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COST IMPACT OF INTRODUCING ALPHA-STIM MEDICAL TECHNOLOGY AS A SECOND LINE TREATMENT FOR ANXIETY AND DEPRESSION IN SLOVENIA

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"Father, give us courage to change what must be altered, serenity to accept what cannot be helped and the insight to know the one from the other." – The Serenity Prayer, R. Niebuhr

Abstract

Mental disorders affect a substantial proportion of our society and the importance of mental health became an even hotter topic after the Covid-19 pandemic resulted in social isolation. For most national health care systems, being understaffed and underfinanced are key defining characteristics. Pharmaceuticals tend to be overprescribed and in depth face-to-face cognitive-behavioural therapy remains reserved mostly for those able to afford it. Alpha-Stim® medical technology is an innovative approach recognized by the American and British national health services alike. Thus, a cost analysis was performed to assess if a nationwide implementation as a second-line modality is economically sound also in Slovenia.

Keywords

Alpha-Stim, cranial electrotherapy stimulation (CES), cognitive-behavioural therapy (CBT), cost analysis, economic analysis, mental disorders, major depression (MD), generalized anxiety disorder (GAD), psychiatry, psychiatric care, second-line, decision tree, Slovenia

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PRIMER ON PSYCHIATRIC EPIDEMIOLOGY

In the European Union (EU), mental disorders affect 38% of the population (Wittchen et al. 2011a). Depression is the largest cause of disability worldwide and its burden has been increasing (Vos et al. 2016; WHO 2017; UN 2017). Generalized anxiety disorder is also highly impairing (R. Lieb, Becker, and Altamura 2005).

At any given moment, depression affects 7% to 12% of the adult population, whereas lifetime prevalence is estimated to be between 11% and 18% (Bromet et al. 2011; Lim et al. 2018; Wittchen et al. 2011a).

The existing estimates of point prevalence of anxiety disorders vary between 14% and 41% of adult population (Guo et al. 2016; Munir, Zafar Gondal, and Takov 2017; Remes et al. 2016; Wittchen et al. 2011a). Among those above 82 years of age, the estimates are somewhat lower, going from 7% to 17% (Leray et al. 2011; Rezapour et al. 2020; Welzel et al. 2019). While its one-year prevalence is 9% (Watterson et al. 2017), the lifetime prevalence of anxiety disorders is between 5% and 9% (Kessler et al. 2011; Ruscio et al. 2017; Watterson et al. 2017).

For comparison, during the Covid-19 outbreak, the prevalence of general anxiety disorders, depressive symptoms and insomnia in the Chinese adult population were 35%, 20%, and 18%, respectively (Gao et al. 2020; Huang and Zhao 2020). In addition, 54% of Chinese respondents rated the psychological impact of the Covid-19 outbreak as moderate or severe; 29% reported moderate to severe anxiety symptoms; and 17% reported moderate to severe depressive symptoms (Wang et al. 2020). The Americans were most concerned about facing increased anxiety (41%), more than about insolvency or reduced job security (UOPX 2020).

Even in high-income countries, nearly 50% of people who suffer from mental disorders do not get treated (WHO 2012). For example, despite Singapore ranking as 9th on the 2019

Human Development Index (HDI), 62% of Singaporeans with anxiety disorders had not sought help after one year (Chang et al. 2019). Globally, the vast majority of patients is seen only in primary care and most treatments are often inadequate in relation to minimal standards published in treatment guidelines (Wittchen et al. 2011b). In general, the obstacles to mental health include lack of appropriate responses from health systems, such as lack of psychologists/psychiatrists or barriers in access to mental health care as well as lack of awareness and social stigma.

This study considers a new medical technology for the treatment of mental disorders, Alpha Stim, which has the potential of addressing some of those obstacles. I focus on Slovenia, a country with significant shortage of clinical psychologists/psychiatrist, high regional differences in accessibility and increasing demand for psychiatric services.

1ST LINE TREATMENT FOR MENTAL DISORDERS: PSYCHOTROPIC DRUGS

Antidepressants (SSRIs)

The average clinical response rate to antidepressants is around 50% (i.e. 50% reduction in symptomatology) (IQWiG 2017). While the efficacy measured during clinical trials is one of the most influential measures in treatment assessment, its external validity may be jeopardized by non-adherence to medication in real life (Pedersini and Kuehl 2014). The most comprehensive review of clinical trials found that all SSRIs were more effective than placebo, with relatively low odds ratios, between 2.1 and 1.4. Most of them were also associated with more dropouts than placebo. Only 18% of the trials included in this review were rated as low risk of bias (Cipriani et al. 2018). The English National Health Service (NHS) responded to this study, explaining that SSRIs are not highly effective; only more effective when compared to placebo (NHS 2018). An older paper with 3,500 citations reports only 37% response rate for monotherapy, no better than placebo (Rush et al. 2006; Santarsieri and Schwartz 2015).

Even though SSRIs might have statistically significant effects on depressive symptoms, trials often have high risk of bias and the clinical significance (outside the context of the trial) seems questionable (Procopio 2005). In addition, many trials and meta-analyses of SSRIs are authored by or linked to the industry and almost never report any caveats about SSRIs in their abstracts. Ebrahim et al. (2016) found that 29% of meta-analyses' authors were employees of the drug manufacturer and 79% had at least some industry link. The meta-analyses including an employee of the manufacturer were 22 times less likely to have any criticism on the drug. Often there is misclassification, misrepresentation and under-reporting of serious harm, which means that we cannot be confident about the risk-benefit ratio of the drugs (Moncrieff 2016).

In Denmark, the most frequent calls to the national medical advice hotline were inquiries relating to SSRIs withdrawal phenomena (Geffen et al. 2007). The current UK and USA Guidelines underestimate the severity and the duration of SSRIs withdrawal with significant clinical implications, as 56% of people experience withdrawal effects upon attempting to quit SSRIs, with 46% of people describing them as severe and often lasting for several weeks or months (Davies and Read 2019). The Royal College of Psychiatrists has since changed its guidelines accordingly (Council For Evidence-Based Psychiatry 2018; 2019).

The withdrawal effects include sexual problems (72%), weight gain (65%) and adverse emotional effects, such as feeling emotionally numb (65%) and addicted (43%) (Cartwright et al. 2016). Other side effects include stroke, falls and fractures, epileptic seizures in the elderly, diabetes, deep vein thrombosis, gastrointestinal and intracranial bleeding (Kirsch 2019). "Brain zaps" are another underappreciated symptom (Papp and Onton 2018). Lastly in children and adolescents, there appears to be an increased risk of suicidality and aggression (Sharma et al. 2016; Spielmans, Spence-Sing, and Parry 2020).

In summary, SSRIs significantly increase the risk of both serious and non-serious adverse events (Jakobsen et al. 2017). Their benefits seem to be minimal, possibly without any

importance to the average patient with a major depressive disorder, and thus should not be used for adults with major depressive disorders before valid evidence has shown that the potential beneficial effects outweigh the harmful effects (Jakobsen, Gluud, and Kirsch 2019). The National Alliance of Mental Illness, the main funder of which is Pharma, lobbied for legalization of certain medicines (Harris 2009)and also disputed the 'black box' warnings on SSRIs causing suicide (CCHR International 2009; Harris 2009). Even the WHO had to officially retract its controversial guidelines on the use of opioid analgesics after accepting that the industry had an influence (Dyer 2020). A global team of influential researchers, clinicians and regulators are calling for trustworthy evidence and breaking ties with pharmaceutical companies not just on research but also on practice guidelines and education (Moynihan et al. 2019; Spilde, Bergstrøm, and Bazilchuk 2020).

Anxiolytics

While long term benzodiazepines (BZDs) use is not endorsed in the treatment guidelines for anxiety disorder, it is prevalent in real-world clinical settings. There is no evidence of a significant difference in response compared to placebo (Shinfuku et al. 2019). One study reports that 83% of patients were still anxious after the third month of treatment with BZDs (Barthelmé and Poirot 2008). Without strong evidence of efficacy and with significant evidence of risks, a variety of evidence-based treatments should be considered prior to initiating BZDs (Fluyau, Revadigar, and Manobianco 2018; Guina and Merrill 2018; Lader 2008). There is significant concern regarding overprescribing of BZDs and the resulting harms (Brett and Murnion 2015; Weaver 2015). Despite all this, pharmacotherapy abuse may occur because we are treating mental health problems almost exclusively with drugs, with 90% of patients staying in primary care. (Ávila 2015). With the current pandemic, anti-anxiety medication prescriptions are up 34% and SSRIs prescriptions are up 19% in the US (Express Scripts 2020).

2nd LINE TREATMENT FOR MENTAL DISORDERS: iCBT

Individual cognitive-behavioural therapy (iCBT) for the treatment of mental disorders can include 1 to 20 session of 30 to 120 min (Li et al. 2014; Laird et al. 2017). The standard is 8 to 10 60-minute sessions (Morriss et al. 2019; Psychiatric Association of Slovenia 2017).

