients resulted an increase of the LOS by 22% (1.22; 95% CI: 1.20, 1.25), the model for the males showed an increase by 24% (1.24; 95% CI: 1.22, 1.27).

The primary outcome was further examined in a subgroup analysis, stratified by sex (Figure 1). The association of ancillary depression with a longer LOS among males with other/unknown marital status was statistically insignificant. The only subgroup with a potential reduction of LOS associated with ancillary depression was females with alcohol misuse, however, that association was statistically insignificant, too. All other subgroups showed statistically significant associations of ancillary depression with longer LOS. Ancillary depression seemed to increase LOS more among patients aged ≥65 than for the patients

aged ≤49. In the subgroup of patients with metastatic cancer, ancillary depression seemed to increase LOS the most, for both sexes.

Secondary end points

Main diagnoses

After controlling for multiple testing, 16 main diagnosis categories showed a statistically significant association of ancillary depression with increased LOS (Figure 2).

The top LOS increases were identified for the main diagnosis categories “Failure and rejection of transplanted organs and tissues” (ICD-10 code category T86; predominantly concerning lung transplants; LOS increased by 121%), “Other noninfective gastroenteritis and colitis” (K52; e.g. drug-induced gastroenteritis and colitis; LOS increased by 75%), and “Other soft tissue disorders, not elsewhere classified” (M79; e.g. fibromyalgia; LOS increased by 69%).

Readmissions

After adjusting for co-variables, the logistic regression models showed that ancillary depression was independently associated with an increase in the odds of being readmitted within 1 month (30 days), 3 months, 6 months, 12 months, and 24 months after discharge. Depressed patients were also more frequently readmitted, as demonstrated by adjusted Poisson regression models (Table 3).

Discussion

The present study shows that ancillary depression is independently associated with increased LOS and more frequent readmissions in multimorbid hospitalized patients in which a physical disease is the primary diagnosis. These results still apply after controlling for the influence of several potentially confounding factors, including demographics and physical comorbidities. The findings of this study highlight ancillary depression as an important contributory factor in resource utilization among multimorbid hospitalized patients with a primary, non-psychiatric diagnosis.

We investigated a comprehensive range of multimorbid inpatients with a main diagnosis other than depression. Our cohort was large and included more than 90% of all inpatients normally discharged from our institution over the course of approximately eight years. The routinely and prospectively collected electronic health record data enabled us to run adjusted regression models comparing depressed patients to those without depression. In an innovative analysis, we identified 16 main diagnosis clusters in which ancillary depression was associated with particularly substantial LOS increases.

Similar studies, but with considerably smaller sample sizes, investigated the additive effect of psychiatric diseases, including depression, on LOS. They observed increases in LOS by 2.6 to 2.8 days [52,53] due to psychiatric diseases. A recent meta-analysis pooled data of 5,044 inpatients and calculated that depressed patients had an additional LOS of 4.38 days [54]. Only two studies that reported a positive relationship between depression and LOS used both non-psychiatric diagnoses as index and a similarly broad selection of non-psychiatric diagnoses [55,56]. In one of these two studies, [55] scores from a self-report instrument for depression severity did correlate positively with LOS, but the psychiatric

diagnosis for depression did not. In the other study, [56] which is partially comparable to the present study, there was a significant effect of “mood disorder” on LOS but of only 0.26 days. However, it seems the authors did not account for the skewed distribution of LOS.

In our study, the effect of depression on LOS may have multiple reasons. Generally, depression associates with the severity and complexity of disease management of concurrent conditions [14,22,57,58]. Patients with comorbid depression have more medical symptoms (after controlling for the severity of non-psychiatric conditions) in diseases such as diabetes, cardiac disease, and arthritis [59,60]. Somatization makes diagnosis and disease management more difficult. Physical disorders may have a poorer treatment response in patients with concurrent depression [61]. Poorer treatment response may be due in part to effects of polypharmacy and drug-drug and drug-disease interactions and complications [22,62–65]. Symptoms of depression such as loss of interest and energy and poor concentration may impact treatment adherence, physical functioning, and recovery during the hospital stay [17,18,66].

