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Study to determine the epidemiology of treatment-resistant depression among the Saudi Arabian population: A cross-sectional study

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Abstract:

BACKGROUND: Depression is a common mental health disorder that affects millions of people worldwide. Globally, major depressive disorder (MDD) is a public health concern; nearly, it affects more than 300 million people. The coronavirus disease 2019 (COVID-19) pandemic lockdown, travel restrictions, social distancing, and COVID-19 vaccine acceptance have aggravated psychological disorders, such as depression and suicidal tendencies. Treatment-resistant depression (TRD) is typically defined as a lack of response to at least two different antidepressant medications or psychotherapies. TRD is common and has been associated with higher comorbidities and prolonged duration of illness, leading to a substantial medical and economic burden.

MATERIALS AND METHODS: A cross-sectional study was designed to determine the epidemiology and estimate the prevalence of TRD in Abha City, Assir Region, Kingdom of Saudi Arabia. The study includes adult patients who were attended to the psychiatry department and aged 18–65 years diagnosed with major depressive depression. A total of 651 study participants were recruited.

RESULTS: Of the total 651 depressive disorder cases, 134 (20.6%) were reported as TRD and the remaining 517 (79.4%) were nontreatment-resistant depressive cases. Of the 651 depression participants, 176 (27%) were males and 475 (73%) were females. More than one-quarter (180 (28%)) had been associated with chronic morbidity. One-tenth of the depressive patients were suffering from thyroid disorders, followed by hypertension (10%), autoimmune diseases (10%), and diabetes mellitus (8%).

CONCLUSIONS: TRD emerged as a threat to public health and challenging psychiatric care providers, and further innovative techniques and effective newer drugs to treat depression need to be researched. The treatment complaint mechanism is warranted, encouraging people to get treatment from the psychiatrist by removing the stigma of mental illness, which is needed to improve the quality of life of TRD patients.

Keywords:

Antidepressants, Beck's Depression Inventory, epidemiology, nontreatment-resistant depression, treatment-resistant depression

Introduction

Depression is a common mental health disorder that affects millions of people worldwide. Globally, major depressive disorder (MDD) is a public health concern; nearly, it affects more than 300 million people.[1,2] MDD has a substantial impact on essential activities of life, including sleeping, eating, intellect, and self-worth.

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Depression can occur in anyone who is exposed to severe loss, abuse, or other stressful life events. Women are more prone to depression than men.[3] In 2020, the estimated MDD prevalence among adults was 8.4% in the USA, and the major depressive episode was highest among individuals aged 18–25 (17.0%), almost double the prevalence in females compared with males.[4] Numerous large-scale clinical trials have studied the treatment response rates of depressive disorders to conventional therapeutic approaches. The cumulative remission rate was 67% (within 14 months).[5] MDD can happen at any age of life, depending on biological susceptibility, risk factors, symptomatic presentation, and comorbidities present among people with the same diagnosis.[6]

According to a 2021 study published in the International Journal of Clinical and Health Psychology, the prevalence of depression in Saudi Arabia is estimated to be around 26.4%. Coronavirus disease 2019 (COVID-19) causes neurological problems such as headaches, olfactory dysfunction, loss of taste, and cognitive impairments.[7] The COVID-19 pandemic lockdown, travel restrictions, social distancing, and COVID-19 vaccine acceptance have aggravated psychological disorders, such as depression, suicidal tendencies, and anxiety.[8] However, it is important to note that these data may be subject to variations depending on the methodology and criteria used in different studies. Additionally, depression is a complex and multifactorial condition, and its prevalence may be influenced by a range of environmental, cultural, and individual factors.[9]

What is Treatment-Resistant Depression (TRD)?

Treatment-Resistant Depression: When Standard Treatments Fail

While antidepressants and psychotherapy are often prescribed as standard treatments, some patients do not respond well to these interventions. This phenomenon is known as TRD.[10] TRD is typically defined as a lack of response to at least two different antidepressant medications or psychotherapies. However, there is some variation in the definition across studies. Some experts include failure to respond to multiple treatment modalities, including electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), which can significantly impact an individual's quality of life and increase their risk of suicide. The European Medicines Agency (EMA) defines TRD as a lack of clinically meaningful improvement despite the use of adequate doses of at least two first-line antidepression agents prescribed for an adequate duration with adequate treatment adherence.[11] TRD is common and has been associated with higher comorbidities and prolonged duration of illness, leading to a substantial medical and economic burden, and approximately 33% of patients with depression failed to achieve remission even after four consecutive trials of antidepressant treatments.[12]