Although the evidence-base of CBT is enormous, almost 80% of meta-analyses statistically significantly favour psychotherapy, and only 7% to 22% provided convincing evidence without biases. Furthermore, studies demonstrate small to moderate effects when compared to more conservative control groups, such as care-as-usual and pill placebo (Cuijpers et al. 2018; Dragioti et al. 2017; Hofmann et al. 2012). Furthermore, therapy experiences are associated with significant increases in undesirable traits and markers (e.g. chronic stress, depression, neuroticism) and significant decreases in desirable traits (e.g. self-esteem, conscientiousness) (Chow et al. 2017). In addition, conflicts of interest were confirmed in a systemic review (K. Lieb et al. 2016). Since it is still unknown whether therapies work through common or specific factors, it can be regarded as highly unstandardized (Cuijpers, Reijnders, and Huibers 2019). While it may be effective, the evidence is, due to bias, not conclusive (Cuijpers, Reijnders, and Huibers 2019; Okumura and Ichikura 2014; Yang et al. 2017). Despite the criticism, it is also argued that CBT is based on rigorous empirical basis (David, Cristea, and Hofmann 2018) and is considered valid (Chand, Kuckel, and Huecker 2020; Lopez and Basco 2014; Titov et al. 2018; Tay, Subramaniam, and Oei 2019).

On the other hand, with CBT 55% of patients with social anxiety disorder responded, and 15% achieved remission (Hunger et al. 2019). Upon that, the meta-analysis showed that response occurs in approximately 50% of all clients that are administered iCBT, whereas about a third reach remission, and a quarter fail to respond (Andersson, Carlbring, and Rozental 2019; Rozental, Andersson, and Carlbring 2019). When used as a second-line treatment, the success rate in the UK was found to be at 52% (Gyani et al. 2013). Finally, the

European Association of Psychotherapy references an average success rate of 65% to 72% (Carr 2012). Even though online therapy room approach has an odds ratio of only 1.1, the odds ratio for face-to-face intervention is between 2.5 and 3.0 (Carpenter et al. 2018; Ewbank et al. 2020; Santoft et al. 2019). Hence, the effectiveness should not be lower than that of pharmacological approach. To conclude, iCBT proved effective across 4 main disorders: major depression, generalized anxiety disorder, social anxiety disorder and panic disorder (Andrews et al. 2018).

ALPHA-STIM® DEVICE FOR ANXIETY, INSOMNIA, DEPRESSION AND PAIN

Alpha-Stim is a cranial electrotherapy stimulator (CES), produced by Electromedical Products International, Inc (EPI). The NHS is the most recent organism to recognize Alpha-Stim, after a clinical effectiveness and economics study conducted by the National Institute for Health Research (NIHR), published in the Journal of Affective Disorders, provided favourable results (add reference). Subsequently, an innovation briefing was developed by The National Institute for Health and Care Excellence (NICE), specifying that the current care pathway would be changed to start providing the device through primary care and mental health services for patients to use at home (NICE 2019). The brief includes comments from specialists and patient organizations, noting the potential for Alpha Stim to be used by those who do not want to undergo pharmacological or psychological treatments, to reduce the need for psychological treatment and to reduce the cost of care. NICE MedTech guidance is currently under development and includes 42 registered stakeholders, from patient organizations to professional groups and the manufacturer.

The U.S. Food and Drug Administration (FDA) reclassified Alpha Stim from the risk III class into a less risky II class just 6 months ago (Federal Register 2019). Based on a review of the scientific literature, the FDA concluded that there is reasonable assurance of safety and

effectiveness of CES devices. This decision was accompanied by 303 testimonials, mostly coming from board certified medical doctors, therapists and researchers, and can be accessed on the Federal Register's webpage. In the US, the medical device is extensively used by the US Army, with every single deployed unit being equipped with one (Chicago Psychology Podcast 2020). A colonel and chief psychologist of the US Army Reserve testified to the FDA: "In my experience, without exception, there is no more powerful form of therapeutic intervention, either as an adjunct or a stand-alone treatment, than Alpha-Stim" (FDA 2012).

While in the US the device is obtainable solely if prescribed, in Europe Alpha-Stim is IIa classified, which means that it can be sold freely in any store. It goes without saying that also in Europe, the Directive (93/42/EEC) and accompanying Guidelines demand sufficient clinical evidence to confirm compliance with safety and performance requirements. In Slovenia, Alpha-Stim has been used by individual psychiatrists since early 2018, and it has been distributed in selected European countries for even longer.

Even though interactions between electrical and chemical synapses are likely to have important pathological implications, we are still far from understanding the full scope of their prevalence (Nagy, Pereda, and Rash 2018; Pereda 2014). Currently a registered PTSD trial is underway (ClinicalTrials.gov 2019). The results from a recent systematic review supported the notion that CES is safe, and provided suggestive evidence of a beneficial association in patients with anxiety disorders and major depression (Shekelle et al. 2018). Alpha-Stim safety and efficacy is supported by over 100 research studies, most done by independent researchers who have attained institutional review board (IRB) approval without funding by EPI (Marksberry 2018), of which NICE referenced 4. The NHS study was partially funded by the manufacturer, but any other role or conflict of interest were negated (Morriss et al. 2019).

Finally, it is important to differentiate between CES devices with different settings/treatment parameters and to note that Alpha-Stim has a patented waveform (Mischoulon et al. 2015) (Patent no.: US 8,612,008 B2).

For anxiety and depression symptoms, the efficacy of Alpha-Stim ranged from 48% for NHS patients that had not reached remission with a therapist or full guided self-help to 82% in a randomized, 5-week double blind, placebo controlled study (Barclay and Barclay 2014; Morriss et al. 2019). The NHS study found that 63% of patients achieved reliable improvements at 12 weeks, with most of the effect experienced in the first 6 weeks. CES was found to be effective against anxiety and depression symptoms, with rates of remission being only 13% lower than that of iCBT but with a 42% lower cost (Morriss et al. 2019). Furthermore, a pending publication of a retrospective study by Morris & Price for subjects with generalized anxiety disorders and comorbid depression showed that on the Patient Health Questionnaire (PHQ-9) basis, 72% of depressed patients achieved remission by week 12 and 80% by week 24. Finally, only 2.5% experienced side effects. The device's user manual explains that no significant lasting side effects have been reported. An occasional headache, discomfort or skin irritation under the electrodes or light-headedness may occur (EPI 2020a).

CURRENT STATE OF PSYCHIATRIC CARE IN SLOVENIA

Epidemiological review

Psychotherapeutic services are urgently needed by 5% of Slovenian adult population and less urgently by 20%. This means that 100,000 Slovenians are in urgent need of care. Since a psychotherapist can, on a conservative basis, see 15 to 30 patients per month, 5,000 psychotherapists would be needed, although on the basis of the European Association for Psychotherapy's more conservative estimate the number drops to "only" 2,000 (Možina 2010). This estimation can only be a best-case scenario if no other treatments were utilized.

For comparison, Switzerland, being the European country with by far the most psychiatrists, has 51.72 per 100,000 inhabitants (Eurostat 2020). If Slovenia had the same, 1,076 would be providing psychotherapy.

In the 2014 European Health Interview Survey (EHIS 2, second wave), 5.5% of Slovenian interviewees (15+ years) rated themselves as depressed. This low "prevalence" is probably due to self-reporting; it is inconsistent with the fact that Slovenia is consistently among the 3 countries in the EU with the highest rates of death by intentional self-harm (Eurostat 2016). The prevalence of depression is estimated at 12%, and it is believed that only up to 50% of people are getting treated.

In 2018, 83,158 new cases of mental and behavioural disorders were identified at the primary care level, corresponding to 4% of the population (NIJZ 2019d). At the secondary outpatient level, 61,355 first psychiatric visits were made and further visits amounted to 251,183. Thus, for each first visit there were additional 4.1 follow-up visits on average (NIJZ 2019e). This ratio is topped only by the outpatient oncology.

In 2018, SSRIs were prescribed to 7% of Slovenians, with an average prescription duration of 79 days. According to the Anatomical Therapeutic Chemical Classification System (ATC), 586 thousand prescriptions were made (code N06A) or 283 per 100,000, which amounts to 11.1 million € and an average prescription value of 18.9 € (NIJZ 2019a). Applying the cost of a defined daily dose (DDD) to a minimum treatment duration of 6 months, the cost of SSRIs amounts to a minimum of 43 € per one full treatment. Anxiolytics, of which most are BZDs, were prescribed to 6.9% of Slovenians - 409 thousand times (code N05B) or 198 times per 100,000, which in total amounts to 2.8 million euros or an average prescription value of 6.7 € (NIJZ 2019a). The average prescription duration is 24 days, as BZDs can cause dependence after 3 to 4 weeks (Brett and Murnion 2015).

Long waiting times

Waiting for treatment has become a defining characteristic of Slovenian health care. Based on the EHIS (wave 2), the prevalence rate of unmet health care needs that was due to long waiting lists was estimated at 19.6% of the population, being the highest of all causes (NIJZ 2019f). The maximum permissible waiting times are set at 14 days for "very quick," at 3 months for "quick" and at 6 months for "regular" referrals (Rules on the Referral of Patients, the Management of Waiting Lists and the Maximum Permissible Waiting Times 2018). These limitations are lifted for (routine) check-ups at later appointments, for which no data is provided. In psychiatric care, the queues have been unacceptably long over the years (Polanec Klemen 2019). The National Institute of Public Health (NIJZ) publishes queue reports monthly, and the last available is of March. The average waiting times for the first psychiatric appointment were as follows: 92.5 days with "regular," 57.6 days with "quick" and 36.6 days with "very quick" referral, with the total number of patients on the waiting list amounting to 2,131. In addition, 264 patients (12.39%) had been waiting above the permissible limits.

