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Treatment and long-term outcome of mental disorders: The grim picture from a quasi-epidemiological investigation in 54,826 subjects from 40 countries

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ABSTRACT

Introduction: This study registered rates of specific treatment options for mental disorders as well as their long-term outcome.
Material and methods: The history of mental disorders was used as a proxy for diagnosis. The data came from the COMET-G study (40 countries; 54,826 subjects, 64.73 % females, 35.45±13.51 years old). The analysis included descriptive statistics, Risk Ratios, *t*-tests, and ANCOVA's.
Results: [24].14 % reported a history of any mental disorder (depression >12 %, non-affective psychosis and Bipolar disorder 1 % each, >20 % self-injury, >10 % had attempted suicide, 7.17 % illegal substance abuse). Most patients were not under any kind of treatment (59.44 %) and most were not receiving treatment as recommended (e.g. 90 % of Bipolar and 2/3 of psychotic patients). No treatment at all and psychotherapy as monotherapy were consistently related to poorer outcomes. In anxiety or depression, only antidepressant monotherapy and benzodiazepines, in Bipolar disorder only antipsychotic monotherapy in males and antidepressant monotherapy in females and in non-affective psychosis antipsychotics and psychotherapy in females only, were related to good outcomes. No treatment modality was related to a good outcome in those with a history of self-harm, suicidal attempts, or illegal substance use. Only depression and treatment with antidepressants were related to metabolic syndrome.
Discussion: In the community, the overwhelming majority of mental patients do not receive appropriate treatment or, even worse, no treatment at all. The outcome is unfavourable for the majority and only a few selective treatment options seem to make a difference.

1. Introduction

How mental disorders are treated in the real world is not well studied and much of the pharmacoepidemiology of mental disorders is unknown. As a consequence, the data on the real-world outcomes of mental disorders is scant and often restricted to specific populations (Bartova et al., 2016). Thus, while data coming from clinical settings are abundant (Bartova et al., 2016; Mojtabai and Olfson, 2010), and we know the efficacy of therapeutic interventions in mental disorders, we are unaware of what the real effect is on the global real population of patients, and whether these notionally successful and efficacious treatment options make any difference and influence the global burden of mental disorders.

Mental disorders usually manifest first during adolescent or early adulthood (Eranti et al., 2013; Immonen et al., 2017; Myles et al., 2012; Solmi et al., 2022), and there is a latency from the first onset of symptoms until the diagnosis, measured in years (Medici et al., 2015; Plana-Ripoll et al., 2022; Scott et al., 2018; Solmi et al., 2022). They inflict a

heavy burden on the patients, their families and society as a whole, and despite efforts for early diagnosis and intervention (Angermeyer et al., 2013; Bijjal et al., 2018; Correll et al., 2018; Crump et al., 2013; Fusar-Poli et al., 2017; Kumar et al., 2015a; Schomerus et al., 2012; Taipale et al., 2018; Tiihonen et al., 2011, 2009, 2016; Tiihonen et al., 2006; Torniainen et al., 2015; Vanasse et al., 2016), individuals suffering from mental disorders have a shorter life expectancy in comparison to that of the general population, and this gap could be as large as 10–15 years (Bagewadi et al., 2016; Bitter et al., 2017; Hjorthoj et al., 2017; Manjunatha et al., 2019; Olfson et al., 2015; Robinson, 2016; Saha et al., 2007; Walker et al., 2015), while disability is huge and rates of remission and rehabilitation are generally unsatisfactory (Jaaskelainen et al., 2013; Suresh et al., 2012).

While the epidemiology of mental disorders is more or less known, at least roughly, the pharmacoepidemiology and the epidemiology of treatment in general, are not well studied and little is known. Most of our knowledge concerns prescription volume, but there is literally no detailed data on the real-world outcome of mental disorders in combination with specific modes of treatment. If such knowledge existed, it would help us to further validate the usefulness of treatment options and to focus public health actions to improve the outcomes.

The **current study aimed** to investigate the rates of specific treatment received by those with mental disorders in the general population as well as their long-term outcomes, using the COMET-G dataset. Secondary aims were the investigation of treatment appropriateness as well as of the relation of specific treatment options with the existence of the metabolic syndrome.

The history of mental disorders was used as a proxy for the diagnosis since all major mental disorders are generally lifelong, episodic, or chronic disorders. Participating in the study was used as a proxy for at least fair functioning.

2. Material and methods

The data came from the COVID-19 MEntal health inTernational for the General population (COMET-G) study, whose main findings have already been published (Fountoulakis et al., 2021a, 2022a, 2022b; Fountoulakis et al., 2022c, 2024; K et al., 2023; Patsali et al., 2020). The full protocol used is available in the webappendix of the first published COMET study (Fountoulakis et al., 2022b) and also in the webappendix of the current study.

The data were collected NNYY and anonymously from April 2020 through March 2021. Announcements and advertisements were done on social media and through news sites, but no other organized effort had been undertaken. The first page included a declaration of consent which everybody accepted by continuing with the participation. Approval was initially given by the Ethics Committee of the Faculty of Medicine, Aristotle University of Thessaloniki, Greece, and locally concerning each participating country.

The study sample included data from 40 countries concerning 55,589 responses, but for the current paper, complete data were available for 54,826 subjects (64.73 % females; 34.15 % males; 1.11 % non-binary gender). The contribution of each country and the gender and age composition, as well as details concerning various sociodemographic variables (marital status, education, work, etc.), have been reported (Fountoulakis et al., 2021a, 2022a, 2022b; Fountoulakis et al., 2022c, 2024; K et al., 2023; Patsali et al., 2020).

The study population was self-selected, and the only limitation was age 18 or above. It was not possible to apply post-stratification on the sample as it was done in a previous study (Fountoulakis et al., 2021a), because this would mean that we would need to utilize a similar methodology across many different countries and the population data needed were not available for all countries.

The protocol, which is also available in previous publications (Fountoulakis et al., 2022b), and is also included here in the webappendix, included the registration of already existing (not emerged during the pandemic) somatic and mental disorders as well as specific treatment modalities with antipsychotics, antidepressants, benzodiazepines, and psychotherapy as monotherapies as well as in combination. The questions B2, B3, B5, B6, and M2 and M3 were used as the source of variables for the current study. The current treatment status was registered but not its history. The COVID-19 pandemic acted as a stressful condition and triggered the emergence of both somatic and mental disorders even de novo, but previous history could serve as a fair approximation for the lifetime prevalence of various medical conditions in the study sample in a quasi-epidemiological frame for the time point just before the pandemic.

A composite score reflecting the presence of hypertension, dyslipidemia, diabetes mellitus, and obesity (0–4) was created and used as a factor reflecting the presence and severity of the metabolic syndrome.

The complete list of mental conditions and treatments registered and their rates are shown in Table 1. All the data were self-reported, no clinical assessment was made, and this constitutes a significant factor for the interpretation of the results.

In terms of diagnostic group, subjects without any history of any mental disorder were assigned to group N, those with any type of history of any mental disorder were assigned to group M, those with a history of anxiety disorder to group A, with depression to group D, with Bipolar disorder to group B, with non-affective psychosis to group P, self-harm to group H, with history of suicidality to group S and those with history of illegal substance use the IS.

Note that self-harm and suicidality had shown a transdiagnostic distribution and therefore although allocation to groups A, D, B, P, and N was mutually exclusive, this was not the case between these groups and groups H and S. Interestingly, a significant number of subjects belonging to the N group also belonged both to the H and S groups. In the comparison between H and S groups with the N group, the Nn group was used, that is the N group with the exclusion of these subjects belonging also to the H and S groups.

