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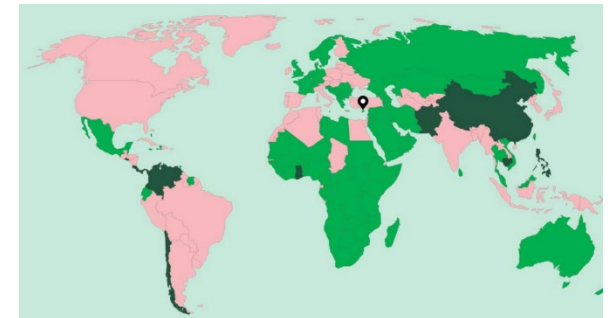
# **Anksioznost, uzroci i posledice (šta utiče na njen porast) i kada je treba medikamentozno lečiti ?**

*Čedo D. Miljević*

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# predavanje je sponzorisano

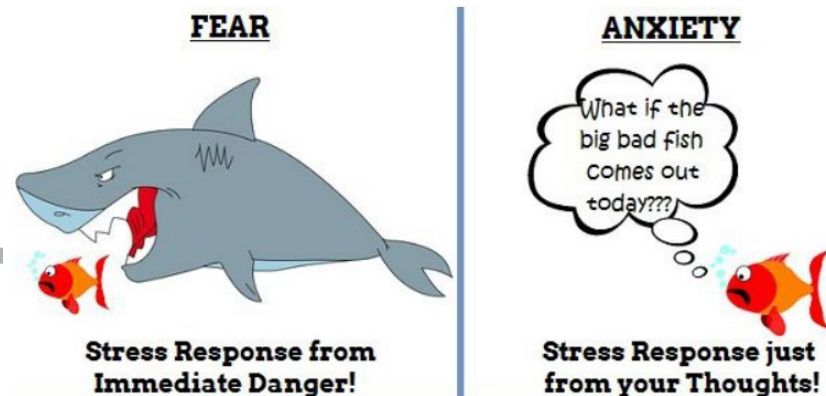
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# Strah i anksioznost...

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- Strah i anksioznost su blisko povezani.
- Oboje sadrže ideju opasnosti/ mogućnost povrede...
- Uopšteno, strah se posmatra kao reakcija na specifičnu, jasnu opasnost, dok se anksioznost posmatra kao difuzni, nefokusirani, bezobjektni, strah orijentisan ka budućnosti (Barlow, 2002)



