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RESEARCH: EPIDEMIOLOGY

Achieving diabetes treatment targets in people with registered mental illness is similar or improved compared with those without: Analyses of linked observational datasets

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Abstract

Aims: To determine the association between registered mental illness and type 2 diabetes mellitus treatment targets, while taking into account the effects of health expenditure and social determinants of health.

Methods: This observational cross-sectional study was based on routine primary care data, linked to socio-economic and medical claims data. The main outcomes, analysed by multivariate logistic regression, were achieving primary care guideline treatment targets for HbA_{1c}, systolic blood pressure (SBP) and LDL-cholesterol in 2017. We examined the association with diagnosed mental illness registered by the general practitioner (GP) or treated via specialist' mental healthcare between 2016 and 2018, adjusting for, medication use, body mass index, co-morbidity, smoking, and additionally examining effect-modification of healthcare expenditures, migration status, income and demographics.

Results: Overall ($N = 2862$), 64.0% of participants achieved their treatment targets for HbA_{1c}, 65.1% for SBP and 53.0% for LDL-cholesterol. Adjusted for migrant background, income and care expenditures, individuals <65 years of age with mental illness achieved their HbA_{1c} treatment target more often than those without (OR (95% CI)): treatment by GP: 1.46 (1.01, 2.11), specialist care: 1.61 (1.11, 2.34), as did men with mental illness for SBP: GP OR 1.61 (1.09, 2.40), specialist care OR 1.59 (1.09, 2.45). LDL-cholesterol target was not associated with mental illness. A migrant background or low income lowered the likelihood of reaching HbA_{1c} targets.

Conclusions: People with registered mental illness appear comparable or better able to achieve diabetes treatment targets than those without. Achieving HbA_{1c} targets is influenced by social disadvantage.

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KEYWORDS

diabetes mellitus, type 2, electronic health record data, healthcare expenditures, mental disorders, observational data, social determinants of health, treatment targets

1 | INTRODUCTION

Type 2 diabetes mellitus and mental illness often co-occur,¹ and are associated with decreased quality of life and co-morbidity.² People with type 2 diabetes are not only more likely to develop a mental illness; the causal link is bi-directional.^{3,4} In people with mental illness, decreased self management, use of psychiatric medication and genetic predisposition may increase diabetes risk, and (when already present) influence diabetes regulation,^{2,5,6} whereas diabetes itself can lead to depressive symptoms and cognitive decline.^{3,4,7}

To reduce the risk of cardiovascular complications, diabetes treatment aims to control HbA_{1c}, blood pressure and cholesterol levels, and for this purpose, personalised treatment targets have been advised by the Dutch primary care guidelines. Existing research on the effect of mental illness on diabetes regulation is inconclusive. Rather than poorer glycaemic control and diabetes monitoring,^{2,6} it has been observed that people with type 2 diabetes with hospital-diagnosed depression or antidepressant treatment are actually more likely to achieve HbA_{1c} treatment targets compared with people without.⁸ This could be a consequence of beneficial antidepressant medication or the more intensive delivery of healthcare in patients with diabetes receiving treatment for depression. Compared with people not affected by mental illness, Smith et al.⁹ found similar mean HbA_{1c} regulation but improved systolic blood pressure (SBP) regulation in individuals with severe mental illness. However, it should be noted that severe mental illness was associated with more extreme risk values (very high or very low) for HbA_{1c}.

Due to their need for both mental and physical care, individuals with diabetes and mental illness make greater use of healthcare and require higher healthcare expenditure.¹⁰⁻¹³ In the Netherlands, type 2 diabetes care is well organised within care groups and is mainly delivered by general practitioners (GPs) and their teams.¹⁴ GPs are also the gatekeeper for mental healthcare and low-intensity conditions are mainly treated in GP practice centres, whereas people with greater treatment demands are treated in specialist care. The diverse treatment needs of people with multiple morbidities may lead to fragmented care, with possible adverse effects on outcomes. If diabetes treatment targets are not reached despite intensive use of healthcare, there may be room for improvement regarding the delivery of healthcare. Conversely, when treatment

What's new?

- Type 2 diabetes and mental illness exhibit a bi-directional relationship in terms of disease control as well as prevalence. Social determinants of health are associated with both diseases.
- In terms of reaching treatment targets, adults with diabetes and registered mental illness were comparable or better than those without mental illness. Income or a migrant background was independently associated with disease regulation, whereas healthcare expenditure was not.
- When mental illness is registered (thus diagnosed) and diabetes is monitored in people with diabetes, diabetes treatment targets can be achieved. Diabetes care providers should therefore consider recognition and prevention of mental illness.

targets are reached, efforts may be justified despite high expenditure.

The prevalence and persistence of both mental illness and type 2 diabetes is associated with social determinants of health such as income, employment, migrant background and access to healthcare delivery.^{5,15} Previous research examining the association between lower SES and healthcare delivery¹⁶ produced mixed results, as any association is highly dependent on the specifics of local healthcare organisation.^{17,18} A lower socio-economic status (SES) is associated with poorer achievement of treatment targets for HbA_{1c}, SBP and lipids in people with diabetes.^{18,19} Social determinants of health should therefore be considered when examining the quality of chronic care delivery in socio-economic diverse populations.