The proxy for the outcome is described below in the statistical analysis section

Treatment was registered by the responder and it is self-reported

Treatment appropriateness was defined as a general idea suggesting that antipsychotics are necessary for non-affective psychosis, antidepressants or psychosocial treatment for anxiety and depression and monotherapy or combinations of antipsychotics and anidepressants for Bipolar disorder.

Because of the nature of the data (self-report), the NbN nomenclature was not used in the current paper.

2.1. Statistical analysis

Data only from males and females were used because the overall contribution of non-binary gender in the total study sample was too small to calculate the contribution in age groups divided additionally by treatment options.

- Detailed descriptive statistics were calculated and tables were created
- Subjects were classified into 13 age groups as well as in two major but arbitrary groups, above 45 and below 46.
- Percentages in age groups were compared between diagnostic groups. In total, the percentage of subjects over 45 years old in 6 diagnostic groups by 8 treatment categories and by two genders was compared to the respective percentages of subjects without any mental health history. In total 112 comparisons were performed and the p-level of $p < 0.01$ was accepted as the level of significance.
- Risk Ratios (RR) were calculated as the ratio of the percentage of the pathological state divided by the percentage of the non-pathological state.
- T-test was used to assess the difference between two groups
- Analysis of Covariance (ANCOVA) with Scheffe as a post-hoc test

Table 1
Frequencies (N) and percentages of the total sample (%) of subjects of diagnostic groups; proportions (%) of age groups within each diagnostic group and the relative contribution (ratio) of age groups to the population within each diagnostic group in comparison to the 21–25 age group (standardized as equal to 1). RR corresponds to the risk ratio for subjects over 45 years of age not to participate in the study in comparison to group N.

History of																							
	Group N No history of mental disorder N = 40,492 (73.8 5 %)			any mental disorder N = 14,334 (26.1 4 %)		Group A anxiety disorder N = 4267 (7.78 %)		Group D depression N = 6943 (12.66 %)		Group B Bipolar disorder N = 643 (1.17 %)		Group P psychosis N = 539 (0.98 %)		Other mental disorder N = 1489 (2.71 %)		Group H self-harm N = 11,844 (21.6 0 %)		Group S Suicide attempt N = 5862 (10.69 %)		Group IS Illegal substance use N = 3934 (7.17 %)	
age	%	ratio		%	ratio	%	ratio	%	ratio	%	ratio	%	ratio	%	ratio	%	ratio	%	ratio	%	ratio		
<21	9.83	0.51		9.13	0.46	7.66	0.42	7.85	0.39	18.35	0.69	19.29	0.74	11.62	0.74	16.59	0.61	17.18	0.63	10.32	0.41		
21–25	19.32	1.00		19.75	1.00	18.19	1.00	20.14	1.00	26.59	1.00	25.97	1.00	15.65	1.00	27.33	1.00	27.07	1.00	25.47	1.00		
26–30	14.30	0.74		16.23	0.82	15.49	0.85	16.92	0.84	15.09	0.57	11.50	0.44	16.32	1.04	16.82	0.62	15.86	0.59	22.19	0.87		
31–35	13.55	0.70		14.27	0.72	14.11	0.78	14.60	0.73	12.44	0.47	12.43	0.48	14.17	0.91	12.22	0.45	12.81	0.47	17.92	0.70		
36–40	10.69	0.55		11.04	0.56	11.32	0.62	10.86	0.54	7.93	0.30	9.28	0.36	13.90	0.89	8.19	0.30	8.58	0.32	10.22	0.40		
41–45	8.65	0.45		8.49	0.43	9.59	0.53	8.20	0.41	5.60	0.21	6.12	0.24	8.60	0.55	5.61	0.21	5.49	0.20	6.10	0.24		
46–50	7.10	0.37		6.66	0.34	7.55	0.41	6.63	0.33	6.38	0.24	6.49	0.25	5.71	0.36	4.29	0.16	4.74	0.18	3.51	0.14		
51–55	5.41	0.28		5.09	0.26	5.53	0.30	5.23	0.26	2.02	0.08	3.15	0.12	5.64	0.36	2.85	0.10	3.07	0.11	1.80	0.07		
56–60	4.51	0.23		4.15	0.21	4.83	0.27	4.29	0.21	2.02	0.08	2.23	0.09	3.76	0.24	2.39	0.09	2.49	0.09	1.12	0.04		
61–65	3.23	0.17		2.86	0.14	3.26	0.18	2.97	0.15	2.02	0.08	1.48	0.06	2.35	0.15	1.79	0.07	1.45	0.05	0.58	0.02		
66–70	1.85	0.10		1.50	0.08	1.59	0.09	1.45	0.07	1.40	0.05	1.30	0.05	1.61	0.10	1.21	0.04	0.82	0.03	0.53	0.02		
71–75	0.82	0.04		0.54	0.03	0.52	0.03	0.65	0.03	0.16	0.01	0.56	0.02	0.27	0.02	0.55	0.02	0.22	0.01	0.18	0.01		
>75	0.25	0.01		0.27	0.01	0.37	0.02	0.22	0.01	0.00	0.00	0.19	0.01	0.40	0.03	0.16	0.01	0.20	0.01	0.05	0.00		
>45	23.17			21.07		23.65		21.44		14.00		15.40		19.74		13.24		12.99		8.24			
>45 RR				1.10		0.98		1.08		1.66		1.50		1.17		1.75		1.78		2.98			

The core assumption in the analysis that could lead to conclusions on the outcome is that there is a specific age distribution of subjects participating in this kind of online research, meaning that younger ages are over-represented in comparison to a truly representative epidemiological sample with similar clinical characteristics. Thus, the expected age composition is reflected in the age composition of group N. Since the major mental disorders assessed in the current study have a median age at onset at the age of mid-20 s to mid-30 s (Solmi et al., 2022), and since there is a latency time since the first onset of symptoms to diagnosis (Medici et al., 2015; Plana-Ripoll et al., 2022; Scott et al., 2018; Solmi et al., 2022), it is reasonable to assume that the expected age distribution of mental patients participating in the study should be shifted towards greater median age, but this should not affect participation after the age of 45 (arbitrary taken as cut-off). Any reduced participation in any mental patient group after the age of 45 could be an indirect indication or increasing disability or even mortality (loss of functioning or reduced life expectancy). Participation as in group N could be also considered to be an indication of increasing disability or reduced life expectancy since the age at onset implies an increase in median age in the patient groups in comparison to normal subjects. However, there is no sufficient data to precisely estimate the expected age participation in the patient groups. The increased participation in comparison to group N should be considered as an indication of no increasing disability or reduced life expectancy.

The alternative explanation that treatments that do not contribute with a favorable outcome manifest significant attrition due to drop-out from the group and entering another until a suitable treatment option is found should be rejected, because in that case there should be a difference between treatment options, with the most successful ones having the biggest subsamples and high late-age participation in the study.

As a standard for the creation of the pattern of age distribution, the age group of 20–25 was used since this was the biggest age group in group N. Thus, all age groups were standardized as their % size in comparison to the 20–25 age group (equal to 100 %). See Fig. 1 for a detailed explanation.

The statistical package SPSS v.29, provided by the Aristotle University of Thessaloniki, Greece, was used for the analysis. The comparison of proportions and percentages was done with the MedCalc Software v.23.0.6 (Campbell, 2007; Richardson, 2011).

