

Medication non-adherence in patients with varying levels of depression symptoms measured using the Medication Adherence Reasons Scale

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Introduction

Depression – Prevalence and Global Burden

Depression affects
~280 million people
worldwide (WHO) ¹



5.0% among all adults and **5.7%**
among adults **older than 60**
years of age



According to the European Health
Interview Survey with **27 European**
countries²:

- **6.38%** suffered from depression
- **Older Individuals** reported more depression than younger population
- **4.89% of men** and **7.74% of women** reported depression



In Europe, in 2018 the economic
cost of mental health was more
than **600 billion euros**^{3, 4}

- **190 billion euros** on direct health care spending
- **170 billion euros** on social security programs
- **240 billion euros** on indirect costs due to lower employment and productivity at work

Adherence to Antidepressant Medicines

Antidepressant medications can ease depression symptoms.


Adherence to antidepressants can affect treatment response, costs, as well as relapse.

Non-adherence to antidepressants immediately after the start of treatment was **13 to 55.7%** and **by six months was 52%.**⁵



Medication nonadherence can be caused by⁵

- Unreliable information e.g., myths about depression
- Lack of support from family
- High cost of hospitalizations and medications
- Concern about side effects
- Fears of addiction
- Clinician factors (e.g.: inadequate patient education and poor follow-up)



Study Objective

This study focuses on **the extent of non-adherence among adults** diagnosed with depression based on their level of depression severity via the PHQ-9



Methods

Sample



Data was from the **2022 National Health and Wellness Survey (NHWS)**, a self-administered, annual, internet-based cross-sectional survey of adults (age 18+) in:



Germany



Spain



France



Italy



The United Kingdom



NHWS uses a quota sampling framework (sex and age) to ensure that it is representative of the demographic composition of the adult population.



The NHWS has been classified as exempt by Pearl IRB (Indianapolis, IN, USA).



Respondents who self-reported a physician diagnosis of depression and reported taking daily prescription medication(s) to treat their depression were given the Medication Adherence Reasons Scale.

- Depression medication daily use (n=4,008)

Medication Adherence Reasons Scale (MAR-Scale)

The scale has 19 specific reasons for non-adherence and one global item.

Respondents were shown the 19 items from the MAR-Scale and were asked to select all the items that were reasons for their non-adherence **in the past week**.

For the items chosen by the respondent, they then selected the number of days, using a 7-point scale (1 day to 7 days) in which that reason was a cause of their non-adherence.

Over the last **7 days**, which of the following were reasons you did **NOT** take the medicine or medicines above as prescribed?

1	I had side-effects from the medicine.
2	I did not have money to pay for the medicine.
3	I was not comfortable taking it for personal reasons (e.g. tired of taking medicine, too sick, my religious beliefs).
...	...

The global item provides an overall estimate of the frequency of the medication adherence.

Respondents use an 8-point scale (0 days to 7 days) to report the number of days they took the medicine as prescribed **in the past week**.

Over the last **7 days**, how many days were **YOU ABLE TO** take your **DAILY** medicine or medicines for **depression** exactly as prescribed?

0 days (have not taken the medicine or medicines in the last 7 days)	1 day	2 days	3 days	4 days	5 days	6 days	7 days (took the medicine or medicines on all of the 7 days)
0	1	2	3	4	5	6	7

Medication Adherence Reasons Scale (MAR-Scale)



Perfectly Adherent

Did not miss the medication for any reason for even one day in the **past 7 days** on the 19 items



Non-adherent

Missed medication for one day with any of the 19 items in the **past 7 days**

PHQ-9 Scale

Depression severity was measured using the Patient Health Questionnaire - 9 (PHQ-9) scale. The total scores help identifying patients with symptoms of depression.⁶

0-4 None
5-9 Mild Depression
10-14 Moderate Depression
15-19 Moderately Severe Depression
20-27 Severe Depression

Statistical Analysis



Results are displayed descriptively with percentages for categorical variables and means for continuous variables.