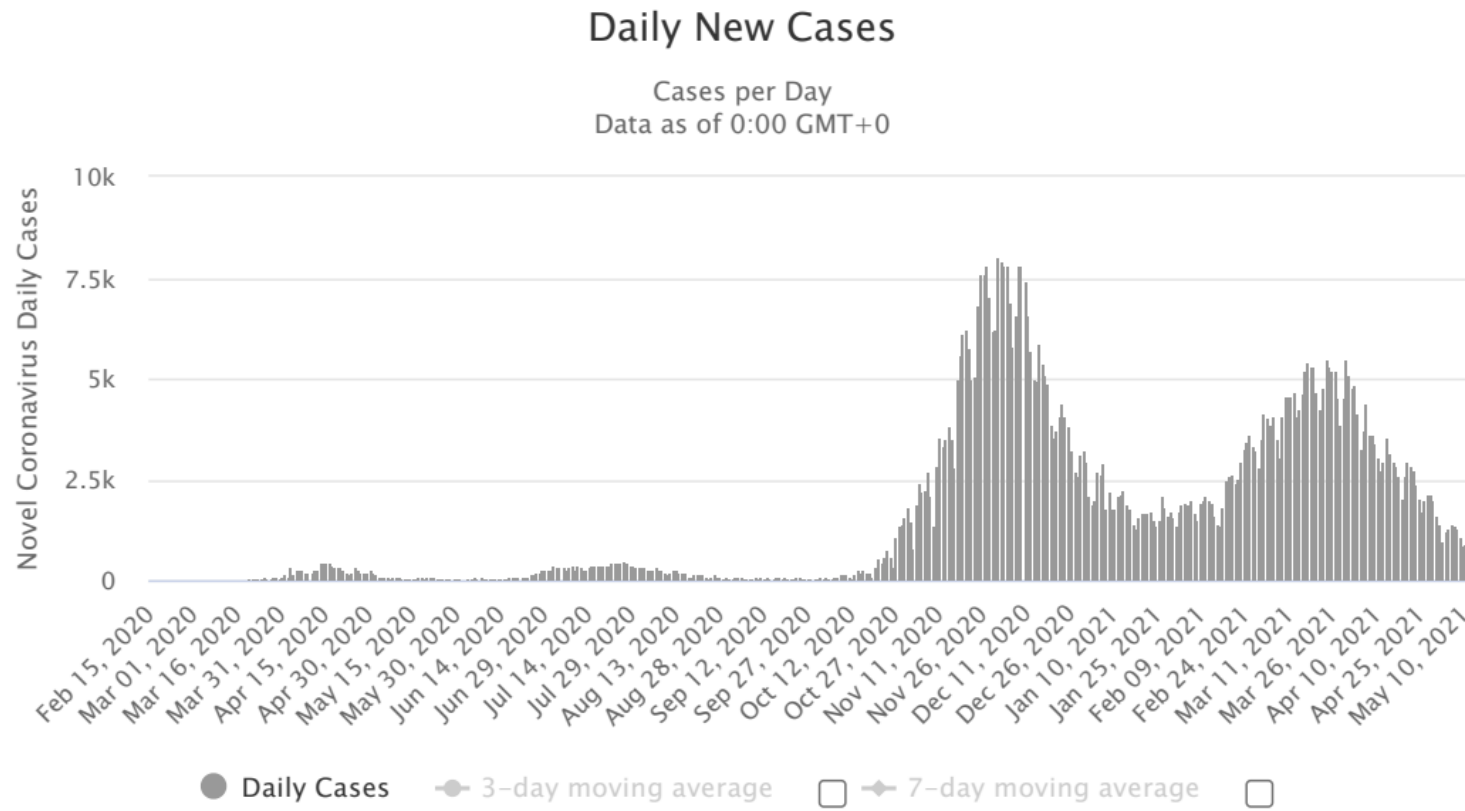
# Sta smo prezivali





# Sta smo preziveli

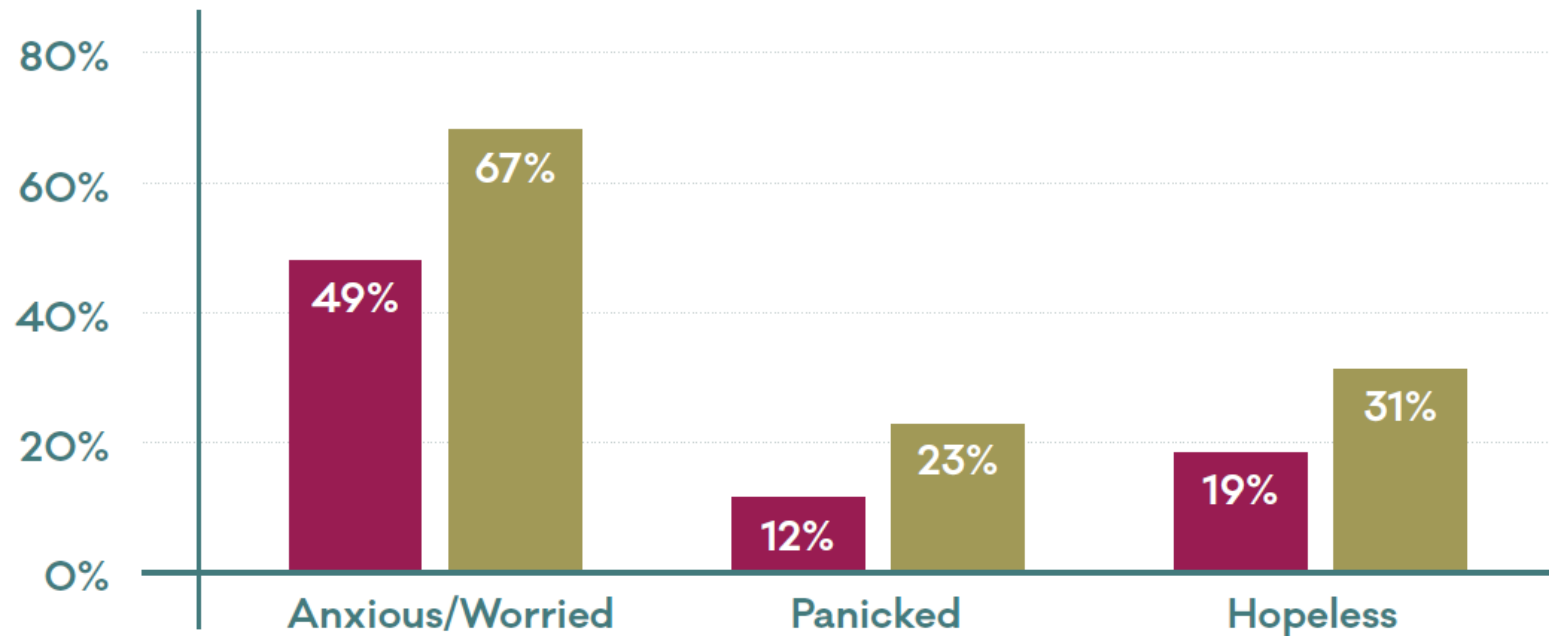
## Daily New Cases in Serbia





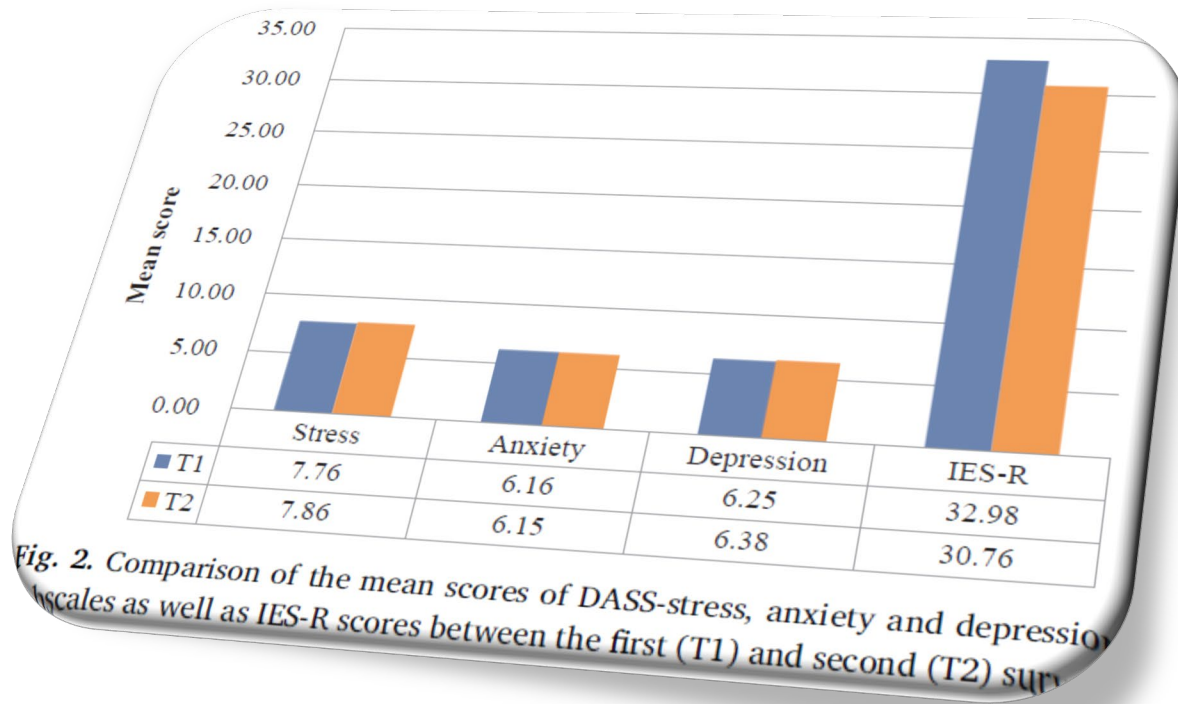
Which of the following emotions have you felt as a result of COVID-19 in the last two weeks?

■ Total population  
■ Have mental health condition



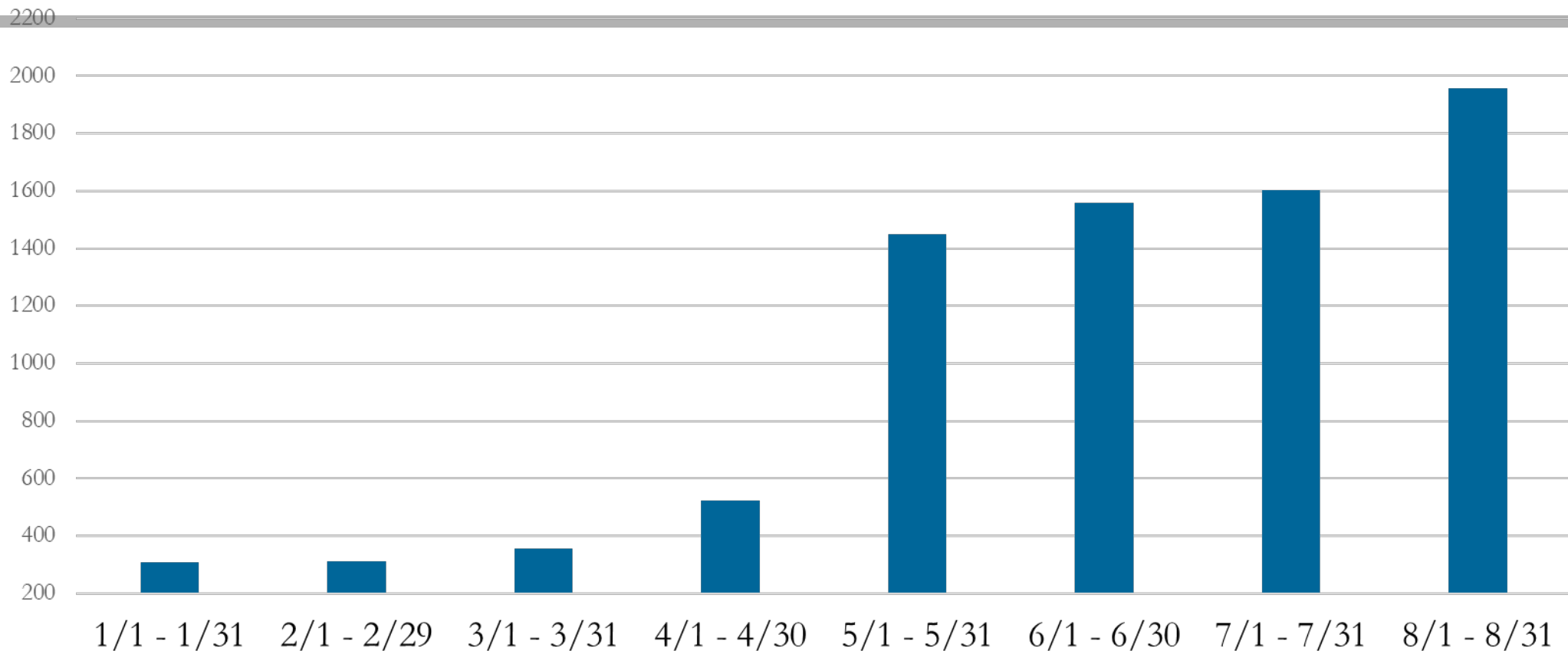
# A longitudinal study on the mental health of general population during the COVID-19 epidemic in China

Brain, Behavior, and Immunity 87 (2020) 40–48



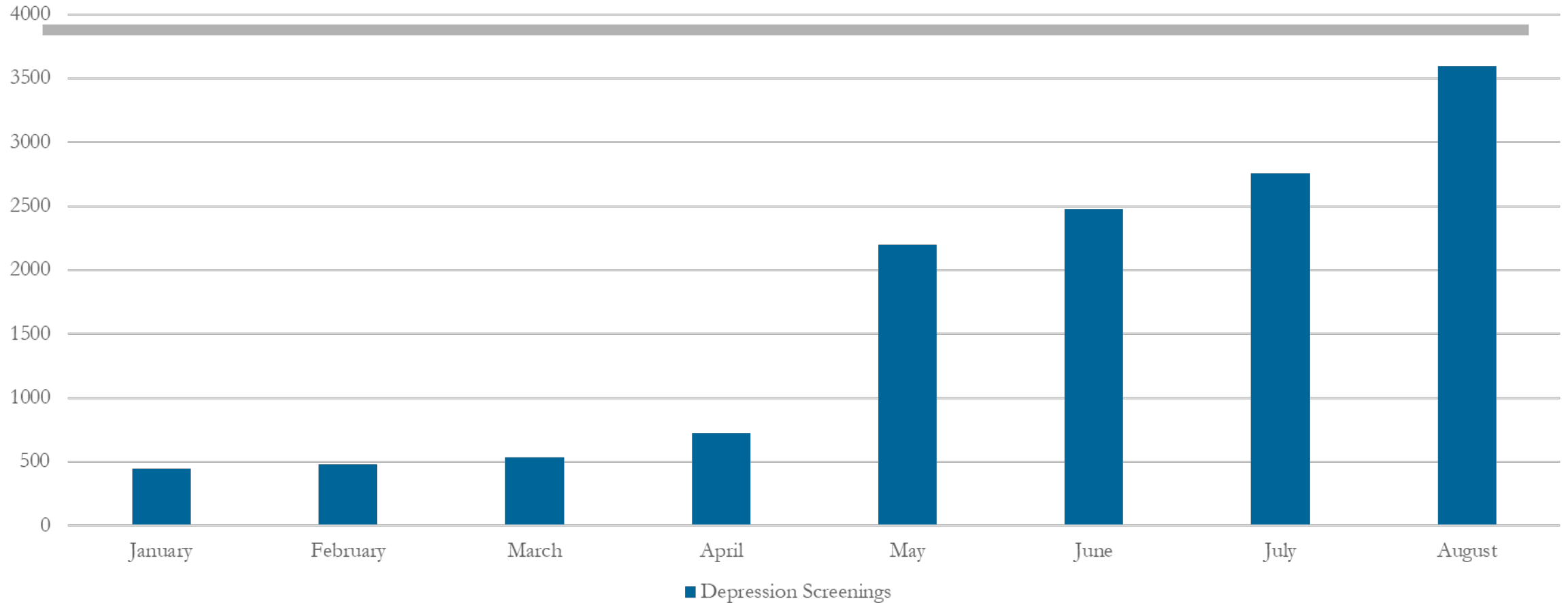
A longitudinal study of psychological symptoms in 1738 respondents from 190 Chinese cities during the initial outbreak in Wuhan, China, repeated 4 weeks later at the peak of the epidemic revealed 28% reported high levels of anxiety, 17% reported depression, and 8% reported stress and distress was stable over time.

