

*NEW*

# **SCIENTIFIC BULLETIN**

of the  
**INSTITUTE of MENTAL HEALTH**



No. 01/2022



# SCIENTIFIC BULLETIN

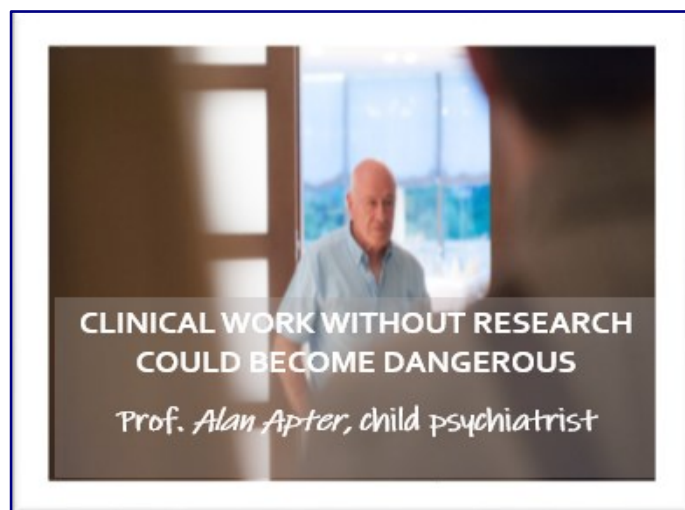
## of the INSTITUTE OF MENTAL HEALTH

Edition 01/2022

### PREFACE

The first issue of the Scientific Bulletin of the Institute of Mental Health (IMH) is being published at a time where IMH is nearing its seventh decade of existence. Since the very beginnings of IMH (1963) whose main task was improvement of mental health care, scientific work was held in high regards as one of the building blocks of an institution that is both medical and academic. The science department at IMH was founded shortly after the Institute's inception (1964) and was led by Professor Predrag Kaličanin.

In his monography "Research in psychiatry" which was first published in 1976, Professor Kaličanin stated in the introduction: *"Thus far, in the education of psychiatrists and their associates, not enough attention has been brought upon enabling scientific work, which should and must become an integral part of everyday professional activities. Literature is lacking in our language... when such a situation occurs, researchers in the field of psychiatry must cross a long and hard path to learn the basic principles and methods of scientific work"*.



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Without a doubt, the past 45 years have changed many things. **Each year, dozens of new studies are initiated at the Institute. Researchers at IMH take part in many national and international projects, frequently receive rewards and take part in educations with the help of the Institute.**

If one were to take only a glimpse at the webpage listing scientific articles published by researchers from the Institute over the past few years, it would be easy to notice that this page is too small to list everything that the Institute can and should share with the national and international public. **For this reason, among others, we were motivated to begin publishing this Bulletin.**

This Bulletin is being published during a digital era, where communication moves faster than ever. Hence, the Bulletin will be published electronically, and the scientific information will be brief and illustrated. Besides news from the Institute, we will report on both experienced and young researchers from Serbia, write about one or two important international studies, and share news from international events that might be useful to our scientific and professional community.

We believe that this way of reporting scientific news can inspire new research, as well as help maintain and improve mental health care, which is our most important goal.

On behalf of the editorial board,  
Prof. Dr Nađa P. Marić, scientific advisor

# OUR RESEARCH

## On mental health among refugee youth

### PREVALENCE OF ALCOHOL AND SUBSTANCE ABUSE AMONG YOUNG REFUGEES RESIDING IN THE REPUBLIC OF SERBIA AND EXPERIENCED PSYCHOLOGICAL DIFFICULTIES

In the November 2021 issue of the “Frontiers in Psychiatry” journal, the research team from IMH presented their research entitled “[Mental health, alcohol and substance use of refugee youth](#)”. Professor Milica Pejovic Milovancevic - the last/senior author of the paper led the research team made up of two trainees in child psychiatry from the IMH – MD Jelena Vasic (first author) and MD Roberto Grujicic, as well as professor Oliver Toskovic from the Faculty of Philosophy, University of Belgrade.

Millions of children from all over the world are currently displaced from their countries of origin due to war, persecution and poverty. **Childhood and adolescence are challenging life periods, especially in the context of exile or migration, which makes these young individuals susceptible to various psychiatric disorders.** This study aimed to explore the prevalence of alcohol and substance use among young refugees residing at two refugee centers in the Republic of Serbia (Krnjaca and Bogovadja), along with the indicators of experienced psychological difficulties. Data collection began in October 2020, and despite numerous difficulties facing the researchers – such as beginning of the C-19 pandemic, cultural and linguistic diversity and high respondents’ illiteracy rate, it was successfully completed in February 2021. The sample consisted of 184 children and adolescents aged 11–18 years (14 years on average), whereby the majority were male, Muslims, living in rural areas - mostly from Afghanistan, prior to migration.