We found only studies with small sample sizes that have investigated the impact of depression on readmissions. The finding that a secondary diagnosis of depression is associated with more frequent readmissions is consistent with studies for psychiatric comorbidity in general [67] and those that specifically examined the role of depression in readmissions. One study on 374 patients with congestive heart failure found that depression increased the risk for readmission at three and twelve months [68]. Another study on 273 medical and surgical inpatients report a two-fold increase in days re-hospitalized over four years [67]. A further study that included 144 medical patients reported a three-fold increase in the likelihood of readmission due to depression [69]. The few studies on elderly patients show increase likelihood of readmission due to a history of depression or current depressive

symptoms [70,71]. Considered together, our and these findings are consistent in showing that depression is a major risk factor for hospital readmission.

The reasons for depression as a risk factor for hospital readmission are not well studied. Depression is associated with poor adherence to medication and behavioural regimens, including diet and exercise, which lead to or contribute to readmission [72–75]. One review suggests that depression is associated with a lack of social support that might otherwise facilitate recovery after discharge, [76,77] reduce stressful events, [78] or increase positive symptoms both before or after hospital discharge [76,79]. Pre-existing or post-discharge depression may impair recovery of activities of daily living (ADL) function [66,80]. Comorbid depression is also associated with complications such as in diabetes or new cardiovascular events [63,64]. Somatization and symptom overlap of physical disease and depression may render diagnosis and disease management more difficult and enhance likelihood of readmission [69,81,82].

Limitations

Limitations of this study should be noted. First, this was a single center study. On the one hand, generalizability of results from a single institution is often lower than from multi-center studies. On the other hand, inclusion of more than 90% of a large inpatient cohort over a long time period may enhance generalizability. More specific patient populations are referred to our hospital and there is a bias towards multimorbidity and complexity which may include psychiatric comorbidity. Also, some of our patients will have been readmitted to other institutions. However, readmissions to other hospitals would most likely not have biased our conclusions. Second, this was a retrospective analysis of electronic health record data. Yet these data were routinely and prospectively collected. In this study, the diagnosis

of depression was based on ICD-10 codes that are added to the diagnosis lists by professional ICD-10 coding staff after the patients are discharged. This procedure does not allow to analyze changes of severity of depression over time during hospital stays. Such an analysis may have provided further insights into the relationship between ancillary depression and LOS. Third, no prospective screening of depression was performed during the study period. In fact, the hospital in which the data were collected does not routinely screen for depression. This might explain the low rate of prevalence of depression in our dataset (4.9%) compared with a prevalence of 12% averaged across numerous studies on hospitalized patients [6]. While our study focused on patients with a recognized diagnosis of depression, the low rates of depression suggest that there may be underdiagnosis of depression, and it can be assumed that severe cases had been more likely to be diagnosed. However, low rates of detection are not unusual in hospitalized patients, [83,84] especially in specific disease populations, such as diabetes or cancer [61,85]. Fourth, our models did not control for the potential confounders education level, disability measures, and drug treatment (e.g. use of antidepressants). Interestingly, a recent study by Angermann et al. [86] showed no benefit of escitalopram in terms of mortality, hospitalization, or depression improvement among patients with chronic heart failure and depression.

Implications and conclusions

The present study suggests important implications on clinical care and resource use: Depression may determine worse clinical outcomes among multimorbid inpatients, independent of the main diagnosis. According to our results, depression could be considered a risk marker that should be more actively detected, diagnosed and coded, whereas its role as a modifiable risk factor in subjects with multimorbidity has yet to be investigated. Therefore, whether screening for, targeted treatment, and ongoing monitoring of

depression in selected inpatient populations may reduce LOS and readmissions should be object of further study.

In conclusion, based on a large cohort with a broad range of multimorbid inpatients, ancillary depression was independently associated with longer LOS and readmissions, after controlling for potentially confounding factors. This study augments the dearth of comparable data on multimorbid patients with concurrent depression and LOS and adds support to available studies on readmissions. This study indicates that ancillary depression is an important contributory factor in resource utilization among multimorbid inpatients with a primary, non-psychiatric diagnosis. Further studies are needed in order to confirm our findings, improve our understanding of the relationship between ancillary depression, healthcare utilization, and health outcomes, and to identify ways needed to improve outcomes in this fragile, multimorbid population.

