Original Article

Challenges in the Transition from In-Patient to Out-Patient Treatment in Depression

An Analysis of Administrative Health Care Data From a Large German Health Insurer

Hauke Felix Wiegand, Joachim Saam, Ursula Marschall, Andrea Chmitorz, Levente Kriston, Mathias Berger, Klaus Lieb, Lars P. Hölzel

Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Mainz, Germany: Hauke Felix Wiegand, MD/PhD, Prof. Dr. med. Klaus Lieb

Department of Medicine and Health Services Research, BARMER Statutory Health Insurance Fund, Wuppertal, Germany: Joachim Saam, Dr. med. Ursula Marschall

Faculty of Social Work, Health and Nursing Sciences, Esslingen University of Applied Sciences, Esslingen, Germany: Prof. Dr. rer. biol. hum. Andrea Chmitorz

Department of Medical Psychology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany: PD Dr. phil. Levente Kriston

Department of Psychiatry and Psychotherapy, University Hospital Freiburg, Freiburg, Germany: Prof. Dr. med. Mathias Berger

Oberberg Parkklinik Wiesbaden Schlangenbad, Wiesbaden, Germany: Dr. phil. Lars P. Hölzel

Summary

Background: Few data are available on the characteristics of inpatient treatment and subsequent outpatient treatment for depression in Germany. In this study, we aimed to characterize the inpatient and outpatient treatment phases, to determine the rates of readmission and mortality, and to identify risk factors.

Methods: We carried out a descriptive statistical analysis of routine administrative data from a large health-insurance carrier (BARMER). All insurees aged 18 to 65 who were treated in 2015 as inpatients on a psychiatry and psychotherapy service or on a psychosomatic medicine and psychotherapy service with a main diagnosis of depression were included in the analysis. Risk factors for readmission and death were determined with the aid of mixed logistic regression.

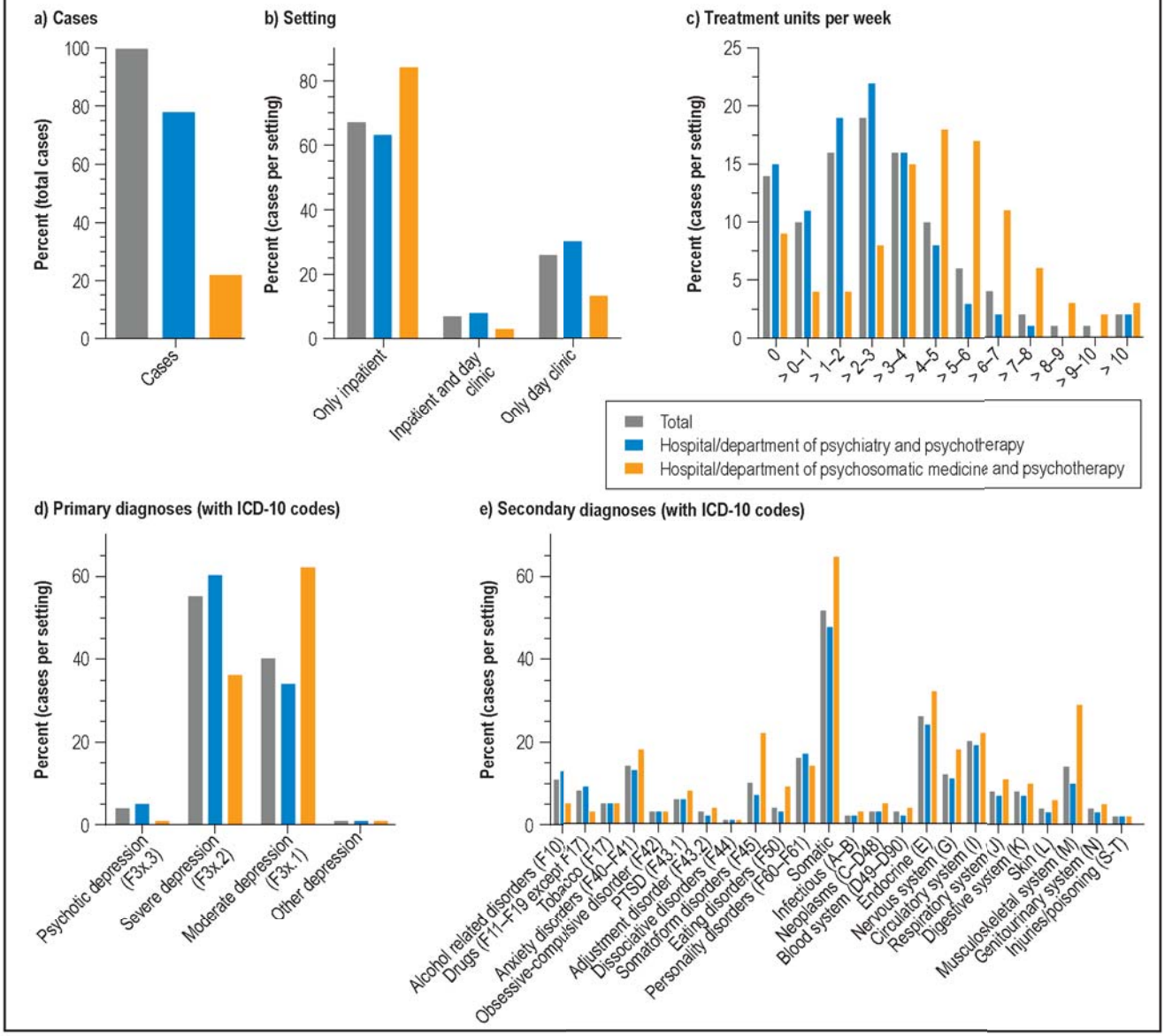
Results: Of the 22 893 patients whose data were analyzed, 78% had been hospitalized on a psychiatry and psychotherapy service and 22% on a psychosomatic medicine and psychotherapy service. The median length of hospital stay was 42 days. Follow-up care in the outpatient setting failed to conform with the recommendations of the pertinent guidelines in 92% of the patients with a main diagnosis of severe depression during hospitalization, and in 50% of those with moderate depression. 21% of the patients were readmitted within a year. The mortality at one year was 961 per 100 000 individuals (adjusted for the age and sex structure of the German population), or 3.4 times the mortality of the population at large. In the regression model, more treatment units during hospitalization and subsequent treatment with psychotherapy were associated with a lower probability of readmission, while longer hospitalization with subsequent pharmacotherapy or psychotherapy was associated with lower mortality.

Conclusion: The recommendations of the national (German) S3 guidelines for the further care of patients who have been hospitalized for depression are inadequately implemented at present in the sectored structures of in- and outpatient care in the German health care system. This patient group has marked excess mortality.