**Table 1. The comparative perspective of Vasic et al. (2021) and ESPAD research results on the prevalence (%) of psychoactive substance use**

	Vasic et al. (2021)	ESPAD 2019*
Tobacco	28	41
Alcohol	13	79
Cannabis	4.6	16
LSD i hallucinogens	2.7	2.1
Amphetamines	2.3	1.7
Cocain	1.7	1.9
Inhalants	1.7	7.2
Tranquilizers	1.7	6.6

\*ESPAD Group (2019), ESPAD report 2019 Results from the European School Survey Project on Alcohol and Other Drugs



The authors reported that **more than a half of the participants displayed clinically significant symptoms of PTSD** - more frequently females, those who resided in a greater number of refugee camps and those who were exposed to abuse and domestic violence. Half of the respondents consumed energy drinks, slightly less than a third of them used tobacco, 13% consumed alcohol, whereby the frequency of other substance use was significantly lower – Table 1.

The significant indicators of individual propensity to use alcohol and substances were shown to be older age (14-18 years), male gender, lower education, unaccompanied migration and exposure to emotional abuse. The authors concluded that the burden of migration increases proneness to substance use in children and youth, especially in those who traveled alone. The proximity of parents, relatives and familiar adults is a strong risk or protective factor for children’s and adolescents’ mental health. The authors’ recommendation is that a coordinated network of professionals should be established to make as early as possible initial contact with young migrants and refugees in order to detect the substance use (or only suspicion) and their timely referral to an appropriate health institution.

Roberto Grujicic, MD, presented part of the results from the aforementioned research at the 28th International Symposium on Controversies in Psychiatry (2021, Barcelona) and **was awarded for the best poster presentation** entitled - "Does abuse and neglect lead to PTSD and alcohol and substance use in refugee youth".

## GUEST OF THE BULLETIN

**Prof. Ljiljana Mihić, PhD**

**Faculty of Philosophy,  
University of Novi Sad**



**Professor Ljiljana Mihić is a full professor at the Department of Psychology, Faculty of Philosophy, University of Novi Sad. Her field of expertise is the subject of vulnerability for development of mental disorders.**

**As a guest of the Bulletin, she will share her thoughts on ruminative thinking, as well as the scale for its assessment that was adapted for our population. She will also reflect on the possibilities of implementing novel findings about ruminations in everyday clinical practice.**

**Which definition of ruminative thinking do you consider the most appropriate?**

People with depression ruminate as a reaction to their own mood state, which is characterized by passive and repetitive orientation of thinking towards depression. By doing so, an attempt is made to discover potential causes and consequences of the depressed state. This style of reacting to depressive symptoms leads to a vicious circle of negative thoughts that further worsen the already depressed mood state. These ruminations are known in literature as depressive ruminations, and they can be evaluated through the Response Style Questionnaire. Depressive ruminations occur more often in depressive episodes of longer duration or shortly after the occurrence of a new episode.

**Can ruminations be seen as a transdiagnostic construct?**

There has been criticism concerning the concept of depressive ruminations. Some of the criticisms have been pointed towards the connection between ruminations and depression, and the tendency for this connection to be accentuated by using questionnaires that use both sadness and depressive mood as a common denominator. Perhaps what should be criticized more is that research mostly focuses on depression itself, and not the process of ruminations. On the other hand, scientific and clinical work has proven that excessive mental activity similar to ruminations can be present in many other disorders – excessive worry in generalized anxiety disorder, excessive self-analysis of behavior after social interactions in social anxiety disorder, intrusive memory in PTSD, etc. Therefore, these findings lead us to an assumption that excessive mental activity in a variety of mental disorders may be a single mental process manifested in different ways.

In other words, authors are beginning to define ruminations as a repetitive, intrusive thinking style which is manifested even when the person does not have other symptoms. This thinking style is unproductive and removes cognitive resources that could be used for more efficient problem solving.