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Competing interests statement

The authors declare no competing interests.

Contributorship statement

PEB and EB conceived this study. PEB and UH designed the study, PEB processed the data and performed the statistical analyses. PEB, MC, UH and EB interpreted data. PEB drafted previous versions, PEB and MC drafted the final version of the manuscript, with MC, UH and EB critically commenting on the drafts. All authors approved the final submitted version of the manuscript.

Ethics approval

The present investigation used completely anonymous data and conformed with the local law and the ethical review and research policies.

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Figures and tables

Table 1. The baseline characteristics.

	No depression (n=240,574)	Ancillary diagnosis of depression (n=12,435)	*P* value	Overall (n=253,009)
Demographics				
Age, median years [IQR]	57.00 [38.00, 70.00]	56.00 [44.00, 67.00]	0.07	57.00 [38.00, 70.00]
Female sex, n (%)	121317 (50.4)	6934 (55.8)	<0.001	128251 (50.7)
Marital status, n (%)			<0.001	
Married/partnered	131953 (54.8)	5573 (44.8)		137526 (54.4)
Single	51701 (21.5)	2816 (22.6)		54517 (21.5)
Widowed/divorced/separated	50858 (21.1)	3725 (30.0)		54583 (21.6)
Other/unknown	6062 (2.5)	321 (2.6)		6383 (2.5)
Number of diagnoses*, median [IQR]	5.00 [3.00, 8.00]	7.00 [4.00, 11.00]	<0.001	5.00 [3.00, 8.00]
Comorbidities				
Alcohol misuse, n (%)	6514 (2.7)	1053 (8.5)	<0.001	7567 (3.0)
Metastatic cancer, n (%)	17530 (7.3)	1090 (8.8)	<0.001	18620 (7.4)
Chronic heart failure, n (%)	15587 (6.5)	1025 (8.2)	<0.001	16612 (6.6)
Chronic pain, n (%)	8582 (3.6)	1623 (13.1)	<0.001	10205 (4.0)
Diabetes, n (%)	26783 (11.1)	1887 (15.2)	<0.001	28670 (11.3)
COPD, n (%)	9169 (3.8)	804 (6.5)	<0.001	9973 (3.9)
Outcomes				
Length of stay, median days [IQR]	5.00 [3.00, 9.00]	9.00 [4.00, 17.00]	<0.001	5.00 [3.00, 9.00]
Had a 30-day readmission, n (%)	31592 (13.3)	2031 (16.5)	<0.001	33623 (13.4)