# In August, Per Day Anxiety Screenings Increased by 535% over January (USA)

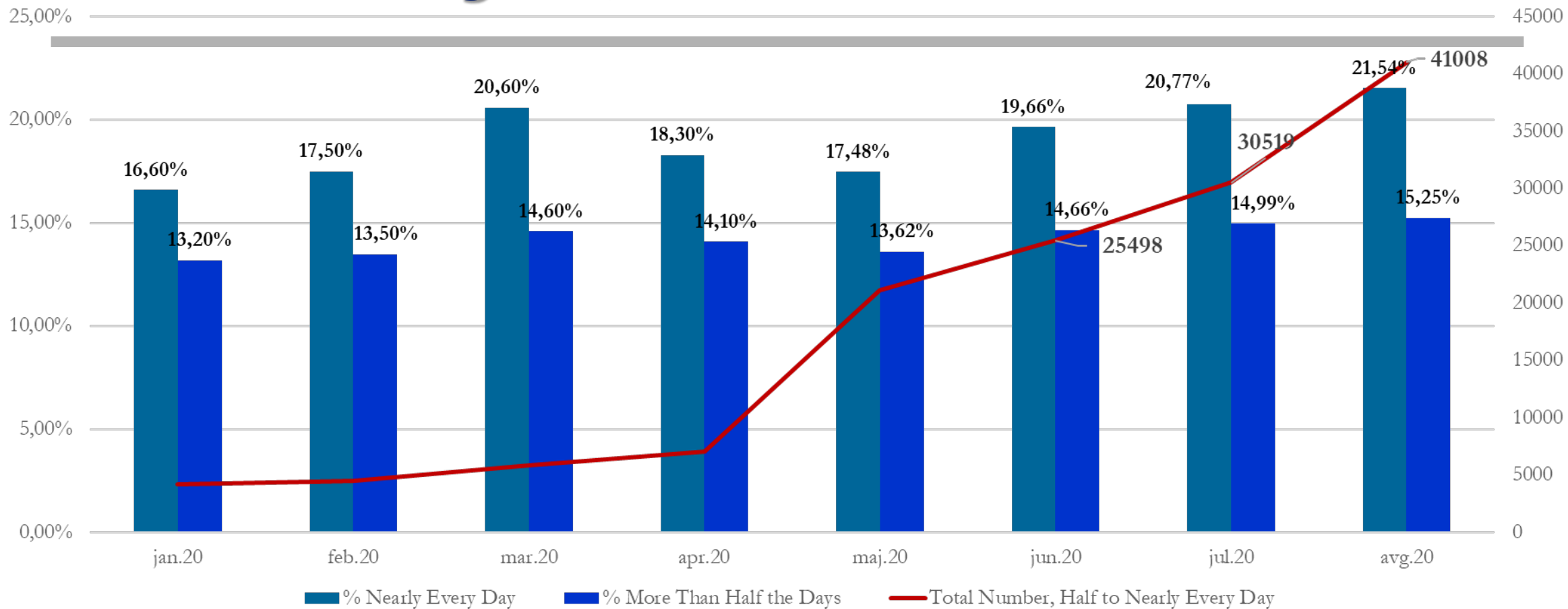




# In August, Per Day Depression Screening Increased by 709% over January (USA)



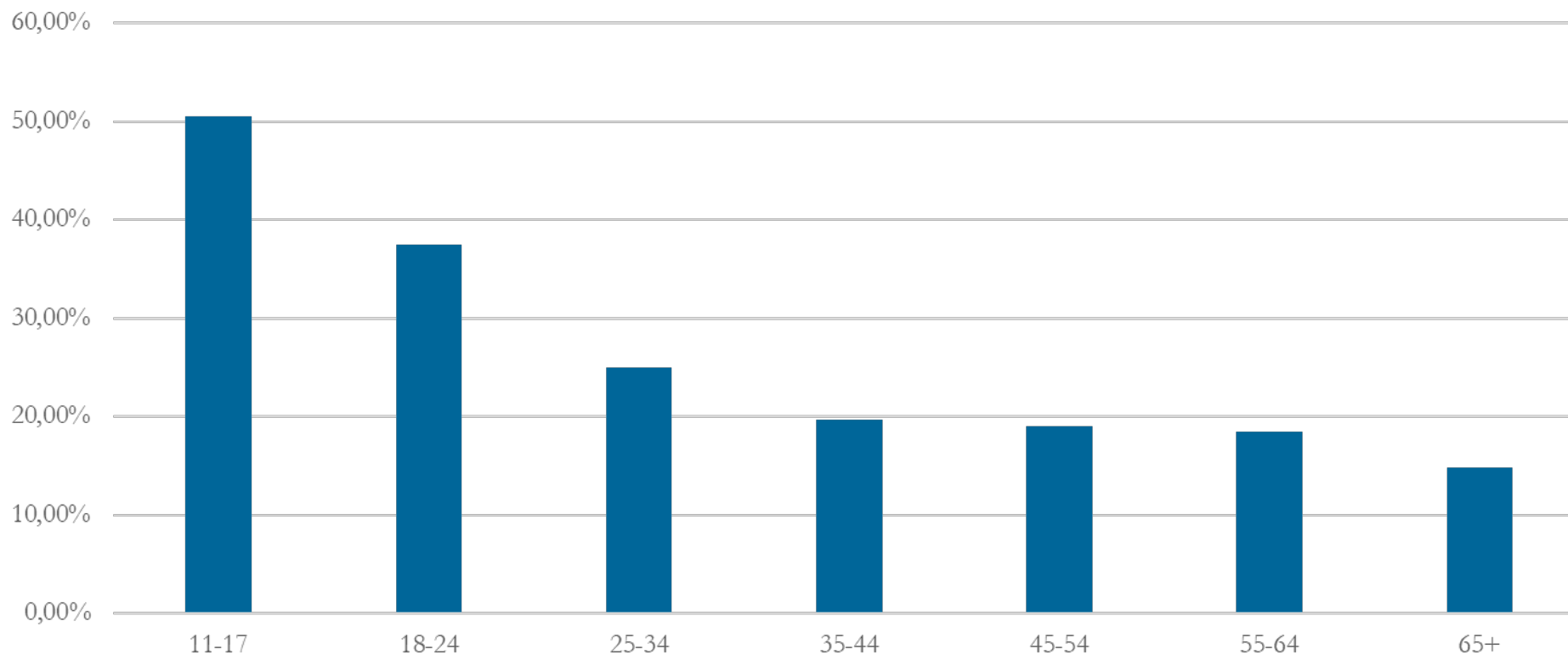
# More Than 40,000 People Considered Self-Harm or Suicide in August (USA)



# Young People Experiencing Highest Rates Suicidal Ideation



Percent with Suicidal Ideation More than half or Nearly every day, August  
2020



**17,497**  
**11-17-year-**  
**olds with**  
**suicidal**  
**ideation**



# August Anxiety Screeners: The Main Things Contributing to Mental Health Problems Right Now

Reason	Number of Responders	Percent of Respondents
Loneliness or isolation	23437	64.42%
Past trauma	17379	47.77%
Relationship problems	14537	39.95%
Current events (news, politics, etc.)	10953	30.10%
Coronavirus	10717	29.46%
Grief or Loss	9210	25.31%
Financial Problems	9197	25.28%
Racism	3289	9.04%

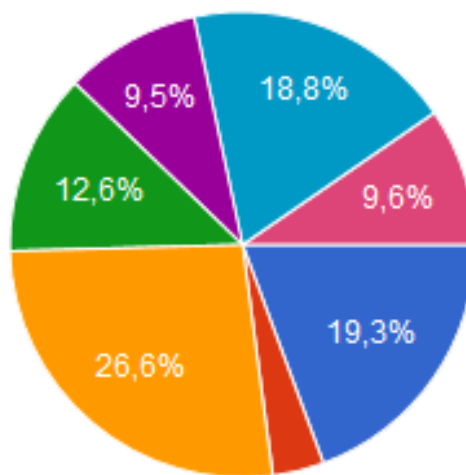
N=36,384, scoring moderate to severe 8/1-8/31, "Choose up to 3"

# Šta nas je najviše brinulo?

Šta Vas najviše brine tokom pandemije?

2.399 odgovora

Loneliness or isolation  
 Past trauma  
 Relationship problems  
 Current events (news, politics, etc.)  
 Coronavirus



- Ograničena mogućnost šetnje
- Izmenjen rad prodavnica/uslužnih/ugostiteljskih delatnosti.
- Strah od zaraze.
- Finasijske brige.
- Nemogućnost direktnog komuniciranja sa starijim članovima porodice.
- Smanjena mogućnost druženja.
- Problemi vezani za roditeljstvo (školske obaveze, nemogućnost dečije razono...

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# Šta je bilo posle...

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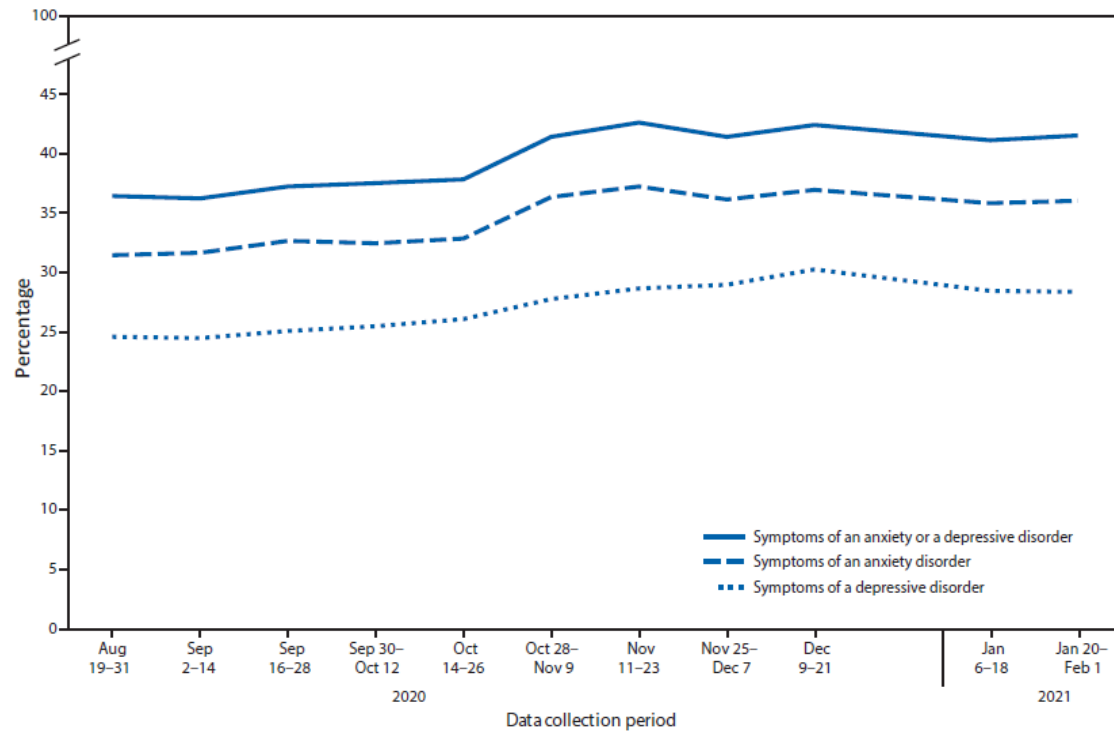
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## Symptoms of Anxiety or Depressive Disorder and Use of Mental Health Care Among Adults During the COVID-19 Pandemic — United States, August 2020–February 2021