Although individual impacts of social determinants of health on the prevalence and outcomes of mental illness or type 2 diabetes are well established, the association of mental illness with achieving diabetes targets in relation to social determinants of health remains unclear. Furthermore, healthcare expenditures, as a measure of delivered care, may play a role in achieving targets. We, therefore, investigated associations between mental illness and achieving diabetes treatment targets for HbA_{1c}, SBP, and LDL-cholesterol. As healthcare expenditures

and/or social determinants of health may be associated with mental illness or the above outcomes, we also investigated effect modification and adjusted our analysis in relation to these determinants.

2 | METHODS

In this observational cross-sectional study, we used pseudonymised routine GP care data from The Hague area that were derived from our 'Extramural Academic Network of the Leiden University Medical Centre' data warehouse (data of approximately 180,000 citizens from 1 January 2007 to 31 December 2019).²⁰ Included individuals were informed about use of their data for research purposes and could withdraw via an informed opt-out procedure. Healthcare data were linked to socio-economic data within the Social Statistical Datasets from Statistics Netherlands.²¹ These datasets cover longitudinal micro-data on several domains (demographics, socio-economic details, including migration background, residence, income, and statutory basic health insurance claims data from all Dutch health insurers) for registered residents of the Netherlands. International Classification of Primary Care (ICPC) codes, body measurements and metformin prescriptions (7-digit Anatomical Therapeutic Chemical Classification System code (ATC)) were derived from the GP data. Demographics, social determinants of health, death records, medication use and healthcare expenditures were derived from the Social Statistical Datasets for the year 2017. Medication use was derived from claims data, aggregated on an annual basis per person using a 4-digit ATC. A code book with a detailed description of the determinants is available on request. The ethics Committee Leiden-The Hague-Delft exempted this study.

2.1 | Study population

Adults (18–80 years of age) with an active ICPC-code for type 2 diabetes (T90 and T90.02) and alive in the year 2017 were included. Exclusion criteria included a diabetes duration of <1 year (as diabetes outcomes may be unregulated in the first year after diagnosis²²), likely type 1 diabetes, Latent Autoimmune Disease of the Adult, Maturity-Onset Diabetes of the Young, gestational diabetes or dementia (being more of a neurological aetiology and occurring at older age) Those with data missing on all three treatment targets were excluded, indicating that individuals included attended at least one annual diabetes monitoring visit.

2.2 | Mental illness groups

Three mental illness groups were defined: (1) no mental illness; (2) mental illness in 2017 registered in GP data (i.e., individuals with ICPC-code for mental illness, but no expenditures via specialised mental healthcare) and (3) mental illness identified via mental healthcare expenditure data (i.e. specialist mental healthcare between 2016–2018).

2.3 | Treatment targets

Mean HbA_{1c}, SBP and LDL-cholesterol were calculated from all registered measurements in 2017. Treatment targets were defined by the 2017 Dutch treatment guidelines for primary care.^{13,23} HbA_{1c} targets were ≤7.0% (≤53 mmol/mol) for those aged <70 or aged ≥70 years without medications or metformin monotherapy and ≤7.5% (≤58 mmol/mol) for those aged ≥70 years with additional blood glucose lowering medication or insulin.²³ The treatment target for SBP was <140 mmHg.¹³ The target level for LDL-cholesterol was ≤2.5 mmol/L, but only for individuals with an indication for primary or secondary prevention of cardiovascular disease (CVD). Indications were secondary prevention of manifest CVD and primary prevention for individuals without CVD but >20% risk of 10-year fatal and non-fatal CVD risk score defined by the Systematic Coronary Risk Evaluation function.¹³ Reimbursed lipid-lowering medication in 2017 was defined as an additional indication.

2.4 | Medical determinants

Diabetes duration was identified using the first ICPC-code registration date and was categorised into tertiles of 12–50, 50–85, or 85–120 months. As data were available from 2007 on, the maximum diabetes duration was 10 years. Smoking status was defined as 'non-smoker', 'previous smoker' or 'current smoker' in 2016–2018. Mean body mass index (BMI (kg/m²)) was calculated from all BMI registered in 2016–2018.

Diabetes-related vascular co-morbidity was defined as the presence of one or more ICPC-codes for manifest micro- or macrovascular disease. Other chronic co-morbidity was defined as the presence of one or more chronic diseases selected based on their high prevalence among the Dutch population.²⁴

Three diabetes treatment categories were defined: (1) lifestyle advice only (no reimbursed glucose-lowering medication), (2) oral blood glucose-lowering medication

or GLP-1 agonists (ATC A10B, no A10A) and (3) use of insulin (ATC A10A). Metformin monotherapy was identified from prescription data on ATC-7 level from the GP data for people >70 years, to allow their treatment target for HbA_{1c} to be determined. Other medication groups were categorised as 'yes' and 'no' regarding usage of psychiatric/anti-hypertensive/lipid-lowering medication.