3. Results

3.1. Demographics

The study sample included data from 40 countries. In total data from 54,826 participants from the original study sample of 55,589 subjects (Fountoulakis et al., 2021a, 2022b, 2024), were utilized, since for them, treatment data were available. These subjects were 35.45±13.51 years old; of them 35,489 were females (64.73 %; aged 35.80±13.61) and 18, 725 males (34.15 %; aged 34.90±13.29), while 612 declared 'non-binary gender' (1.11 %; aged 31.64±13.15). The age means and standard deviations were identical to the original study sample. <6.5 % were older than 60 years.

3.2. Rates of mental disorders

These rates have been reported in detail previously in combination with the rates of somatic disorders (Fountoulakis et al., 2024). Approximately 24.14 % of the study sample had a history of any mental disorder. If self-injury or suicidality were included, the percentage climbs to 39.62 % (15.48 % reported a history of self-harm or suicidal attempts but no formal diagnosis of mental disorder). History of depression (group D) was the most frequently reported mental disorder (>12 %) followed by anxiety (group A; approximately 8 %). History of non-affective psychoses (group P) and Bipolar disorders (group B) were reported by approximately 1 % each. A striking >20 % had a lifetime

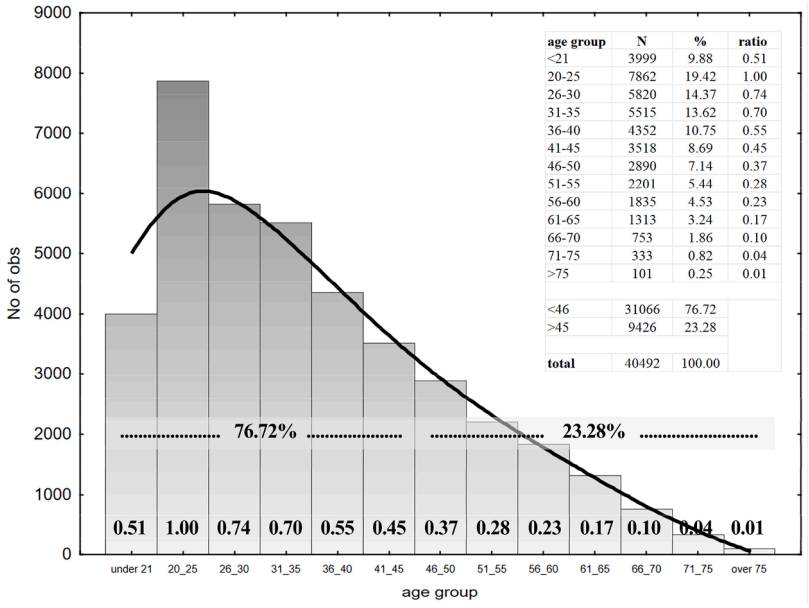

Fig. 1. Histogram of age distribution in group N. The age subgroup of 20–25 was the bigger in this group and therefore it was used as the reference to standardize all other age subgroups as their % size in comparison to the 20–25 age group (equal to 100 %).

history of self-injury (group H) and >10 % had attempted suicide (group S) in the past. A history of illegal substance abuse was reported by 7.17 % (Table 1).

3.3. Treatment of mental disorders

The basic results concerning treatment options have been published (Fountoulakis et al., 2024). The treatment options by diagnostic category and age (above and below 45) at the time of the questionnaire completion are shown in Table 2.

Any treatment was received by 40.56 % of patients with a mental health history, corresponding to 10.60 % of the total study sample. The respective numbers for any pharmacotherapy were 28.75 % and 7.51 %. Within the subsample of persons with mental health history, the rates between males and females receiving any treatment (38.95 % vs. 40.88 %) and any medication (28.57 % vs. 28.71 %) were similar.

Table 2
Percentages of treatment options in the diagnostic subgroups of subjects with a mental health history. For Anxiety, Depression, and 'other' one can not be certain whether not receiving any treatment at present represents a problem since some patients might not need treatment after a certain period of time and after the first episode of the disorder. However, this is not the case with Bipolar disorder and non-affective psychosis, for whom one can definitely conclude on their treatment quality.

	History of							
Treatment option	**Anxiety**	**Depression**	**Bipolar disorder**	**Non-affective Psychosis**	**Other**	**Self-harm**	**Suicide attempt**	**Illegal Substance use**
Any kind of treatment	33.58	44.61	67.19	67.35	30.69	21.38	25.84	26.35
No treatment of any kind	66.42	55.39	32.81	32.65	69.31	78.62	74.16	73.65
Antipsychotics	1.62	3.28	28.15	36.18	1.07	3.57	6.09	4.78
Antipsychotic monotherapy	*1.22	1.27	7.31	20.04	0.60	1.47	2.92	2.49
Antidepressants	11.09	28.33	43.23	26.90	2.96	10.64	12.74	10.98
Antidepressant monotherapy	7.73	16.89	*15.55	*11.50	1.14	5.46	6.32	5.56
Benzodiazepines	9.89	10.18	19.28	16.33	7.79	5.55	6.32	6.18
Psychotherapy	16.01	18.38	27.68	21.89	22.63	10.16	11.39	13.83
Only Psychotherapy treatment	12.89	10.4	*7.62	*10.20	20.15	6.19	6.87	9.45
Only medication treatment	17.58	26.23	39.5	45.45	8.06	11.22	14.44	12.53
No medication	79.31	65.79	40.44	42.86	89.46	84.81	81.03	83.09
One class of medications	18.84	27.26	36.39	40.82	9.47	11.44	14.09	12.88
Two classes of medications	1.8	6.29	15.24	10.39	0.87	2.89	3.56	2.99
Three classes of medications	0.05	0.65	7.93	5.94	0.20	0.84	1.31	1.02
Mean number of medication classes	0.23	0.42	0.91	0.79	0.11	0.20	0.25	0.22
Mean number of medication classes when under medication	1.09	1.22	1.52	1.40	1.12	1.30	1.33	1.30
Antipsychotic plus antidepressant	0.16	1.83	17.26	10.76	0.40	1.77	2.74	1.83
Antidepressant plus benzodiazepine	1.62	5.69	*12.60	*8.72	0.87	2.63	3.19	2.94
Antipsychotic plus psychotherapy	0.21	1.05	11.66	7.42	0.40	1.16	1.63	1.37
Antidepressant plus psychotherapy	2.16	7.17	*16.80	*7.24	1.61	3.32	3.90	3.66
Benzodiazepines plus psychotherapy	1.34	2.85	*7.47	*5.57	1.48	1.73	1.94	2.06
Treatment not as recommended	**≥66.42	**≥57.71	60.04	43.23	**≥69.31			

* not recommended treatment option.
** not under treatment.

As reported before (Fountoulakis et al., 2024), most patients with mental disorders were not receiving any kind of treatment at all (59.44 %). This was true mainly for anxiety and depression while in the more severe disorders, most patients were under some kind of treatment. Unfortunately, of those patients under treatment, only a small minority received treatment as recommended, e.g. 7.62 % of Bipolar patients and 10.2 % of psychotic patients were treated with psychotherapy alone and respectively 16.8 % and 7.24 % with antidepressant plus psychotherapy and 15.55 % and 11.5 % with antidepressant monotherapy. This pattern impacted the vast majority of patients under treatment in the Bipolar (60.04 % of 67.19 %; that is 9/10 of patients under any kind of treatment) and the psychotic groups (43.23 % of 67.35 %; that is 2/3 of patients under any kind of treatment) (Fountoulakis et al., 2024).