In the first section of article 2.2 of the Resolution on the National Mental Health Program 2018-2028 (RNMHP), it is written: "The waiting times, especially for psychotherapy, are long. The field of psychotherapy is not regulated in Slovenia; the Health Insurance Institute of Slovenia (ZZZS) recognizes the cost of this service only to clinical psychologists and psychiatrists. There are too few clinical psychologists, as only one in three psychologists is a specialist in clinical psychology. The specialization of clinical psychology depends on the interest of practitioners and does not rest on the actual needs of the population." Patients can wait on recurring examinations and therapies for up to a year, and considering the current outlook, psychotherapy is by all means reserved only for those able to afford it (24UR 2017). Based on the European Quality of Life Survey (EQLS 2016) responses about the difficulty in affording psychological or psychiatric services, the only 2 countries that ranked worse than

Slovenia on EU-28 level were Greece and Cyprus (Ludwinek, Sandor, and Clevers 2019). The report mentions that due to this reason, the young people (18-24 years) in these countries would not even consider turning to support services for mental health issues. This is very alarming, as almost 40% experience their first episode of depression before the age of 20 (Malhi and Mann 2018). This means that besides pharmacotherapy, patients are presented with 2 choices: to suffer in long waiting lines in the public sector or to pay out of their pocket and seek treatment from private providers, some of dubious professional backgrounds, using pseudoscientific methods, causing even more psychological pain (Polanec Klemen 2019).

Severe shortage of staff

The number of patients is increasing and there are too few psychiatrists, about 50% of the European average (ZZZS 2019), which implies that 315 more are needed. If instead of the EU average, Swiss level would be targeted, 760 would be needed. While in 2017 Switzerland had 52 psychiatrists per 100,000 inhabitants and Germany 27, Slovenia had only 14 (Eurostat 2020). Note that this number includes all training statuses and all industries. When counting only fully certified adult specialists, Slovenia is left with only 207 out of the 277 professionals (NIJZ 2019b). As shown in Tables 6 - 8, the number of professionals has been increasing but way too slowly to have any noticeable impact. Counting all the psychiatrists, to achieve the German level Slovenia would need an additional 254 psychiatrists. In addition to the staff shortage, burnout is an issue, as working conditions are getting unbearable. As new specialists appear nowhere to be found, the psychiatric hospital Vojnik is conducting interviews with specialists from abroad. Future outlooks are unfavourable and the announced vacancies for specialists in training are not going to meet the increasing needs (RTV Slovenija 2019).

As already mentioned, ZZZS recognizes psychotherapy services only to psychiatrists and clinical psychologists and not to unspecialized psychologists, who are not allowed to diagnose. In general, they (only) provide psychological evaluations in terms of occupational

medicine. Psychologists with or without clinical specialization are not allowed to prescribe medications. Because clinical psychologists are not recognized as medical doctors, the government does not provide funding for their specialization and institutions must finance it themselves, which costs around of 150,000 € (Vignjevič Pupovac 2019). Based on the 2018 report on resources, Slovenia had 4.7 clinical psychologists per 100,000 inhabitants, 97 in total. When counting only fully certified adult specialists employed in the health service, 73 are left (NIJZ 2019b). To put things in perspective; the UK has 17, while Norway has 62 clinical psychologists per 100,000 inhabitants (Polanec Klemen 2019). Slovenia is thus at the European bottom (Čoderl Dobnik 2020). Finally, the number of forensic psychologists (expert witnesses) is so low that the Human Rights Ombudsman of the Republic of Slovenia is warning about a possible human rights violation (STA 2019c).

Substantial regional differences in service accessibility

Regional differences in service accessibility are quite high in Slovenia; they are shown in Tables 4 - 5 and Figures 3 - 4. Regions with higher risk tend to have smaller numbers of psychiatry specialists, generally above-average disease identification at the primary care level and below-average identification at the secondary care level. Regional variations (measured by the percentage point difference between the best and the worst regions) are the lowest in outpatient antidepressant prescription, followed by anxiolytics prescription, because these prescriptions can also be made by general practitioners. On the contrary, the variations are the highest in the numbers of clinical psychologists. One may conclude that while accessibility to pharmacological treatment is relatively equal across regions, the opposite is true for professional psychological or psychotherapeutic care. This could lead to tremendous inequalities if the pharmacological treatment fails.

Absenteeism, sick leave and statutory social security

For full-time employees in Slovenia, mental and behavioural disorders accounted for 995,596 lost workdays in 2018. Mental and behavioural disorders are the 3rd biggest cause of sick leave and represent the 4th longest sick leave duration, on average 46.3 days. This compares to average duration of leave in case of pregnancy and delivery of 54 days, whereas a general average is of 16.4 days (NIJZ 2019c).

When it comes to hospitals beds, psychiatric care comes 3rd (NIJZ 2019b). Furthermore, psychiatric illnesses are the second cause of all permanent disability cases (ZPIZ 2020).

The Resolution on the National Mental Health Program (RNMHP 2018-28) and outlook

The Resolution on the National Mental Health Program (2018-28) should enable equal accessibility to mental health facilities for all residents and address the increasing number of patients, stigma, lack of experts, long-term hospitalizations and absenteeism from work, numerous institutionalizations and the low number of persons with mental disorders included in the labour market (K. Juričič et al. 2018). This would be mainly achieved by financing teams for 50 new regional mental health centres (RMHCs), 7 subspecialist outpatient teams complementing 22 already existing interdisciplinary teams, amounting to a yearly cost of 97.8 million € at the end of RNMHP (18-28). In 2018, ZZZS spent 63.06 million € on mental health, corresponding to 2.25% of total healthcare budget or 3.03 € per capita (Zupanič Milena 2018). The comparison between the proposed and the accepted budget is given in Table 10. In Europe, the average spending on mental health amounts only to 1% of total health spending by governments, with 69% of it going to psychiatric hospitals (WHO 2019).

In spite of a what should end the “considerable chaos” (Janičijević 2018) and start the “revolution in Slovenian mental health care” (Zajec 2018), the realization of the clinical psychology program was, according to the ZZZS, low (91.48%). In its yearly business report

for 2019, published in March 2020, ZZZS also remarks that: “In practice, it turned out that on the labour market, the RMHCs were not able to acquire the majority of the projected labour force needs, so the funding was reduced for the missing staff. This brings us to the question if in the light of the human resources shortage, it is realistic to expect that the centres’ teams will be successfully assembled and if the currently agreed arrangement of this field is even appropriate” (fifth section of Article 1.4.1.1). Thus, the RMHCs have been opening in a reduced structure, and psychologists without the specialization will, under the supervision of a mentor, substitute clinical psychologists, which happened without the consent of the professional community, because psychologists are required to perform work for which they are not qualified (Polanec Klemen 2019; Vignjevič Pupovac 2019). Thus, the Chamber of Clinical Psychologists believes that the NHMBR will not deliver what it promised, and The National Youth Council of Slovenia states that although highly needed, the mental health remains at the bottom of the government’s priorities (NYCS 2019; Polanec Klemen 2019).

COST QUANTIFICATION OF ALPHA-STIM IMPLEMENTATION

In Europe, the total cost of mental health problems was estimated at more than 4% GDP, of which 32% represent direct healthcare costs, 19% direct costs to social security and 49% indirect labour market costs — i.e. sick days and disability, early retirement, undetected decreases in productivity (OECD/EU 2018). Thus, effective treatment may have substantial consequences outside immediate treatment settings (Knapp and Wong 2020; Sobocki et al. 2006; Wittchen et al. 2011a). From the employers perspective, 2 separate large-scale randomized workplace depression treatment trials found positive returns-on-investment (Kessler 2012). As for the treatments, iCBT has been found to be the most cost-effective intervention even without considering the side-effects of drugs (Heuzenroeder et al. 2004; Mavranezouli et al. 2015; Yan et al. 2019), and an Alpha-Stim intervention in the NHS setting was found to be even more cost-effective (Morriss et al. 2019).

Psychotropic non-adherence is a widely known phenomenon, with 50% of patients not taking antidepressants as prescribed (Sansone and Sansone 2012; Semahegn et al. 2020). In the US, non-optimized medication therapy was estimated to represent an annual cost of 528.4 billion $, equivalent to 16% of total 2016 US health care expenditures (Watanabe, McInnis, and Hirsch 2018). Thus, non-adherence is a significant challenge for patients with psychiatric disorders, physicians and healthcare systems and places a large resource burden on healthcare systems (Chapman and Horne 2013; Lloyd et al. 2019). Alpha-Stim has a non-resettable cumulative timer, allowing for usage control and better adherence.

Methodology

To determine the cost impact of introducing CES into the care pathway for mental disorders in Slovenia, as a second-line treatment instead of or prior to a second-line iCBT, a cost minimization analysis was undertaken using a health economics model decision tree (Fig. 1). The second-line comparison is made because it is the most realistic nationwide implementation option at the time, and because it allows for a results comparison between the UK and the former Yugoslavian country, with much lower wages and thus lower iCBT costs. For iCBT, a remission rate of 54.2% was used, which is the average remission rate between guided and full self-help groups in the study by Gyani et al. 2013. For the second-line use of Alpha-Stim, the response rate ranged from 47.2% for depression to 63.4% for anxiety but the former was utilized (the conservative approach and similarly to Morriss et al. 2019).