**You tested Ruminative Thought Questionnaire (RTQ) on our population. When can we expect this scale to be available for use?**

The purpose of our work was to validate the Serbian version of RTQ which measures ruminations defined as intrusive, repetitive pattern thoughts, whose content valences can be different (positive, negative, even neutral) and for which the temporal direction varies (content is both centered around the past and future). Literature contains two more similar questionnaires, but RTQ has an advantage of encompassing a wider array of potential repetitive thought patterns, and every item was deliberately chosen to measure problematic thought patterns. Our results, which we obtained in three different, non-clinical samples, show that the Serbian version of the instrument measures a non-functional mental process which is manifested through repetitiveness, intrusiveness and non-productive problem solving, such as imagining better alternative outcomes compared to those that really occurred. The total score is useful in anticipating future symptoms six month after the testing – particularly depression, social anxiety, and excessive worry in the student population.

**Besides scientific work, is RTQ also useful in everyday clinical practice?**

Repetitive cognitive styles can be found in varying degrees in most people. We still do not have an answer to the question of when these thought patterns become dysfunctional. One of the suggestions was to categorize repetitive thoughts as dysfunctional when they mostly consist of abstract mental representations.

For everyday clinical work, many therapeutic interventions have been developed with the goal of reducing dysfunctional thought patterns (i.e., Mindfulness Based CBT, Rumination Focused CBT, Acceptance Based Therapy). RTQ can be a useful instrument for tracking treatment progress. Finally, it can be useful in identifying persons at risk of development of certain mental disorders.



# THE PROMISING PROJECT

## What is the PsyCise project novelty?

**Associate professor Marin Jukić, PhD, Faculty of Pharmacy, University of Belgrade Farmaceutski fakultet**

The PsyCise project - "Utility of plasma drug level monitoring and CYP2C19/CYP2D6 genotyping in dose personalization of antidepressants and antipsychotics" with the overall budget of approximately 200.000 EUR was launched two years ago. The Institute of Mental Health has participated in this project from the very beginning ([more information on this project](#)).

**The associate professor Marin Jukic, PhD, project leader, has received numerous awards for his scientific work, including three consecutive awards for the best scientific paper published at the University of Belgrade and three International Medis Awards for the best work in the field of pharmacy in the region. For the first issue of the Bulletin, we asked him a few questions.**

### What is the main research question of the PsyCise project?

The overall goal is to establish an algorithm for precise dosing of the antidepressants escitalopram and sertraline, as well as the antipsychotics risperidone and aripiprazole. This algorithm would include data related to patients' characteristics such as body weight, liver status, kidney status, and the genotype of genes encoding the CYP2C19 and CYP2D6 enzymes, that metabolize these drugs. The minimal goal is for the algorithm to accurately predict the dose in more than 68% of cases (mathematical confidence level one-sigma), and the more ambitious goal is to predict the exact dose in 95% of cases (mathematical confidence level two-sigma).

**How similar are the PsyCise participants to the patients whom we see in our everyday practice?**

The participants are precisely the patients from our real-life practice. The focus is on the patient who comes to the psychiatric clinic to seek help and who is prescribed some of the abovementioned medications for the first time. Actually, such situation where the psychiatrist is looking for an adequate dose, is at the same time a situation where dosing errors are the most common and where the abovementioned algorithm would be the most helpful.

### At the moment, what are the losses due to not taking into account the liver enzymes of our patients?

Psychiatric drugs are predominantly metabolized by the CYP2C19 and CYP2D6 enzymes and the patient's metabolic capacity to metabolize psychiatric drugs depends on their genotype. For example, there are patients who, due to a genetic defect, lack one or even both of these enzymes. In such patients, the drug accumulates, which increases the chance of adverse drug reactions. Conversely, a patient who is a rapid metabolizer may fail to achieve adequate plasma level of drug leading to insufficient effectiveness. It is difficult to estimate the magnitude of the loss, but the papers that I published in recent years show that about 45% of drug exposure depends on the CYP genotype, suggesting that almost half of those patients who received inadequate dose at the start of their treatment would have received the appropriate dose right away had the CYP genotype been known and taken into account.

### What has the PsyCise taught you so far?

The main thing this project has taught me is to always keep my eyes open. The project is simple and complex at the same time. It is based on routine psychometric assessment, routine measurement of drug concentration, routine genotyping and routine biochemical analyzes. Each technique is well known and relatively easy to perform. However, there are certain standards that a clinical study has to meet and some mistakes that occasionally occur are not allowed, which makes it difficult to complete the given protocol in an adequate way. Also, the coordination and dedication of persons performing these techniques are very important. The problems occur on a weekly basis and it is essential to react properly - so the project can proceed adequately.