Cite this as:
Wiegand HF, Saam J, Marschall U, Chmitorz A, Kriston L, Berger M, Lieb K, Hölzel LP: Challenges in the transition from in-patient to out-patient treatment in depression—an analysis of administrative health care data from a large German health insurer. Dtsch Arztebl Int 2020; 117: 472–9. DOI: 10.3238/arztebl.2020.0472

Depression is one of the most common and most debilitating illnesses worldwide (1). It causes significant individual suffering (2) and is associated with increased mortality, due to suicide and comorbidities (3). In Germany, about three per cent of patients with depression are currently treated on an inpatient basis (4). After discharge from hospital, the risks of suicide (5, 6), recurrence and—if the patient does not achieve remission—chronification are increased (7, 8). To achieve complete remission or to prevent a chronic or recurrent course of the illness as well as suicide, the German National Disease Management Guideline ("S3 guideline") recommends adequate follow-up care in the form of remission-stabilizing maintenance therapy. In patients with severe depression, treatment should consist of a combination of pharmacotherapy and psychotherapy. In patients with moderate depression, pharmacological or psychotherapeutic treatment alone, depending on the patient's preference, is sufficient (9). These guideline recommendations are supported by the highest level of evidence (grade of recommendation "A"), i.e. they are based on multiple randomized controlled trials. Analyzes of routine health insurance data as well as surveys assessing the outpatient care of patients with depression found evidence of care deficits (4, 10–13). Data on the characteristics of inpatient treatment of depression in

FIGURE 1



Characteristics of inpatient index treatment. PTSD, posttraumatic stress disorder

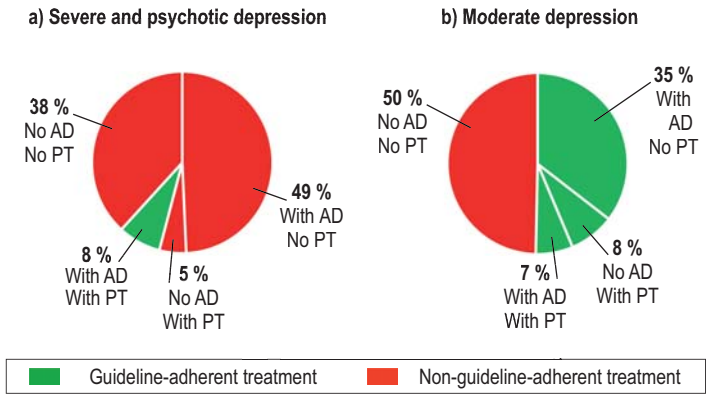
Germany and the current state of follow-up outpatient treatment are scarce, making it difficult to assess the required health policy measures in the context of the current health policy debates about mental health care. Therefore, our study addresses—based on the routine data set of BARMER, a large German health insurer, covering more than 9 million persons in Germany—the following questions:

- How and for how long are patients with a depressive episode treated in a hospital/department of psychiatry and psychotherapy or a hospital/department of psychosomatic medicine and psychotherapy?
- Is the follow-up outpatient treatment guideline-adherent?
- What are the annual readmission and mortality rates and
- by which sociodemographic, illness-related or treatment-related variables are they influenced?

Methods

From the about 9.4 million persons insured with BARMER in 2015, those were selected who were between 18 and 65 years of age and discharged from psychiatric-psychotherapeutic or psychosomatic-psychotherapeutic inpatient treatment with an ICD-10 diagnosis of F32.x (major depressive disorder, single episode) or F33.x (major depressive disorder, recurrent). If the patient was discharged in 2015, the inpatient stay was regarded as an index stay. Subsequent to

FIGURE 2



Guideline-adherent follow-up treatment
AD, antidepressant; PT, psychotherapy

TABLE 1

Outpatient psychotherapy in the observation interval

	Cases*		Service items	
	N	%	N	%
Total	7951	100	218 254	100
CBT individual	4335	55	103 084	47
CBT group	108	1	2014	1
PP individual	3403	43	89 380	41
PP group	174	2	4866	2
AP individual	273	3	17 416	8
AP group	<50	<1	1494	1

*In one index patient, several types of psychotherapy may have been billed during the observation interval, resulting in a total >100%
AP, analytical psychotherapy; PP, psychodynamic psychotherapy; CBT, cognitive behavioral therapy

discharge, a 365-day observation interval was defined during which guideline-adherent follow-up treatment with medication and psychotherapy as well as readmission and mortality rates were assessed (short version, see *eMethods*).

Results

Characteristics of the index population

22 893 of the approximately 9.4 million persons insured with BARMER (equaling a one-year prevalence of an inpatient stay of 0.25%) fulfilled the inclusion criteria (= index population). 66% (n = 15 059) were females. The age median was 47 years (range 47). 39% (n = 8991) of the index population were registered in a city (>100 000 inhabitants).

Characteristics of the index hospital treatment

The median length of inpatient stay was 42 days (minimum 1, maximum 816). At discharge from the index stay, 78% (n = 17 799) of the index population were treated in a hospital/department of psychiatry and psychotherapy and 22% (n = 5094) in a hospital/department of psychosomatic medicine and psychotherapy. *Figure 1* and *eTable 1* provide an overview of the distribution of cases *(Figure 1a)*. What was striking was the small proportion of day-clinic treatment, especially in psychosomatic medicine (*Figure 1b*), and a significantly higher treatment density by physicians/psychologists in hospitals/departments of psychosomatic medicine and psychotherapy compared to hospitals/departments of psychiatry and psychotherapy, (*Figure 1c*), where, however, the vast majority of patients with severe or psychotic depression were treated (*Figure 1d*). With regard to secondary diagnoses, there were no major differences between the two types of hospitals/departments (*Figure 1a)*.

Severity-adapted guideline-adherent follow-up treatment

With regard to the severity-adapted guideline recommendations, 92% (n = 12 395) of the patients with severe depression did not receive guideline-adherent follow-up treatment with a combination of pharmacotherapy and psychotherapy (*Figure 2a*). Of the patients with moderate depression, 50% (n = 4605) did not receive guideline-adherent follow-up treatment with either medication or psychotherapy (*Figure 2b*).

The analysis of outpatient pharmacotherapy found that 84% of the 13 427 patients with severe depression (F3X.2 or F3X.3) and 70% of the 9270 patients with moderate depression (F3X.1), filled at least one antidepressant prescription during the follow-up year. However, only 57% (n = 7651) and 42% (n = 3908) of the patients with moderate depression and severe depression, respectively, were given a prescription—as recommended in the guideline—during the first quarter after discharge and, where appropriate, follow-up prescriptions with defined daily doses (DDDs) sufficient for a period of at least four months For an overview of the DDDs of the prescribed substances see the *eFigure*.

For the outpatient follow-up treatment, it was found that only 33% (n = 4428) and 37% (n = 3474) of the patients with severe and moderate depression, respectively, received one hour of psychotherapy within the one-year observation interval at all. Only 12% (n = 1676) and 15% (n = 1376) of patients with severe and moderate depression, respectively, received the first hour of psychotherapy within the first quarter after discharge and at least eight hours of psychotherapy during the one-year observation interval, as recommended in the guideline.