It is estimated that between 10 and 30 percent of patients with depression experience TRD, and the prevalence increases with the duration and severity of symptoms.[13] Individuals with TRD often have a more chronic course of depressive illness and a higher risk of suicidal tendencies. In Europe and Hungary, it has been demonstrated that 8.3% of MDD patients met the criteria for TRD. While women represented 66.6% of the total study population, a significantly larger proportion of the TRD population were women (71.0%).[14] Another retrospective study was conducted in Poland, and the TRD patients constituted 25.2% of all MDD patients,[15] while in Asia, a pharmaceutically treated depression (PTD) (2.0%) and TRD (4.17% of PTD) developed and the TRD was greatest in males aged 18 to 29 and in females aged 30 years and above.[16]

Pseudo-resistance of medication may incorporate the profile of patients who inappropriately were prescribed inadequate doses or underdosing of antidepressants, including intolerable side effects and poor treatment compliance (discontinuation) of medication for any reason.[17] Maybe the patients suffering from substance use disorders or other physical and mental comorbidities, such as personality disorders and anxiety disorders, might have deleterious effects on treatment response. Sometimes, while interviewing the patients for the assessment of TRD, the recall bias about the medication trials and responses is one of the common potential threats to misdiagnose TRD. The majority of studies defined the term TRD as at least two suitable trials of antidepressants without adequate response. The depressive illness that is not adequately responding to treatment for that condition is "difficult-to-treat depression."[18] With this background, this study has been planned to study the epidemiology of TRD among the Saudi population.

Materials and Methods

Study design and setting

A cross-sectional study was designed to determine the epidemiology and estimate the prevalence of TRD in Abha City, Assir Region, Kingdom of Saudi Arabia.

Study population and sampling

The study includes adult patients who were admitted to the psychiatry department and aged (18–65 years) and diagnosed with major depressive depression. A simple random sampling technique was used to recruit the study subjects. The researcher collected the data from the patients who were attending the psychiatry outpatient

department and inpatient department with the inclusion criteria.

Sample size

The minimum sample size calculated based on the prevalence of TRD in a previous study conducted by Zhadanava *et al*.[19] was 30.9%; substituting in the formula $4pq/d^2$ (where p = 30.9% and q is 100-p; d allowable error is constant 5), the minimum sample size required for the study is expected to be around 535 participants. However, adjustments were made for any possible attrition; thus, a minimum of 588 participants needed to be included in the study, but, finally, a total of 651 samples were studied.

Data collection tool and technique

Research tool

The self-structured questionnaire was carefully designed and validated to address the objectives of the study. Cronbach's alpha is used for measuring the internal consistency, that is, the validity and reliability of the data, and it was found that Cronbach's alpha is 0.84. The questionnaire consists of close-ended responses such as (a) socio-demographic information; (b) physical and mental health information of the respondents; and (c) Beck's Depression Inventory among respondents (using a 4-point Beck's Depression Inventory scale, with scores ranging from 0 to 3). The values have been divided as follows: minimal depression (0–9), mild depression (10–18), moderate depression (19–29), severe depression (30–49), and extreme depression (50–63).[18]

The participants who were suffering from MDDs and attended the psychiatry department were recruited. Informed consent was obtained from the patient's first-degree relatives after explaining the objectives of the study. The data were collected by the researcher through the validated, predesigned questionnaire electronically in Google Forms.

The following are the inclusive and exclusive criteria.

Participants above 18 years old, those given informed consent, and those residing in Saudi Arabia were included. Participants who have a history of bipolar and psychosis, pregnant women, those unable to provide complete information, severe medical illness, or any contraindications for depression medication or psychotherapy, and substance abuse persons were excluded from the study.

Statistical analysis

All the data were downloaded from Google Forms in the Microsoft Office (MS) 2019 Excel spreadsheet. All the data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 21 for Windows (SPSS Inc., Chicago, IL, USA) and Microsoft Excel spreadsheets. Qualitative variables were expressed in proportions, and to test the hypothesis, the Chi-square test was applied. All reported *P* values are 2-sided at the level of a 95% confidence interval, where a *P* value of <0.05 was considered significant.