To estimate the cost of iCBT, actual patient data was obtained from moj.zzzs.si portal ("my.zzzs.si"), a user accessible portal of the National Health Insurance Institute providing patients with transparent and accurate insights into costs of their service utilization. For each 1-hour session, 3 distinctive service codes are used (96190, 11305 and 02003/05), which checked against the latest ZZZS's code register (ZZZS 2020b), and the official 2020 price list (ZD Koper 2019) results in a total cost of 48.68 €. For the medical device, the total cost was

set at 70 € ex./VAT per a 12-week treatment, including the supplier's reimbursement, consumables, postage and 13.7 € worth of additional specialist time, valued through service codes (11305 for treatment continuation, 02003/05 for examination and 91100 for making a prescription). For non-responders to second-line iCBT, a further course of the same number of iCBT sessions would follow (8 and 10 sessions were compared), with the same/constant remission probability. For non-responders to second-line CES, up to two further courses of iCBT were included in the decision tree. Nevertheless, results are provided also for the case if only 1 or none further iCBT courses followed.

Next, to estimate staff and Alpha-Stim needs at the national level, a top-down approach was utilized[1]. Hence, the number of missing psychiatrists was estimated on the basis of the EU average (315) (ZZZS 2019), the German level (250) and a basic arbitrarily set need (150). The estimate of how many patients one psychiatrist could treat in a year is based on the normative duration of 1 session being 1 hour (Psychiatric Association of Slovenia 2017), 224 workdays, 7 hours of daily productive time and provided for 2 treatment duration scenarios: 8-session (Option A) and 10-session iCBT (Option B). Based on these assumptions, 1 specialist could provide iCBT treatment for 157-196 patients per year. Because the device was found to be 13% less effective on the secondary level than iCBT, effectiveness was adjusted so that the original number of devices needed was increased accordingly. Since 1 Alpha-Stim can provide four 12-week treatments in a year, the need is estimated with a scenario analysis provided for all previously mentioned options. Finally, since effective treatment has even greater effects on employment-related costs than the direct healthcare cost, a basic budget impact analysis was done (Woo et al. 2011). Note that in Slovenia, the employer must cover the first 30 days of sick leave, and ZZZS pays only for the subsequent days. ZZZS is also the institution that would cover the costs of the Alpha-Stim implementation.

[1]A bottom-up approach was hampered by lack of data (e.g. how many patients receive iCBT).

It was estimated that the implementation of RNMHP 11-16 would decrease the number of hospitalizations by 10%, decrease their duration by 3% and reduce the number of sick days by 10%. In our case, only the decrease in sickness absence was quantified and is provided as a scenario analysis in Table 2. Pay-outs are based on the average gross salary of 1,799.66 € and the official 90% gross salary compensation (SURS 2020; ZZZS 2020a). Furthermore, an opportunity cost reduction was quantified through a trickle-down effect from an incremental increase in net added value per worker for the reduced absence duration, via corporate tax of 19%, to the ZZZS through its governmental budget participation of 7.7% (AJPES 2019; EUGO 2020; Ministry of Finance 2020).

Results

When Alpha-Stim is compared to 8-session iCBT solely on the first round's head-to-head basis, 1,000 patients could be treated without therapists for 319,400 € less, at an incremental loss of 70 patients that do not respond to treatment (Fig. 1). Next, if Alpha-Stim is introduced as a second-line intervention prior to a double round second-line iCBT, a cost reduction of 198 € per patient is observed. With 1,000 patients, a cost saving of 198,000 € is achieved, with 99 more patients responding. The threshold price is 268 €. Finally, if Alpha-Stim is used instead of just the 1st-legged iCBT, an additional incremental saving of 94.000 € is observed but at an incremental cost of 131 not responding. The threshold price is at 362 €.

When Alpha-Stim is compared to a 10-session iCBT solely on the first round's head-to-head basis, 1.000 patients could be treated without therapists for 416.800 € less, at an incremental loss of 70 patients (Fig. 2). Next, if Alpha-Stim is introduced as a second-line intervention prior to a double round second-line iCBT, a cost reduction of 198 € per patient is observed. In a pool of 1.000 patients, a cost saving of 198 thousand € is achieved, with 99 more patients responding. The threshold price is for this case 268 €.

Finally, if Alpha-Stim is used instead of just the 1st-legged iCBT, an additional incremental saving of 94 thousand € is observed but at an incremental cost of 131 patients not responding. The threshold price is for this case at 362 € per treatment.

Regarding the results for overall care needs at the national level, the number of yearly treatments needed was estimated between 79,966 and 27,034, the number of devices needed between 17,741 and 6,759 and the direct Alpha-Stim costs between 1.89 million and 4.97 million €, depending on treatment duration (Option A or Option B). The intermediate values of these intervals were used for the analysis: 49,000 for treatments needed, 12,250 for devices needed, and 3.43 million € for the direct Alpha-Stim costs.

To provide a regional perspective, the number of circulating devices was broken down to the municipal level for 2 Slovenian statistical regions and epidemiologically compared (Table 1).

Lastly, the budget impact analysis is presented in Table 2. Based on the results, the direct social security cost savings were estimated at 10.14 million € for a 15% reduction in the average duration of sick leave, while the indirect opportunity benefits were estimated at 339 thousand, together amounting to a 10,5 million € net monetary benefit to the ZZZS' budget.

Thus, the direct yearly average Alpha-Stim cost of 3.43 million € derived from the health economics decision tree for 2-round 8-session iCBT is more than 3 times offset solely by the social security budget impact. Factoring in the average number of additional yearly treatments needed (49.000), multiplied by an individual net cost benefit of 198 €, gives "direct" cost savings of 9.70 million € that could be obtained. Since this effect would be accompanied by the mentioned indirect impact on the social security budget of another 7.30 million to 10.48 million € (for a 10% or a 15% reduction in sick-leave duration), the final yearly net cost effect sums up to a minimum 17 million € saved.

Figure 1: Decision tree model for comparison of Alpha-Stim pathway with 8-session individual cognitive behavior therapy (iCBT) treatment as usual.

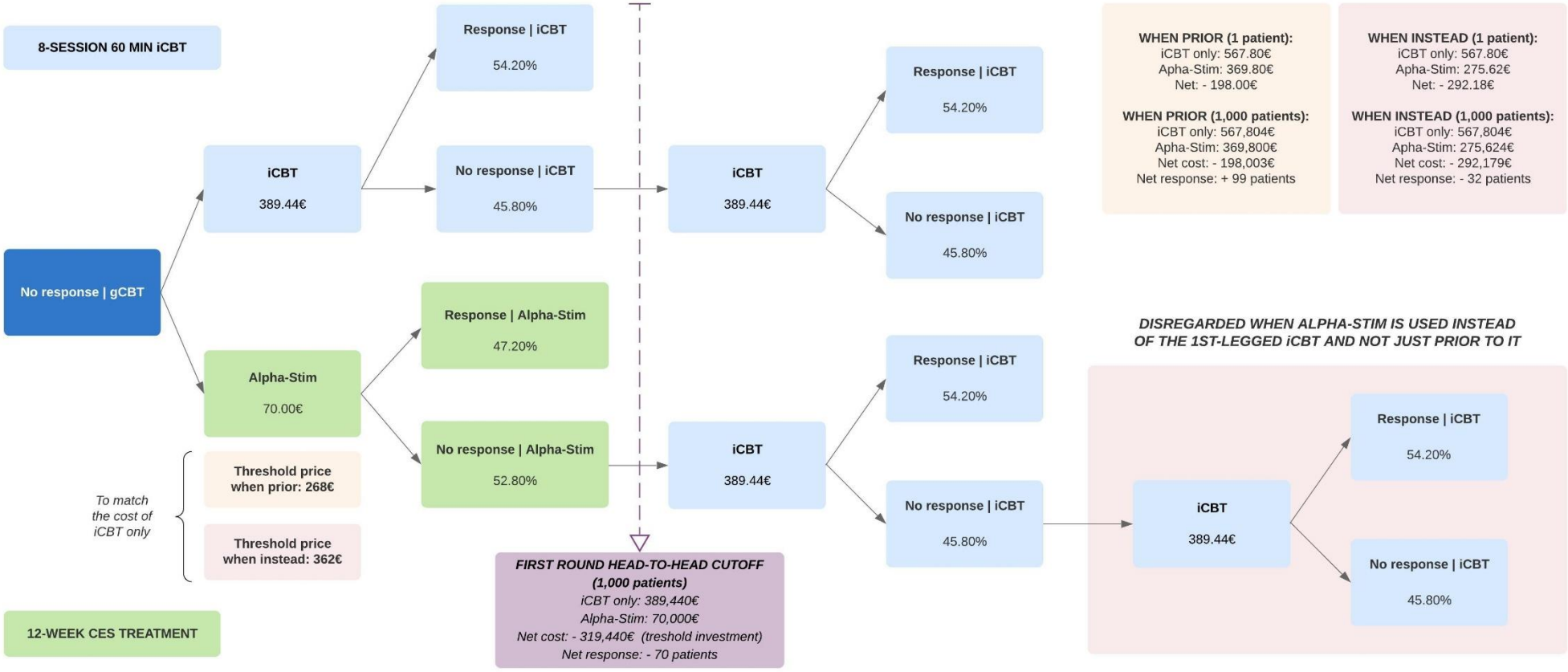

Figure 2: Decision tree model for comparison of Alpha-Stim pathway with 10-session individual cognitive behavior therapy (iCBT) treatment as usual.