The interval between discharge from hospital and the first hour of psychotherapy was assessed in the 4311 patients who had not received psychotherapy in the year prior to hospital admission. Among these patients, the median interval between discharge and start of psychotherapy was 111 days (95% confidence interval: [106; 115]). Psychotherapy was primarily

TABLE 2

3-level regression model readmission in the second half of the year after discharge

Variable	Covariance parameter estimate	Standard error
Random intercepts of the null model		
Hospital	0.09	0.02
Region (post code 2 digits)	0.02	0.01
Random intercepts of the predictor model		
Hospital	0.04	0.02
Region (post code 2 digits)	0.02	0.01

Variable	Odds ratio*1		F value	p
Fixed effects of the predictor model				
Sociodemographic factors				
– Age (per year)	1.00	[1.00; 1.01]	14.42	0.0001
– Male sex	0.95	[0.85; 1.05]	1.18	0.2769
Illness-related factors				
– Secondary diagnosis personality disorder (F60–F61)	1.70	[1.51; 1.90]	82.11	<0.0001
– Secondary diagnosis posttraumatic stress disorder (F43.1)	1.53	[1.30; 1.81]	25.81	<0.0001
– Primary diagnosis severe depression (F3x.2–F3x.3)	1.50	[1.35; 1.66]	55.26	<0.0001
– Secondary diagnosis obsessive-compulsive disorder (F42)	1.32	[1.01; 1.72]	4.18	0.0408
– Secondary diagnosis drugs (F11–F19 except F17)	1.28	[1.09; 1.51]	9.19	0.0024
– Secondary diagnosis alcohol-related disorders (F10)	1.21	[1.05; 1.39]	6.75	0.0094
– Secondary diagnosis dissociative disorder (F44)	1.13	[0.77; 1.65]	0.37	0.5456
– Secondary diagnosis somatoform disorders (F45)	1.09	[0.93; 1.28]	1.16	0.2816
– Charlson index (somatic comorbidities)	1.09	[0.99; 1.20]	2.82	0.0931
– Secondary diagnosis tobacco (F17)	1.07	[0.87; 1.31]	0.43	0.5097
– Secondary diagnosis anxiety disorders (F40–F41)	0.99	[0.87; 1.14]	0.01	0.9042
– Secondary diagnosis eating disorders (F50)	0.92	[0.72; 1.18]	0.39	0.5322
– Secondary diagnosis adjustment disorders (F43.2)	0.75	[0.53; 1.05]	2.78	0.0953
Treatment-related factors				
– Guideline-adherent follow-up treatment with antidepressants	1.49	[1.35; 1.64]	63.13	<0.0001
– Treatment in hospital/department of psychiatry*2	1.30	[1.12; 1.51]	11.97	0.0005
– Length of stay (per day)	1.00	[1.00; 1.00]	0.19	0.6603
– Treatment units (per 25 min TU per week)	0.96	[0.95; 0.98]	14.94	0.0001
– Guideline-adherent follow-up treatment with psychotherapy	0.78	[0.67; 0.90]	10.67	0.0011

*1 95% confidence intervals
*2 As opposed to hospital/department of psychosomatic medicine
TU, treatment unit

individual therapy with cognitive behavioral therapy (55%) or psychodynamic psychotherapy (43%), whereas psychoanalysis and group therapy played only a marginal role (*Table 1*).

eTable 3 shows whether a specialist or general practitioner/internist was consulted during the first quarter of treatment in the observation interval.

Readmissions

During the observation interval, 21% (n = 4798) of the index population were readmitted to inpatient or day-patient psychiatric-psychotherapeutic or psychosomatic treatment, 5% (n = 1103) twice or more. To evaluate whether guideline-adherent follow-up treatment helps to prevent readmission, we looked for

TABLE 3a

3-level regression model—random intercepts of the null model and predictor model

Variable	Covariance parameter estimate	Standard error
Random intercepts of the null model		
Hospital	0.38	0.11
Region (post code 2 digits)	0	–
Random intercepts of the predictor model		
Hospital	0.25	0.11
Region (post code 2 digits)	0	0

evidence of risk factors of readmission in the second half of the year after discharge, using a multi-level regression model. In the random intercept null model, hospital and region explained a substantial proportion of the variation with regard to readmission. In the three-level regression model, older age was a sociodemographic factor that increased the likelihood of readmission. With regard to disease-related factors, the primary diagnosis of severe depression and the secondary diagnoses of personality disorder, posttraumatic stress disorder, obsessive-compulsive disorder, addiction or alcohol-related disorders significantly increased the likelihood of readmission in the model. With regard to treatment-related factors, the likelihood of readmission increased with treatment in a hospital/department of psychiatry and psychotherapy as well as with guideline-adherent follow-up treatment with antidepressants. In contrast, more treatment units during index treatment and guideline-adherent psychotherapeutic follow-up treatment decreased the likelihood of readmission. McFadden's Pseudo R^2 was 0.03; the predictors thus explained a moderate proportion of the variation beyond the hospital-related and regional variation (14) (*Table 2*).

Mortality

Within the observation period, 1.1% (n = 256) of the index population died. The result was adjusted with regard to age and sex to the German general population aged 18 to 65 years (15). With 961/100 000 population, the one-year mortality was 3.4-times higher compared to the age- and sex-matched general population (282/100 00). The cause for mortality is not recorded in the available data. In the random intercept null model, "hospital", but not "region", explained variation in mortality. In the 3-level regression model, with regard to fixed effects, age and male sex as sociodemographic risk factors, a primary diagnosis of severe depression as well as psychiatric secondary diagnoses and severe somatic comorbidities (represented by the Charlson index) as illness-related factors, and treatment in a hospital/department of psychiatry and psychotherapy as treatment-related factors were associated with an increased likelihood of mortality. By contrast, prolonged length of inpatient stay and (at least minimal) antidepressant and psychotherapeutic follow-up treatment decreased the likelihood of mortality. McFadden's Pseudo R^2 was 0.16; the predictors thus explained a significant proportion of the variation beyond the hospital-related and regional variation (14) (*Table 3 a, b*).

To obtain evidence of preventative effects of guideline-adherent treatment, we initially planned to repeat the regression analysis using the more extensive indicators "guideline-adherent medication" and "guideline-adherent psychotherapy" for the deaths that occurred during the second half of the year after discharge; however, none of the patients who died during the second half of the year received guideline-adherent treatment during the first half of the year.

Discussion

Inpatient treatment

The routine data of BARMER show that in Germany inpatient treatment of depression was provided by hospitals/departments of psychiatry and psychotherapy in three of four patients. In 2015, the number of beds was 50 972 in psychiatry (without addiction) to 10 439 in psychosomatic medicine (16). The hospitals/departments of psychiatry and psychotherapy primarily treated patients with severe and psychotic depression, while the hospitals/departments of psychosomatic medicine primarily treated patients with moderate depression. However, treatment density was considerably lower in hospitals/departments of psychiatry and psychotherapy compared to hospitals/departments of psychosomatic medicine. This is due to the requirements of the approximately 30-year-old German Psychiatry Personnel Regulation Act (PsychPV, *Psychiatrie-Personalverordnung*) which limits the possibilities to provide intensive and guideline-adherent psychotherapy (17, 18). Since staffing in hospitals/departments of psychosomatic medicine is usually not regulated by the PsychPV, in this setting one full-time physician/psychologist is only responsible for the treatment of half as many patients compared to hospitals/departments of psychiatry (19, 20). With 42 days, the length of stay was overall shorter compared to, for example, the situation 15 years ago (21). In the light of the goal to promote the integration of patients into their living environment and the comparable low costs of this care strategy, it is surprising that treatment in day clinics, especially in hospitals/departments of psychosomatic medicine, is the exception, not the rule.