2.5 | Social determinants

Demographic determinants included sex and age on 1 January 1 2017; social determinants of health included migration status and income. Migration status was clustered into two groups, 'Dutch origin' or 'migrant background', based on the individual's or parents' country of origin. Standardised disposable household income was used, which represents the net amount a household can spend on an annual basis, adjusted for household size and composition and divided into percentiles on a population-wide national level: low (0–33 percentile), middle (33–66 percentile), high (66–100 percentile). Job status was defined by the main source of household income and classified into two groups: (1) income from wages or pension benefits, and (2) income from social security benefits.

2.6 | Healthcare expenditures

Total reimbursed healthcare expenditures minus expenditures for mental healthcare were used as an indicator of healthcare utilisation and analysed as tertiles. For baseline characteristics, total expenditures were further grouped into GP expenditure, medical specialist expenditure and pharmacy expenditure.

2.7 | Missing data

Missing data were handled using multiple imputation generating 10 imputed datasets (supplementary material (SM) A).²⁵ Variables in the imputation procedure included all predictors and the outcome variables of the final analysis, plus a two-digit postal code. Pooled results were calculated using Rubin's rules.

2.8 | Statistical analysis

All analyses were performed using SPSS version 25. Descriptive statistics for all determinants were provided in *n* (%), mean ± standard deviation (SD) or median (interquartile range (IQR)), as appropriate. Continuous data

were normally distributed, except for income and healthcare expenditures, which were categorised for the main analyses.

The main analyses were multivariate logistic regression models with the outcomes being achieved treatment targets for (1) HbA_{1c} (2) SBP and (3) LDL-cholesterol.

The models were built using the following steps: for each outcome variable a basic model was performed including only demographic and medical determinants. Interaction terms for sex and age were added to examine effect modification with mental illness. Second, (1) migration status and (2) income were added and effect modification with mental illness was examined. Finally, total healthcare expenditures were added and effect modification examined. When effect modification was present, models were stratified into appropriate groups. All final models included demographics (sex, age), medical factors (mental illness group, diabetes-related co-morbidity, other chronic co-morbidity, BMI, diabetes duration, psychiatric medication, diabetes treatment category (HbA_{1c}), use of anti-hypertensives (SBP), use of lipid lowering medication (LDL model)), social factors (migration status, income) and healthcare expenditures.

To assess the associations of migration status, income and healthcare expenditures with mental illness, multinomial multivariate regression analysis was performed on the full population, adjusted for all relevant confounders.

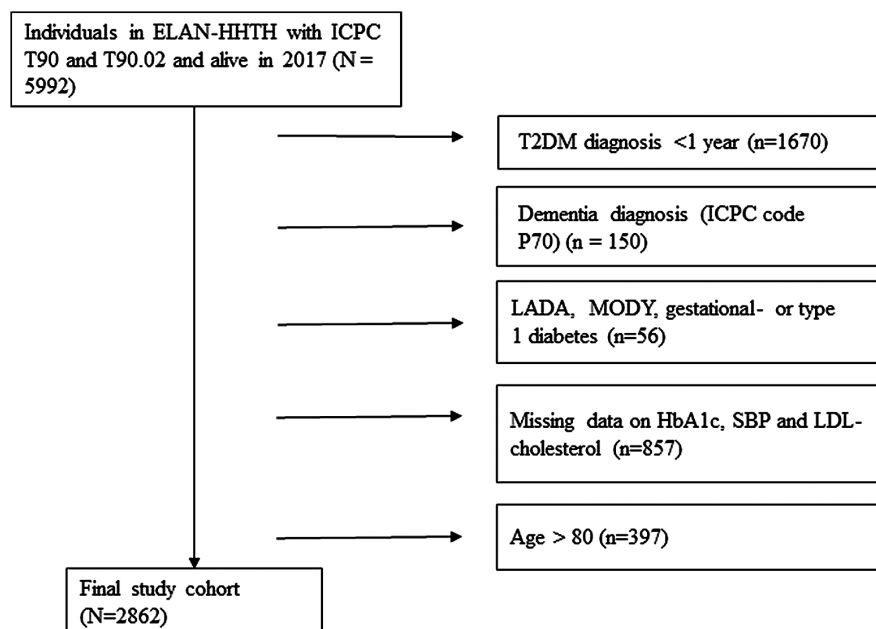
We performed several sensitivity analyses. First, using multilevel logistic regression we investigated to what extent differences in outcome variables could be attributed to between-GP practice differences. Furthermore, we examined the associations of job status as a substitute for income, and mental illness duration <1 year versus >1 year as a substitute for a mental illness group. Lastly, we substituted total healthcare expenditures with pharmacy expenditures only.

Area-under-the-curves (c-statistic) were calculated to assess internal validity of the main analysis.

3 | RESULTS

Of the 5992 living adults with type 2 diabetes identified in the data warehouse in 2017, 2862 were included in the analyses (Figure 1). Most individuals were excluded based on diabetes duration <1 year and missing data on all three outcome measurements. Almost a quarter of all included participants (23%: *n* = 644) had a mental illness diagnosis, of which 323 received specialist care. Half of the population had a low income (50%) and half (52%) had a migrant background. Median total healthcare expenditures in 2017 were 2560 (IQR 1324–5855) euros (Table 1). Compared with those without mental illness, individuals

FIGURE 1 Flowchart of patient inclusion



with mental illness were younger and were more likely to have/more often had a lower income, receive social benefits, and generate higher healthcare expenditures (Table 2, Figure 3, SM B Table S1).