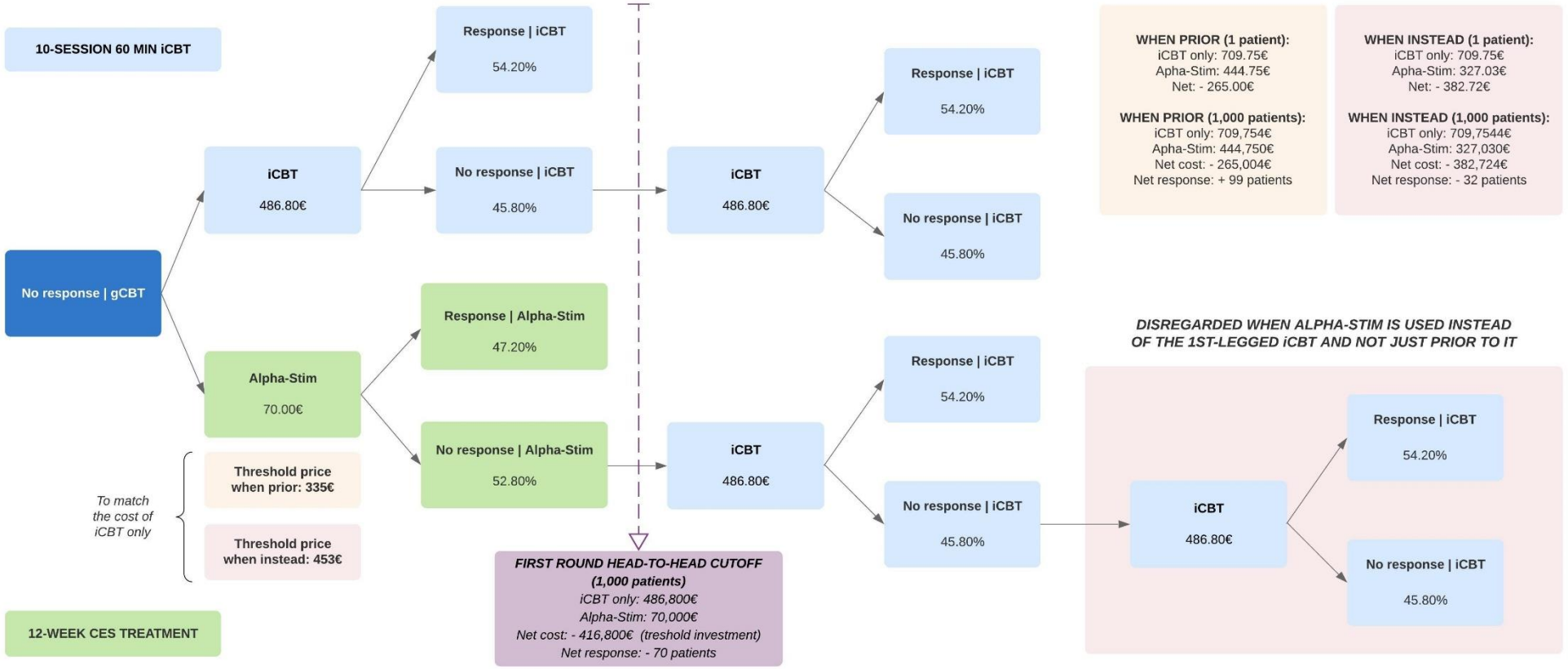

Table 1: Municipal Alpha-Stim allocation breakdown example and epidemiological perspective.

		Inhabitants	National weight	EU level scenario: MAX number of AS devices in circulation	Basic level scenario: MIN number of AS devices in circulation	**Average number of AS devices in circulation**	Average number of people with at least 1 prescription of SSRI	Average number of people with at least 1 prescription of anxiolytic	**Average number of monthly AS treatments**	**Average monthly cost of AS treatment in EUR**
Region:	**Obalno-kraška**	**114.085**	**5,48%**	**973**	**371**	**672**	**7.986**	**7.872**	**448**	**31.355**
Municipalities:	**Ankaran**	3.216	0,15%	27	10	19	225	222	13	884
	Divača	4.093	0,20%	35	13	24	287	282	16	1.125
	Hrpelje - Kozina	4.426	0,21%	38	14	26	310	305	17	1.216
	Izola	16.099	0,77%	137	52	95	1.127	1.111	63	4.425
	Komen	3.523	0,17%	30	11	21	247	243	14	968
	Koper	51.828	2,49%	442	168	305	3.628	3.576	203	14.244
	Piran	17.613	0,85%	150	57	104	1.233	1.215	69	4.841
	Sežana	13.287	0,64%	113	43	78	930	917	52	3.652
Region:	**Goriška**	**117.353**	**5,64%**	**1.001**	**381**	**691**	**8.215**	**8.097**	**461**	**32.253**
Municipalities:	**Ajdovščina**	19.154	0,92%	163	62	113	1.341	1.322	75	5.264
	Bovec	3.052	0,15%	26	10	18	214	211	12	839
	Brda	5.613	0,27%	48	18	33	393	387	22	1.543
	Cerkno	4.584	0,22%	39	15	27	321	316	18	1.260
	Idrija	11.730	0,56%	100	38	69	821	809	46	3.224
	Kanal	5.300	0,25%	45	17	31	371	366	21	1.457
	Kobarid	4.097	0,20%	35	13	24	287	283	16	1.126
	Miren - Kostanjevica	4.885	0,23%	42	16	29	342	337	19	1.343
	Nova Gorica	31.691	1,52%	270	103	187	2.218	2.187	124	8.710
	Renče - Vogrsko	4.345	0,21%	37	14	26	304	300	17	1.194
	Šempeter - Vrtojba	6.201	0,30%	53	20	37	434	428	24	1.704
	Tolmin	11.108	0,53%	95	36	65	778	766	44	3.053
	Vipava	5.593	0,27%	48	18	33	392	386	22	1.537

Table 2: Social security budget impact.

Assumptions	
Average sick days duration	46.34
Average duration that falls on ZZZS	16.34
Workdays in a month	20.75
Number of cases	21,484
Gross salary (EUR)	1,799.66
Compensation	90.0%
Corporate tax	19.0%
ZZZS budget participation	7.7%
Average yearly net added value per worker	44,415.00
Average daily net added value per worker	178.37

Type of payout	ZZZS direct outflow	**Cost decrease**	Increase in net added value	Tax collected	**ZZZS indirect inflow**	**ZZZS total net benefit**
Current	27,401,988 €	- €	- €	- €	**- €**	**- €**
With a 5% duration reduction	23,701,434 €	**3,700,554 €**	8,456,335 €	1,606,704 €	**123,716 €**	**3,824,270 €**
With a 10% duration reduction	20,337,294 €	**7,064,694 €**	16,143,913 €	3,067,343 €	**236,185 €**	**7,300,880 €**
With a 15% duration reduction	17,265,688 €	**10,136,300 €**	23,163,006 €	4,400,971 €	**338,875 €**	**10,475,175 €**
With a 20% duration reduction	14,450,049 €	**12,951,939 €**	29,597,174 €	5,623,463 €	**433,007 €**	**13,384,946 €**

Table 3: Direct costs impact as average of scenario analysis.

Average between MAX of OPTION A and MIN of OPTION B - national level
Average number of psychiatrist missing
233
Average yearly number of treatments (also patients)
49,000
Average number of devices needed
12,250
Average monthly number of treatments
4,083
Average monthly point in time prevalence of AS treatment
0.39%
Average yearly direct cost of implementation
3.43 million €

Of course, multiple other opportunity costs could be accounted for, which is the main limitation of this analysis. As already mentioned, clinical specialization costs an institution 150.000 €. Distributed across a 35-year career, ZZZS would, on a yearly basis, need to spend 4,286 € per doctor, which was not accounted for in the decision tree.

Since Alpha-Stim reduces the number of specialists needed by 50%, this could result, roughly, in yearly savings of 0.5 million €. Of course, if Slovenia were to channel all its medical students to psychiatry to fill the shortage as soon as possible, other great opportunity costs would occur in the form of staff shortages for treating other important conditions.

Next, according to the NIJZ's representative, every euro invested in the preventive social programs used in the RNMHP (18-28) has 33 to 80-fold return (Zajec 2018). This means that if a net monetary benefit of at least 17.5 million € is invested in these programs, a final net impact of at least 577 million € could be assumed in the long run. Therefore, Alpha-Stim implementation could provide an even more substantial value proposition from multiple additional viewpoints in addition to potentially solving the current stalemate state of Slovenian psychiatry in a cost-effective manner.

Next, if Alpha-Stim were implemented to completely replace iCBT, according to the first-round head-to-head comparison coupled with a 5% duration reduction, 24.2 million € would be the minimum final net yearly benefit; 38% higher than in the previously mentioned option of using Alpha-Stim prior to a 2-round iCBT but at the expense of 47% less patients responding (472 vs. 890 in a pool of 1.000 patients).

Finally, the pathway could be optimized by dynamically allocating patients based on their individual preferences and characteristics, thus improving the likelihood of successful response for both options simultaneously. For example, if one prefers human interaction or is a techno-sceptic, CBT could be used instead and vice versa for those doubting psychotherapy.

Discussion

The demand for psychiatric services in Slovenia is increasing, the waiting lines are exceedingly long, and the shortage of specialists is severe and unequal across regions. It seems that Slovenia has reached a stalemate position, where creating a large pool of specialists in psychiatry would result in high opportunity costs at the expense of other specializations that are also critically understaffed (STA 2019a; 2019b).