Ethics and human subject issues

This study followed the Helsinki Declaration for ethical issues. Informed consent was obtained from the first-degree legal hire of the patients. The principal investigator assured the administration of the hospital about the confidentiality of the data and the personal identification of the participants; the data were not given to any outsider who was not involved in this research. The institutional ethical approval (ECM#2023-103) was obtained from the Research Ethics Committee at King Khalid University, Abha, Kingdom of Saudi Arabia.

Results

Of the total of 651 depressive disorder cases, 134 (20.6%) were reported as TRD and the remaining 517 (79.4%) were nontreatment-resistant depressive cases. Of the 651 depression participants, 176 (27%) were males and 475 (73%) were females. Most of the participants are Saudi nationals (623 (95.7%)), of which 131 (21.0%) were TRD and 492 (95.2%) were NTRD individuals, and the remaining 28 (4.3%) were non-Saudis; of this, three (10%) were TRD and 25 (90%) were NTRD. The maximum number of respondents is from the central region of Saudi Arabia (172 (26.4%)), of which 41 (23.8%) were TRD and 131 (76.2%) were NTRD individuals. The marital status of the respondents indicates that of the 432 (66.4%) unmarried respondents, 352 (68.1%) are non-TRD (NTRD) individuals. The education level of respondents concludes that a maximum number of them are graduates, comprising 409 (62.8%), of which 331 (64%) are NTRD individuals. The maximum number of respondents falls under the income category of less than 5000 SAR, among which 373 (72.1%) are NTRD individuals [Table 1].

Of the 651 participants, more than one-quarter (180 (28%)) were associated with chronic morbidity. One-tenth of the depressive patients were suffering from thyroid disorders, followed by hypertension (10%), autoimmune diseases (10%), and diabetes mellitus (8%). Around 7% of them were suffering from cardiac and renal diseases. Of the treatment-resistant depressive persons, around one-fifth of them suffered from thyroid disease (26 (19%)), followed by hypertension (14%), diabetes (9%), cardiac diseases (7%), and renal disorders (7%) [Table 2].

The Beck's Depression Inventory score suggests that of 651 respondents, 142 (18.4%) have moderate

Table 1: Distribution of study population-based socio-demographic characteristics

Characteristics	TRD *n*=134 (20.6%)		NTRD *n*=517 (79.4%)		Total *n*=651 (100%)		*P*
Age, median (IQR), yrs	27 (22–35)		25 (21–30)		25 (21–30)		0.009[a]
Sex, *n* (%)							0.063[b]
Man	45	26%	131	76%	172	100%	
Woman	89	19%	386	81%	475	100%	
Nationality, *n* (%)						#DIV/0!	0.237[b]
Non-Saudi	3	11%	25	89%	28	100%	
Saudi	131	21%	492	79%	623	100%	
Marital status, *n* (%)							0.085[b]
Divorced	13	35%	24	65%	37	100%	
Married	40	23%	137	77%	177	100%	
Single	80	19%	352	81%	432	100%	
Widowed	1	20%	4	80%	5	100%	
Education level, *n* (%)							0.654[b]
Primary	1	25%	3	75%	4	100%	
Intermediate	2	29%	5	71%	7	100%	
High school	44	23%	146	77%	190	100%	
Graduate	78	19%	331	81%	409	100%	
Postgraduate	9	22%	32	78%	41	100%	
Job status, *n* (%)							0.009[b]
Government sector	33	33%	67	67%	100	100%	
Housewife	10	19%	42	81%	52	100%	
Military sector	—		9	100%	9	100%	
Private sector	8	11%	64	89%	72	100%	
Student	42	20%	173	80%	215	100%	
Unemployed	41	20%	162	80%	203	100%	
Income, *n* (%), SAR							0.055[b]
≤5,000	83	18%	373	82%	456	100%	
5,001–10,000	25	25%	77	75%	102	100%	
10,001–15,000	16	27%	44	73%	60	100%	
15,001–20,000	9	39%	14	61%	23	100%	
>20,000	1	10%	9	90%	10	100%	

a=Significant, b=Not significant

depression, 204 (31.3%) have severe depression, and 77 (11.8%) have extreme depression. The personal habits of the respondents suggest that of the 566 (86.9%) nonsmokers, 451 (87.2%) are NTRD individuals. Many of the respondents do not have a healthcare provider, constituting 510 (78.3%), of which 411 (79.5%) are NTRD individuals [Table 3].