Except for HbA_{1c} (6.3%), SBP (7.5%), LDL-cholesterol (13%), smoking (7.7%), BMI (7.7%), the proportion of missing data was less than 1% (SM A).

3.1 | Achieving treatment targets

Overall, 64% of participants ($n = 1831$) achieved their treatment target for HbA_{1c}, 65% ($n = 1863$) for SBP and 53% ($n = 1516$) for LDL-cholesterol.

Regarding the HbA_{1c} target, mental illness by age group (<65 years (mean age 54.1 ± 7.7) versus ≥ 65 years (mean age 71.2 ± 4.1)) showed effect modification. For the SBP target, sex (age men: 62.1 ± 10.4 women: 61.2 ± 10.8) and income showed effect modification. As associations differed between subgroups, all associations are presented for the largest subgroup (age for HbA_{1c}, sex for SBP). No other effect modification was seen (SM B Table S2).

HbA_{1c} Overall, mental illness was not associated with achieving the HbA_{1c}-target (OR (95% CI) GP treatment, 1.26 (0.92, 1.73); specialist care, 1.36 (0.98, 1.88) (SM B, Table S3a). However, adults aged <65 years with mental illness, GP-registered or in specialist care were more likely to achieve their treatment target for HbA_{1c} compared with those without OR (95% CI) GP treatment, 1.46 (1.01, 2.11); specialist care, 1.61 (1.11, 2.34). Adults aged ≥ 65 years with higher incomes were also more likely to achieve their HbA_{1c} target. In both age groups, a migrant background

and diabetes medication lowered the likelihood of achieving targets (Figures 2a and 3a) compared with native Dutch and those without medication.

SBP Overall, mental illness was not associated with the SBP-target (OR (95% CI) GP treatment, 1.10 (0.84, 1.46); specialist care, 1.30 (0.94, 1.80) (SM B, Table S3a). However, men with mental illness, GP-registered or in specialist care, were more likely to achieve the SBP treatment target than men without mental illness OR (95% CI) 1.61 (1.09, 2.40), 1.59 (1.09, 2.45), respectively. For both sexes, higher BMI, higher age, and use of anti-hypertensive medication compared with those without medication negatively affected SBP targets (Figures 2b and 3b).

LDL-cholesterol Mental illness was not associated with achieving LDL-cholesterol targets: OR (95% CI) 1.16 (0.89, 1.52), 1.12 (0.85, 1.49), respectively. Independent from mental illness, use of lipid-lowering medication, a longer diabetes duration, a lower income and higher healthcare expenditures were all associated with achieving LDL-cholesterol targets (Figures 2c and 3c).

Regarding area-under-the-curves, the 95% CI for the three main analyses indicated moderate to good internal validity (HbA_{1c} <65: 0.78 (0.76, 0.80) ≥ 65 : 0.79 (0.76, 0.82); SBP men: 0.65 (0.63, 0.68) women: 0.67 (0.64, 0.70); LDL: 0.64 (0.62, 0.66)).

Sensitivity analysis (results available on request) showed small practice variations concerning achieving treatment targets, with intraclass correlation coefficients between 0.5 (0.09%–3.0%)–4.3% (1.7%–10%) for the different models. There was no association of job status with achieving diabetes treatment targets. Individuals with a mental illness duration >1 year were more likely to achieve HbA_{1c} and SBP targets compared with individuals