Considering everything, it is hard to believe that Slovenia is prepared for the after-effects of what seems to be the largest pandemic of our time. Hence, professional warnings about the aftermath of Covid-19 should be taken even more seriously. One of the warnings was published last month in *Lancet Psychiatry*, stating that the epidemic has caused a parallel epidemic of fear, anxiety and depression (Yao, Chen, and Xu 2020). Another similar warning comes from the editor-in-chief of the American Journal of *Current Psychiatry*. Even the Chinese, Singaporean and Australian governments have voiced concerns that the long-term psychological side effects of Covid-19 and isolation could cause more harm in the community than the virus (Zhou et al. 2020). A list of other academically published warnings about the parallel epidemic is provided in the Appendix. In Slovenia, even though free psychological support helplines are being offered, the majority of consultations have been suspended and the new regional mental health centres were no exception. The NIJZ's update on monthly waiting times is running late.

Given the burden of poor mental health, the economic case for preventing mental illnesses and promoting better mental health may be very strong, but too often it attracts little attention and few resources (Chisholm et al. 2016; McDaid, Park, and Wahlbeck 2019). Hence, there is still a substantial unmet need, especially among treatment-resistant depression patients in Europe (Jaffe, Rive, and Denee 2019). Alpha-Stim is a cost-effective, transportable, pocket-sized, readily available and clinically tested treatment intervention that can also help improve

regional discrepancies in service accessibility as well as provide a new treatment option which may be more appropriate to some patients.

To put the estimated direct yearly costs of nationwide Alpha-Stim implementation into perspective, it represents less than a quarter of Slovenian yearly spending on antidepressants and anxiolytics, less than 10% of what would need to be spent just on specializations, less than 4% of total costs planned at the end of the RNMHP (18-28) and less than 2% of what was spent on personal protective equipment during the Covid-19 pandemic. The RNMHP planned for ZZZS to gradually increase investment in mental health from 63.1 to 97.8 million €, which due to staff shortages turned out to be unfeasible. Hence, 3.5 million € is a minor direct cost for an estimated net benefit of at least 18 million €, offsetting no less than 50% of the RNMHP's planned cost increase. While NICE guidance is being prepared by a mix of more than 40 organizational stakeholders, in Slovenia the decision on Alpha-Stim implementation will be left in the hands of 5 psychiatrists constituting the Ministry of Health's General Advisory Board for Psychiatry and a ZZZS' committee. Furthermore, at the beginning of 2020, EPI's application for a Healthcare Common Procedure Coding System (HCPCS) with the Centres for Medicare and Medicaid Services in the US was approved, and an insurance billing code for CES devices was issued (EPI 2020b). Private insurance companies are soon to follow (Chicago Psychology Podcast 2020).

Researchers must work extra hard to find alternative methods for psychiatric treatment and both the NHS and the US Army have embraced the potential of Alpha-Stim medical technology (P. Nuse 2017). Since we are already stimulating our muscles to a speedy recovery after various injuries, doing the same to an organ that can generate enough electricity to power a low-wattage bulb (Hofman 2014) may be associated with less stigma than the pharmacological or psychological treatments. It is time to take electrified medicine seriously (Park 2019).

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APPENDIX

Table 4: Regional differences in access to pharmacological and psychiatric specialist care – absolute values.*

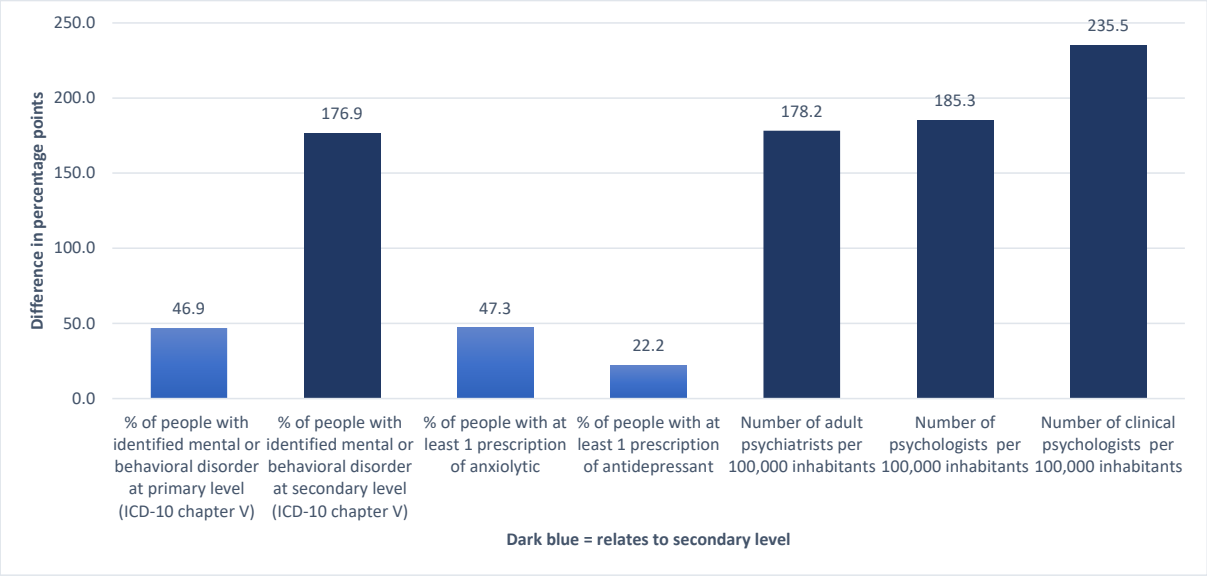
Data source:	*A (2011)	*B (2018)	*C (2018)	*D (2018)	*D (2018)	*E (2018)	*E (2018)	*E (2018)	*E (2018)
	Risk degree of developing mental disorder	% of people with identified mental or behavioral disorder at primary level (ICD-10 chapter V)	% of people with identified mental or behavioral disorder at secondary level (ICD-10 chapter V)	% of people with at least 1 prescription of anxiolytic	% of people with at least 1 prescription of antidepressant	Number of adult psychiatrists per 100,000 inhabitants	Number of psychologists per 100,000 inhabitants	Number of clinical psychologists per 100,000 inhabitants	Number of child and adolescent psychiatrists per 100,000 inhabitants
Pomurska	12	4.8	3.4	8.5	7.4	4.4	9.6	4.4	0.0
Zasavska	11	4.9	1.5	6.9	8.1	3.5	5.3	0.0	1.8
Posavska	10	3.0	1.5	7.6	6.6	6.6	13.3	2.7	0.0
Primorsko-notranjska	9	4.6	0.9	7.7	7.1	3.8	3.8	0.0	0.0
Podravska	8	4.1	4.0	8.4	7.3	11.5	12.7	3.7	1.2
Savinjska	7	3.5	1.9	7.5	7.2	6.3	11.3	2.3	0.0
Koroška	6	4.6	0.3	7.9	7.7	5.7	8.5	2.8	1.4
Jugovzhodna Slovenija	5	4.2	2.0	7.4	6.9	3.5	7.0	1.4	0.0
Obalno-kraška	4	3.8	2.6	6.5	6.9	8.8	8.8	0.0	0.9
Gorenjska	3	4.6	3.0	5.1	6.7	10.8	8.4	6.4	0.5
Goriška	2	4.0	3.0	7.1	7.9	17.9	14.5	3.4	0.0
Osrednjeslovenska	1	3.7	4.6	5.7	6.5	14.3	23.3	6.6	1.3
Average	6.5	4.2	2.4	7.2	7.2	8.1	10.5	2.8	0.6

Table 5: Regional differences in access to pharmacological and psychiatric specialist care – relative deviations and their respective averages.*

Data source:	*A (2011)	*B (2018)	*C (2018)	*D (2018)	*D (2018)	*E (2018)	*E (2018)	*E (2018)	*E (2018)
	Risk degree of developing mental disorder	% of people with identified mental or behavioral disorder at primary level (ICD-10 chapter V)	% of people with identified mental or behavioral disorder at secondary level (ICD-10 chapter V)	% of people with at least 1 prescription of anxiolytic	% of people with at least 1 prescription of antidepressant	Number of adult psychiatrists per 100,000 inhabitants	Number of psychologists per 100,000 inhabitants	Number of clinical psychologists per 100,000 inhabitants	Number of child and adolescent psychiatrists per 100,000 inhabitants
Pomurska	84.6%	15.2%	42.6%	18.2%	2.9%	-46.1%	-8.9%	55.2%	-100.0%
Zasavska	69.2%	19.1%	-39.4%	-4.1%	12.6%	-56.6%	-50.1%	-100.0%	197.7%
Posavska	53.8%	-27.8%	-38.5%	5.7%	-8.2%	-18.0%	25.8%	-5.6%	-100.0%
Primorsko-notranjska	38.5%	11.2%	-62.4%	7.1%	-1.3%	-52.7%	-63.7%	-100.0%	-100.0%
Podravska	23.1%	-0.9%	68.1%	16.8%	1.5%	42.1%	20.9%	32.6%	111.0%
Savinjska	7.7%	-15.5%	-21.4%	4.3%	0.1%	-22.6%	7.6%	-16.5%	-100.0%
Koroška	-7.7%	9.8%	-85.8%	9.8%	7.1%	-29.9%	-19.3%	0.8%	140.5%
Jugovzhodna Slovenija	-23.1%	0.4%	-16.8%	2.9%	-4.1%	-56.9%	-33.8%	-50.4%	-100.0%
Obalno-kraška	-38.5%	-7.9%	9.1%	-9.6%	-4.1%	8.4%	-16.8%	-100.0%	48.9%
Gorenjska	-53.8%	10.6%	26.3%	-29.1%	-6.8%	33.7%	-20.7%	127.2%	-16.6%
Goriška	-69.2%	-4.2%	27.1%	-1.3%	9.8%	121.3%	37.5%	21.3%	-100.0%
Osrednjeslovenska	-84.6%	-9.7%	91.1%	-20.7%	-9.6%	77.3%	121.6%	135.5%	118.5%
Average	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Max difference (p.p.)	/	46.9	176.9	47.3	22.2	178.2	185.3	235.5	/
Diff. 4 high/low (p.p.)	/	29.3	113.7	28.9	15.3	121.7	93.5	175.2	/

Color coding = relative changes. *A (2011): (Šprah, Tatjana, and Zvezdana Dernovšek 2011), *B (2018): (NIJZ 2019g) and own calculations, *C (2018): (NIJZ 2019h) and own calculations, *D (2018): (NIJZ 2019a), *E (2018): (NIJZ 2019b) and own calculations.