The Beck's Depression Inventory characteristics suggest that of 651 respondents, 134 are TRD individuals, and 56 (41.8%) of them feel sad frequently, and among 517 NTRD individuals, nearly half of them, that is, 254 (49.1), feel sad frequently, constituting a significant *P* value between TRD and NTRD as 0.001. As per the past failure concern, around 247 (37.9%) feel that they have failed more than the average person, and 203 (39.3%) are NTRD individuals, constituting a significant *P* value between TRD and NTRD as 0.29. The satisfaction, guilt, punishment, and dislike characteristics responded that 273 (41.9%) do not get real satisfaction out of anything anymore; 250 (38.4%) feel quite guilty most of the time; 216 (33.2%) do not feel that they are being punished; 345 (53%) feel disappointed in themselves; and the major respondents are NTRD individuals: 226 (43.7%), 207 (40%), 174 (33.7%), and 288 (55.7%), respectively, constituting the significant *P* value between TRD and NTRD as 0.07, 0.01, 0.65, and <0.001.

The response for characteristics such as crying, irritability, interest in others, indecisiveness, and worthlessness is that 251 (38.6%) blame themselves all the time for their faults; 393 (60.4%) do not have any thoughts of killing themselves; 284 (43.6%) used to cry, but now they cannot cry even though they want to; 207 (31.8%) feel irritated all the time; 246 (37.8%) have lost most of their interest in other people; 282 (43.3%) have greater difficulty making decisions more than they used to; and 192 (29.5%) feel there are permanent changes in their appearance that make them look unattractive. The pessimism characteristic suggests that major respondents (208 (32%)) have nothing to look forward to and are depressed, and 174 (33.7%) are NTRD individuals, constituting a significant *P* value between TRD and NTRD as 0.08 [Table 4].

The response for characteristics such as sleep, fatigue, appetite, weight, and health worry is that 313 (48.1%) have to push themselves very hard to do anything; 209 (32.1%) do not sleep as well as they used to; 252 (38.7%) get tired from doing almost anything; 259 (39.8%) the respondent's appetite is not as good as it used to be; 358 (55%) have not lost much weight; 316 (48.5%) are worried about physical problems such as aches, pains, upset stomach, or constipation; and 261 (40.1%) have not noticed any recent change in their interest in sex [Table 5].

Table 2: Distribution of the study populations' comorbid condition vs resistant depression

	TRD		NTRD		Total		*P*
	n	%	*n*	%	*n*	%	
Any chronic diseases, *n* (%)							0.065[b]
No	88	66%	383	74%	471	72%	
Yes	46	34%	134	26%	180	28%	
Cardiac diseases							0.848[b]
No	124	93%	482	93%	606	93%	
Yes	10	7%	35	7%	45	7%	
Renal diseases							1[b]
No	125	93%	483	93%	608	93%	
Yes	9	7%	34	7%	43	7%	
Diabetes mellitus							0.862[b]
No	122	91%	474	92%	596	92%	
Yes	12	9%	43	8%	55	8%	
Hypertension							0.076[b]
No	115	86%	471	91%	586	90%	
Yes	19	14%	46	9%	65	10%	
Thyroid diseases							0.104[b]
No	108	81%	446	86%	554	85%	
Yes	26	19%	71	14%	97	15%	
Autoimmune diseases							0.419[b]
No	118	88%	468	91%	586	90%	
Yes	16	12%	49	9%	65	10%	
Immunocompromised participant							0.671[b]
No	132	99%	511	99%	643	99%	
Yes	2	1%	6	1%	8	1%	
Any other chronic diseases							1[b]
No	127	95%	487	94%	614	94%	
Yes	7	5%	30	6%	37	6%	

b=Not significant

Discussion

In this cross-sectional study, the burden of TRD was determined to be 20.6% in a hospitalized depressive disorder patient. Fekadu *et al*. study observed 35% had treatment-resistant depression longitudinally defined poor outcome.[20] study estimates that 34% showed clinical remission, 31% had partial remission, and 37% remained in a depressive episode at discharge.[20] Pilon D *et al*. study observed 10.9% were TRD,[21] observed. Another study conducted by Trivedi MH *et al.* also observed TRD ranging from 15% to 35%.[22] Another study conducted byBerlim MTnoted that Up to 15% of depression patients eventually present with treatment-resistant or refractory depression (TRD) Altshuler noted that TRD prevalence was 30%.[19,23,24]