TABLE 1 Baseline characteristics

Baseline characteristics of the total study population and numbers reaching treatment targets				
	On target HbA _{1c}	On target systolic blood pressure	On target LDL-cholesterol	Total n, (% of total N)
	<i>n</i> = 1831 (64%)	<i>n</i> = 1863 (65%)	<i>n</i> = 1516 (53%)	<i>N</i> = 2862
Women	851 (66%)	854 (66%)	636 (49%)	1290 (45%)
Men	980 (62%)	1009 (64%)	880 (56%)	1572 (55%)
Age (years)	63.6 ± 10.0	60.4 ± 10.8	61.7 ± 11.1	61.8 ± 10.6
Mental illness				
No mental illness	1428 (64%)	1407 (63%)	1153 (52%)	2218 (77%)
Mental illness registration GP	208 (65%)	217 (67%)	177 (55%)	321 (11%)
Specialist mental healthcare	195 (60%)	240 (74%)	186 (57%)	323 (11%)
Medical determinants				
Diabetes duration (months)	65 (40–91)	67.8 (41–93)	71 (44–95)	68 (41–93)
BMI (kg/m ²)	29.9 ± 5.3	29.9 ± 5.2	30.3 ± 5.5	30.2 ± 5.4
HbA _{1c} mmol/mol; (%)	47 ± 5 (6.4 ± 2.6%)	54 ± 14 (7.1 ± 3.4%)	54 ± 14 (7.1 ± 3.4%)	54 ± 4 (7.1 ± 3.4%)
LDL-cholesterol (mmol/l)	2.6 ± 0.9	2.6 ± 0.9	2.1 ± 0.5	2.7 ± 0.9
SBP (mmHg)	136 ± 13.7	128 ± 8.5	135 ± 13.7	136 ± 14.3
Medication usage (<i>n</i> %)				
Diabetes medication				
None	624 (94%)	438 (66%)	297 (45%)	663
Oral blood-glucose-lowering drugs or GLP-1 agonists	1132 (61%)	1209 (65%)	1006 (54%)	1850
Insulin use	75 (21%)	217 (62%)	213 (61%)	349
Psychiatric medication	530 (64%)	556 (67%)	446 (54%)	831
Anti-hypertensives	1296 (66%)	1165 (59%)	1106 (56%)	1964
Lipid-lowering medication	1316 (63%)	1375 (66%)	1238 (60%)	2082
Smoking				
Never	679 (63%)	740 (68%)	564 (52%)	1084
Before	737 (68%)	654 (60%)	593 (55%)	1088
Current	415 (60%)	470 (68%)	359 (52%)	691
Co-morbid conditions				
No	543 (62%)	615 (70%)	465 (53%)	882
Micro- or macrovascular	516 (62%)	515 (62%)	491 (59%)	836
Other chronic	1172 (65%)	1131 (63%)	949 (53%)	1791
Total healthcare expenditures tertiles and healthcare expenditures median (IQR)				
1st tertile	670 (66%)	670 (66%)	490 (48%)	1013
2nd tertile	635 (66%)	647 (67%)	512 (53%)	967.2
3rd tertile	526 (60%)	547 (62%)	514 (58%)	882
Total minus mental healthcare expenditures	1914 (961–4219)	1974 (998–4329)	2212 (1105–5044)	2018 (1006–4550)
Migration status				
Dutch origin	965 (70%)	827 (60%)	726 (53%)	1373
Migrant background	866 (58%)	1036 (70%)	790 (53%)	1489
Job status				

TABLE 1 (Continued)

Baseline characteristics of the total study population and numbers reaching treatment targets				
	On target HbA _{1c}	On target systolic blood pressure	On target LDL-cholesterol	Total n, (% of total N)
Salary or pension benefit	1546 (66%)	1497 (64%)	1232 (52%)	2349
Social security benefit	285 (56%)	366 (71%)	284 (55%)	513
Standardized household income in percentiles				
Low (0–33)	869 (61%)	927 (66%)	791 (56%)	1416
Middle (33–66)	487 (64%)	494 (65%)	401 (53%)	764
High (66–100)	475 (70%)	442 (65%)	324 (48%)	682

Note: Data represent *n* (% of total per category), mean ± SD or median (interquartile range).

Results are pooled from the results of 10 multiple imputed datasets.

with a mental illness duration of <1 year: OR (CI 95%) HbA_{1c} <65 years: >1 year: 1.56 (1.15, 2.12), <1 year: 1.37 (0.70, 2.66); and SBP men: >1 year: 1.63 (1.17, 2.29), <1 year: 1.42 (0.68, 2.95). Pharmaceutical care appeared to be the primary contributor to the association of healthcare expenditure with achieving treatment targets for SBP (in men) and LDL-cholesterol: OR (CI 95%) high pharmaceutical expenditure SBP men, 1.55 (1.13, 2.12); high pharmaceutical expenditures LDL-cholesterol, 1.49 (1.20, 1.86).

4 | DISCUSSION

In this study, we explored the complex relationship of mental illness with type 2 diabetes treatment targets in a multi-ethnic socio-economically diverse urbanised population. Younger adults (<65 years) with mental illness were more likely to achieve HbA_{1c} treatment targets. Adults with a migrant background, compared with Dutch or older adults with a low income, compared with those with a high income were less likely to achieve HbA_{1c} targets, independent of mental illness. Men with mental illness were more likely to achieve SBP treatment targets. By contrast, mental illness was not associated with achieving LDL-cholesterol targets. Healthcare expenditure had no confounding or effect-modifying association with target achievement. A longer duration of mental illness was positively associated with reaching targets, suggesting that disruption due to mental illness can only be improved by recognition and treatment of problems.

Previous studies have reported both impaired^{6,26,27} and improved^{8,12,28} glycaemic control in people with diabetes and depression. Improved HbA_{1c} and SBP control in adults with mental illness might have been influenced by healthcare and self management, as only care users were included in our study. Lister et al.¹² found a positive association between health checks and HbA_{1c}, SBP and LDL-cholesterol levels in people with severe mental

illness. An alternative explanation might be the recognition and treatment of mental illness, as treatment of depression reportedly improves glycaemic control.²⁸ People with mental illness also received more GP, specialist or pharmaceutical care, as indicated by higher healthcare expenditures, although no evidence was found for effect-modification through or an independent contribution of healthcare expenditure.

Consistent with previous research,^{5,12} mental illness was associated with socio-economic factors, and migrant background and low income were negatively associated with achieving HbA_{1c} targets independent of mental illness.^{18,19} However, achieving SBP targets was not associated with migration status or income, perhaps due to adequate healthcare delivery or self management in our population.¹⁷ People with a higher income were less likely to achieve LDL-cholesterol targets, possibly as a result of a lower prevalence of vascular co-morbidity and less use of lipid-lowering medication in the high-income population, both of which are important predictors for achieving LDL targets.