Follow-up outpatient treatment

After discharge, only 8% of patients with severe depression and 50% of patients with moderate depression received guideline-adherent follow-up treatment. In the group of patients with severe depression, only 12% received the follow-up treatment with psychotherapy

TABLE 3 b

3-level regression model mortality—<sociodemographic, illness- and treatment-related factors

Variable	Odds ratio*1		F value	p
Fixed effects of the predictor model				
Sociodemographic factors				
– Male sex	1.8	[1.39; 2.34]	19.24	<0.0001
– Age (per year)	1.05	[1.04; 1.07])	66.21	<0.0001
Illness-related factors				
– Charlson index (somatic comorbidities)	1.77	[1.52; 2.06]	53.21	<0.0001
– Primary diagnosis severe depression (F3x.2–F3x.3)	1.71	[1.26; 2.32]	11.78	0.0006
– Secondary diagnosis drugs (F11–F19 except F17)	1.70	[1.15; 2.50]	7.21	0.0073
– Secondary diagnosis obsessive-compulsive disorder (F42)	1.57	[0.68; 3.63]	1.12	0.2905
– Secondary diagnosis alcohol related disorders (F10)	1.51	[1.11; 2.05]	7.01	0.0081
– Secondary diagnosis adjustment disorders (F43.2)	1.25	[0.60; 2.62]	0.35	0.5542
– Secondary diagnosis somatoform disorders (F45)	1.20	[0.75; 1.93]	0.59	0.4405
– Secondary diagnosis personality disorder (F60–F61)	1.05	[0.71; 1.54]	0.05	0.8169
– Secondary diagnosis posttraumatic stress disorder (F43.1)	0.95	[0.50; 1.78]	0.03	0.8664
– Secondary diagnosis anxiety disorders (F40–F41)	0.79	[0.50; 1.25]	1.06	0.3037
– Secondary diagnosis tobacco (F17)	0.76	[0.44; 1.30]	1.00	0.3165
– Secondary diagnosis eating disorders (F50)	0.66	[0.21; 2.11]	0.49	0.4837
– Secondary diagnosis dissociative disorder (F44)	0.44	[0.06; 3.26]	0.64	0.4250
Treatment-related factors				
– Treatment in hospital/department of psychiatry*2	2.69	[1.52; 4.75]	11.58	0.0007
– Treatment units (TU) (per 25 min TU per week)	1.00	[0.96; 1.03]	0.08	0.7772
– Length of stay (per day)	0.99	[0.98; 0.99]	23.34	<0.0001
– Minimal antidepressant follow-up treatment	0.53	[0.40; 0.71]	18.61	<0.0001
– Minimal psychotherapy follow-up treatment	0.29	[0.18; 0.45]	29.87	<0.0001

*1 95% confidence intervals
*2 As opposed to hospital/department of psychosomatic medicine

recommended in the guidelines. The study data did not allow to determine the exact reasons behind this finding. The important role of structural deficits in the German healthcare system, causing this long interval of 16.7 weeks until the start of treatment, is highlighted by the information of the Federal Chamber of Psychotherapists (BPtK, *Bundespsychotherapeutenkammer*) that nationwide the mean waiting time for a space in psychotherapy is 19.9 weeks, with a high patient preference for this treatment modality (22). These long intervals are of concern because data from the British healthcare system show that with waiting times of more than four weeks the chance of a positive effect of outpatient psychotherapy decreases considerably (23). Structural support could be provided by improved coordination between hospitals, specialists in psychiatry and psychotherapy/general practitioners and guideline psychotherapists (24–26). Furthermore, although group therapy could expand the psychotherapy offering to compensate for the lack of resources, this rarely happens in Germany, according to chambers of psychotherapists because of bureaucratic hurdles (27).

With regard to follow-up treatment with medication, again significant deficits were identified. Only 57% of patients with severe or psychotic illness received medication for an adequate period of time and in adequate doses—and the indicator chosen for this study represents a very conservative estimate. The available data did not allow conclusions about to what extent this was due to patient concerns about long-term medication use or physicians not adhering to the guideline recommendations.

Readmissions

The association of comorbidities and advanced age with less favorable courses is consistent with the findings reported in the literature (28). The finding that patients treated in a hospital/department of psychiatry and psychotherapy are at a higher risk of readmission can be explained by differences in the patient mix and the

Key messages

- 78% of all patients, especially with severe and psychotic depression, received inpatient treatment in hospitals/departments of psychiatry and psychotherapy where the treatment provided by physicians and psychotherapists was considerable less intensive compared to the treatment that could be offered in hospitals/departments of psychosomatic medicine and psychotherapy.
- In hospitals/departments of psychosomatic medicine and psychotherapy, primarily patients with moderate depression were treated, in most cases on an inpatient basis and rarely in day clinics.
- After discharge, 92% of patients with severe depression did not receive the outpatient follow-up treatment with combined pharmacotherapy and psychotherapy recommended in the German clinical practice (S3) guideline on unipolar depression.
- 21% of patients with depression were readmitted within one year after discharge; in the regression model, more intensive treatment und follow-up treatment with psychotherapy were associated with a lower likelihood of readmission.
- The standardized one-year mortality rate was 3.4 times as high as the rate for the general population. In the sample of 22 893 affected persons, 151 persons more died than would have been expected in the general population. Treatment-related risk factors for this phenomenon included, among others, a lack of follow-up treatment with medication and psychotherapy.

more acute treatment setting. The association between inpatient treatment intensity and readmission rates identified in the regression model raises the question of the adequacy of staffing in hospitals/departments of psychiatry and psychotherapy. After discharge, patients receiving follow-up treatment with psychotherapy have a lower risk of readmission in the model, indicating the importance of implementing this guideline recommendation. The finding that guideline-adherent follow-up treatment with medication is associated with an increased likelihood of readmission in the model seems counterintuitive, but may be explained by the fact that the indication for consistent treatment with medication is stricter in patients with more severe illness who consequently are at a greater risk of relapse and recurrence. Alternatively, the finding could be explained by the rebound phenomenon which is triggered by improper discontinuation of antidepressant treatment and has only recently been reported in the literature (29).

Mortality

Deaths are a key outcome measure of high clinical relevance which is available in the routine data. This study found a mortality rate which was higher than expected. In the year following discharge from hospital after inpatient treatment of depression, the mortality rate was 3.4 times higher compared to the general population. Instead of the expected 65 deaths among 22 893 persons in the general population, 151 more persons died in the (adjusted) index sample of this study. It can be assumed that mortality was reliably recorded in the available dataset. While factors such older age, male sex, severity of depression, combined addictions, the Charlson index, and treatment in a hospital/department of psychiatry and psychotherapy can be used to identify high-risk populations, treatment-related factors highlight the risk of increased mortality associated with a lack of follow-up treatment with psychotherapy and medication as well as shorter inpatient stays. Of particular concern was the finding that none of the patients who died in the second half of the year after discharge had received guideline-adherent treatment in the first six months.