MMWR / April 2, 2021 / Vol. 70 / No. 13

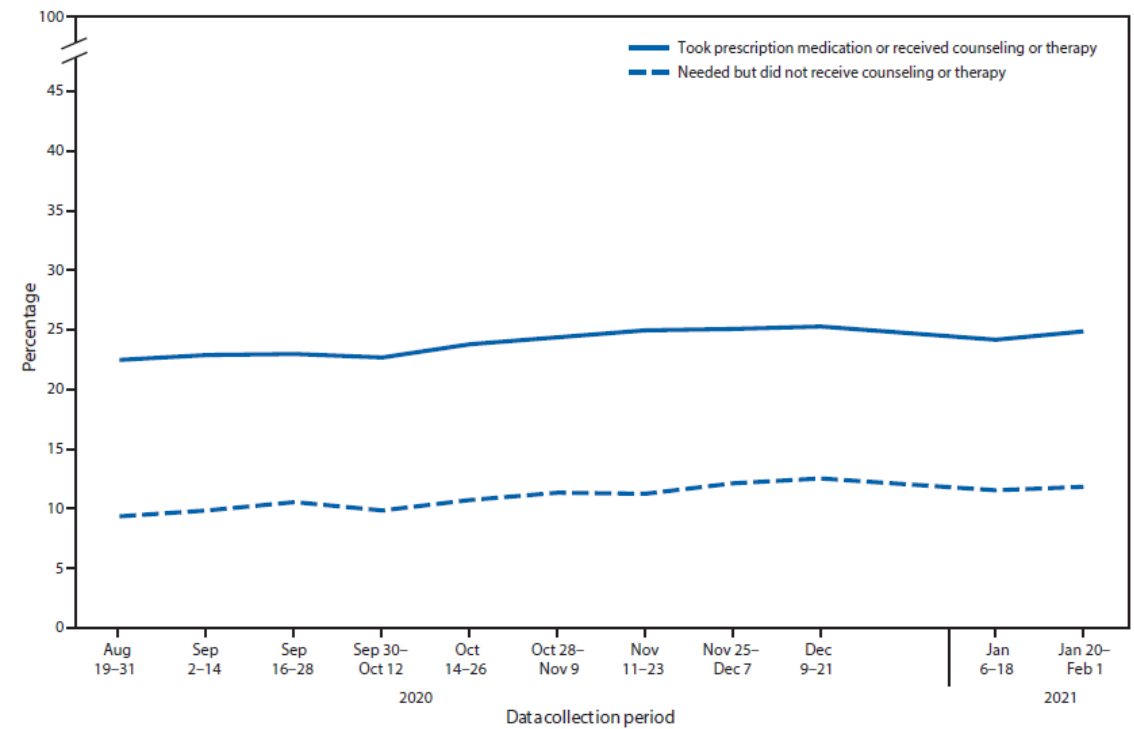
US Department of Health and Human Services/Centers for Disease Control and Prevention

FIGURE 1. Percentage of adults aged  $\geq 18$  years with symptoms of anxiety disorder, depressive disorder, or anxiety or depressive disorder during past 7 days, by data collection period — Household Pulse Survey, United States, August 19, 2020–February 1, 2021\*



\* Household Pulse Survey data collection included a 1-day break between the conclusion of one data collection period and the start of the next, as well as a 2-week break during December 22, 2020–January 5, 2021.

FIGURE 2. Percentage of adults aged  $\geq 18$  years who took prescription medication for mental health or received counseling or therapy during past 4 weeks and percentage who needed but did not receive counseling or therapy during past 4 weeks, by data collection period — Household Pulse Survey, United States, August 19, 2020–February 1, 2021\*



\* Household Pulse Survey data collection included a 1-day break between the conclusion of one data collection period and the start of the next, as well as a 2-week break during December 22, 2020–January 5, 2021.



---

### What is added by this report?

During August 2020–February 2021, the percentage of adults with recent symptoms of an anxiety or a depressive disorder increased from 36.4% to 41.5%, and the percentage of those reporting an unmet mental health care need increased from 9.2% to 11.7%. Increases were largest among adults aged 18–29 years and those with less than a high school education.

### What are the implications for public health practice?

Trends in mental health can be used to evaluate the impact of strategies addressing adult mental health status and care during the pandemic and to guide interventions for disproportionately affected groups.



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# Šta je još problem ?

Loneliness or isolation

Past trauma

Relationship problems

Current events (news, politics, etc.)

Coronavirus

---

# Depresija i anksioznost kao posledica medija?



Vojnosanit Pregl 2020; 77(11): 1201–1209.

VOJNOSANITETSKI PREGLED

Page 1201

ORIGINAL ARTICLE

(CC BY-SA)



UDC: 613.86:616-051]:616-036.22

<https://doi.org/10.2298/VSP200713108M>

## Public trust and media influence on anxiety and depression levels among skilled workers during the COVID-19 outbreak in Serbia

Uticaj poverenja javnosti i medija na nivoe anksioznosti i depresije među stručnim radnicima tokom COVID-19 epidemije u Srbiji

Ivan Marković\*, Srdjan Nikolovski<sup>†</sup>, Stefan Milojević<sup>‡§</sup>, Dragan Živković<sup>||</sup>, Snežana Knežević<sup>¶</sup>, Aleksandra Mitrović<sup>\*\*</sup>, Zlatko Fišer<sup>††</sup>, Dragan Djurdjević<sup>‡‡</sup>

### Abstract

**Background/Aim.** Along with the great impact of 2019 coronavirus disease (COVID-19) on physical health, social functioning, and economy, this public health emergency has significant impact on mental health of people as well. The aim of this study was to assess the impact of outbreak-related information and public trust in the health system and preventive measures during the COVID-19 outbreak in Serbia in 2020 on levels of anxiety and depression in education, army and healthcare professionals. **Methods.** An anonymous questionnaire was disseminated to skilled professionals working in fields of education, army, and healthcare. The questionnaire included the Beck Anxiety Inventory, Zung Self-Rating Depression Scale, as well as the section assessing the perceived disturbance by the outbreak-related information and the trust of participants in healthcare system and preventive measures proposed by the crisis team. **Results.** Out of 110 subjects enrolled in this study (mean age  $35.25 \pm 9.23$  years), 59.1% were women. Among healthcare workers, the frequency of perceiving outbreak-related information available in public media as disturbing, as well as the average level of anxiety, were

higher compared to the group of army professionals ( $p < 0.05$ ). Women also perceived outbreak-related information available in public media as disturbing in a higher percentage compared to men ( $p < 0.01$ ), and had higher levels of anxiety ( $p = 0.01$ ) and depression ( $p < 0.05$ ). The lack of public trust was associated with higher levels of depression, and the perception of outbreak-related information as disturbing with higher levels of both anxiety and depression. **Conclusion.** Significant perception of outbreak-related information as disturbing among healthcare workers, as well as the lack of trust in healthcare system and preventive measures proposed by the crisis team are important factors influencing the mental state. This finding has the guiding purpose for competent institutions to make efforts to increase public trust, as one of the important preventive measures, in order to preserve and improve the mental well-being of the population in outbreak conditions.

### Key words:

anxiety; communications media; covid-19; depression; medicine, preventive; mental health; surveys and questionnaires.