Statistical testing between groups was done using chi-square tests for categorical variables and t-tests for continuous variables.



Results



<i>Table 1. Characteristics by Adherence</i>	Perfectly adherent (n=2,299)	Non-adherent (n=1,709)
Female	64%	65%
Mean Age	51.0	44.9
% Married	38%	32%
% Single, never married	28%	35%
% Retired	24%	15%
% College graduate (four year) or more	28%	29%
Mean number of adults in the household	1.9	2.0
Mean number of children in the household	0.4	0.5
% Annual Household Income < €50K/£40K	76%	78%
% Overweight / Obese^	68%	60%
% Currently Smoke Cigarette	33%	39%
% Drink Alcohol	66%	69%
Mean days exercising in the past month	5.0	5.4
% Currently taking steps to lose weight	37%	40%

^Different base size

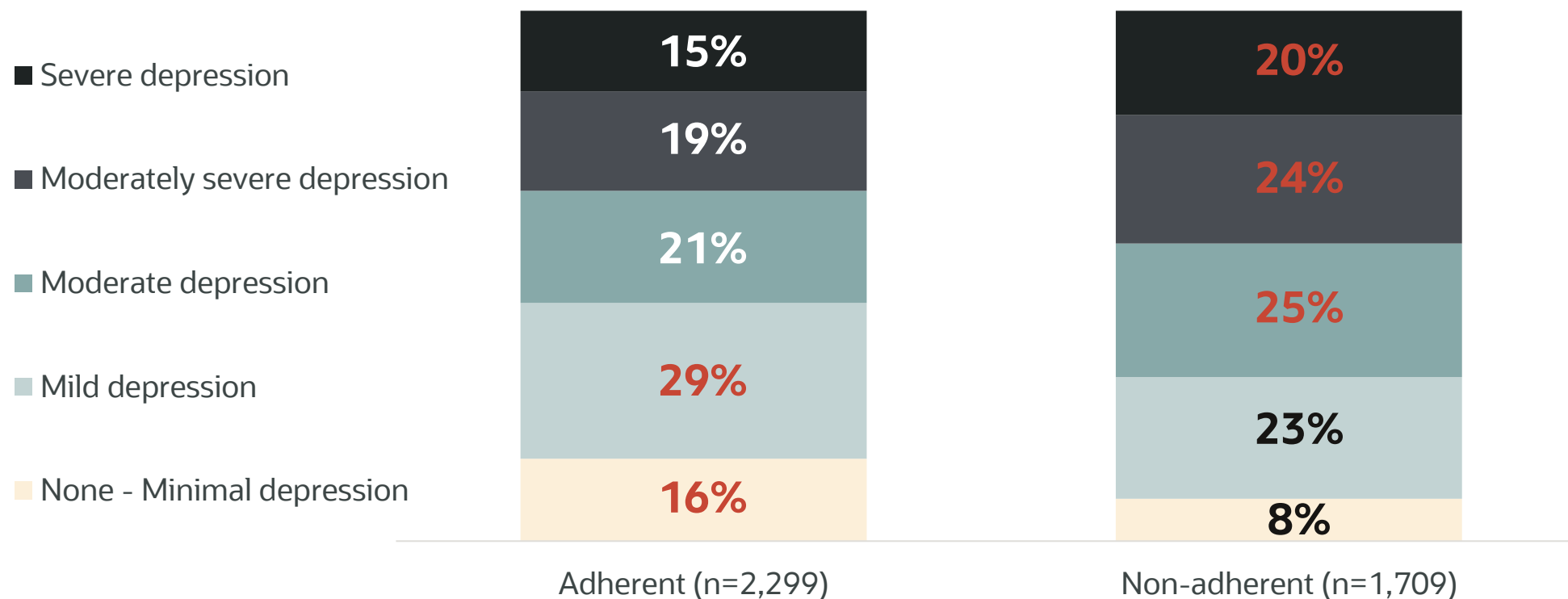
Note: Bold font indicates a statistically significant difference, $p < 0.05$

Of the 4,008 respondents in the sample, 57% were perfectly adherent.