3.4. Long term outcome

In Table 3 the percentage of subjects in the various diagnostic groups by treatment option and age above 45 are included. The p-level corresponds to the comparison of the specific proportion to the corresponding proportion in the group of subjects without any mental disorder. Thus, the percentage of subjects over 45 years old in 6 diagnostic groups by 8 treatment categories and by two genders was compared to the respective percentages of subjects without any mental health history. In total 112 comparisons were performed and the p-level of $p < 0.01$ was accepted as the level of significance. From these comparisons, 29 were-non-significant, suggesting a distribution of ages similar to non-mental patients (but also in some cases very small subsamples) and 10 comparisons were significant but suggested that relatively more subjects over 45 years old were included in the patient group in comparison to non-mental patients. Seventy-three comparisons (65.18 %) were significant, reflecting that fewer patients over the age of 45 participated in the study in comparison to normal subjects. This could suggest that in almost 2/3 of diagnosis-by-sex groups, the long-term outcome is poor.

No treatment at all was consistently related to poorer outcome irrespective of gender or diagnostic group. The same was true for psychotherapy as monotherapy. In patients with a history of anxiety or depression, only antidepressant monotherapy and benzodiazepines were related to good outcome. In Bipolar disorder, only antipsychotic monotherapy in males and antidepressant monotherapy in females were related to better outcome. The same treatment options were superior to other options for the opposite sex. In non-affective psychosis, the combination of antipsychotics and psychotherapy in females only, produced the best outcome, while in males they had better effects in comparison to other options. Interestingly, psychotherapy as monotherapy performed worse than no treatment at all in this diagnostic group. In those with a history of self-harm, suicidal attempts, and illegal substance use no treatment modality was related to a good outcome, but probably benzodiazepines performed better than other treatment modalities.

The complete results are shown in Table 3 and a visual depiction of the data, after assigning to age groups values relative to the 20–25 age group and smoothing the line with the least squares method, is shown in Figs. 2 and 3.

3.5. Metabolic syndrome

Patients with psychiatric disorders had a slightly higher but significant composite metabolic score in comparison to the general population (group M vs. group N; 0.09±0.32 vs. 0.08±0.29, $t=-3.529$, df: 54,824, $p < 0.001$). ANCOVA with diagnostic groups as grouping variable and age and gender (males and females) as covariates produced a significant effect for diagnosis (SS=2.993, df:5, MS: 0.598, F: 6.850; $p < 0.0001$). The post-hoc test revealed that at $p < 0.01$, the significant difference concerned group D vs group N only. ANCOVA of group H vs. group Nn with age and gender as covariates returned no significant results (SS=0.024, df:1, MS: 0.024, F: 0.294; $p = 0.587$). Similarly non-significant was the comparison of group S vs. group Nn (SS=0.233, df:1, MS: 0.233, F: 2.802; $p = 0.094$). The ANCOVA of treatment options as a grouping variable with age and gender as covariates returned significant results (SS=4.795, df:5, MS: 0.951, F: 11.016; $p < 0.001$). The post-hoc analysis revealed that this difference concerned only antidepressant monotherapy or in combination with antipsychotics vs. all the other options (at $p < 0.01$; Table 3).

ANCOVA with diagnostic group by treatment as grouping variable (see Table 3 for grouping) age and gender (males and females) as covariates produced significant effect for diagnosis by treatment groups (SS=4.795, df:5, MS: 0.959, F: 11.016; $p < 0.0001$). The post-hoc test revealed that at $p < 0.001$, the significant differences concerned antidepressant monotherapy (irrespective of diagnosis) vs. all other groups and no treatment vs. only psychotherapy. The means and standard deviations for each diagnosis by treatment group are shown in Table 4. A visual depiction of the composite metabolic score in the various diagnostic groups is shown in Fig. 4.

4. Discussion

The results of this study suggest that >39 % reported a history of any mental disorder, including history of self-injury or suicidality. A history of depression was reported by >12 % while non-affective psychosis and Bipolar disorder were present in approximately 1 % each. A history of illegal substance abuse was reported by 7.17 %. Interestingly, the

Table 3
Mean and standard deviation of the composite metabolic score for each treatment option.

treatment category	gender	N	age		metabolic syndrome composite score		RR
			mean	SD	mean	SD	
No mental health history	females	25,050	35.92	13.80	0.08	0.29	1.00
	males	15,061	35.14	13.40	0.09	0.31	1.00
Mental health history but no treatment	females	4191	34.62	13.05	0.08	0.31	1.06
	males	1347	34.28	12.62	0.12	0.37	1.21
Antidepressant monotherapy	females	1253	40.15	14.22	0.13	0.41	1.40
	males	412	36.59	14.24	0.18	0.48	1.55
Antipsychotic monotherapy	females	126	34.26	13.20	0.06	0.24	0.84
	males	163	31.33	13.00	0.06	0.24	0.78
Only psychotherapy	females	1271	33.86	10.84	0.06	0.24	0.84
	males	380	32.57	11.87	0.08	0.31	1.01
Antipsychotic plus antidepressant	females	205	32.23	12.06	0.08	0.29	1.01
	males	94	31.83	10.76	0.06	0.29	0.92
Various treatments	females	3393	35.81	13.28	0.08	0.29	1.01
	males	1268	33.62	12.79	0.10	0.33	1.08

The ANCOVA of treatment options as a grouping variable with age and gender as covariates returned significant results (SS=4.795, df:5, MS: 0.951, F: 11.016; $p < 0.001$). The post-hoc analysis revealed that this difference concerned only antidepressant monotherapy or in combination with antipsychotics vs. all the other options at $p < 0.01$.

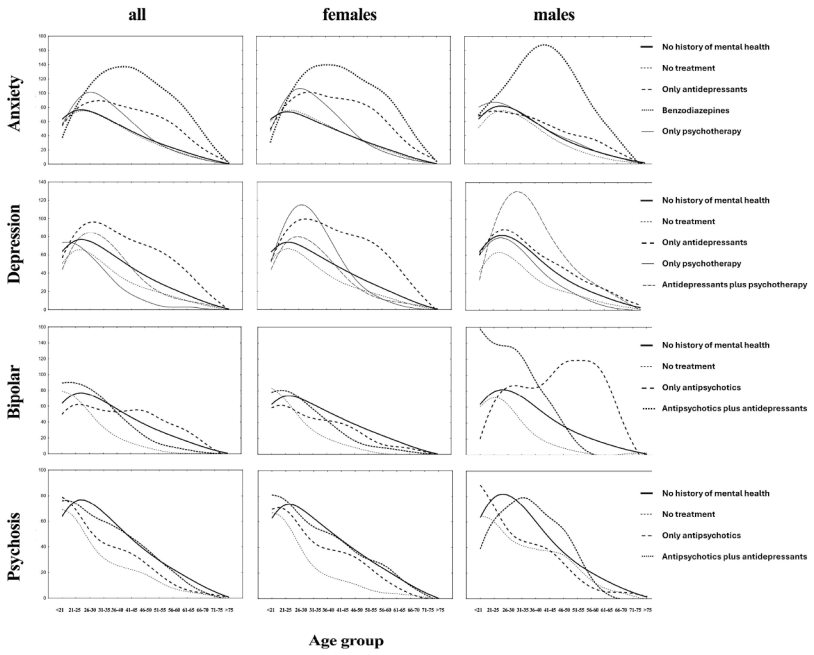

Fig. 2. Visualization of the age distribution data in the diagnostic by treatment groups for groups A, D, B, and P after assigning to age subgroups values relative to the 20–25 age group and smoothing the line with the least squares method.