# Depresija i anksioznost kao posledica medija?

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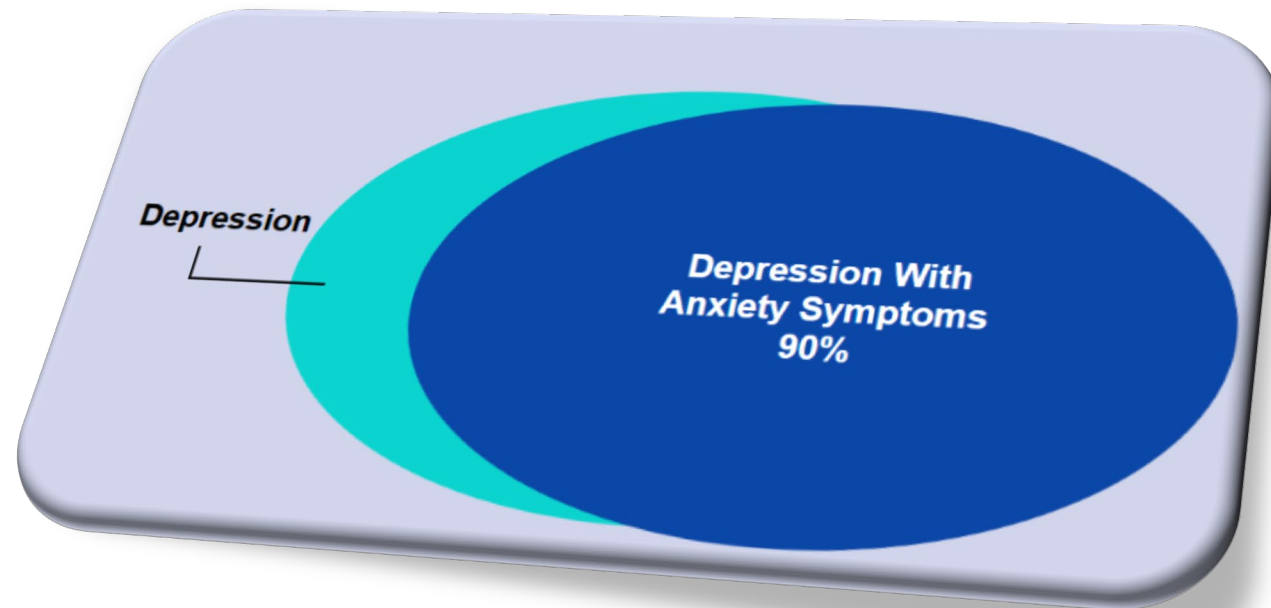
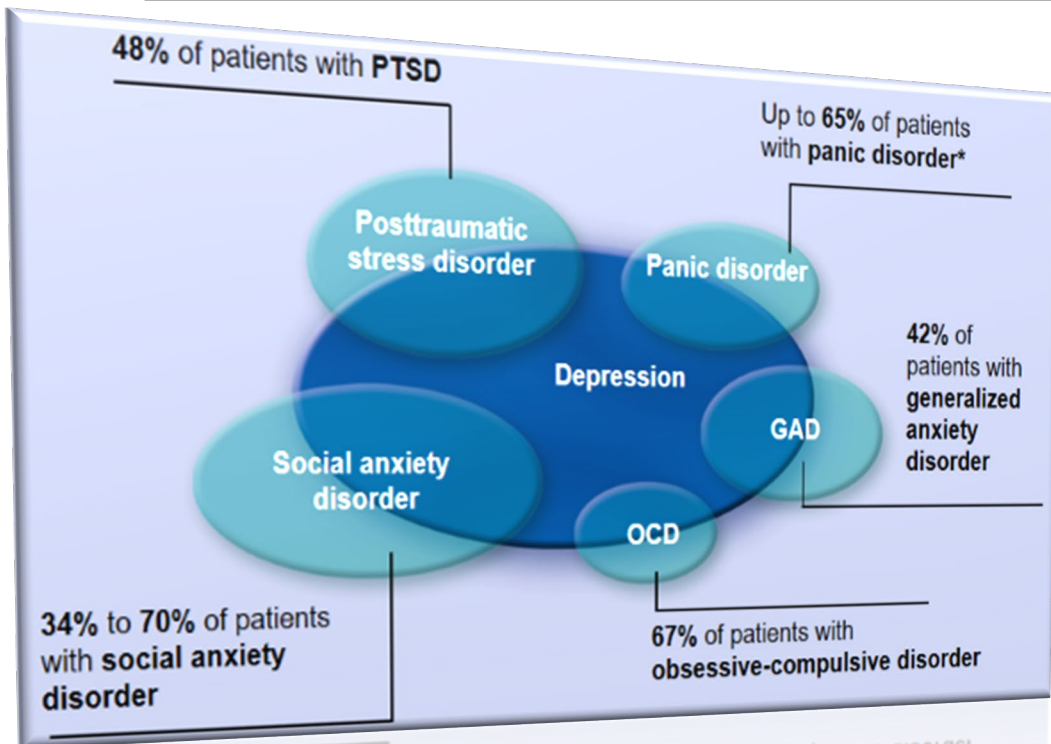
## Rezultati

- Nedostatak poverenja javnosti je bio povezan sa višim nivoima depresije, a doživljavanje informacija u vezi sa stanjem epidemije kao uznemirujućih, sa nivoima i anksioznosti i depresije.

## Zaključak

- Izraženo doživljavanje informacija u vezi sa stanjem epidemije kao uznemirujućih među zdravstvenim radnicima, kao i značajno odsustvo poverenja u zdravstveni sistem i u preventivne mere predložene od strane kriznog štaba, predstavljaju značajne činioce sa uticajem na mentalno stanje.

# Anksioznost i depresija...





# Anksioznost i depresija II...

---

- Comorbid depression and anxiety disorders occur in up to 25% of general practice patients
- About 85% of patients with depression have significant anxiety, and 90% of patients with anxiety disorder have depression.
- Despite the availability of treatments, 40% of patients with depression or anxiety do not seek treatment, and of those who do, less than half are offered beneficial treatment.

# Neuroanatomija anksioznosti i depresije

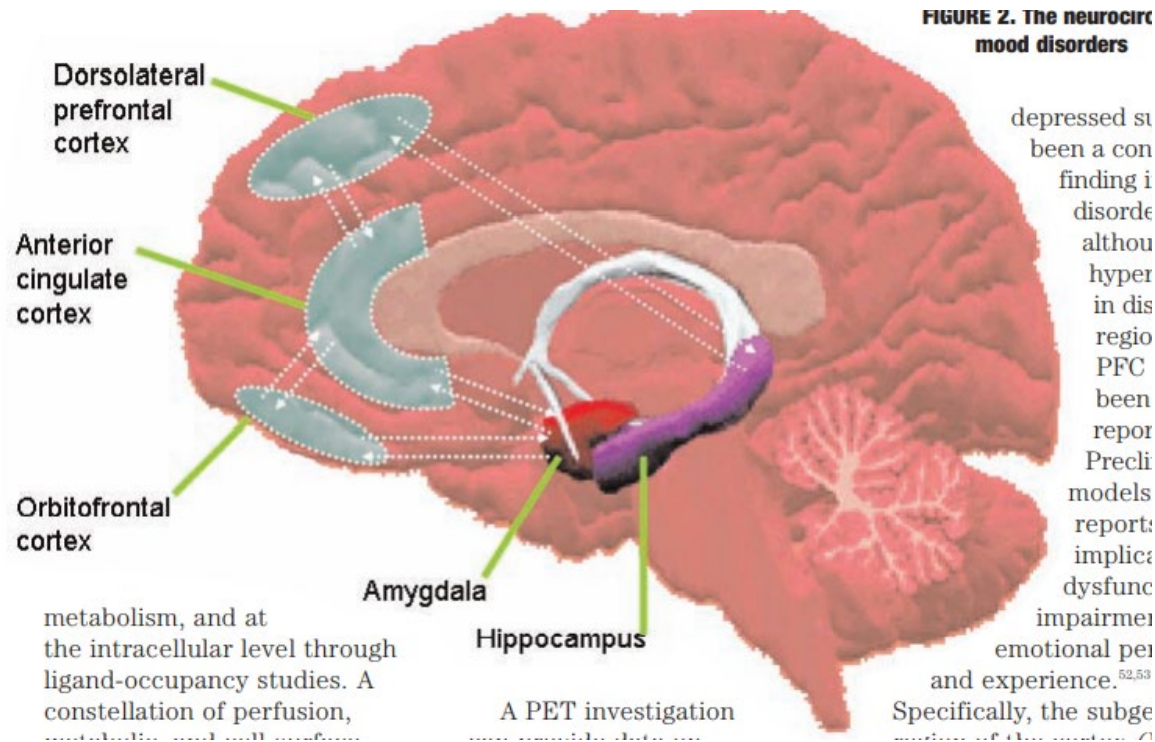
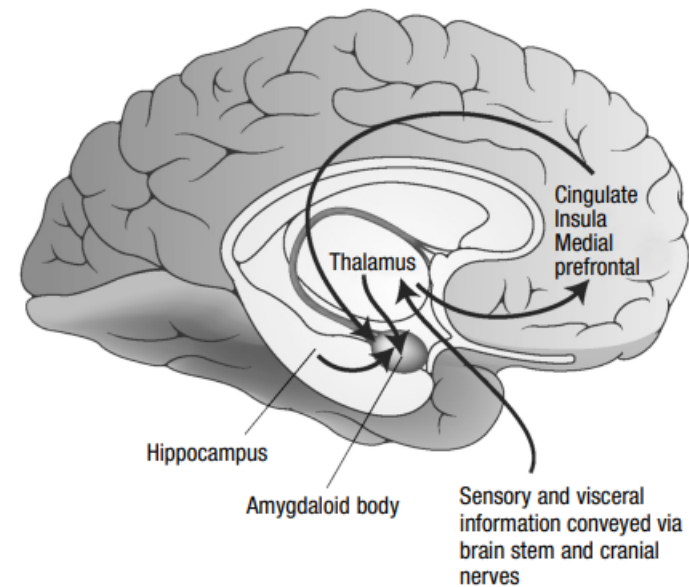
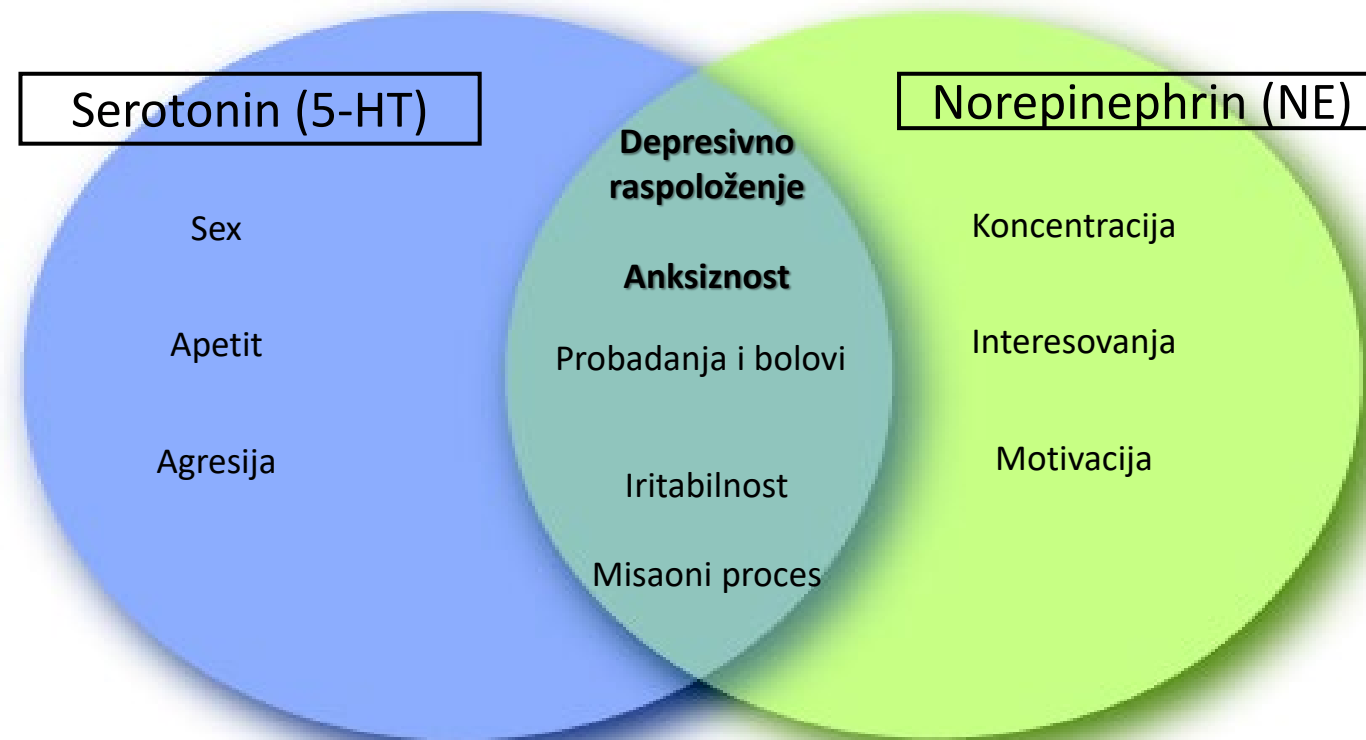