People prescribed anti-diabetic or anti-hypertensive medication were less likely to achieve their HbA_{1c} or SBP targets, respectively, which may be explained by a tendency amongst doctors to prescribe medication in response to a failure to reach targets. This suggests that diabetes and cardiovascular risk management was properly initiated, although time or adherence effects were not investigated.

Subgroups revealed effect differences regarding age and HbA_{1c}, and sex and SBP. People receiving treatment for mental illness were significantly younger, which might explain the effect differences on HbA_{1c} targets between people <65 and ≥65 of age, although underdiagnosis or undertreatment of mental illness in the elderly could also be an explanation.²⁹ Little is known about sex differences in achieving diabetes treatment targets in people with mental illness. A Norwegian study³⁰ found that depression

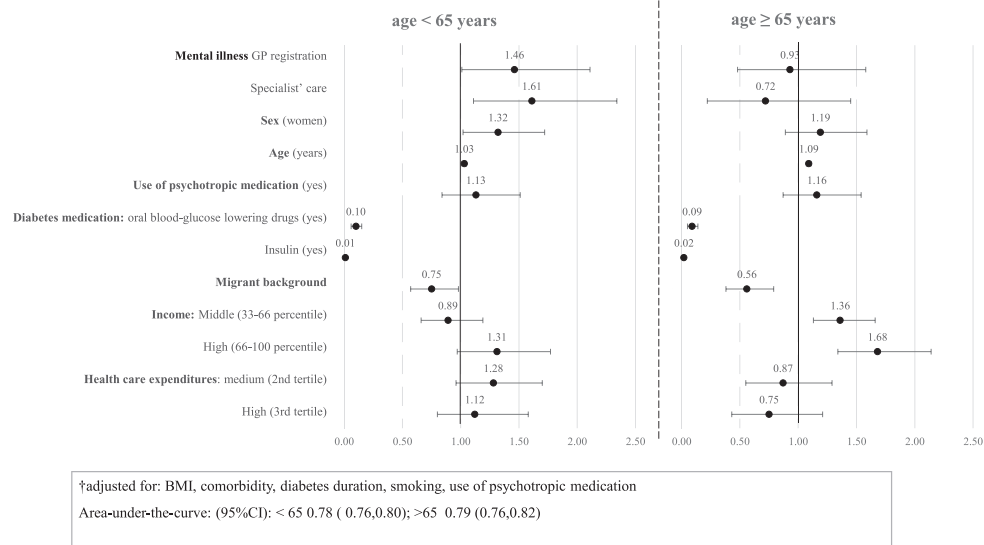
TABLE 2 Characteristics of individuals with and without mental illness

Baseline characteristics by mental illness status			
Characteristic	No mental illness (n = 2218)	Mental illness, monitoring by general practitioner (GP) (n = 321)	Mental illness, specialist mental healthcare (n = 323)
Female sex	969 (44%)	163 (51%)	158 (49%)
Age	62.9 ± 10.4	59.8 ± 10.5	56.4 ± 10.4
Mental illness duration median years (IQR)	n/a	5.5 (3.4–8.0)	5.1 (2.2–8.0)
HbA _{1c} mmol/mol; %	54 ± 13 7.1 ± 3.4%	54 ± 14 7.0 ± 3.4%	56 ± 16 7.2 ± 3.6%
SBP mmHg	137.0 ± 14.2	135.4 ± 14.1	133.1 ± 14.6
LDL-cholesterol	2.67 ± 0.88	2.65 ± 0.85	2.65 ± 0.93
Healthcare expenditures (Euros)			
Total minus mental healthcare	1851 (946–4153)	2217 (1064–5183)	3036 (1584–6150)
General practitioner care	157 (120–230)	185 (131–269)	214 (144–327)
Hospital care	558 (132–1957)	661 (150–2484)	765 (203–2963)
Pharmaceutical care	400 (192–916)	574 (234–1088)	829 (384–1653)
Medication usage			
Diabetes medication			
None	519 (24%)	83 (26%)	62 (19%)
Oral blood-glucose lowering drugs or GLP-1 agonists	1454 (66%)	191 (60%)	206 (64%)
Insulin	245 (11%)	47 (15%)	56 (17%)
Anti-hypertensives	1544 (70%)	219 (68%)	202 (62%)
Lipid-lowering medication	1606 (72%)	223 (70%)	253 (78%)
Psychiatric medication			
Antipsychotics	19 (0.9%)	12 (3.7%)	115 (6%)
Anxiolytics	299 (14%)	83 (26%)	141.6 (44%)
Antidepressants	158 (7.1%)	86 (27%)	136 (42%)
Drugs for addictive disorders	48 (2.2%)	11 (3.4%)	24 (7.4%)
Social determinants of health			
Migration status			
Dutch origin	1100 (50%)	141 (44%)	132.1 (41%)
Migrant background	1118 (50%)	180 (56%)	191.1 (59%)
Household income			
Low	1036 (47%)	176 (55%)	204 (63%)
Middle	617 (28%)	79 (25%)	68 (21%)
High	565 (26%)	66 (21%)	51 (16%)
Job status			
Salary or pension benefit	1929 (87%)	238 (74%)	183 (57%)
Social benefit	289 (13%)	84 (26%)	141 (44%)