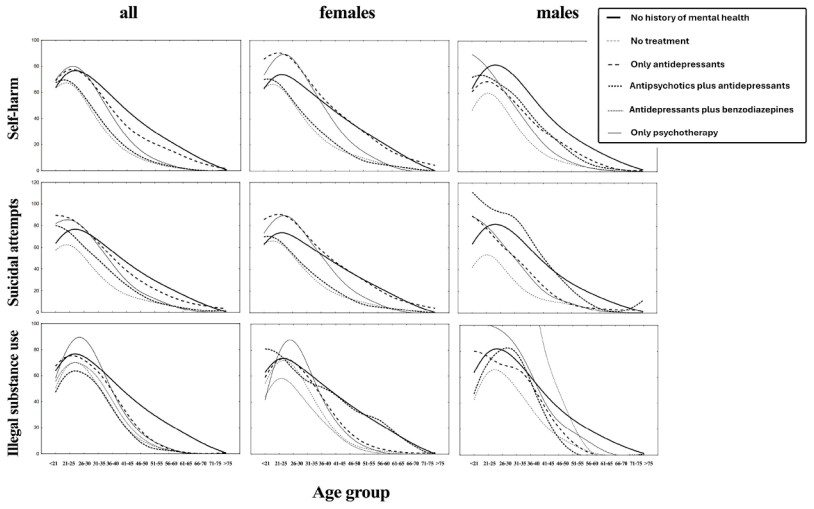

Fig. 3. Visualization of the age distribution data in the various diagnostic by treatment groups after assigning to age subgroups values relative to the 20–25 age group for groups H, S, and IS, and smoothing the line with the least squares method.

majority of patients with mental disorders were not receiving any kind of treatment at all (59.44 %), and additionally, of those patients under treatment, the vast majority were not receiving treatment as recommended (90 % of treated patients with Bipolar disorder and 2/3 of psychotic patients). The analysis of the proportion of patients over 45 years of age participating in the current study suggested that no treatment at all was consistently related to poorer outcomes irrespective of gender or diagnostic group. The same was true for psychotherapy as monotherapy. The above results should be considered only by bearing in mind that they were not derived either from blind controlled trials or from formal epidemiological datasets. Instead, they could reflect some biases and confounding by indication in methodology.

In patients with a history of anxiety or depression, only antidepressant monotherapy and benzodiazepines were related to good outcome. In Bipolar disorder, only antipsychotic monotherapy in males and antidepressant monotherapy in females were related to better outcome. The same treatment options were superior to others in the opposite sex. In non-affective psychosis, the combination of antipsychotics and psychotherapy in females only, produced the best outcome, while in males they had better effects in comparison to other options. Interestingly, psychotherapy as monotherapy performed worse than no treatment at all in this diagnostic group. In a history of self-harm and suicidal attempts, no treatment modality was related to a good outcome, but probably benzodiazepines performed better than other treatment modalities.

Patients with a history of depression had a significantly higher metabolic syndrome burden. This was at least partially associated with treatment with antidepressants. No other medication was related to the metabolic syndrome.

Some treatments by sex groups included a very low number of subjects (males with antipsychotic monotherapy in Bipolar disorder or without any kind of treatment in non-affective psychosis). This means

Table 4
Percentage of subjects in the various diagnostic groups by treatment option and classified into two age groups with 45 years as the cut-off. The p-level corresponds to the comparison of the specific proportion to that of group N and specifically for groups H and S with group Nn. The p-level of $p < 0.01$ was accepted as the level of significance.

		N, aged <46	N, aged >45	% >45	RR	p-level
Total study sample ($N = 54,214$, 100 %)	females	27,016	8473	23.87		
	males	14,851	3874	20.69		
Normal ($N =$ 4011, 73.98 %)	females	18,890	6160	24.59	1.00	
	males	11,867	3194	21.21	1.00	
Anxiety (N=4216, 7.78 %)						
Only psychotherapy	females	357	64	15.20	0.62	<0.001
	males	93	24	20.51	0.97	0.895
No treatment	females	1331	385	22.44	0.91	0.006
	males	419	88	17.36	0.82	0.003
Both antidepressants and psychotherapy	females	58	13	18.31	0.74	<0.001
	males	16	5	23.81	1.12	0.051
Both antipsychotics and psychotherapy	females	3	1	25.00	1.02	0.607
	males	5	0	0.00	0.00	<0.001
Both antidepressants and antipsychotics	females	3	0	0.00	0.00	<0.001
	males	4	0	0.00	0.00	<0.001
Antipsychotic monotherapy	females	16	5	23.81	0.97	0.326
	males	27	1	3.57	0.17	<0.001
Antidepressant monotherapy	females	153	94	*38.06	1.55	<0.001
	males	57	25	*30.49	1.44	<0.001
Benzodiazepines	females	195	141	*41.96	1.71	<0.001
	males	52	31	*37.35	1.76	<0.001
Depression ($N = 6858$, 12.65 %)						
Only psychotherapy	females	501	60	10.70	0.43	<0.001
	males	126	20	13.70	0.65	<0.001
No treatment	females	1426	366	20.42	0.83	<0.001
	males	442	108	19.64	0.93	0.146
Both antidepressants and psychotherapy	females	350	61	14.84	0.60	<0.001
	males	60	18	23.08	1.09	0.085
Both antipsychotics and psychotherapy	females	48	7	12.73	0.52	<0.001
	males	13	3	18.75	0.88	0.022
Both antidepressants and antipsychotics	females	75	12	13.79	0.56	<0.001
	males	34	3	8.11	0.38	<0.001
Antipsychotic monotherapy	females	32	6	15.79	0.64	<0.001
	males	44	1	2.22	0.10	<0.001
Antidepressant monotherapy	females	558	335	*37.51	1.53	<0.001
	males	195	74	27.51	1.30	0.011
Benzodiazepines	females	383	177	*31.61	1.29	<0.001
	males	87	50	*36.50	1.72	<0.001
Bipolar disorder ($N = 612$, 1.13 %)						
Only psychotherapy	females	24	2	7.69	0.31	<0.001
	males	19	2	9.52	0.45	<0.001
No treatment	females	88	7	7.37	0.30	<0.001
	males	35	3	7.89	0.37	<0.001
Both antidepressants and psychotherapy	females	63	5	7.35	0.30	<0.001
	males	34	1	2.86	0.13	<0.001
Both antipsychotics and psychotherapy	females	39	4	9.30	0.38	<0.001
	males	24	0	0.00	0.00	<0.001
Both antidepressants and antipsychotics	females	67	8	10.67	0.43	<0.001
	males	30	1	3.23	0.15	<0.001
Antipsychotic monotherapy	females	21	6	22.22	0.90	0.272
	males	8	11	*57.89	2.73	<0.001
Antidepressant monotherapy	females	40	21	*34.43	1.40	<0.001
	males	25	6	19.35	0.91	0.512
Benzodiazepines	females	63	13	17.11	0.70	<0.001
	males	36	4	10.00	0.47	<0.001
Non-affective Psychosis ($N = 517$, 0.95 %)						
Only psychotherapy	females	18	2	10.00	0.41	<0.001
	males	30	3	9.09	0.43	<0.001
No treatment	females	40	7	14.89	0.61	<0.001
	males	22	8	26.67	1.26	0.040
Both antidepressants and psychotherapy	females	14	3	17.65	0.72	0.007
	males	18	4	18.18	0.86	0.253
Both antipsychotics and psychotherapy	females	13	9	*40.91	1.66	<0.001
	males	13	5	27.78	1.31	0.013
Both antidepressants and antipsychotics	females	27	8	22.86	0.93	0.505
	males	15	5	25.00	1.18	0.154
Antipsychotic monotherapy	females	28	8	22.22	0.90	0.361
	males	55	10	15.38	0.73	0.028
Antidepressant monotherapy	females	36	3	7.69	0.31	<0.001
	males	21	2	8.70	0.41	<0.001
Benzodiazepines	females	40	12	23.08	0.94	0.561
	males	27	7	20.59	0.97	0.815
Self-harm ($N = 11,270$, 20.79 %)						
Only psychotherapy	females	467	37	7.34	0.30	<0.001
	males	184	16	8.00	0.38	<0.001
No treatment	females	1200	102	7.83	0.32	<0.001
	males	345	37	9.69	0.46	<0.001
Both antidepressants and psychotherapy	females	275	32	10.42	0.42	<0.001
	males	57	14	19.72	0.93	0.043
Both antipsychotics and psychotherapy	females	84	7	7.69	0.31	<0.001
	males	34	5	12.82	0.60	<0.001
Both antidepressants and antipsychotics	females	138	8	5.48	0.22	<0.001
	males	46	7	13.21	0.62	<0.001
Antipsychotic monotherapy	females	61	4	6.15	0.25	<0.001
	males	94	6	6.00	0.28	<0.001
Antidepressant monotherapy	females	374	98	20.76	0.84	<0.001
	males	136	24	15.00	0.71	<0.001
Benzodiazepines	females	381	123	24.40	0.99	0.687
	males	104	27	20.61	0.97	0.416
Suicidal attempt ($N = 5713$, 10.54 %)						
Only psychotherapy	females	210	23	9.87	0.40	<0.001
	males	137	15	9.87	0.47	<0.001
No treatment	females	559	89	13.73	0.56	<0.001
	males	188	30	13.76	0.65	<0.001
Both antidepressants and psychotherapy	females	144	25	14.79	0.60	<0.001
	males	44	7	13.73	0.65	<0.001
Both antipsychotics and psychotherapy	females	55	7	11.29	0.46	<0.001
	males	26	3	10.34	0.49	<0.001
Both antidepressants and antipsychotics	females	99	12	10.81	0.44	<0.001
	males	36	6	14.29	0.67	<0.001
Antipsychotic monotherapy	females	51	4	7.27	0.30	<0.001
	males	95	12	11.21	0.53	<0.001
Antidepressant monotherapy	females	201	57	22.09	0.90	<0.001
	males	95	11	10.38	0.49	<0.001
Benzodiazepines	females	196	65	24.90	1.01	0.616
	males	75	18	19.35	0.91	0.054
Illegal substance use $N = 3934$ (7.17 %)						
Only psychotherapy	females	208	11	5.02	0.20	<0.001
	males	117	15	11.36	0.54	0.008
No treatment	females	1304	103	7.32	0.30	<0.001