Figure 1. Schematized Diagram Indicating Critical Pathways in Threat Assessment and Responding, Relevant to Neurocircuitry Models in Post-traumatic Stress Disorder, Panic Disorder, and Social Anxiety Disorder



environmental information.<sup>10</sup> Overall, these findings support involvement of thalamus, amygdala, dACC, hypothalamus, hippocampus, and mPFC in fear circuitry.<sup>12</sup> These regions

# Neurotransmiteri



## References:

1. Adapted from: Stahl SM. In: *Essential Psychopharmacology: Neuroscientific Basis and Practical Applications*: 2<sup>nd</sup> ed. Cambridge University Press 2000.
2. Blier P, et al. *J Psychiatry Neurosci*. 2001;26(1):37-43.
3. Doraiswamy PM. *J Clin Psychiatry*. 2001;62(suppl 12):30-35.
4. Verma S, et al. *Int Rev Psychiatry*. 2000;12:103-114.





Molecular Psychiatry (2012), 1–7  
© 2012 Macmillan Publishers Limited All rights reserved 1359-4184/12



NATURE NEUROSCIENCE | ARTICLE

**ORIGINAL ARTICLE**

[www.nature.com/mp](http://www.nature.com/mp)

The serotonin transporter gene-linked polymorphic region (5-HTTLPR) and cortisol stress reactivity: a meta-analysis

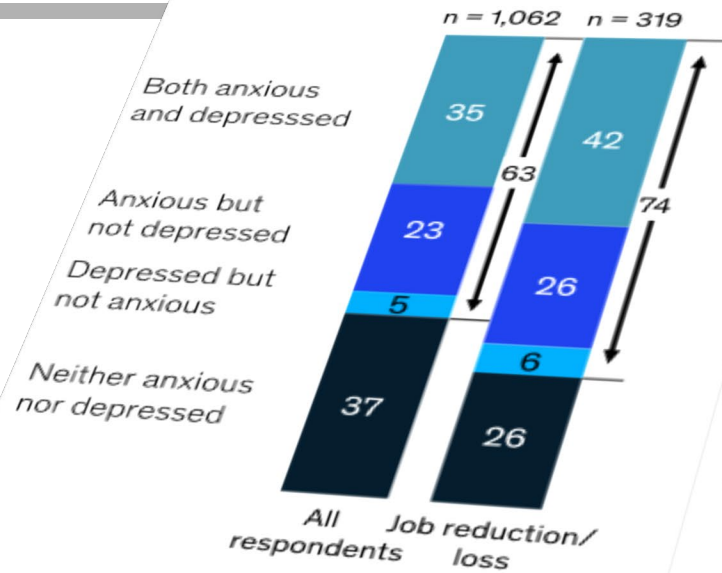
R Miller, M Wankerl, T Stalder, C Kirschbaum and N Alexander

CRF receptor 1 regulates anxiety behavior via sensitization of 5-HT<sub>2</sub> receptor signaling

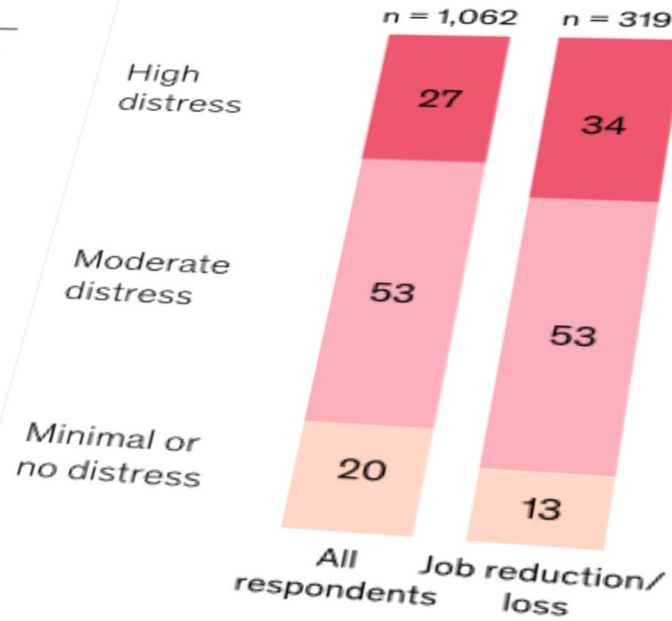
Nature Neuroscience 13, 622–629 (2010) | doi:10.1038/nn.2529

## Reported signs of distress related to COVID-19 in the United States




Respondents reporting feeling anxious or depressed in past week  
% of respondents



Respondents' reported level of distress related to COVID-19  
% of respondents



Respondents' levels of reported substance use

- 
**1 out of 4** reported **binge drinking\*** at least once in the past week
- 
**1 out of 5** reported taking **prescription drugs** for non-medical reasons
- 
**1 out of 7** reported using **illicit drugs**

\* As defined by National Institute on Alcohol Abuse and Alcoholism,  $\geq 5$  drinks for men and  $\geq 4$  drinks for women

QFEEL1. Over the past week have you felt anxious?  
QFEEL2. Over the past week have you felt depressed?  
QFEEL2a. Please indicate your level of distress related to the Coronavirus/COVID-19 pandemic (10-point scale from least distressed to most distressed. "High" is 8-10, "Moderate" is 4-7, and "Low" is 1-3).  
QFEEL2b. Since the Coronavirus/COVID-19 began impacting the US, has the number of hours you have worked increased, decreased, or stayed the same?

# Šta da se radi?

---

Kako se nosimo/prevladavamo (sa) stresom?

Kriza je uvek mogućnost

---

## MALADAPTIVE COPING



## ADAPTIVE COPING



# **Mehanizam prevladavanja stresa je uvek individualan**

One size doesn't fit all... we can't hand out a comprehensive coping manual and tell everyone to have at it.

# могућности...

(али увек изаберите  
оно што Вам  
лично одговара!)



Брините се о физичком здрављу



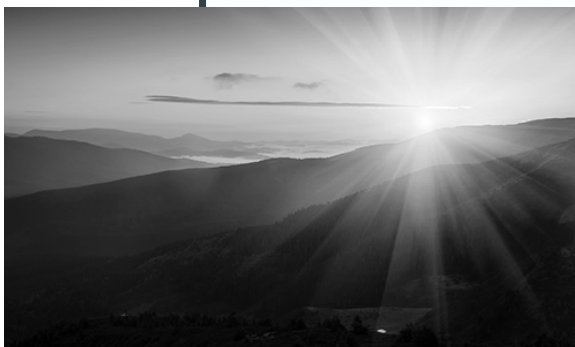
Одржавајте социјални  
контакт



Одмор, пауза



Održavajte rutinu



priroda



Zatražite pomoć

**mogućnosti...**

(ali uvek izaberite  
ono što Vama  
lično odgovara!)