- The perfectly adherent group was older, married, retired, and overweight/obese
- The non-adherent group had more adults and children in the household and had a greater proportion of current smokers
- Both groups were mostly female, non-college graduates with an annual income below €50K/£40K, drank alcohol, and exercised an average of 5 days a month.



Non-adherent respondents are significantly more likely to report moderate to severe symptoms of depression (69%) than adherent respondents (55%)



Note: Bold font indicates a statistically significant difference, $p < 0.05$



Non-adherent with moderate to severe depression were younger, female and single compared to those with none to minimal depression.

Non-adherents with none to minimal depression were retired and spent more days exercising compared to those with more severe depression.

Table 2. Characteristics by PHQ-9 Depression Severity among Non-adherent Respondents	Perfectly adherent	Non-adherent	Non-adherent				
			None - Minimal depression	Mild depression	Moderate depression	Moderately severe depression	Severe depression
	(n=2,299)	(n=1,709)	(n=137)	(n=392)	(n=430)	(n=414)	(n=336)
Female	64%	65%	54%	63%	64%	68%	68%
Mean Age	51.0	44.9	48.6	47.5	45.2	43.4	42.0
% Married	38%	32%	42%	39%	31%	31%	19%
% Single, never married	28%	35%	29%	32%	34%	36%	43%
% Retired	24%	15%	22%	18%	15%	13%	11%
% College graduate (four year) or more	28%	29%	34%	34%	29%	23%	28%
% Annual Household Income < €50K/£40K	76%	78%	72%	73%	78%	80%	85%
% Overweight / Obese^	68%	60%	58%	62%	59%	64%	56%
% Currently Smoke Cigarette	33%	39%	34%	38%	40%	38%	44%
% Drink Alcohol	66%	69%	63%	73%	69%	71%	65%
Mean days exercising in the past month	5.0	5.4	7.0	6.3	5.4	4.6	4.7