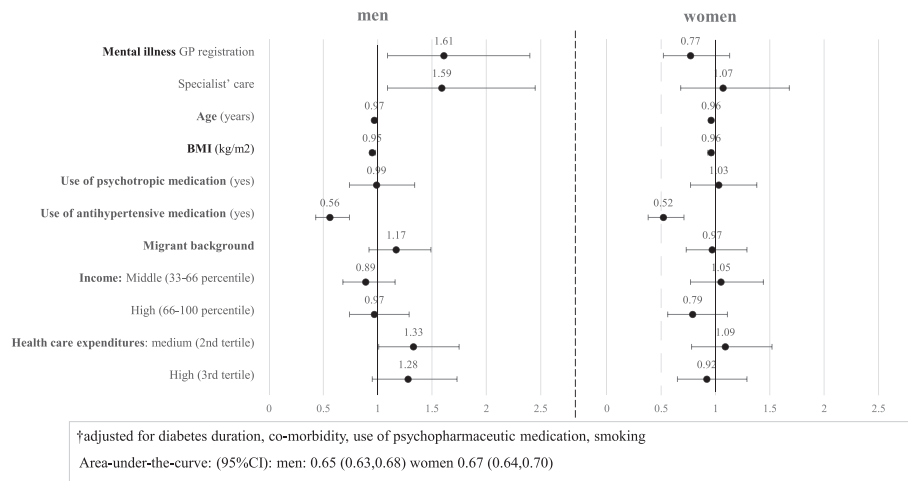
Note: Data represent n (% of total per mental illness category), mean ± SD or median (interquartile range).

Results are pooled from the results of 10 multiple imputed datasets.

(a) Achieving HbA1c treatment target (OR, 95% CI) †



(b) Achieving systolic blood pressure treatment target (OR, 95% CI) †



(c) Achieving LDL-cholesterol treatment target (OR, 95% CI) †

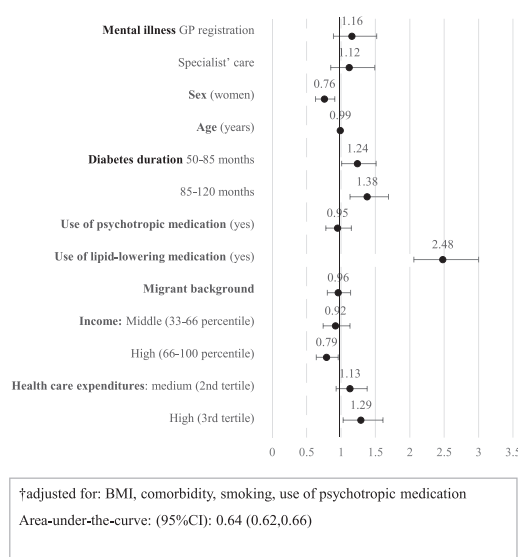


FIGURE 2 Legend on next page

and anxiety were associated with higher HbA_{1c} levels but not SBP levels in men. Another study³¹ showed that diabetes distress, but not depression, was associated with higher HbA_{1c} levels but only in women. Scores for factors such as well-being and diabetes quality of life in women were lower in that study, possibly indicating different care demands between genders/sexes.

4.1 | Strengths and limitations

Some limitations should be considered. First, the cross-sectional design precludes identification of causal relationships between mental illness, social determinants of health and healthcare expenditures. However, possible links of these domains to frailty were found. Given the limited geographic study area, our results are only relevant to comparable healthcare systems and socio-economic compositions.

Another important factor was missing data due to registration and attendance bias.³² We excluded those with missing data on all three outcome variables, most likely including non-attenders and those treated via specialist' healthcare. Care avoiders could not be examined but may be at higher risk of missing targets. Additionally, mental illness registration may reflect GP motivation, and practices with better registration may have better treatment outcomes. However, we found little practice variation in achieving treatment targets, although the small number of practices did limit power.³³

In including persons with reimbursed expenditures of mental illness care in 2018, persons in the 'mental illness' group with mental illness treatment after the year of the measured outcomes (2017) may have been included. We included these persons in the main analysis, as the waiting period between application and treatment in specialist' care are often considerable, and it is likely these persons already have mental (untreated) complaints in 2017. This may have led to underestimation of our results, which was confirmed by our sensitivity analysis that showed that those with mental illness duration <1 year (thus, including those with incident reimbursed expenditures in 2018) in both mental groups were less likely to achieve their targets.

Finally, although treatment location implied severity, we did not actively distinguish between categories of mental illness. This was a clinical decision, as regardless of the diagnosis all mental illnesses interfere with self management skills. Nevertheless, severity of disease might influence diabetes self management.¹²

Overall, this study suggests that diabetes targets can be achieved by people with diagnosed mental illness in an urbanised, socio-economically diverse area. Diabetes monitoring and recognition of mental illness appear to represent the 'protective key' in the association of mental illness with achieving treatment targets. All diabetes monitoring visits should therefore address psychological disturbance, and attendance should be encouraged.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTION

RV, EN and JS designed the study. JS conducted database management quality assurance. EN carried out data management and data analysis; EN, RV and JS interpreted the data. EN wrote the first draft and revised the manuscript, incorporating contributions from co-authors. RV, JS, SS and MN critically revised the manuscript. All authors agreed on submission and are joint guarantors of this work.