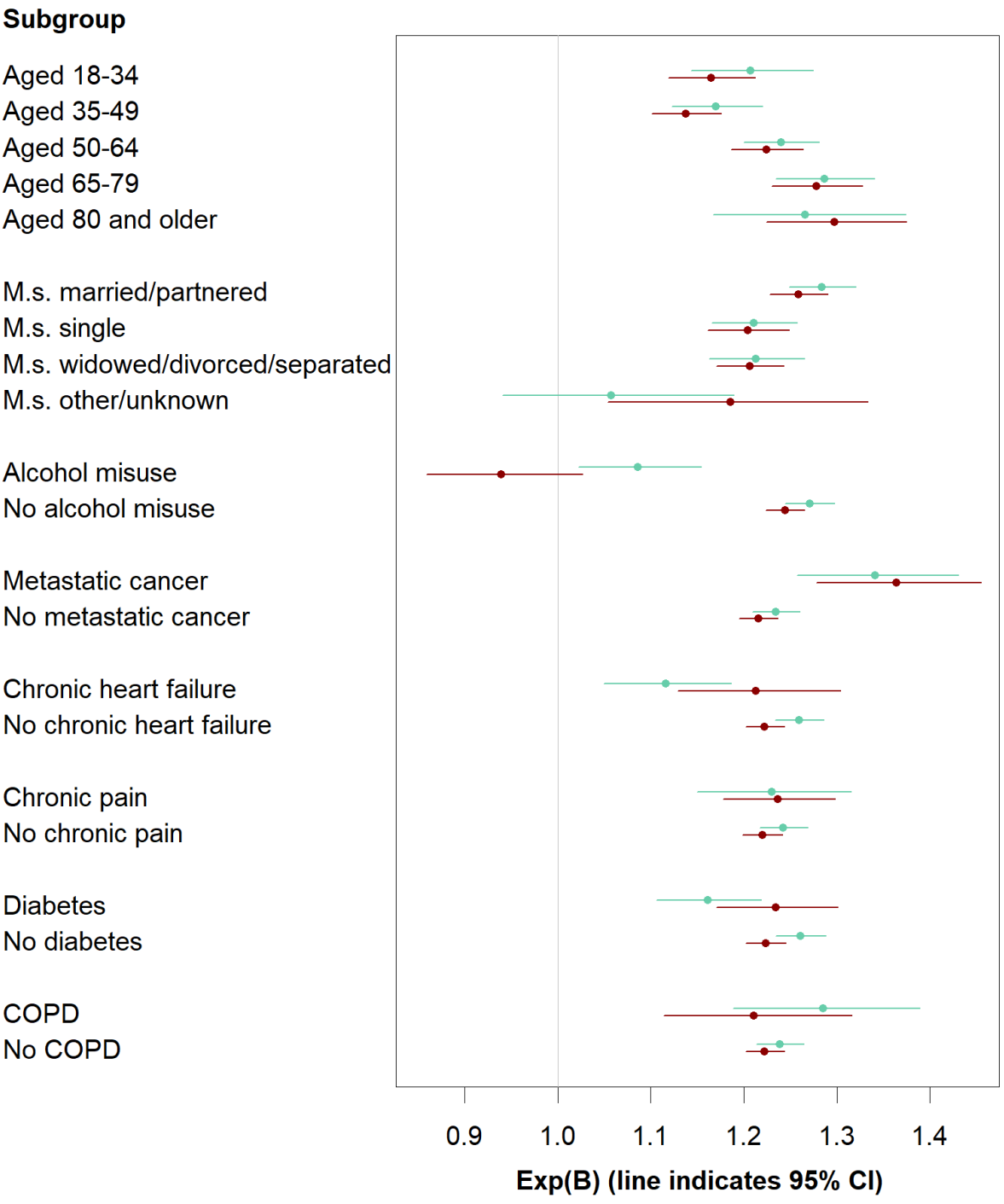
*The number of diagnoses excludes depression. IQR: interquartile range. COPD: Chronic obstructive pulmonary disease.

Table 2. Adjusted multivariable linear regression. Ancillary depression was independently associated with an increased LOS in multimorbid hospitalized patients.

Variable	Exp(B)	(95% CI)
Ancillary depression	1.24	(1.22,1.25)
Age, per additional year	1.00	(1.00,1.00)
Female sex	1.03	(1.03,1.04)
Marital status		
Married/partnered	ref	
Single	0.97	(0.96,0.97)
Widowed/divorced/separated	0.99	(0.98,0.99)
Other/unknown	0.98	(0.96,1.00)
Number of diagnoses, per additional diagnosis*	1.10	(1.10,1.10)
Year discharged	0.99	(0.99,0.99)
Alcohol misuse	0.88	(0.87,0.90)
Metastatic cancer	1.15	(1.14,1.17)
Chronic heart failure	0.91	(0.90,0.92)
Chronic pain	1.23	(1.21,1.24)
Diabetes	0.86	(0.85,0.87)
COPD	1.00	(0.99,1.02)

LOS: length of stay. 95% CI: 95% confidence interval. *The number of diagnoses excludes depression. COPD: Chronic obstructive pulmonary disease.