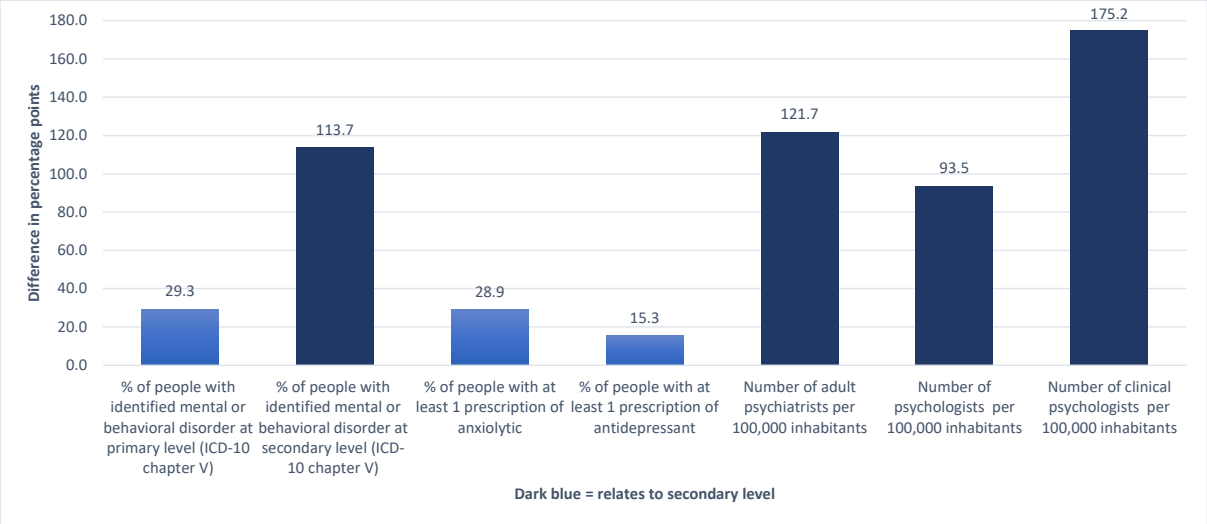
Figure 3: Percentage points differences of maximum regional relative deviations from the average access to psychiatric treatment.



Interpretation: Perc. point difference is for number of psychiatrists per 100.000 inhabitants highest between Goriška (+121,3%) and Jugovzhodna Slovenija region (-56,9%) and is 178,2.

Source: Own calculations based on Table 4 and 5.

Figure 4: Percentage points differences of relative deviations from the average access to psychiatric treatment between the average levels of highest and lowest 4 regions.



Interpretation: 121,7 is the perc. points difference for number of psychiatrists per 100.000 inhabitants between the average values of 4 highest (68,6%) and 4 lowest regions (-53,1%).

Source: Own calculations based on Table 4 and 5.

Table 6: Total number of adult psychiatrists in Slovenia, by the training status.

Year	Specialists	Specialist registrar (in training)	Total adult psychiatry specialists	Adult psychiatrists per 100,000 inhabitants
2005	179	31	210	10.4
2006	175	28	203	10.0
2007	172	21	193	9.5
2008	179	22	201	9.9
2009	186	25	211	10.3
2010	184	25	209	10.2
2011	187	32	219	10.7
2012	181	43	224	10.9
2013	195	43	238	11.5
2014	194	42	236	11.4
2015	196	47	243	11.8
2016	205	47	252	12.2
2017	206	50	256	12.4
2018	210	67	277	13.3

Source: NIJZ Data portal https://podatki.nijz.si/pxweb/sl/) and Statistical Office of the Republic of Slovenia (https://pxweb.stat.si/).

Note: While Table 1 and 2 only include specialists with finished training, that were working in healthcare related institutions in 2018 (207), this table includes them all no matter the training or industry status, i.e. also governing bodies and ministries, educational institutions, the pharmaceutical industry, and other non-medical organizations (277).

Table 7: Total number of child and adolescent psychiatrists in Slovenia, by training status.

Year	Specialists	Specialist registrar (in training)	Total child and adol. psychiatry specialists	Child and adol. psychiatrists per 100,000 inhabitants
2005	0	3	3	0.1
2006	0	3	3	0.1
2007	0	4	4	0.2
2008	0	3	3	0.1
2009	1	3	4	0.2
2010	3	4	7	0.3
2011	3	4	7	0.3
2012	3	7	10	0.5
2013	5	9	14	0.7
2014	5	12	17	0.8
2015	7	17	24	1.2
2016	7	20	27	1.3
2017	10	19	29	1.4
2018	15	24	39	1.9

Source: NIJZ Data portal https://podatki.nijz.si/pxweb/sl/) and Statistical Office of the Republic of Slovenia (https://pxweb.stat.si/).

Note: While Table 1 and 2 only include specialists with finished training, that were working in healthcare related institutions in 2018 (15), this table includes them all no matter the training or industry status, i.e. also governing bodies and ministries, educational institutions, the pharmaceutical industry, and other non-medical organizations (39).

Table 8: Total number of clinical psychologists in Slovenia, by training status.

Year	Specialists	Specialist registrar (in training)	Total clinical psychology specialists	Clinical psychologists per 100,000 inhabitants
2005	86	6	92	4.5
2006	82	6	88	4.3
2007	82	4	86	4.2
2008	81	5	86	4.2
2009	84	4	88	4.3
2010	83	6	89	4.3
2011	81	5	86	4.2
2012	76	6	82	4.0
2013	75	6	81	3.9
2014	78	6	84	4.1
2015	81	8	89	4.3
2016	87	10	97	4.7
2017	81	10	91	4.4
2018	86	11	97	4.7

Source: NIJZ Data portal https://podatki.nijz.si/pxweb/sl/) and Statistical Office of the Republic of Slovenia (https://pxweb.stat.si/).

Note: While Table 1 and 2 only include specialists with finished training, that were working in healthcare related institutions in 2018 (73), this table includes them all no matter the training or industry status, i.e. also governing bodies and ministries, educational institutions, the pharmaceutical industry, and other non-medical organizations (97).

Table 9: Total number of psychologists in Slovenia.

Year	Total psychologists	Psychologists per 100,000 inhabitants
2005	183	9.0
2006	188	9.3
2007	186	9.2
2008	194	9.6
2009	211	10.3
2010	221	10.8
2011	220	10.7
2012	220	10.7
2013	235	11.4
2014	256	12.4
2015	274	13.3
2016	296	14.3
2017	320	15.5
2018	365	17.6

Source: NIJZ Data portal https://podatki.nijz.si/pxweb/sl/) and Statistical Office of the Republic of Slovenia (https://pxweb.stat.si/).

Note: While Table 1 and 2 only include psychologists that were working in healthcare related institutions in 2018 (266), this table includes them all no matter the industry status, i.e. also governing bodies and ministries, educational institutions, the pharmaceutical industry, and other non-medical organizations (365).

Table 10: RNMHP (18-28) total costs comparison between suggested and accepted plan.

The Health Insurance Institute of Slovenia -The Resolution on the National Mental Health Programme 2018-2028 - total cost in million €												
DISPOSITION												
Year	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**
Marginal in	0	0	3.01	3.01	5.72	5.72	5.415	5.415	4.545	4.545	3.14	3.14
Yearly spen	63.06	63.06	66.07	69.08	74.8	80.52	85.935	91.35	95.895	100.44	103.58	**106.72**
ACCEPTED												
Year	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**
Marginal in	0.00	0.00	4.75	4.21	3.87	3.54	3.55	3.68	3.51	3.87	2.41	1.32
Yearly spen	63.06	63.06	67.81	72.03	75.90	79.44	82.99	86.66	90.17	94.05	96.46	**97.78**

Source: Official Gazzete and Ministry of Health of the Republic of Slovenia.

Table 11: Yearly patient intake estimation if only 8 or 10-session iCBT would be performed.

Question: How much patients can a specialist doing solely iCBT treat in a year?						
Estimating monthly and yearly patient intake if only 8 or 10-session 60min iCBT therapy would be provided						
Assumptions		Number of iCBT sessions needed: 8 --> OPTION A				
Workdays in a year	249	Frequency	Monthly patient intake	Yearly cycle repetition factor	Yearly patient intake	Average monthly intake
Vacation days in a year	25	iCBT done daily	16.3	12,0x	196	
Net yearly workdays	**224**	iCBT done weekly	32.7	6,0x	196	16.3
Working hours per day	8	iCBT done monthly	130.7	1,5x	196	
Lunch time loss per day	0.5	Number of iCBT sessions needed: 10 --> OPTION B				
Administrative time loss per day	0.5	Frequency	Monthly patient intake	Yearly cycle repetition factor	Yearly patient intake	Average monthly intake
Net productive hours	**7**	iCBT done daily	13.1	12,0x	156.8	
Net workdays in a month	18.66666667	iCBT done weekly	32.7	4,8x	156.8	13.1
Net monthly productive hours	130.7	iCBT done monthly	130.7	1,2x	156.8	

Table 12: Yearly number of treatments comparison.