Limitations

By analyzing administrative health insurance data, large populations and the reality of treatment can be explored over time outside of studies. A disadvantage of routine data is the limited validity of the diagnoses, especially of the severity grading used in this study. Since this study focused on patients who were treated in a specialist hospital or department, a higher validity at least of mental health diagnoses can be assumed; on the other hand, this focus also allowed to capture the reality of outpatient treatment of some of the most severely affected patients. By combining inpatient stays, this study provides a more realistic view on readmissions and the length of hospital stays than previous studies. Since health insurance providers are not allowed to have access to further clinical variables, indicators have to be used to make these accessible. Thus, treatment reality may differ in individual cases. Furthermore, analyzes of routine data can only describe the existing care situation. The regressions performed on the administrative data can only indicate plausible relationships, but do not allow for causal interpretations. In addition, the relationships identified in the regression models are only valid, even on the basis of correlative interpretation, if no unconsidered confounders with substantial effects on the studied outcomes are present. Due to the relatively low number of events compared to the complexity of the statistical models, some results may show bias. Furthermore, it should be taken into account that "guideline adherence" could only be operationalized very broadly in this study, because guidelines, although making general recommendations, explicitly allow to deviate from these recommendations and to take into account factors when making individualized decisions that extend beyond illness severity.

Conclusion

Despite its methodological limitations, which need to be considered, our study reveals potential shortcomings in the care of patients undergoing inpatient treatment. Inpatient treatment in specialist hospitals and departments of psychiatry and psychotherapy was characterized

by lower treatment intensity compared to specialist hospitals and departments of psychosomatic medicine and psychotherapy, despite the higher proportion of patients with severe depression and the fact that in the model, intensification of inpatient treatment could counteract readmissions. In addition, longer inpatient stays were associated with reduced mortality risk in the model. Furthermore, our study shows deficits of the follow-up treatment with medication and psychotherapy. Only in a minority of patients, the current guideline recommendations were implemented, despite the fact that in regression models the recommended follow-up treatment could reduce the likelihood of readmissions and death. These results underscore the high relevance of current efforts in research, professional and health policy to improve healthcare structures in a way that enables guideline-adherent treatment in an inpatient care setting independent of the type of hospital/department and in outpatient care within the currently existing sectored structures.

Conflict of interest statement
Mr. Wiegand received co-authorship fees from Springer Medizin Verlag.
The remaining authors declare no conflict of interest.

Manuscript received on 19 September 2019, revised version accepted on 26 March 2020

Translated from the original German by Ralf Thoene, MD.

References

1. Vigo D, Thornicroft G, Atun R: Estimating the true global burden of mental illness. Lancet Psychiatry 2016; 3: 171–8.
2. Rubio JM, Olfson M, Pérez-Fuentes G, Garcia-Toro M, Wang S, Blanco C: Effect of first episode axis I disorders on quality of life. J Nerv Ment Dis 2014; 202: 271–4.
3. Chesney E, Goodwin GM, Fazel S: Risks of all-cause and suicide mortality in mental disorders: a meta-review. World Psychiatry 2014; 13: 153–60.
4. Melchior H, Schulz H, Härter M: Faktencheck Gesundheit. Bertelsmann Stiftung 2014: 1–144.
5. Nordentoft M, Mortensen PB, Pedersen CB: Absolute risk of suicide after first hospital contact in mental disorder. Arch Gen Psychiatry 2011; 68: 1058–64.
6. Simon GE, VonKorff M: Suicide mortality among patients treated for depression in an insured population. Am J Epidemiol 1998; 147: 155–60.
7. Melartin TK, Rytsälä HJ, Leskelä US, Lestelä Mielonen PS, Sokero TP, Isometsä ET: Severity and comorbidity predict episode duration and recurrence of DSM-IV major depressive disorder. J Clin Psychiatry 2004; 65: 810–9.
8. Holma KM, Holma IAK, Melartin TK, Rytsälä HJ, Isometsä ET: Long-term outcome of major depressive disorder in psychiatric patients is variable. J Clin Psychiatry 2008; 69): 196–205.
9. DGPPN, BÄK, KBV, AWMF: S3-Leitlinie/Nationale VersorgungsLeitlinie Unipolare Depression – Langfassung, 2. Auflage. Version 5. 2017: 1–238. www.awmf.org/leitlinien/detail/ll/nvl-005.html (last accessed on 16 April 2020).
10. Wiegand HF, Sievers C, Schillinger M, Godemann F: Major depression treatment in Germany - descriptive analysis of health insurance fund routine data and assessment of guideline-adherence. J Affect Disord 2016; 189: 246–53.
11. Gaebel W, Kowitz S, Zielasek J: The DGPPN research project on mental healthcare utilization in Germany: inpatient and outpatient treatment of persons with depression by different disciplines. Eur Arch Psychiatry Clin Neurosci 2012; 262: 51–5.
12. Trautmann S, Beesdo-Baum K, Knappe S, et al.: The treatment of depression in primary care— a cross-sectional epidemiological study. Dtsch Arztebl Int 2017; 114: 721–8.
13. Herzog DP, Wagner S, Ruckes C, et al.: Guideline adherence of antidepressant treatment in outpatients with major depressive disorder: a naturalistic study. Eur Arch Psychiatry Clin Neurosci 2017; 267: 711–21.
14. McFadden D: Quantitative methods for analyzing travel behavior of individuals. Cowles Foundation Discussion Paper No. 474, 1977.
15. Statistisches Bundesamt: Bevökerungsvorrausberechnung 2015. https://service.destatis.de/bevoelkerungspyramide/#!y=2015&v=2 (last accessed on 16 April 2019).
16. Statistisches Bundesamt: Gesundheit; Grunddaten der Krankenhäuser – Fachserie 12 Reihe 6.1.1 – 2015. 2016; 1–155. www.destatis.de/GPStatistik/servlets/MCRFileNodeServlet/DEHeft_derivate_00031004/2120611157004.pdf (last accessed on 2 January 2020).
17. Normann C, Wolff J, Hochlehnert A, et al.: Resource use and financing of guideline-adherent psychotherapeutic inpatient care. Nervenarzt 2015; 86: 534–41.
18. Berger M, Wolff J, Normann C, et al.: Guideline-adherent psychiatric-psychotherapeutic hospital care. Nervenarzt 2015; 86: 542–8.
19. Godemann F, Wolff-Menzler C, Löhr M, et al.: Calculating personnel allocation at 100 % implementation of the psychiatry personnel act. Nervenarzt 2015; 86: 845–51.
20. Friederich HC, Heuft G, Cuntz U, et al.: Staffing level: Survey among psychosomatic-psychotherapeutic institutions in Germany. Z Psychosom Med Psychother 2018; 64: 334–49.
21. Härter M, Sitta P, Keller F, et al.: Externe Qualitatssicherung bei stationarer Depressionsbehandlung Modellprojekt der Landesarztekammer Baden-Württemberg. Dtsch Arztebl 2004; 101: A 197074.
22. McHugh RK, Whitton SW, Peckham AD, Welge JA, Otto MW: Patient preference for psychological vs pharmacologic treatment of psychiatric disorders. J Clin Psychiatry 2013; 74: 595–602.
23. Clark DM, Canvin L, Green J, Layard R, Pilling S, Janecka M: Transparency about the outcomes of mental health services (IAPT approach): an analysis of public data. Lancet 2018; 391: 679–86.
24. Bermejo I, Hölzel LP, Voderholzer U, van Elst LT, Berger M: Optimal versorgt bei Depression – Freiburger Modell zur Integrierten Versorgung depressiver Erkrankungen. Z Evid Fortbild Qual Gesundhwes 2012; 106: 625–30.
25. Schmid P, Steinert T, Borbé R: Systematische Literaturübersicht zur Implementierung der sektorübergreifenden Versorgung (Regionalbudget, integrierte Versorgung) in Deutschland. Psychiatr Prax 2013; 40: 414–24.
26. Deuschle M, Scheydt S, Hirjak D, et al.: Track treatment in psychiatry: the CIMH track model to overcome sector boundaries. Nervenarzt 2020; 91: 50–6.
27. Bundespsychotherapeutenkammer: Ein Jahr nach der Reform der Psychotherapie-Richtlinie – Wartezeiten 2018.
28. Hölzel L, Härter M, Reese C, Kriston L: Risk factors for chronic depression—a systematic review. J Affect Disord 2011; 129: 1–13.
29. Henssler J, Heinz A, Brandt L, Bschor T: Antidepressant withdrawal and rebound phenomena—a systematic review. Dtsch Arztebl Int 2019; 116: 355–61.
30. Statistisches Bundesamt: Gemeindeverzeichnis-Sonderveröffentlichung Gebietsstand: 31.12.2011. 2013 Jul pp. 1–5. www.destatis.de/DE/Themen/Laender-Regionen/Regionales/Gemeindeverzeichnis/Administrativ/05-staedte.html (last accessed on 16 April 2019).
31. Kassenärztliche Bundesvereinigung. Einheitlicher Bewertungsmaßstab (EBM). Berlin; 2015: 1–1546. www.kbv.de/html/arztgruppen_ebm.php#content2403 (last accessed on 16 April 2020)
32. Lambert NJ: Bergin and Garfield's handbook of psychotherapy and behavior change. New Jersey: John Wiley & Sons 2013.
33. Armitage JN, van der Meulen JH: Identifying co-morbidity in surgical patients using administrative data with the Royal College of Surgeons Charlson Score. Br J Surg 2010; 97: 772–81.