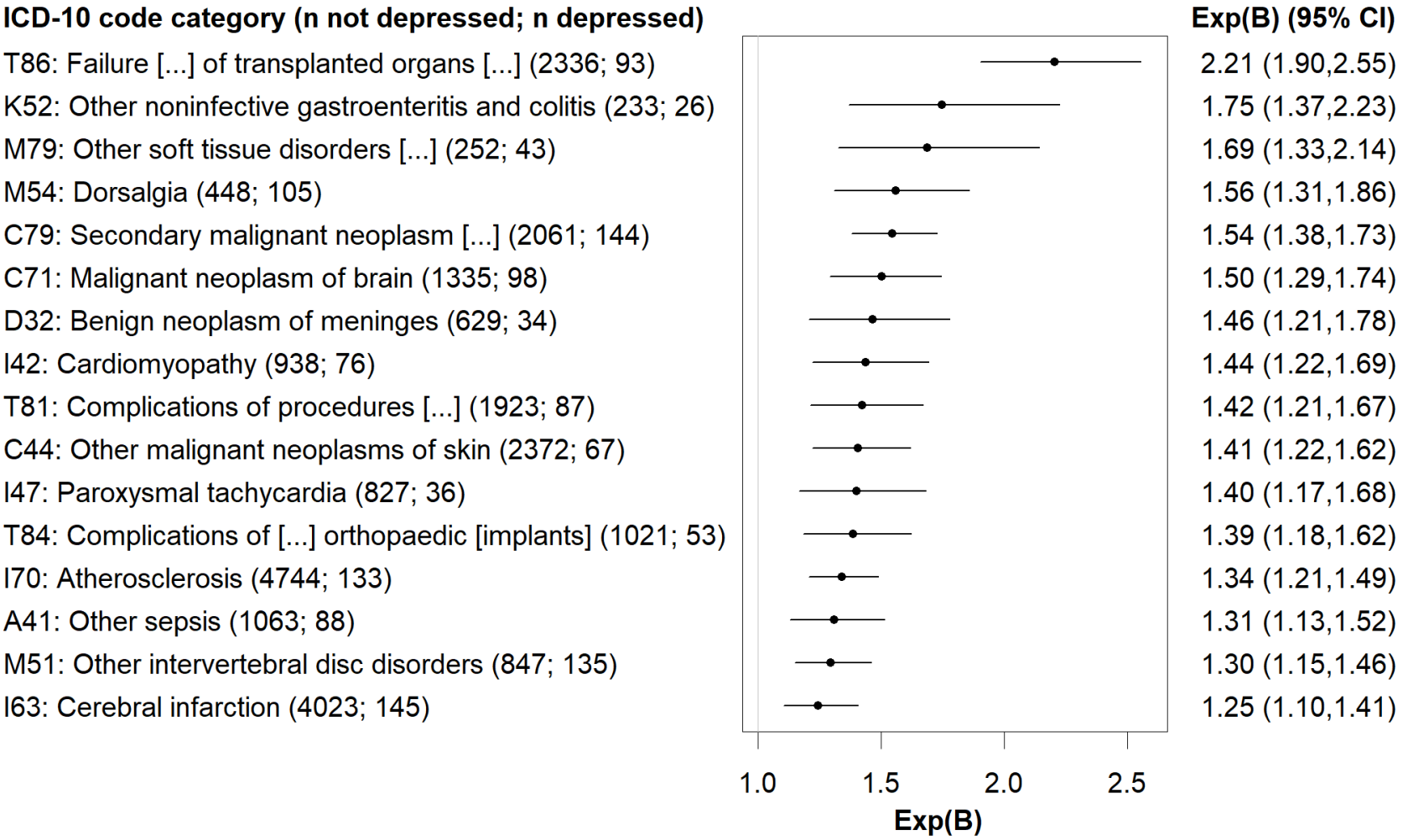
Figure 1. Subgroup analysis of the association of ancillary depression with increased LOS. Each subgroup model was adjusted, where appropriate, for age, marital status, diagnosis count (excluding depression), year the patient was discharged, and for six chronic diseases.



Red (dark): female patients. Aquamarine (bright): male patients.

LOS: length of stay. COPD: Chronic obstructive pulmonary disease. 95% CI: 95% confidence interval.

Figure 2. After controlling for multiple testing with the Bonferroni correction, 16 out of 135 main diagnosis categories showed statistically significant associations of ancillary depression with increased LOS. In parentheses on the left of the figure are the numbers of not depressed and depressed patients shown, respectively. Only main diagnosis categories were considered if at least 25 patients per subgroup had ancillary depression (n=135). Each subgroup model was adjusted, where appropriate, for age, sex, marital status, diagnosis count (excluding depression), year the patient was discharged, and for six chronic diseases.



LOS: length of stay. n: number of stays of patients. 95% CI: 95% confidence interval.