DATA AVAILABILITY STATEMENT

As data contain personal health information and individual socio-economic information, data were strictly used under license for the current study and are, therefore, not publicly available.

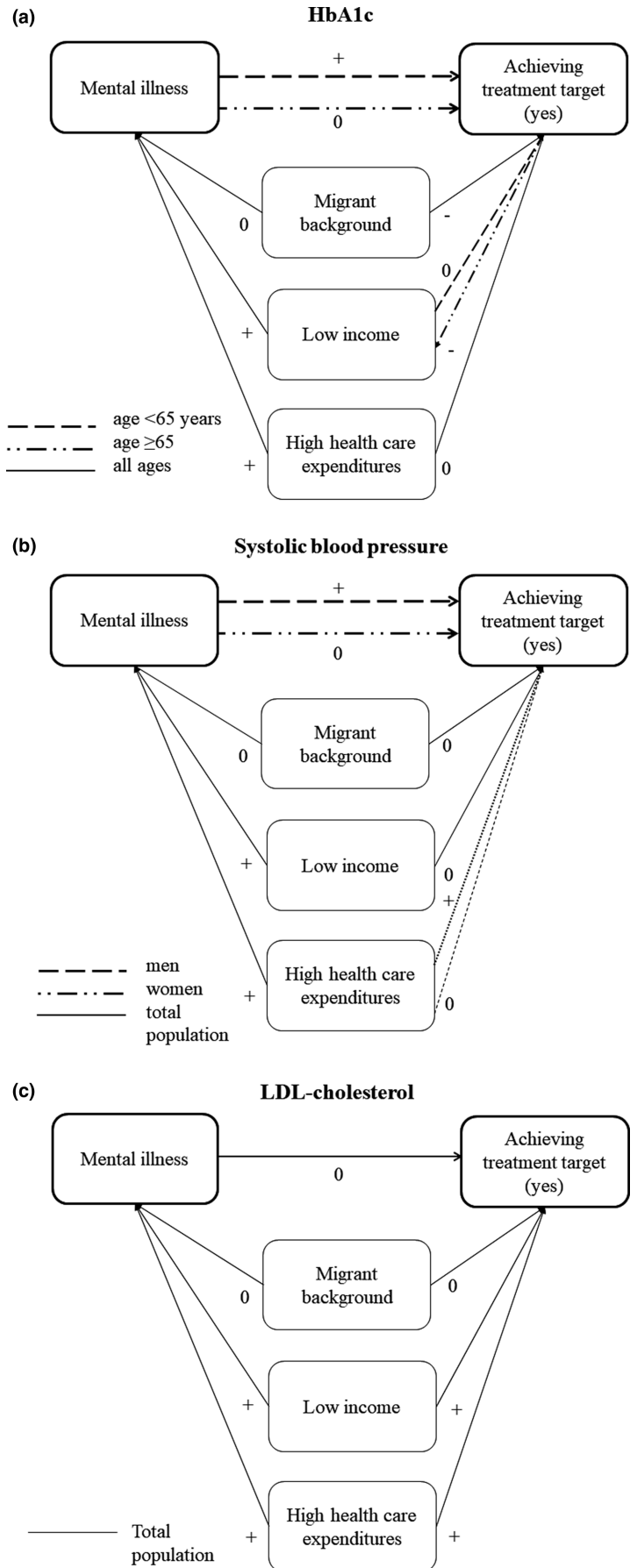
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FIGURE 2 (a–c) Multivariate logistic regression model: achieving cardiovascular treatment targets, mental illness, income, migration status and healthcare expenditures. (a) Achieving the HbA_{1c} target. (b) Achieving the systolic blood pressure target. (c) Achieving the LDL-cholesterol target. Multivariate logistic regression models of mental illness, income, migration status and healthcare expenditures associated to achieving cardiovascular treatment targets. Not achieving treatment targets was the reference group for the analyses. Results are presented as adjusted odds ratios (OR), with 95% confidence intervals (95% CI), for the pooled results of the imputed data analyses. Exact numbers are displayed in SM B, Table S3. Reference groups for categorical determinants: no mental illness, no anti-diabetes medication, no anti-hypertensive medication, no lipid-lowering medication, diabetes duration 12–50 months, Dutch origin, low income, low healthcare expenditures (first tertile). Odds ratios of the associations are displayed in SM B, Table S3

FIGURE 3 (a–c) Associations of mental illness, social determinants, healthcare expenditures with reaching treatment targets. – Negative association. + Positive association. 0 no association. Associations with treatment targets are adjusted for sex, age, BMI, diabetes duration, co-morbidities, smoking, income, migration status, healthcare expenditures, as well as use of psychopharmaceuticals, diabetes medication (HbA_{1c}), anti-hypertensive medication (systolic blood pressure) and lipid-lowering medication (LDL-cholesterol). Associations with mental illness are adjusted for sex, age, BMI, diabetes duration, co-morbidities, income, migration status, smoking, diabetes medication and psychopharmaceuticals (healthcare expenditures). Odds ratios of the associations are displayed in SM B



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