(*continued on next page*)

Table 4 (*continued*)

		N, aged <46	N, aged >45	% >45	RR	p-level
	males	1315	118	8.23	0.39	<0.001
Both antidepressants and psychotherapy	females	86	3	3.37	0.14	<0.001
	males	41	6	12.77	0.60	0.018
Both antipsychotics and psychotherapy	females	24	0	0.00	0.00	0.006
	males	23	1	4.17	0.20	0.045
Both antidepressants and antipsychotics	females	34	1	2.86	0.12	0.004
	males	32	1	3.03	0.14	0.123
Antipsychotic monotherapy	females	26	2	7.14	0.29	0.037
	males	62	1	1.59	0.07	<0.001
Antidepressant monotherapy	females	130	11	7.80	0.32	<0.001
	males	70	5	6.67	0.31	0.002
Benzodiazepines	females	126	12	8.70	0.35	<0.001
	males	80	10	11.11	0.52	0.025

* The proportion of subjects aged >45 is higher than in the population without a history of mental disorder.

that conclusions could not be considered as solid, however, these groups come from a huge quasi-epidemiological sample of >50,000 persons.

The interpretation of the above results should take into consideration the major factors that determine the findings (apart from methodological design). Disability and premature death is the factor that determines the age distribution horizontally across all subgroups of patients in the study sample, by reducing the participation in advanced age groups. Another major factor that affects the age distribution is the age at onset and the latency from onset to diagnosis. This shifts the peak age away from the early 20 s and close to the early 30 s (see Fig. 5). In general it is accepted that the diagnosis follows the onset of symptoms with a latency time of 5–10 years depending on the specific disorder, but this latency tends to be shorter and subsequently, a diagnosis of mental disorders tends to occur sooner in recent years than the past (Medici et al., 2015; Plana-Ripoll et al., 2022; Scott et al., 2018; Solmi et al., 2022). This is probably a result of long-term efforts and campaigning against stigma and the usefulness of early diagnosis and intervention (Angermeyer et al., 2013; Schomerus et al., 2012). However, the data on the age at onset and subsequently of diagnosis are conflicting, and important methodological limitations make any conclusions problematic (Chen et al., 2018; Fagerlund et al., 2021; Fountoulakis et al., 2019, 2021b; Jones, 2013; Xu et al., 2020), despite the several meta-analyses that exist (Eranti et al., 2013; Immonen et al., 2017; Myles et al., 2012; Solmi et al., 2022). The most recent and reliable meta-analysis (Solmi et al., 2022) reported a median age at onset of 25 for schizophrenia, 30 for unipolar depression, 33 for Bipolar disorder, 13–32 for anxiety disorders depending on the specific disorder, and 22 for cannabis use. The proportion of patients at the age of 25 was 50 % for non-affective psychosis, 47 % for unipolar depression, 70 % for Bipolar disorder, 30–80 % for anxiety disorders, and 80 % for substance use.

Diagnosis was delayed as long as 4 years for depression and 1 year for Bipolar disorder. The respective period varied for anxiety while it was very short for non-affective psychosis. In Fig. 5 the distributions of age at onset for various mental disorders are shown (Solmi et al., 2022). On the other hand, individuals suffering from mental disorders have a shorter life expectancy in comparison to that of the general population, and this loss could be as big as 10–15 years (Hjorthoj et al., 2017; Saha et al., 2007; Walker et al., 2015). Since two opposite trends exist (one is the introduction of new cases by passing the years (incidence) and the other is the drop-out because of loss of functioning and shorter life expectancy), the net outcome is unknown.

One of the aims of the study was to investigate whether there is any data in support of a different long-term outcome for different diagnostic