### Physical Wellbeing



**7-Minute Workout ML**  
Access guided workouts for any activity level



**Fooducate**  
Create your healthy diet toolbox



**Headspace ML**  
Access guided meditations and mindfulness activities

### Emotional Wellbeing



**Happify ML**  
Play games to reduce stress, overcome negative thoughts, and build resilience



**MindShift ML**  
Access resources to help manage anxiety



**Happy Color™- Color by Number**  
Engage in coloring activities as a positive coping strategy

### Physical Wellbeing



**Hoopla ML**  
Access e-books, music, audiobooks, and movies



**Khan Academy ML**  
Learn online with interactive exercises and videos



**Luminosity ML**  
Improve memory and increase focus with brain training games

### Financial Wellbeing



**DPSS Mobile ML**  
Fill out forms and skip a trip to the office

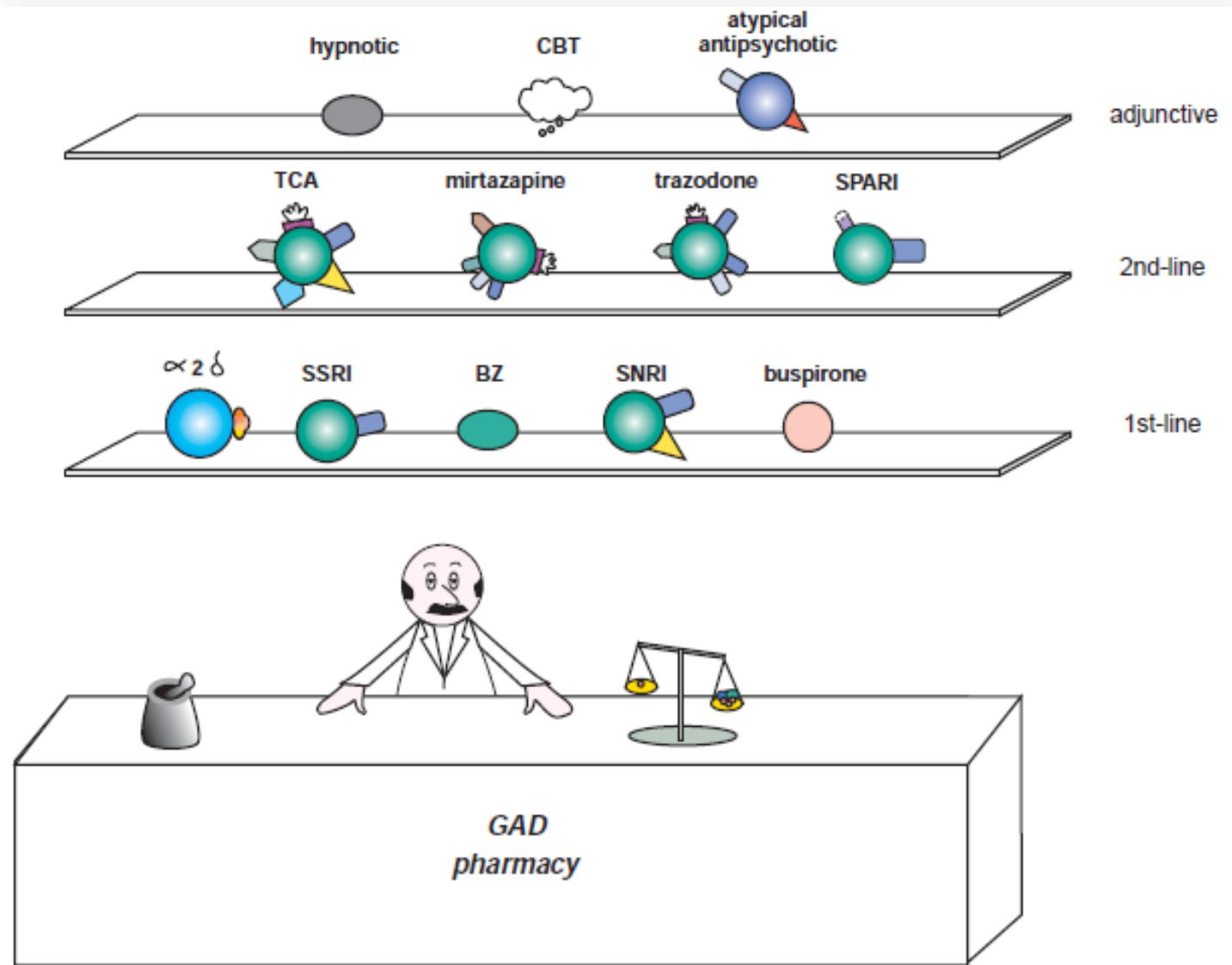


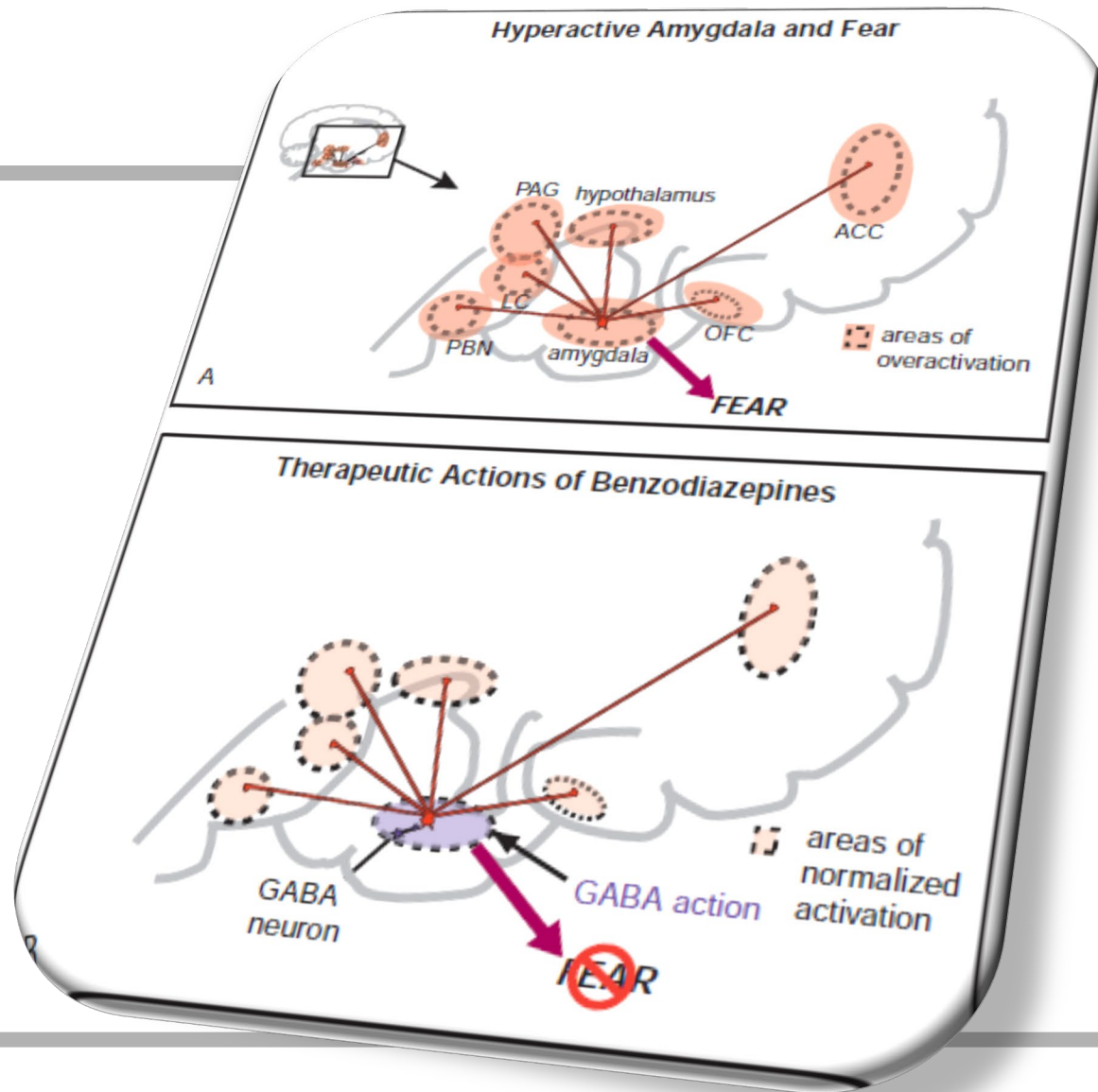
**Keeper ML**  
Store and manage passwords securely



**Mint ML**  
Develop and manage a personal budget







## Clonazepam for the Treatment of Panic Disorder

Patients (n)	Diagnosis	Active Treatment and Duration	Outcome	Adverse Events	Authors
29	DSM-III PD or agoraphobia with panic attacks	Clonazepam, dose titrated for 2 weeks (average 2.2 mg/day). Total treatment 4 weeks.	Clonazepam significantly better than placebo for CGI-S, HAM-A, and GAS. Number, intensity, and duration of situational attacks, anticipatory attacks, and spontaneous attacks.	Drowsiness in 9/13 patients. Other AEs with clonazepam but not placebo: memory/concentration, sexual problems	Beauclair <i>et al.</i> , 1994
413	DSM-III PD	Clonazepam, fixed daily doses up-titrated over 3 weeks to 0.5 mg, 1.0 mg, 2.0 mg, 3.0 mg, and 4.0 mg. Maintained for 6 weeks and then tapered for 7 weeks.	Clonazepam (dose of 1 mg and above) significantly better than placebo for CGI-S, PGI-C, and HAM-A. Doses of 1-2 mg considered to have the best benefit/risk ratio.	Somnolence, ataxia, depression, dizziness, fatigue, and irritability more frequent with clonazepam than with placebo.	Rosenbaum <i>et al.</i> , 1997
		Clonazepam, uptitrated for 3 weeks, maintained for 3 weeks	Clonazepam clinically and statistically superior to placebo in change in the number of panic attacks and CGI-S, CGI-C, and PGI-C.	Gradual withdrawal not associated with withdrawal symptoms. No evidence of rebound. Main AE associated with clonazepam therapy: somnolence.	Moroz and Rosenbaum, 1999

438

DSM-III  
PD with or without  
agoraphobia

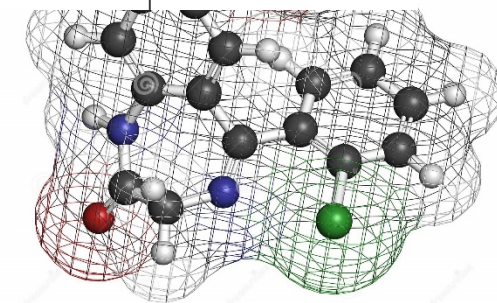
Clonazepam, uptitrated for 3 weeks, maintained for 3 weeks (total 6-week therapeutic phase) at a daily dose of 0.25 to 4.0 mg/day. Doses tapered gradually to zero for 7 weeks.