^Different base size

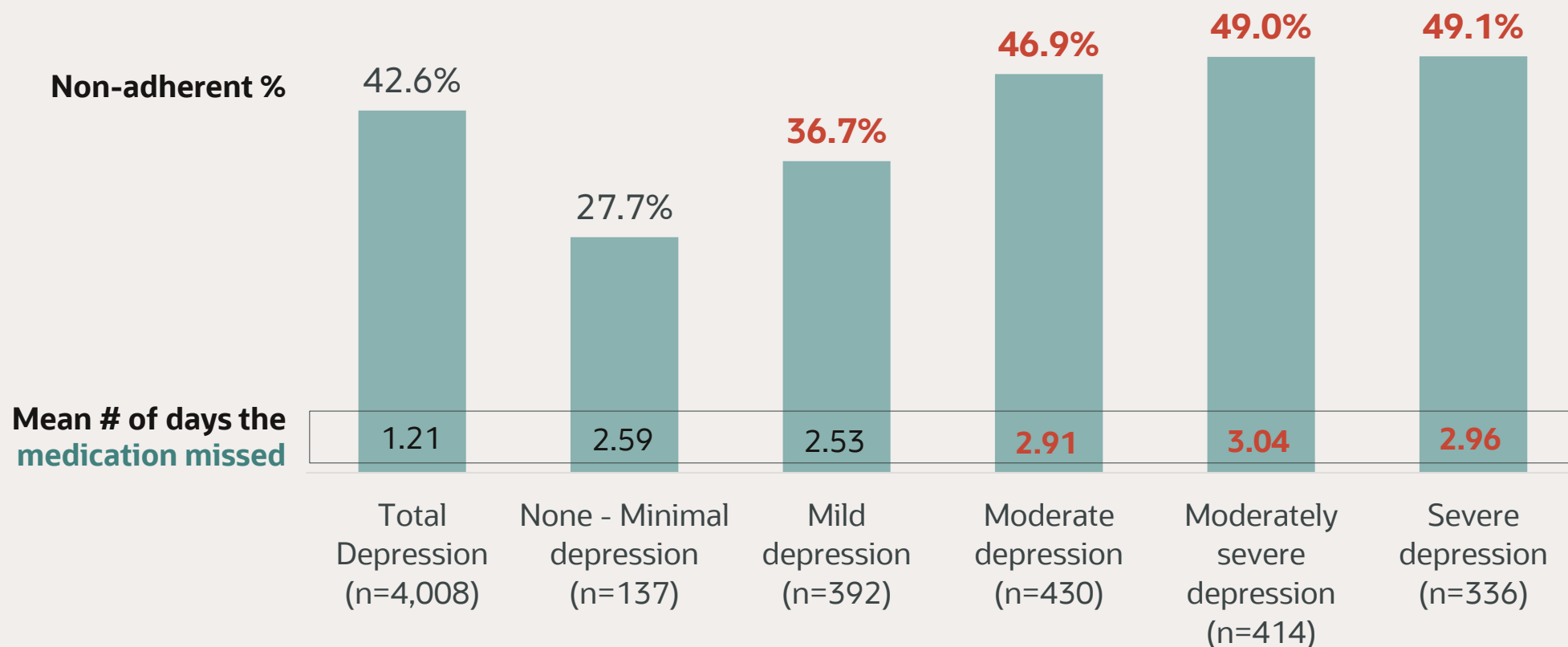
Note: Bold font indicates a statistically significant difference, $p < 0.05$

Note: All tests for the non-adherent groups are compared to the none-minimal depression category.



Among the respondents with moderate to severe depression almost 50% reported being non-adherent. The numbers of days moderate to severe respondents missed was significantly higher than respondents with mild severity.

Figure 2. Non-adherence by PHQ-9 Depression Severity



Note: Bold font indicates a statistically significant difference, $p < 0.05$



Top Reasons for Medication Non-Adherence

<i>% of patients who missed vs Mean # days missed</i>	Total Depression (n=4008)	
	%	#
Concerned about long-term effects from the medicine	21.5	2.49
Concerned about possible side-effects from the medicine	18.2	2.56
Simply missed the medicine	17.6	2.10
Sometimes skip the medicine to see if it is still needed	14.7	2.68
Don't think medicine is working	11.5	2.91
Missed it because of busy schedule/change in routine	10.5	2.32
Difficulty remembering things in daily life	10.4	2.46
Not comfortable taking it for personal reasons	9.5	2.74
Side-effects from the medicine	9.3	3.18
Do not consider taking the medicine as a high priority in my daily routine	8.7	2.76
Don't think need the medicine anymore	8.3	3.16
Pharmacy/provider was out of this medicine, out of refills, or the mail order did not arrive in time	7.9	2.52
Trouble managing all the medicines I have to take	7.8	2.52
Not comfortable taking it for social reasons	7.2	2.58
Didn't have a way to get to the pharmacy/provider	6.4	2.57
Don't have money to pay for the medicine	5.9	2.64
Difficulty swallowing/applying/inhaling/injecting the medicine	5.7	2.80
Difficulty opening the container or getting the injection ready to use	4.9	2.84
Not sure how to take this medicine	4.3	2.93

Top Reasons for Medication Non-Adherence

Table was sorted on the severe group (%)