Corresponding author
Hauke Felix Wiegand, MD/PhD
Klinik für Psychiatrie und Psychotherapie, Universitätsmedizin Mainz
Untere Zahlbacher Str. 8
55131 Mainz, Germany
haukefelix.wiegand@unimedizin-mainz.de

Cite this as:
Wiegand HF, Saam J, Marschall U, Chmitorz A, Kriston L, Berger M, Lieb K, Hölzel LP: Challenges in the transition from in-patient to out-patient treatment in depression—an analysis of administrative health care data from a large German health insurer. Dtsch Arztebl Int 2020; 117: 472–9. DOI: 10.3238/arztebl.2020.0472

► **Supplementary material**

eMethods, eTables:
www.aerzteblatt-international.de/20m0472

Supplementary material to:

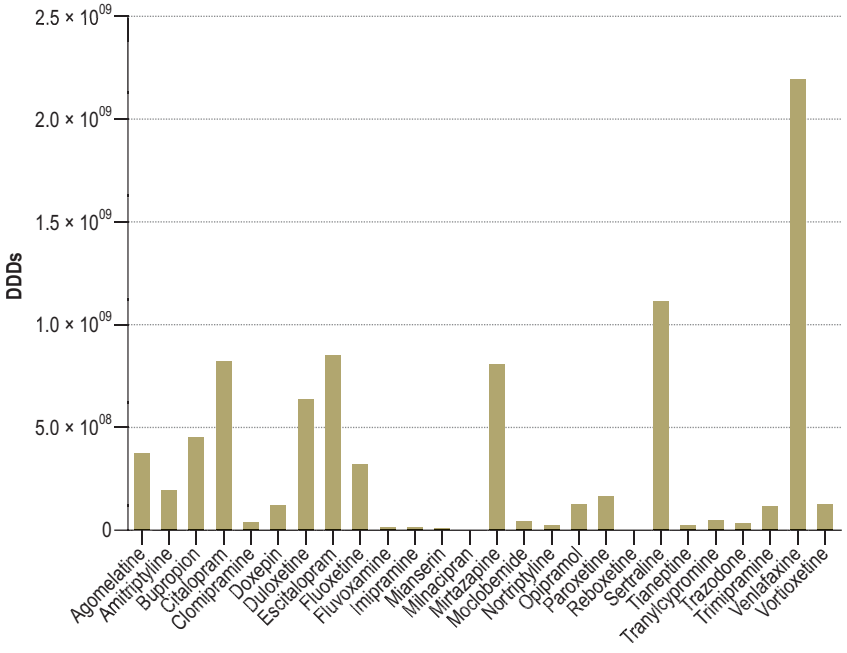
Challenges in the Transition from In-Patient to Out-Patient Treatment in Depression

An Analysis of Administrative Health Care Data From a Large German Health Insurer

by Hauke Felix Wiegand, Joachim Saam, Ursula Marschall,
Andrea Chmitorz, Levente Kriston, Mathias Berger, Klaus Lieb, and Lars P. Hölzel

Dtsch Arztebl Int 2020; 117: 472–9. DOI: 10.3238/arztebl.2020.0472

eFIGURE



ATC	Name	DDD
N06A	**Antidepressants**	
N06AX22	Agomelatine	25 mg
N06AA09	Amitriptyline	75 mg
N06AX12	Bupropion	0.15 g
N06AB04	Citalopram	20 mg
N06AA04	Clomipramine	0.1 g
N06AA12	Doxepin	0.1 g
N06AX21	Duloxetine	60 mg
N06AB10	Escitalopram	10 mg
N06AB03	Fluoxetine	20 mg
N06AB08	Fluvoxamine	0.1 g
N06AA02	Imipramine	0.1 g
N06AX03	Mianserin	60 mg
N06AX17	Milnacipran	0.1 g
N06AX11	Mirtazapine	30 mg
N06AG02	Moclobemide	0.3 g
N06AA10	Nortriptyline	75 mg
N06AA05	Opipramol	0.15 g
N06AB05	Paroxetine	20 mg
N06AX18	Reboxetine	8 mg
N06AB06	Sertraline	50 mg
N06AX14	Tianeptine	37.5 mg
N06AF04	Tranylcypromine	10 mg
N06AX05	Trazodone	0.3 g
N06AA06	Trimipramine	0.15 g
N06AX16	Venlafaxine	0.1 g
N06AX26	Vortioxetine	10 mg