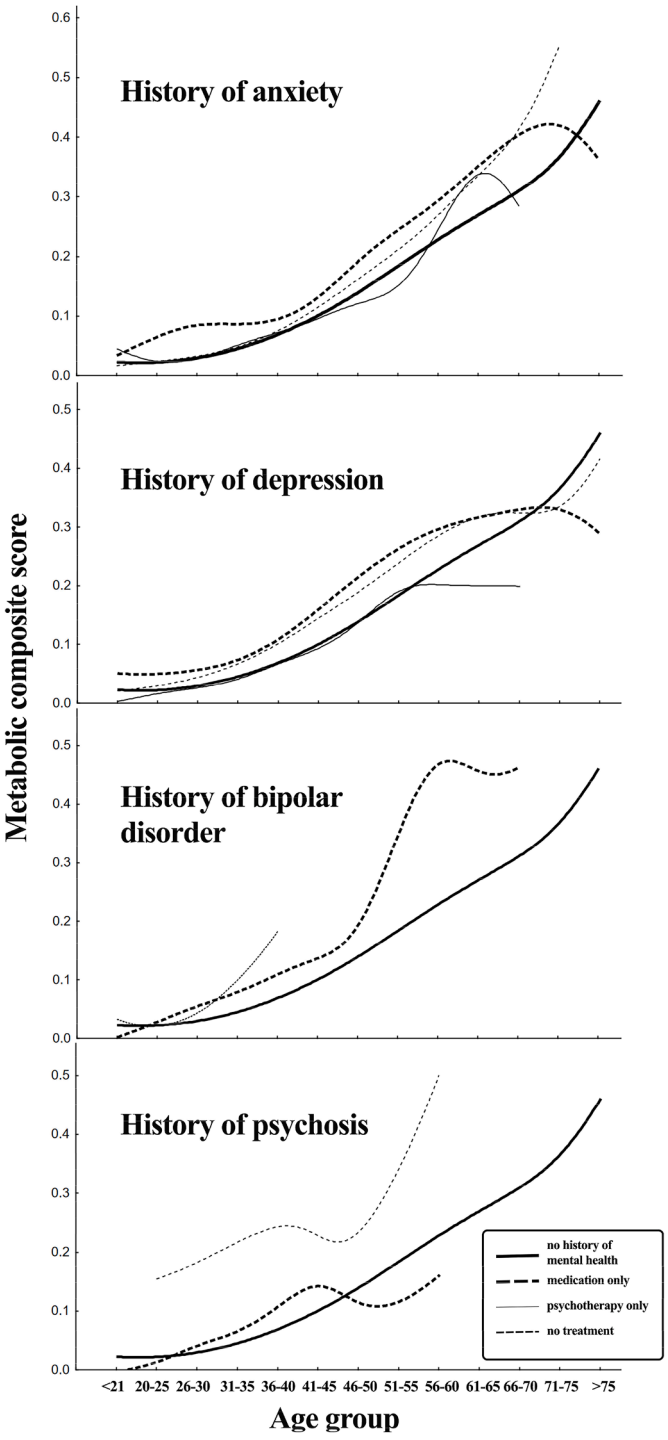

Fig. 4. Metabolic composite score in the four major mental disorders by treatment option vs. age subgroup.

groups receiving different treatment options. It is known that proper treatment especially as early as possible could improve the outcome and reduce the loss in life expectancy and also it could sustain better functioning (Correll et al., 2018; Fusar-Poli et al., 2017; Reddy et al., 2017).

Major mental illnesses accounted for 24.14 % of the total study sample and this is like the 23.1 % reported by the NIMH and the 2022 NSDUH Annual National Report for 2022. Interestingly, the majority of patients with mental disorders were not receiving any kind of treatment at all (59.44 %), and this is in contrast to the NIMH 2022 NSDUH Annual National Report as well as previous reports (Kessler et al., 2001; Narrow

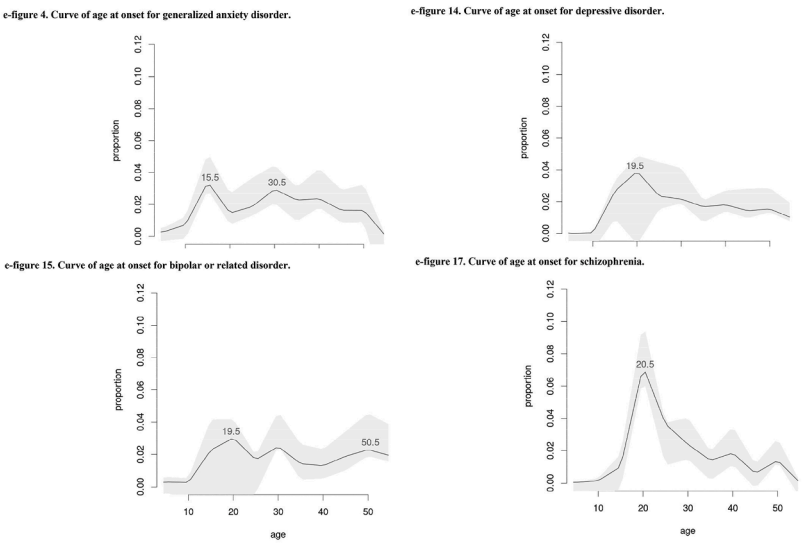

Fig. 5. The distributions of age at onset for various mental disorders (after permission from Solmi et al. (2022) Mol Psychiatry 27,281–295).

et al., 2000), that suggest only one-third to less than half of patients are not under treatment. This could possibly reflect a difference between the US (and possibly Europe, Canada, etc.) and the rest of the world (https://www.nimh.nih.gov/health/statistics/mental-illness). Any treatment was received by 40.56 % of patients with a mental health history, corresponding to 10.60 % of the total study sample. The respected numbers for any pharmacotherapy were 28.75 % and 7.51 %. Within the subsample of persons with mental health history, the rates between males and females receiving any treatment (38.95 % vs. 40.88 %) and any medication (28.57 % vs. 28.71 %) were similar. These findings are half in size in comparison to the US CDC report for 2021–2023 (https://www.statista.com/statistics/252316/type-of-mental-health-service-used-by-us-adults-since-2002/) and their consistency (same findings for all therapies and for medication separately and same finding for both sexes) adds to their reliability and validity. Additionally, in our study, of those patients under treatment, the vast majority were not receiving treatment as recommended (90 % of patients treated for Bipolar disorder and 2/3 of psychotic patients).

The finding that no treatment at all leads to poor outcome was expected. This is not the case however with psychotherapy when used as monotherapy which was almost always related to a worse long-term outcome. It would be expected that at least in some diagnostic groups (e.g. anxiety, depression) psychotherapy should perform better than no treatment at all (Kamenov et al., 2017; Munder et al., 2019). In non-affective psychosis, psychotherapy performed worse even in comparison to no treatment at all. This finding is in sharp contrast with the literature which supports at least some efficacy for psychotherapy in psychotic patients, especially in combination with pharmacotherapy (Haram et al., 2019; Health Quality, 2018; Turner et al., 2014). However, it should be noted that the literature on psychotherapy seems flawed (unblinded trials, super-selective samples, investigators with a strong allegiance to the specific psychotherapy, lack of adequate placebo condition or comparison to nocebo conditions such as waitlist, etc.) (Fountoulakis and Tsapakis, 2024). One could argue, however, that under the umbrella 'psychotherapy', patients could include any kind of unsystematic regular contact with a therapist, rather than specific and proper psychotherapy per se. However, it is difficult to argue in favor of this in those cases in our study sample that reported psychotherapy as monotherapy. Interestingly, in depression, the rates of monotherapy with psychotherapy or antidepressants and their combination were roughly equal, while in anxiety psychotherapy monotherapy was received by most subjects under treatment.

The treatment rates for depression reported here are similar (though a little lower) to what is reported in the literature e.g. by >75 % of patients even in homeless populations (Bartova et al., 2016) or approximately 50 % in depressives living with family (Olie et al., 2002). In anxiety and depression, the only treatments that seem to relate with a favorable outcome are antidepressant monotherapy and benzodiazepines, and interestingly they seem to exert an effect similar in size. The lack of better outcome for the combination of antidepressants with psychotherapy is not in accordance with the literature (Kamenov et al., 2017).

The literature reports that only one-third of Bipolar patients were not getting treatment (1993). While recent data reflect a trend towards increasing antipsychotic and antidepressant use in Bipolar disorder up to 50 % of patients in the US (Dimellis and Fountoulakis, 2015; Rhee et al., 2020), this is not in accord with our finding of 28.15 % antipsychotic use. Similarly, antidepressant monotherapy was reported by 15.55 which is lower than the 25 % reported by other studies (Lyall et al., 2019). Antipsychotic monotherapy was also lower with 7.31 vs. 13 % in the literature while the combination of an antipsychotic plus an antidepressant was almost triple than that reported in the literature (17.26 vs. 6.2 %) (Lyall et al., 2019). In Scandinavia, antipsychotic use in Bipolar disorder was reported to be as high as 50 % and antidepressants as high as 30 % (Kessing et al., 2016). Much lower rates were reported in the UK and Hong Kong (Ng et al., 2021). Our findings suggest that in Bipolar disorder a favorable outcome is related to antipsychotics in males and antidepressants in females, possibly reflecting differences in predominant polarity (Carvalho et al., 2014a, 2014b; Dell'Osso et al., 2021; Nivoli et al., 2011; Rasgon et al., 2005).