	None - Minimal depression (n=137)		Mild (n=392)		Moderate (n=430)		Moderately severe (n=414)		Severe (n=336)	
<i>% of patients who missed vs Mean # days missed</i>	%	#	%	#	%	#	%	#	%	#
Concerned about long-term effects from the medicine	46.0	2.32	48.7	2.26	53.7	2.52	51.9	2.60	47.9	2.62
Simply missed the medicine	35.8	1.82	39.3	1.91	38.6	2.05	43.7	2.34	46.1	2.13
Concerned about possible side-effects from the medicine	39.4	2.44	40.1	2.37	44.2	2.50	43.5	2.67	44.4	2.75
Don't think medicine is working	19.7	3.11	17.6	2.72	29.5	2.66	27.5	3.12	36.9	3.03
Difficulty remembering things in daily life	11.0	2.13	16.6	2.69	24.0	2.34	26.1	2.62	36.9	2.33
Sometimes skip the medicine to see if it is still needed	31.4	2.74	31.4	2.60	39.3	2.65	37.0	2.61	29.8	2.87
Trouble managing all the medicines I have to take	12.4	2.71	13.0	2.29	17.9	2.70	21.5	2.73	23.8	2.22
Not comfortable taking it for personal reasons	15.3	2.52	18.4	2.58	25.1	2.71	24.2	2.67	23.2	3.09
Side-effects from the medicine	20.4	2.79	17.6	2.84	22.8	3.16	24.4	3.41	22.9	3.34
Missed it because of busy schedule/change in routine	17.5	1.79	20.9	2.43	28.4	2.18	28.0	2.41	22.3	2.48
Do not consider taking the medicine as a high priority in my daily routine	19.0	2.38	19.6	2.70	22.8	2.51	19.3	2.97	20.2	3.07
Pharmacy/provider was out of this medicine, out of refills, or the mail order did not arrive in time	13.1	2.22	16.1	2.35	18.4	2.52	21.5	2.79	19.9	2.40
Don't have money to pay for the medicine	14.6	2.10	10.7	2.98	14.4	2.56	14.7	2.67	15.5	2.62
Didn't have a way to get to the pharmacy/provider	11.7	2.13	11.2	2.52	17.4	2.68	16.7	2.80	15.5	2.27
Not comfortable taking it for social reasons	12.4	2.41	13.8	2.54	19.1	2.45	20.1	2.73	15.2	2.65
Don't think need the medicine anymore	24.8	2.82	18.4	3.36	22.1	2.98	20.1	3.47	14.0	2.94
Difficulty swallowing/applying/inhaling/injecting the medicine	13.9	2.47	11.2	3.02	15.4	2.77	13.8	2.65	12.2	2.98
Difficulty opening the container or getting the injection ready to use	11.0	2.07	9.2	3.14	12.8	2.91	13.3	2.73	11.0	2.92
Not sure how to take this medicine	10.2	2.71	6.9	2.89	13.5	2.72	11.6	3.27	7.7	2.92

Note: Bold font indicates a statistically significant difference, p <0.05

Note: All tests for the non-adherent groups are compared to the none-minimal depression category.



Top 5 Reasons for Medication Non-Adherence by Frequency

Close to 1 in 2 patients, in each severity group, didn't take the daily prescription medication as prescribed by the physician because of concerns about long-term effects.

Forgetfulness was the second highest selected reason for non-adherence followed by concerns about possible side effects.

	None - Minimal depression (n=137)		Mild (n=392)		Moderate (n=430)		Moderately severe (n=414)		Severe (n=336)	
<i>% of patients who missed vs Mean # days missed</i>	%	#	%	#	%	#	%	#	%	#
Concerned about long-term effects from the medicine	46.0	2.32	48.7	2.26	53.7	2.52	51.9	2.60	47.9	2.62
Simply missed the medicine	35.8	1.82	39.3	1.91	38.6	2.05	43.7	2.34	46.1	2.13
Concerned about possible side-effects from the medicine	39.4	2.44	40.1	2.37	44.2	2.50	43.5	2.67	44.4	2.75
Don't think medicine is working	19.7	3.11	17.6	2.72	29.5	2.66	27.5	3.12	36.9	3.03
Difficulty remembering things in daily life	11.0	2.13	16.6	2.69	24.0	2.34	26.1	2.62	36.9	2.33

Note: Bold font indicates a statistically significant difference, $p < 0.05$

Note: All tests for the non-adherent groups are compared to the none-minimal depression category.