Prescribed defined daily doses (DDDs) of the various antidepressants

eTABLE 1

Characteristics of inpatient index treatment (data for Figure 1)

eTable 1b – Length of hospital stay and treatment setting of index treatment

	Total			Psychiatry			Psychosomatic medicine		
	LOS* Median	N	%	LOS* Median	N	%	LOS* Median	N	%
Total	42	22 893	100	42	17 799	100	43	5 094	100
Only inpatient	38	15 418	67	34	11 143	63	42	4 275	84
Only day clinic	51	5967	26	51	5289	30	52	682	13
Inpatient + day clinic combined	80	1508	7	82	1 371	8	70	137	3
of these inpatient	44								
of these day clinic	30								

eTable 1c – Treatment units of index treatment

	Total			Psychiatry			Psychosomatic medicine		
	Median	N	%	Median	N	%	Median	N	%
0	3.5	3135	14	2.4	2669	15	4.9	466	9
> 0–1		2215	10		2021	11		194	4
> 1–2		3574	16		3347	19		227	4
> 2–3		4352	19		3954	22		398	8
> 3–4		3649	16		2902	16		747	15
> 4–5		2316	10		1380	8		936	18
> 5–6		1437	6		576	3		861	17
>6–7		909	4		341	2		568	11
> 7–8		419	2		109	1		310	6
> 8–9		224	1		59	0		165	3
> 9–10		140	1		60	0		80	2
> 10		523	2		381	2		142	3

eTable 1d – Primary diagnoses of index treatment

	Total			Psychiatry			Psychosomatic medicine		
		N	%		N	%		N	%
F3x.3 – Psychotic depression		877	4		841	5		<50	1
F32.3		358	2		344	2		<50	<1
F33.3		519	2		497	3		<50	<1
F3x.2 – Severe depression		12 550	55		10 714	60		1 836	36
F32.2		5201	23		4599	26		602	12
F33.2		7349	32		6115	34		1 234	24
F3x.1 – Moderate depression		9270	40		6093	34		3 177	62
F32.1		4018	18		2840	16		1 178	23
F33.1		5252	23		3253	18		1 999	39
Remainder		196	1		151	1		<50	1

eTable 1e – Secondary diagnoses of index treatment

	Total			Psychiatry			Psychosomatic medicine		
		N	%		N	%		N	%
Alcohol related disorders (F10)		2473	11		2234	13		239	5
Drugs (F11–F19)**		1754	8		1581	9		173	3
Tobacco (F17)		1188	5		912	5		276	5
Anxiety disorders (F40–F41)		3276	14		2342	13		934	18
Obsessive-compulsive disorder (F42)		598	3		449	3		149	3
PTSD (F43.1)		1472	6		1072	6		400	8
Adjustment disorder (F43.2)		647	3		441	2		206	4
Dissociative disorders (F44)		266	1		196	1		70	1
Somatoform disorders (F45)		2368	10		1225	7		1143	22
Eating disorders (F50)		968	4		494	3		474	9
Personality disorders (F60–F61)		3750	16		3053	17		697	14
Somatic		11 924	52		8596	48		3328	65
Infectious (A–B)		542	2		401	2		141	3
Neoplasms (C–D48)		779	3		546	3		233	5
Blood system (D49–D90)		586	3		402	2		184	4
Endocrine (E)		5853	26		4217	24		1636	32
Nervous system (G)		2820	12		1925	11		895	18
Circulatory system (I)		4501	20		3388	19		1113	22
Respiratory system (J)		1874	8		1319	7		555	11
Digestive system (K)		1786	8		1297	7		489	10
Skin (L)		921	4		616	3		305	6
Musculoskeletal system (M)		3305	14		1834	10		1471	29
Genitourinary system (N)		833	4		598	3		235	5
Injuries/poisoning (S–T)		512	2		393	2		119	2

eTable 1f – Comorbidity indices according to the Royal College of Surgeons Charlson Score (RCS)

	Total			Psychiatry			Psychosomatic medicine		
		Mean	SD		Mean	SD		Mean	SD
RCS Charlson score		0.157	0.449		0.157	0.455		0.159	0.430

**except F17 – Tobacco
*LOS, length of stay

eTABLE 2

Included fee scale items (FSIs) from the Uniform Value Scale (EBM, Einheitlicher Bewertungsmaßstab) of the National Association of Statutory Health Insurance Physicians (KBV, Kassenärztliche Bundesvereinigung) 2015/2016

FSI code	Name
35200	PP short-term therapy, individual therapy
35201	PP long-term therapy, individual therapy
35202	PP short-term therapy, large group
35203	PP long-term therapy, large group
35210	AP individual therapy
35211	AP large group
35220	CBT short-term therapy, individual therapy
35221	CBT long-term therapy, individual therapy
35222	CBT short-term therapy, small group
35223	CBT long-term therapy, small group

AP, analytical psychotherapy;
PP, psychodynamic psychotherapy;
CBT, cognitive behavioral therapy

eTABLE 3

Follow-up treatment by specialist*1 or general practitioner/internist*2

eTable 3a – In the entire index year at least one service provided by specialist or general practitioner

	Specialist *1		General practitioner *2	
	n	%	n	%
Number n and % of index population	12 672	55	4276	19

eTable 3b – In the first quarter after discharge at least one service provided by specialist or general practitioner

	Specialist *1		General practitioner *2	
	n	%	n	%
Number n and % of index population	9659	42	2235	10

eTable 3c – Medication and psychotherapy if in the first quarter after discharge at least one service was provided by specialist or general practitioner

Inpatient primary diagnosis	Treatment	Total		Specialist *1		General practitioner *2	
		n	%	n	%	n	%
Severe depression	Total	13 427	100	5879	100	1302	100
	AD	6619	49	3197	54	587	45
	PT	644	5	316	5	88	7
	AD + PT	1032	8	680	12	81	6
	(–)	5132	38	1686	29	546	42
Moderate depression	Total	9270	100	3780	100	933	100
	AD	3289	35	1585	42	284	30
	PT	757	8	363	10	89	10
	AD + PT	619	7	389	10	<50	5
	(–)	4605	50	1443	38	511	55

*1 Specialist: Neurology and psychiatry, psychiatry and psychotherapy, psychosomatic medicine and psychotherapy;
*2 General practitioner: General practice, physician/medical practitioner internist, pediatrician (family physician)
Cases in the specialist category may also have received additional services from their general practitioner.
Included in the general practitioner category are only those cases which have not received additional specialist services
AD, antidepressant; AD + PT, antidepressant + psychotherapy; PT, psychotherapy; (–), neither antidepressant nor psychotherapy
green: guideline-adherent treatment
red: non-guideline-adherent treatment

eMETHODS

Index population and index hospital treatment

Via a secured VPN tunnel, the authors (H.F.W., J.S., U.M.) had access to the BARMER Data Warehouse. From the about 9.4 million persons insured with BARMER in 2015, those were selected who were between 18 and 65 years of age in 2015 and discharged from psychiatric-psychotherapeutic or psychosomatic-psychotherapeutic inpatient treatment with an ICD-10 diagnosis of F32.x (major depressive disorder, single episode) or F33.x (major depressive disorder, recurrent). It is common that patients undergoing prolonged inpatient treatment are occasionally discharged for a short period of time (for example, in case of a long weekend due to a public holiday, transitions between treatment settings or as a discharge on a trial basis to test prolonged exposure to stress). Since these events would confound the information about the length of inpatient stay and readmission rates, we combined hospital stays to one hospital stay if with the same institution identification code (unique for a specific hospital/department) the interval between discharge and readmission was <10 days, or if with different institution identification codes (for example, transfers due to the area of responsibility in care psychiatry) the interval between discharge and readmission was <3 days. This combined hospital stay with first discharge in 2015 was then regarded as the index stay. We defined the observation interval as a period of 365 days after discharge. Consequently, data from the years 2014, 2015 and 2016 were used. Only persons insured with BARMER during the entire observation interval or who died during the interval or during the index hospital stay were included. Based on the list of cities with more than 100 000 inhabitants in 2011 (30) and the available first 3 digits of the postal code of the place of residence of the patients, a patient's place of residence was classed as a "city". In order to estimate the density of treatment provided by physicians and psychotherapists during the index hospital stay, the since 2013 obligatory OPS codes for treatment units were obtained. Treatment units are contacts of ≥ 25 minutes reported in 25-minute increments. For group therapies, the contact period is divided by the number of participants.