## JOURNAL CLUB NEWS



### Critical review of literature

*Journal Club* has been active at the Institute for Mental Health for years now. Young residents choose individual papers at their own discretion to present the methodology and results, with a critical review of the qualities and shortcomings of the published research. In January 2020, *Journal Club* was renamed **Critical Review of Literature (CRL)** with some changes in the format. In October of this year, the fifth CRL meeting was held and Jovana Maslak, a resident, presented a paper entitled - [Reduction in Mental Health Treatment-Utilization Among Transgender Individuals After Gender-Affirming Surgeries: A Total Population Study](#) by Branstrom and Pachankis.

The basic conclusion is that this is a solid paper that has value, but the liberal interpretation of the evidence has spoiled the overall impression. To exemplify, despite the lack of a control group, the authors interpret the gradual, very slight reduction in mental health problems as proof of usefulness of the intervention and conclude that their results "lend support to the decision to provide gender-affirming surgeries to transgender individuals who seek them". Given that a randomized controlled trial is the gold standard for confirming the effectiveness of any intervention and that observational studies provide weaker evidence, the CRL participants agreed to conclude that the recommendation was made lightly (with the caveat that the right to the intervention is not only a medical, but also a philosophical and ethical question of human rights).

Another criticism was the failure of the authors to either notice or comment on a significant increase in mental illness in the period around surgery, relative to the average, which potentially affected the results and the subsequent observed decline in complaints - potentially due to regression to the mean rather than a confirmed positive effect of the surgery.

All in all, the progress of the Institute's youth is obvious in pinpointing high quality and low quality methodologies, as well as in assessing the value of research, as a result of continuous work in this segment of education. Given that the information is now available extensively to all, including the general population, and given the plethora of conflicting information that often come not only from the obscure websites, but also from positions of authority, it is important that as psychiatrists and doctors we know not only to receive information, but also to be able to interpret and comprehend it critically, because only in that way can we be better doctors for our patients.

The next KSL meeting will be held on January 26, 2022 in the Red Hall of the Institute, and the topic will be the paper - [mHealth-Assisted Detection of Precursors to Relapse in Schizophrenia](#), Buck et al. The door will be open to all interested persons from the Institute and beyond.

## INTERNATIONAL NEWS

### Persistent symptoms following SARS-CoV-2 infection amongst children and young people: a meta-analysis of controlled and uncontrolled studies

Pandemic caused by the SARS-CoV-2 virus has been a significant research topic over the past two years. More and more studies are attempting to clarify the long-term consequences caused by this widespread infection.

Illness course in children and young people is most commonly asymptomatic or manifests itself with mild symptoms. Even though most children and young people fully recover from SARS-CoV-2 infection, a part of this population exhibits long-term, persistent symptoms. Persistent post-COVID symptoms can be manifested through a wide array of symptoms. This syndrome has been described as a complex multisystemic illness, typically manifested by persistent heterogenous and recurrent symptoms of varying intensity.



These symptoms most commonly occur in the convalescent phase of the illness, usually four weeks after the SARS-CoV-2 infection. So far, the data published about the effects of SARS-CoV-2 infections in children and young people have been conflicting, and the literature mostly contains uncontrolled studies with small samples that were conducted on a single site.

A [recent meta-analysis](#) published in the Journal of Infection by Behnood et al. attempted to provide an answer to this question by including studies published in the period of December 2019-August 2021. They included all studies that evaluated children and young people younger than 20 with a confirmed or probable SARS-CoV-2 infection and with any symptoms that were reported after the acute phase of the illness.

The meta-analysis included 22 studies, with a total of 23141 children and young people. The primary analysis (random effects meta-analysis evaluating the differences in prevalence of individual symptoms) was done only for the five studies that had a control group. The average time of symptom evaluation was 125 days after the infection. The biggest differences between post-COVID cases and controls were in the following symptoms: cognitive difficulties (3%), headaches (5%), loss of smell (8%), throat ache (2%), eyes swelling (2%). There were no significant differences in the symptoms of abdominal pain, cough, tiredness, myalgia, insomnia, diarrhoea, fever, dizziness, or dyspnoea. **Higher quality of study correlated with a lower prevalence of all symptoms**, other than loss of smell and cognitive difficulties.

The authors conclude that even though the symptom prevalence in the studies was high, when taking into account only the studies with a control group, **almost all persistent symptoms occurred with a similar prevalence in both the post-COVID and the control group. High prevalence of many somatic symptoms in healthy teenagers, such as headache or tiredness implies that more studies should have a control group.** This meta-analysis once again confirms the necessity of using adequate study methodology in order to receive precise data and avoid making judgment based on methodologically lacking studies.

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