Top 5 Reasons for Medication Non-Adherence by Mean Days

In the past week, patients with moderate to severe depression missed their antidepressant medication on average 3.16 – 3.41 days due to side-effects from the medicine.

	None - Minimal depression (n=137)		Mild (n=392)		Moderate (n=430)		Moderately severe (n=414)		Severe (n=336)	
<i>% of patients who missed vs Mean # days missed</i>	%	#	%	#	%	#	%	#	%	#
Side-effects from the medicine	20.4	2.79	17.6	2.84	22.8	3.16	24.4	3.41	22.9	3.34
Not comfortable taking it for personal reasons	15.3	2.52	18.4	2.58	25.1	2.71	24.2	2.67	23.2	3.09
Do not consider taking the medicine as a high priority in my daily routine	19	2.38	19.6	2.7	22.8	2.51	19.3	2.97	20.2	3.07
Don't think medicine is working	19.7	3.11	17.6	2.72	29.5	2.66	27.5	3.12	36.9	3.03
Difficulty swallowing / applying / inhaling / injecting the medicine	13.9	2.47	11.2	3.02	15.4	2.77	13.8	2.65	12.2	2.98

Note: Bold font indicates a statistically significant difference, $p < 0.05$

Note: All tests for the non-adherent groups are compared to the none-minimal depression category.





Strengths

- National database with various quality control measures
- Large sample size for a self-reported study
- Detailed insight and quantification of the various reasons for non-adherence



Limitations

- Analyses are based on self-report data of adherence measures. Recall bias may introduce error, in addition to overestimation of adherence
- Self-reported adherence data are often skewed, correction factors ought to be applied to data for further analysis
- Cross sectional studies account for only one point in time and do not capture adherence behavior over time. Replicating these results with a longitudinal study would be beneficial
- This analysis didn't adjust for baseline characteristics or perform any regression analyses.

Conclusion

The extent of non-adherence, the characteristics of respondents who are non-adherent, the reasons for non-adherence all varied based on the level of depression.

Individuals with higher levels of depression:

- Were more likely to be non-adherent
- Were more likely to be younger, single, and female
- Had forgetfulness issues, logistic issues and belief issues

In summary, individuals with different levels of depression needed to be screened for their specific reasons for non-adherence

Different interventions and specific messages should be developed for individuals with different levels of depression

Questions?



Contact

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for questions regarding use of MAR-Scale



Thank you

Reference

1. World Health Organization, 2023. Depression. <https://www.who.int/news-room/fact-sheets/detail/depression> (accessed 3 October 2023)
2. Arias-de la Torre J, Vilagut G, Ronaldson A, Serrano-Blanco A, Martín V, Peters M, Valderas JM, Dregan A, Alonso J. Prevalence and variability of current depressive disorder in 27 European countries: a population-based study. *Lancet Public Health*. 2021 Oct;6(10):e729-e738. doi: 10.1016/S2468-2667(21)00047
3. European Data Journalism Network, 2018. Mental illness costs Europe 600 billion Euro. <https://www.europeandatajournalism.eu/News/Data-news/Mental-illness-costs-Europe-600-billion-euro> (accessed 3 October 2023)
4. OECD/EU(2018), Health at a glance: Europe 2018: State of Health in the EU cycle, OECD publishing, Paris. https://read.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-europe-2018_health_glance_eur-2018-en#page4
5. Sansone, R. A., & Sansone, L. A., 2012. Antidepressant adherence: are patients taking their medications? *Innov. Clin. Neurosci*. 9(5-6), 41–46.
6. Kroenke, K., Spitzer, R.L., & Williams, J.B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medicine*, 16606-613.



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