Outpatient follow-up treatment with medication

The outpatient follow-up treatment with medication during the observation interval was assessed using the Anatomical Therapeutic Chemical (ATC) codes for antidepressants and the prescribed defined daily doses (DDDs) of the WHO (*eFigure*). The day a prescription was filled and the treatment period achievable with one DDD per day were used to estimate the possible medication treatment period covered by a prescription. Follow-up prescriptions were regarded as continuous if they were filled within 7 days after the end of the period covered by the previous prescription. Hospital stays during the observation interval were recognized and included as a time interval with prescription. In order to assess whether a "guideline-adherent treatment with medication" had been administered, the first prescription in the first quarter after discharge (immediate prescription could not be made a requirement because of the possibility that a patient kept a stock of medication at home) and a continuous supply for four months (since the national clinical practice (S3) guideline on unipolar depression requires continuation of pharmacotherapy after remission for at least 4 to 9 months [9]) were used as an indicator. In the regression analysis of mortality, it was regarded as "minimal medication" if at least one prescription for an antidepressant was filled during the observation interval.

Outpatient follow-up treatment with psychotherapy

In order to assess whether a guideline-adherent treatment with psychotherapy had been administered and to evaluate the type of psychotherapy and its provision in an individual therapy or a group therapy setting, the billed fee scale items (FSIs) were analyzed, based on the catalogues of the 2014/2015 Uniform Value Scale (EBM) of the National Association of Statutory Health Insurance Physicians (KBV) (31). For the FSI numbers, see *eTable 2*. Since evidence from psychotherapy research indicates that measurable changes occur only after eight treatment sessions (32), the indicator "guideline-adherent psychotherapy" was assessed as positive if treatment with psychotherapy was started or continued in the first quarter after discharge and if at least eight treatment sessions (without probationary sessions and biographical history taking) were billed. If at least 1 hour of psychotherapy was billed, it was regarded as "minimal psychotherapy". In order to assess the interval between discharge and start of treatment and to select only patients for this who actually started a new therapy and did not just continue a treatment that had already been approved, only those patients who did not have a psychotherapy fee scale item billed in the year prior to the hospital stay were selected for this analysis.

In order to assess whether a guideline-adherent follow-up treatment had been provided, the two indicators "guideline-adherent medication" and "guideline-adherent psychotherapy" were combined to satisfy the severity-adapted guideline requirements.

Outpatient follow-up treatment by a general practitioner or specialist

Using the billed cases as well as FSI codes it was assessed whether in the first quarter after discharge a specialist visit (specialist groups: neurology and psychiatry, psychiatry and psychotherapy, psychosomatic medicine and psychotherapy) or a general practitioner/internist visit (physician groups: general practice, physician/medical practitioner internist, pediatrician [general practitioner]) occurred. Cases in the specialist category may also have received additional services from their general practitioner. In the general practitioner category appear only those cases which did not receive additional specialist services (*eTable 3*).

Readmissions in the second half of the observation year

For the indicator "readmissions", all inpatient and day-patient admissions to psychiatric and psychosomatic facilities during the observation interval were counted. These stays were combined based on the same criteria used for the index stay. In order to identify risk factors of readmission to inpatient or day-patient psychiatric-psychotherapeutic or psychosomatic care (including for another diagnosis), we chose a random-intercept multilevel model of logistic regression for the categorical indicator "readmission in the second half of the observation year". As random intercepts we first tested the variables hospital/department (in the text "hospital", n = 527) as well as regional variances, using two-digit postal codes (in the text "region", n = 95), in the null model. As fixed effects (predictors), the continuous variables age, hospital length of stay, and treatment units per week (as defined above), as well as the somatic comorbidities of the Charlson comorbidity index in the version of the Royal College of Surgeons were included. This current index awards one point for each diagnosis present in the following categories: myocardial infarction (ICD-10 codes I21, I22, I23, I252), congestive heart failure (I11, I13, I255, I42, I43, I50, I517), peripheral vascular disease (I70–I73, I770, I771, K551, K558, K559, R02, Z958, Z959), cerebrovascular disease (G45, G46, I60–I69), dementia (A810, F00–F03, F051, G30, G31), chronic lung disease (I26, I27, J40–J45, J46, J47, J60–J67, J684, J701, J703), connective tissue disease (M05, M06, M09, M120, M315, M32–M36), liver disease (B18, I85, I864,

I982, K70. K71, K721, K729, K76, R162, Z944), diabetes mellitus (E10–E14), hemiplegia or paraplegia (G114, G81–G83), kidney disease I12, I13, N01, N03, N05, N07, N08, N171, N172, N18, N19, N25, Z49, Z940, Z992), malignancies (C00–C26, C30–C34, C37–C41, C43, C45–C58, C60–C76, C80–C85, C88, C90–C97), metastasized solid tumors (C77–C79), AIDS (B20–B24). Unlike other indices, the Charlson comorbidity index does not include age and the separately analyzed psychiatric comorbidities (33). The following categorical variables were included: sex, presence of a primary diagnosis of severe depression, treatment in a psychiatric facility (as opposed to psychosomatic), guideline-adherent treatment with antidepressants or psychotherapy as defined above, the psychiatric comorbidities of alcohol-related disorder (ICD-10 F10), other addictions (F11–F19 without F17), tobacco dependence (F17), anxiety disorder (F40–F41), obsessive-compulsive disorder (F42), PTSD (F43.1), adjustment disorder (F43.2), dissociative disorders (F44), somatoform disorders (F45), eating disorders (F50), and personality disorders (F60–F61). In addition, we calculated McFadden's R squared to estimate the variation explained by the predictors other than the variation on the hospital and regional level. To be able to reliably estimate the likelihood function despite the multilevel structure of the data, we modelled the region and hospital allocations as fixed effects.

Mortality during the observation interval

The death data in the accessible data set are based on copies of death certificates or letters of the German pension insurance institution about the death of the person insured; thus, they can be considered reliable. We also chose a 3-level regression model to identify the risk factors of mortality (however, the intercept of region was 0) to ensure comparability. This model included the same variables we used for the indicator "readmissions", except for the use of the indicators "minimal antidepressant treatment" and "minimal psychotherapy" instead of the indicators "guideline-adherent treatment with medication" and "guideline-adherent treatment with psychotherapy" in the first half of the year after discharge. The reason for this change was that the described indicators of guideline-adherent treatment with medication and psychotherapy would have confounded the results because of the time criteria and potential death during these time intervals.

Statistical analysis and ethical considerations

A significance level of $p = 0.05$ was used (two-sided). Because of the explorative nature of this study, no correction for multiple testing was applied. For analysis and statistics, SAS Enterprise Edition 7.1. was used on the servers of the BARMER Data Warehouse. For data protection reasons, only the publication of group results with large numbers is permitted. In order to protect individual affected persons from being identified, all N numbers <50 were reported as <50 in the result presentation. The authors are bound to this procedure under a contract with BARMER.

According to a statement of the Rhineland-Palatinate Medical Association, this study which uses administrative routine data does not require special approval by the ethics committee.