In our dataset , 36.18 % of patients with a history of non-affective psychosis were receiving antipsychotics and this is very close to the report by the CATIE study, that 74 % of patients discontinuing treatment within the first year with 30 % doing this in the basis of personal choice for unknown reasons (Lieberman et al., 2005), but in contrast with other studies that report that >2/3 of patients receive some kind of proper treatment (1993; Olfson et al., 2010; Vanelli et al., 2001), but most of these reports concern clinical samples. Our data concerning the use of antidepressants in non-affective psychosis are in accord with the literature (Galling et al., 2018; Himelhoch et al., 2012) and especially the CATIE study (Chakos et al., 2006). Overall, the antidepressant use in non-affective psychosis is equivocal (Buchanan et al., 2010; Lehman et al., 2004; Sepehry et al., 2007; Silver, 2003; Singh et al., 2010) and only a few data exist (Addington et al., 2002; Daniel et al., 1994; Galling et al., 2018; Mojtabai and Olfson, 2010; Mulholland et al., 2003; Sepehry et al., 2007; Whitehead et al., 1996). Our results suggest that in

non-affective psychosis it is the combination of antipsychotics and psychotherapy that is related to better outcome, but this only in females. This probably reflects a more benign subgroup of patients that remain affiliated with the health care system and adhere to treatment with antipsychotics, and it is also in accord with a better outcome for females (Kohler et al., 2009; Ochoa et al., 2012). Unfortunately, all treatment options were similar to non-treatment concerning self-harm and suicidal attempts, with only benzodiazepines having some effect.

A history of illegal substance use was reported by 7 .17 %. Similarly to the other findings, this is half of what has been reported by the NCDAS for the US for 2020 (https://drugabusestatistics.org/ and the SAMHSA for 2023(https://www.hhs.gov/about/news/2024/07/30/samhsa-releases-annual-national-survey-drug-use-and-health.html). However treatment rates are almost identical between our findings and these reports. Treatment and outcome are highly personalized for this group of patients and no reliable epidemiological data exist concerning the long-term outcome (Greenfield et al., 2007; Okrant et al., 2023). There are at least some data suggesting that psychotic patients might use alcohol less than the general population (Kumar et al., 2015b) and comorbidity plays a major role in observed rates (Udupi et al., 2018).

The finding that the metabolic syndrome is related to depression and antidepressants is in accord with the literature (Gramaglia et al., 2018; Kumar et al., 2013; Penninx and Lange, 2018), however, the finding that non-affective psychosis and antipsychotics are not related is not in accord with the literature which suggests that antipsychotics cause more problems in this area (Bernardo et al., 2021; Carli et al., 2021; Penninx and Lange, 2018; Pillinger et al., 2020; Rawat et al., 2018; Zhang et al., 2021). In general, major adverse health outcomes with antidepressants are not supported by the literature (Dragioti et al., 2019).

The current paper reports on the prevalence of mental disorders and their treatment in a large convenient sample from 40 countries. The first question is how appropriate this study sample is for such a quasi-epidemiological study, and subsequently, how reliable and how valid are the rates that are reported. Since the data were obtained by self-reporting from a self-selected sample, the only way to assess validity is to compare the findings concerning a specific topic with already known answers on this topic.

Overall, the findings of the current study are generally in accord with the literature concerning the prevalence of major mental disorders, including anxiety (Bourdon et al., 1992; Wittchen and Jacobi, 2005), depression (Goodwin et al., 2022; Lim et al., 2018), Bipolar disorder (Bebbington and Ramana, 1995; Fountoulakis, 2015; Merikangas et al., 2011; Pini et al., 2005), and psychosis (Eaton, 1991; McGrath et al., 2008), as well as self-injury (Agley and Xiao, 2021; Cipriano et al., 2017; Lucena et al., 2022). While the history of suicidal attempts was found to pass 10 %, the rates reported in the literature vary between 2 and 5 % (Borges et al., 2006, 2010; Fairweather-Schmidt and Anstey, 2012; Fountoulakis et al., 2012; Kessler et al., 1999; Nock et al., 2008; Schmidtke et al., 1996), however, the variability is great and it seems that selective retrieval of memories is involved. This is evident since studies in adolescents report rates around 20 % (Liu et al., 2018; Van Meter et al., 2023) while surveys in middle-aged individuals report much lower lifetime rates. This general agreement with the literature supports the validity of the study sample and the results of the current study.

The finding that most patients were not receiving treatment at all was more or less expected. However, the finding that above 90 % of Bipolar patients and 75 % of patients with non-affective psychosis receive an inappropriate treatment or do not receive any treatment at all, was alarming, but not unexpected since similar reports can be found in the literature (Fond et al., 2019). If these severe mental disorders that have the most clear-cut treatment guidelines are treated so inadequately, then it is likely other mental disorders with less robust guidelines or in the case of milder and not 'classical' manifestations of mental disorders, the lack of treatment or incorrect treatment is probably widespread. It was also expected to find that mental disorders in general cause significant disability and reduce life expectancy. These observations also reject an alternative explanation of our findings, that is, treatments that do not contribute to a favorable outcome manifest significant attrition due to the drop-out of patients from the group only to join another until a suitable treatment option is found.

The finding that antipsychotics were unrelated to the development of metabolic syndrome was also unexpected (Correll, 2007; Fenton and Chavez, 2006; Suppes et al., 2007). The finding that patients with psychiatric disorders have more frequent metabolic syndrome is in accord with the literature (Correll, 2007). Our results point to the urgent need for better training of psychiatrists as well as of all mental health professionals and GPs in the treatment of patients with psychiatric disorders, especially of the most severely ill. Training based on modern technocratic methods and ways of clinical work, which is standard in the rest of medicine, seems to be an unmet need in Psychiatry and it takes a toll on patients. Even if the results of the current study overestimate the problem and are influenced by residual confounding, still there seems to be much room for improvement concerning the treatment and the outcome of patients with psychiatric disorders at an international level and especially at the level of primary care (Ibrahim et al., 2021; Kumar et al., 2017).

5. Conclusion

Unfortunately, most of mental patients might not receive appropriate treatment according to standard recommendations, or, even worse, no treatment at all, and the outcome is unfavorable for the majority of patients. However, a few selective treatment options seem to make a difference and improve functioning and/or life expectancy. It seems that the outcomes could be relatively good in those who continue the prescribed treatment (both medical and psychosocial). The above points to the importance of better teaching psychiatry and mental health in medical schools and also to the need for more technocratically oriented training of psychiatric residents and also during life-long education and training.

5.1. *Strengths and limitations*

The strengths of the current paper include the large number of people who filled out the questionnaire and the large bulk of information obtained. The major limitation was that the data were obtained anonymously online through the self-selection of the responders, via self-report without any clinical or laboratory investigation. The utilization of 'personal medical history' was a fair approximation for the morbidity of the study sample without the effect of the pandemic, but still, it is an approximation open to debate. Also, the use of age distribution above 45 as a proxy for general functioning and life expectancy is a fair proxy, however, the interpretation and the generalization of results should be done with caution. There is always a risk of selection bias and confounding by indication in studies of such methodology.

Funding

None.

CRediT authorship contribution statement

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Declaration of competing interest

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Supplementary materials

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