In this study, 27% of males and 73% of females participated, and among these, the TRD was high in the male gender (26%) compared with the female gender (19%), and the gender difference in depressive disorders was high in women, almost double that of their counterparts, but the treatment resistance was more observed among men than women, but the difference was not statistically significant. A similar study conducted by Moderie C *et al*.[25] observed the TRD at almost the same level in both genders (women: 9.92 ± 1.89, and men: 9.47 ± 1.67).[24,25]

The smoking habit is almost equal to the depressive disorder persons (12.8%) and the general Saudi population (12.2%). A similar study conducted by Qattan AMN *et al*. on Saudi population[26] and Theo Korchia *et al*.[27] on the French population noted that the smoking rate was much higher in TRD women compared with the French general population (34% vs 24%).[27] This difference might be because the study

Table 3: Distribution of the study population depression, smoking, and occupation

	TRD		NTRD		Total		*P*
Beck's Depression Inventory, median (IQR)	27 (17–38)		28 (24–34)		28 (23–34)		
Depression severity, *n* (%)							
Minimal	3	2.5%	117	97.5%	120	100%	0.561
Mild	6	5.6%	102	94.4%	108	100%	
Moderate	33	23.2%	109	76.8%	142	100%	
Severe	54	26.5%	150	73.5%	204	100%	
Extreme	38	49.4%	39	50.6%	77	100%	
Smoking, *n* (%)							
No	115	20.3%	451	79.7%	566	100%	<0.001
Yes	19	22.4%	66	77.6%	85	100%	
Healthcare provider, *n* (%)							
No	99	19.4%	411	80.6%	510	100%	0.001
Yes	35	24.8%	106	75.2%	141	100%	

Table 4: Beck's Depression Inventory of self-feelings of the study population with TRD

Characteristics	Total *n*=651	TRD *n*=134 (20.6)	NTRD *n*=517 (79.4)	*P*
Crying				<0.001
0. I don't cry any more than usual	149 (22.9)	51 (38.1)	98 (19)	
1. I cry more now than I used to	169 (26)	22 (16.4)	147 (28.2)	
2. I cry all the time now	49 (7.5)	12 (9)	37 (7.2)	
3. I used to be able to cry, but now I can't cry even though I want to	284 (43.6)	49 (36.6)	235 (45.5)	
Sadness				0.001
0. I do not feel sad	45 (6.9)	17 (12.7)	28 (5.4)	
1. I feel sad	310 (47.6)	56 (41.8)	254 (49.1)	
2. I am sad all the time and I can't snap out of it	204 (31.3)	33 (24.6)	171 (33.1)	
3. I am so sad that I can't stand it	92 (14.1)	28 (20.9)	64 (12.4)	
Irritability				0.001
0. I am no more irritated by things than I ever was	63 (9.7)	17 (12.7)	46 (8.9)	
1. I am slightly more irritated now than usual	188 (28.9)	50 (37.3)	138 (26.7)	
2. I am quite annoyed or irritated a good deal of the time	193 (29.6)	23 (17.2)	170 (32.9)	
3. I feel irritated all the time	207 (31.8)	44 (32.8)	163 (31.5)	
Satisfaction				0.07
0. I get as much satisfaction out of things as I used to	80 (12.3)	22 (16.4)	58 (11.2)	
1. I don't enjoy things the way I used to	215 (33)	42 (31.3)	173 (33.5)	
2. I don't get real satisfaction out of anything anymore	273 (41.9)	47 (35.1)	226 (43.7)	
3. I am dissatisfied or bored with everything	83 (12.7)	23 (17.2)	60 (11.6)	
Pessimism				0.08
0. I am not particularly discouraged about the future	166 (25.5)	39 (29.1)	127 (24.6)	
1. I feel discouraged about the future	150 (23)	27 (20.1)	123 (23.8)	
2. I feel I have nothing to look forward to	208 (32)	34 (25.4)	174 (33.7)	
3. I feel the future is hopeless and that things cannot improve	127 (19.5)	34 (25.4)	93 (18)	
Energy				0.01
0. I can work about as well as before	86 (13.2)	29 (21.6)	57 (11)	
1. It takes extra effort to get started at doing something	164 (25.2)	34 (25.4)	130 (25.1)	
2. I have to push myself very hard to do anything	313 (48.1)	54 (40.3)	259 (50.1)	
3. I can't do any work at all	88 (13.5)	17 (12.7)	71 (13.7)	

design varies; this study is based on one center, and the France study is a systematic review study.