Table 3. All analyzed time frames showed a statistically significant association of ancillary depression with a readmission event (logistic regression) as well as higher frequencies of readmissions (Poisson regression). These associations stayed valid after applying Bonferroni correction.

	Overall		Patients with ancillary depression		Multivariable logistic regression			Multivariable Poisson regression		
Readmission time frame	Stays considered (% of total study population)	At least 1 readmission (%)	Stays (% of overall considered stays)	At least 1 readmission (%)	Odds ratio (readmission)	95% CI	p value	Relative risk (number of readmissions)	95% CI	p value
30-day	191613 (76)	25417 (13)	9985 (5)	1703 (17)	1.13	(1.07,1.20)	<0.001	1.12	(1.07,1.18)	<0.001
3-month	185894 (73)	40973 (22)	9689 (5)	2726 (28)	1.12	(1.06,1.17)	<0.001	1.14	(1.11,1.18)	<0.001
6-month	177197 (70)	49622 (28)	9215 (5)	3305 (36)	1.15	(1.09,1.21)	<0.001	1.16	(1.13,1.20)	<0.001
12-month	159882 (63)	54814 (34)	8262 (5)	3607 (44)	1.18	(1.13,1.25)	<0.001	1.19	(1.17,1.22)	<0.001
24-month	126366 (50)	52014 (41)	6364 (5)	3242 (51)	1.19	(1.13,1.26)	<0.001	1.21	(1.18,1.24)	<0.001

Ancillary depression was independently associated with (i) readmissions and (ii) higher numbers of readmissions. All models adjusted for age, sex, marital status, LOS, diagnosis count (excluding depression), year the patient was discharged, number of previous stays (within prior two years), and six chronic conditions. Only stays with complete information in respect of prior stays and potential readmission events were considered (depending on analyzed time frame).

95% CI: 95% confidence interval. LOS: length of stay.

Supplementary online material

Supplementary Table ST1. The baseline characteristics stratified by sex.

	Females (n=128,251)	Males (n=124,758)	*P* value	Overall (n=253,009)
Depression as ancill ary diagnosis, n (%)	6934 (5.4)	5501 (4.4)	<0.001	12435 (4.9)
Demographics				
Age, median years [IQR]	50.00 [34.00, 69.00]	61.00 [47.00, 71.00]	<0.001	57.00 [38.00, 70.00]
Marital status, n (%)			<0.001	
Married/partnered	66743 (52.0)	70783 (56.7)		137526 (54.4)
Single	25988 (20.3)	28529 (22.9)		54517 (21.5)
Widowed/divorced/separated	32950 (25.7)	21633 (17.3)		54583 (21.6)
Other/unknown	2570 (2.0)	3813 (3.1)		6383 (2.5)
Number of diagnoses*, median [IQR]	5.00 [3.00, 8.00]	5.00 [3.00, 9.00]	<0.001	5.00 [3.00, 8.00]
Comorbidities				
Alcohol misuse, n (%)	1865 (1.5)	5702 (4.6)	<0.001	7567 (3.0)
Metastatic cancer, n (%)	8095 (6.3)	10525 (8.4)	<0.001	18620 (7.4)
Chronic heart failure, n (%)	5916 (4.6)	10696 (8.6)	<0.001	16612 (6.6)
Chronic pain, n (%)	5752 (4.5)	4453 (3.6)	<0.001	10205 (4.0)
Diabetes, n (%)	9757 (7.6)	18913 (15.2)	<0.001	28670 (11.3)
COPD, n (%)	3270 (2.5)	6703 (5.4)	<0.001	9973 (3.9)
Outcomes				
Length of stay, median days [IQR]	5.00 [3.00, 9.00]	5.00 [3.00, 10.00]	0.179	5.00 [3.00, 9.00]
Had a 30-day readmission, n (%)	14494 (11.4)	19129 (15.5)	<0.001	33623 (13.4)

*The number of diagnoses excludes depression. IQR: interquartile range. COPD: Chronic obstructive pulmonary disease.

Supplementary Figure SF1. The study flow diagram. Monomorbid patients and those being multimorbid only due to ancillary depression (n=24,839) were excluded. Patients with depression as main diagnosis (n=172) were also excluded.