Clonazepam clinically and statistically superior to placebo in change in the number of panic attacks and CGI-S, CGI-C, and PGI-C.

Gradual withdrawal not associated with withdrawal symptoms. No evidence of rebound. Main AE associated with clonazepam therapy: somnolence.

Moroz and  
Rosenbaum,  
1999

144	PD	Clonazepam, uptitrated for 3 weeks, maintained for 3 weeks (6-week therapeutic phase) at a daily dose of 0.25 to 4.0 mg/day. Doses tapered gradually to zero for 7 weeks.	Improvement on the SF-36 MCS scale was more than twice as great with clonazepam as with placebo ( $p=0.03$ ), with highest improvement in "general mental health" in MCS and "freedom from bodily pain" in the PHCS.	See Moroz and Rosenbaum, 1999	Jacobs <i>et al.</i> , 1997 (Data obtained in conjunction with study Moroz and Rosenbaum, 1999)
27	Chest pain. PD with normal angiography	Clonazepam, 1-4 mg/day for 6 weeks.	Reduction of panic attacks >50%; clonazepam 67%; placebo 47%. Reduction in HAM-A score >50%; clonazepam 58%; placebo 14%.	Safety not reported.	Wulsin <i>et al.</i> , 1999
24	PD with agoraphobia	Clonazepam, 2 mg/day for 6 weeks.	Clonazepam superior to placebo for CGI ( $p=0.031$ ).	Main AEs associated with clonazepam therapy: somnolence, ataxia, dizziness.	Valença <i>et al.</i> , 2000



# The Efficacy and Safety of Clonazepam in Patients with Anxiety Disorder Taking Newer Antidepressants: A Multicenter Naturalistic Study

*Clinical Psychopharmacology and Neuroscience 2016;14(2):177-183*

Drug	Group		
	Clonazepam (n=75)	Alprazolam (n=64)	Lorazepam (n=41)
Citalopram	2 (2.7)	0 (0)	0 (0)
Escitalopram	24 (32.0)	25 (39.1)	14 (34.1)
Fluoxetine	7 (9.3)	4 (6.3)	5 (12.2)
Fluvoxamine	0 (0)	1 (1.6)	0 (0)
Paroxetine	22 (29.3)	19 (29.7)	8 (19.5)
Sertraline	6 (8.0)	2 (3.1)	3 (7.3)
Duloxetine	1 (1.3)	0 (0)	3 (7.3)
Milnacipran	1 (1.3)	0 (0)	0 (0)
Venlafaxine	6 (8.0)	4 (6.3)	3 (7.3)
Mirtazapine	3 (4.0)	5 (7.8)	3 (7.3)
Others	3 (4.0)	4 (6.3)	2 (4.9)

**Table 3.** Comparison of efficacy among three benzodiazepines in the treatment of anxiety disorders

Variable	Group		
	Clonazepam (n=75)	Alprazolam (n=64)	Lorazepam (n=41)
<b>CGI-S</b>			
Baseline	4.92±0.93	4.92±0.97	4.76±0.99
Week 6	2.76±0.80	2.77±0.79	2.90±0.89
<b>Change*</b>	<b>2.16±1.12<sup>†</sup></b>	<b>2.16±1.03<sup>†</sup></b>	<b>1.85±0.94<sup>†</sup></b>
<b>CGI-anxiety</b>			
Baseline	4.89±0.94	4.78±0.95	4.78±1.15
Week 6	2.63±0.75	2.69±0.73	2.88±1.01
<b>Change*</b>	<b>2.27±1.15<sup>†</sup></b>	<b>2.09±0.94<sup>†</sup></b>	<b>1.90±0.99<sup>†</sup></b>
<b>CGI-sleep</b>			
Baseline	3.73±1.42	3.56±1.48	3.78±1.39
Week 6	2.07±0.78	2.08±0.98	2.34±0.97
<b>Change*</b>	<b>1.67±1.19<sup>†</sup></b>	<b>1.48±1.08<sup>†</sup></b>	<b>1.44±1.12<sup>†</sup></b>

Values are presented as mean±standard deviation.

\*Change=Week 6–baseline.

<sup>†</sup>p<0.001 for paired t-test.

**Table 5.** Incidence of adverse events among three treatment groups

Adverse event	Group			p value
	Clonazepam	Alprazolam	Lorazepam	
Total	20 (26.7)	31 (48.4)	18 (43.9)	<0.05
Somnolence	7 (9.3)	23 (35.9)	6 (14.6)	<0.001
Ataxia	0	0	0	
Gastrointestinal symptoms	1 (1.3)	3 (4.8)	4 (9.8)	NS
Sexual dysfunction	0 (0)	1 (1.6)	2 (4.9)	NS
Dizziness	6 (6.7)	6 (9.4)	2 (4.9)	NS
Agitation	1 (1.3)	0 (0)	2 (4.9)	NS
Headache	1 (1.3)	3 (4.8)	3 (7.3)	NS
Memory problem	2 (2.7)	7 (10.9)	1 (2.4)	NS



# COVID-19 and Benzodiazepines



## Recommendations

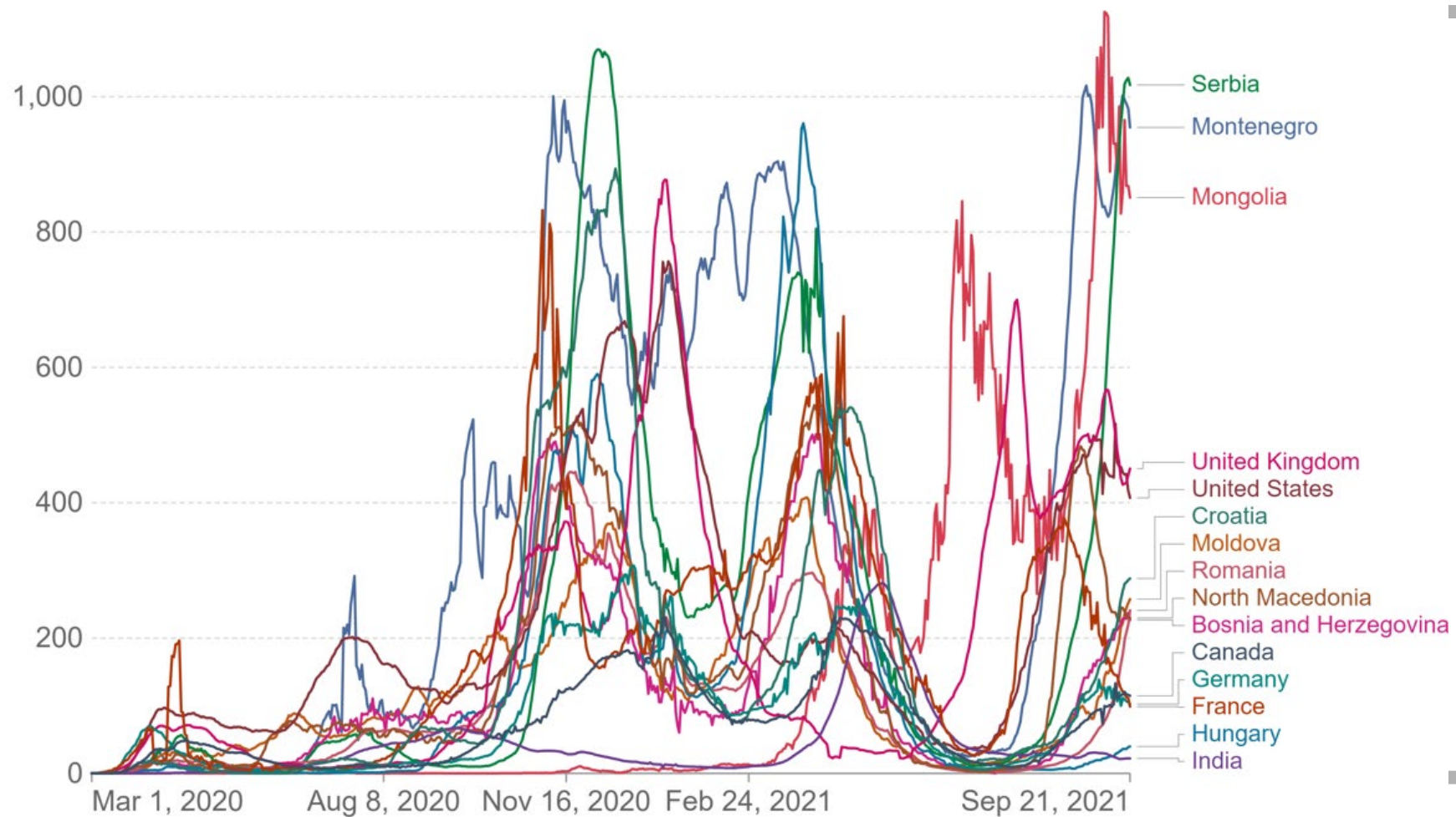
- Benzodiazepines can be used in patients with COVID-19 infection
- Where possible non-benzodiazepine drugs should be tried first
- If it is necessary to prescribe, the lowest dose should be used for the shortest possible time
- Monitoring of respiratory function after administration is recommended each hour until no concerns about physical health status and document on the NEWS chart.

# Sta nas ceka



## Daily new confirmed COVID-19 cases per million people

Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.



---

**Hvala na pažnji 😊**