The poor response to antidepressant treatment among chronic diseases and several psychosocial and physical factors associated with poor treatment response in MDD patients may be due to the associated physical health problems and poor treatment adherence. This study observed that among the treatment-resistant depressive persons, around one-fifth of them suffered from thyroid disease (26 (19%)), followed by hypertension (14%), diabetes (9%), cardiac diseases (7%), and renal disorders (7%). A systematic review study conducted by Chiresh *et al*. observed that diabetes is associated with the prognosis of common mental disorders,[28] and cardiac diseases either cause the persistence of depressive diseases or worsen depression and finally develop TRD.[29] Hypothyroidism is one of the major causes of developing TRD. Depressive patients must be screened for the thyroid to prevent the development of TRD, and treating the underlying hypothyroidism significantly minimizes mood disorders, including depression.[30,31]

In the present study, according to Beck's Depression Inventory score, the severity of the depression is directly proportional to the development of TRD, whereas the NTRD is inversely proportional to the depression severity.

Limitations and recommendation

This study was conducted in one area of the country, and it may not represent the national sample. Furthermore, the study did not distinguish between nonresponse and nonadherence to medication.

Conclusions

The prevalence of TRD (20.5%) among MDD persons is higher compared with the other countries, and this study stresses the importance of newer technologies to the management of depression and further research to determine the etiological factors for TRD and factors affecting treatment compliance.

TRD emerged as a threat to public health and challenged psychiatric care providers, and further innovative techniques and effective newer drugs to treat depression

Table 5: Beck's Depression Inventory general condition of the participants

Characteristics	Total *n*=651	TRD *n*=134 (20.6)	NTRD *n*=517 (79.4)	*P*
Sleep				0.54
0. I can sleep as well as usual	154 (23.7)	37 (27.6)	117 (22.6)	
I don't sleep as well as I used to	209 (32.1)	42 (31.3)	167 (32.3)	
2. I wake up 1–2 hours earlier than usual and find it hard to get back to sleep	166 (25.5)	29 (21.6)	137 (26.5)	
3. I wake up several hours earlier than I used to and cannot get back to sleep	122 (18.7)	26 (19.4)	96 (18.6)	
Fatigue				0.003
0. I don't get more tired than usual	68 (10.4)	19 (14.2)	49 (9.5)	
1. I get tired more easily than I used to	163 (25)	42 (31.3)	121 (23.4)	
2. I get tired from doing almost anything	252 (38.7)	34 (25.4)	218 (42.2)	
3. I am too tired to do anything	168 (25.8)	39 (29.1)	129 (25)	
Appetite				0.19
0. My appetite is no worse than usual	230 (35.3)	54 (40.3)	176 (34)	
1. My appetite is not as good as it used to be	259 (39.8)	47 (35.1)	212 (41)	
2. My appetite is much worse now	94 (14.4)	15 (11.2)	79 (15.3)	
3. I have no appetite at all anymore	68 (10.4)	18 (13.4)	50 (9.7)	
Weight				0.08
0. I haven't lost much weight, if any, lately	358 (55)	83 (61.9)	275 (53.2)	
1. I have lost more than two and a half kilograms	142 (21.8)	19 (14.2)	123 (23.8)	
2. I have lost more than five kilograms	74 (11.4)	14 (10.4)	60 (11.6)	
3. I have lost more than seven and a half kilograms	77 (11.8)	18 (13.4)	59 (11.4)	
Health worry				0.58
0. I am no more worried about my health than usual	198 (30.4)	47 (35.1)	151 (29.2)	
1. I am worried about physical problems like aches, pains, upset stomach, or constipation	316 (48.5)	59 (44)	257 (49.7)	
2. I am very worried about physical problems and it's hard to think of much else	89 (13.7)	18 (13.4)	71 (13.7)	
3. I am so worried about the physical problems that I cannot think of anything else	48 (7.4)	10 (7.5)	38 (7.4)	

need to be researched. The treatment complaint mechanism is warranted to encourage people to get treatment from the psychiatrist by removing the stigma of mental illness, which needs to improve the quality of life of TRD patients.

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Conflicts of interest

There are no conflicts of interest.

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