Question: How much specialists does Slovenia lack and how many patients could they treat?		
Estimating yearly number of patients that would be treated, if a specific number of psychiatrists would be added into the healthcare system		
Number of missing psychiatrist when compared to		
the claimed EU average	**the German level**	**the basic solution of specialists shortage**
315	250	150
Number of patients treated if OPTION A		
61,740 (MAX)	49,000	29,400
Number of patients treated if OPTION B		
49,392	39,200	**23,520 (MIN)**

Table 13: Yearly number of Alpha-Stim devices needed.

Question: What is the number of devices needed to match the number of treatments specialists could've done?		
Estimating number of Alpha-Stim medical devices needed to obtain the same result		
Number of 3-month treatments one Alpha-Stim medical device can do in a year		
4		
Number of Alpha-Stim devices needed to obtain the same result as missing psychiatrists would, if OPTION A and same effectiveness assume		
15,435	12,250	7,350
Number of devices needed when adjusted for cca. 13% lower effectiveness than iCBT		
17,741 (MAX)	14,080	8,448
Number of Alpha-Stim devices needed to obtain the same result as missing psychiatrists would, if OPTION B and same effectiveness assume		
12,348	9,800	5,880
Number of devices needed when adjusted for cca. 13% lower effectiveness than iCBT		
14,193	11,264	**6,759 MIN**

Table 14: Direct yearly costs and number of devices needed when adjusted for effectiveness.

Question: What is the number of effectiveness-adjusted treatments need and how much would they cost in a year?		
Estimating total direct yearly cost of Alpha-Stim treatments to ZZZS		
Total yearly number of Alpha-Stim treatments needed with adjusted effectiveness, if OPTION A		
70,966	56,322	29,400
Total yearly direct cost of Alpha-Stim treatments quoted above (1 treatment = 70,0€, includes also 13€ of additional specialist time) in million EUR		
4.97 (MAX)	3.94	2.06
Total yearly number of Alpha-Stim treatments needed with adjusted effectiveness, IF OPTION B		
56,772	45,057	27,034
Total yearly direct cost of Alpha-Stim treatments quoted above (1 treatment = 70,0€, includes also 13€ of additional specialist time) in million EUR		
3.97	3.15	**1.89 (MIN)**

List 1: Published warnings on Covid-19 psychological crisis and parallel pandemic.

(As of 27. 3. 2020).

1) Management of corona virus disease-19 (COVID-19): the Zhejiang experience.

Xu K., et al. PubMed, 21. 2. 2020.

"Therefore, we established dynamic assessment and ***warning for psychological crisis****."*

2) The Role of Telehealth in Reducing the Mental Health Burden from COVID-19.

Zhou X, et al. Mary Ann Liebert, 23. 3. 2020.

"The Chinese, Singaporean, and Australian governments have highlighted ***the psychological side effects of COVID-19****, and have voiced concerns regarding the long-term impacts of isolation and that the fear and panic in the community* ***could cause more harm than COVID-19****."*

3) Psychological interventions for people affected by the COVID-19 epidemic.

Li D., et al. 19. 2. 2020.

"Studies have confirmed that individuals who have experienced public health emergencies ***still have varying degrees of stress disorders, even after the event is over****, or they have been cured and discharged from hospital, indicating these individuals should not be ignored."*

"Finally, owing to a ***shortage of professionals****, the establishment of psychological intervention teams in many areas is not feasible.*"

4) Prevalence and predictors of PTSS during COVID-19 Outbreak in China Hardest-hit Areas: Gender differences matter.

Liu N., et al. ScienceDirect, 16. 3. 2020.

"The prevalence of ***posttraumatic stress symptoms (PTSS)*** *in China hardest-hit areas* ***a month after the COVID-19 outbreak was 7%.*** *"*

"Therefore, we have reason to believe that ***the prevalence of PTSS*** *among the public of the hardest-hit areas* ***will be more severe than the results of this study****."*

5) Recommended psychological crisis intervention response to the 2019 novel coronavirus pneumonia outbreak in China: a model of West China Hospital.

Zhang J. et al. Oxford Academic, 18. 2. 2020.

"The absence of mental health and psychosocial support systems and ***the lack of well-trained psychiatrists and/or psychologists*** *in these regions* ***increased the risks of*** *psychological distress and* ***progression to psychopathology***."

6) Progression of Mental Health Services during the COVID-19 Outbreak in China.

Li W., et al. IVYSPRING, 23. 2. 2020.

*"The outbreak of the COVID-19 has caused **tremendous psychological problems** in different subpopulations."*

*"Fourth, based on experiences of SARS outbreak, some patients and health professionals **would be traumatized by the COVID-2019 outbreak** and still suffer from **persistent psychiatric symptoms even after the outbreak**."*

7) Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed.

Xiang Y., et al. The Lancet, 1. 3. 2020

*"**Health workers** in a Beijing hospital who were quarantined, worked in high-risk clinical settings such as SARS units, or had family or friends who were infected with SARS, had **substantially more post-traumatic stress symptoms** than those without these experiences.*"

*"In any biological disaster, themes of fear, uncertainty, and stigmatisation are common and may act as **barriers to appropriate medical and mental health interventions**. Based on experience from past serious novel pneumonia outbreaks globally and the psychosocial impact of viral epidemics, **the development and implementation of mental health** assessment, support, treatment, and services are **crucial and pressing goals for the health response to the 2019-nCoV outbreak**."*

8) The National Health Commission has issued guidelines for emergency psychological crisis intervention for people affected by COVID-19.

Li D., et al. The Lancet, 18. 2. 2020.

*"The National Health Commission has issued guidelines for **emergency psychological crisis** intervention **for people affected by COVID-19**."*

*"After the assessment of the mental health states of individuals affected by the epidemic, **patients cannot be assigned** according to the severity of their condition and **difficulty of treatment** to the appropriate department or professionals **for timely and reasonable diagnosis and treatment**."*

9) Public Mental Health Crisis during COVID-19 Pandemic, China.

Dong L., et al. Centers for Disease Control and Prevention, 23. 3. 2020.

"Third, **unprecedented large-scale quarantine** measures in all major cities, which essentially confine residents to their homes, are likely to have a **negative psychosocial effect** on residents."

10) A Novel Approach of Consultation on 2019 Novel Coronavirus (COVID-19)-Related Psychological and Mental Problems: Structured Letter Therapy.

Xiao C. Psychiatry Investigation, 25. 2. 2020.

*"**The epidemic brought** to people in China and the world **not only the risk of** death after virus **infection**, **but also unbearable psychological pressure**."*

11) Mental Health Strategies to Combat the Psychological Impact of COVID-19 Beyond Paranoia and Panic.

Ho C, et al. Annals Academy of Medicine Singapur, 16. 3. 2020.

*"**It is pivotal**, however, that we **do not ignore the psychological impact** that the outbreak has on individuals and **the society**, which is often the **limiting factor** for the nation to **overcome the crisis**. Psychological ramifications can be **long-lasting** even after the epidemic has ended.*"

12) Online mental health services in China during the COVID-19 outbreak.

Liu S., et al. The Lancet, 18. 2. 2002.

*"One such multicentre survey involving **1.563 medical staff**, with our centre at Nanfang Hospital, Southern Medical University (Guangzhou, China) as one of the study sites, found the prevalence of **depression to be 50,7%,** of **anxiety to be 44,7%,** of **insomnia to be 36,1%**, and of **stressrelated symptoms to be 73,4%**.*"

13) Patient Management and Clinical Recommendations During The Coronavirus (COVID-19) Pandemic.

Azziz R., et al. American Society for Reproductive Medicine, 17. 3. 2020.

*"The COVID-19 pandemic presents an **unprecedented threat of unimaginable proportions** to the **psychological and emotional wellbeing** of patients and staff."*

*"Mental health professionals should be utilized to help support **patients and staff** at risk for **serious psychological or emotional issues**."*

14) The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China.

Y. Yang, et al. ScienceDirect, 3. 3. 2020.

*"The costs of the epidemic are not limited to medical aspects, as the virus has led to **significant** sociological, **psychological** and economic **effects** globally."*

*"One must not forget the **psychological impact** of an infection such as this on people who are not even infected or who will never encounter an infected person."*

15) The Risk and Prevention of Novel Coronavirus Pneumonia Infections Among Inpatients in Psychiatric Hospitals.

Zhu Y., et al. Springer Link, 25. 2. 2020.

*"**Panic is inevitable** among patients and **medical staff** and **timely mental health care** for dealing with the novel coronavirus outbreak **is urgently needed**."*

16) Psychological crisis intervention during the outbreak period of new coronavirus pneumonia from experience in Shanghai.

Jiang X., et al. ScienceDirect, 28. 2. 2020.

*"**If medical care is delayed**, affected persons may suffer **inestimable damage** caused by the **psychological crisis**."*

*"During the outbreak period of NCP, **psychological crisis intervention** (PCI) is **urgently need** for all affected, including patients, **medical staff**, close contacts, people in affected areas, as well as the **general public**."*

17) COVID-19 infection epidemic: the medical management strategies in Heilongjiang Province, China.

Wang H., et al. BMC (part of Springer Nature), 18. 3. 2020.

*"**It is crucial** to ensure the stable **psychological state of the medical staffs**. Therefore, **early professional intervention is necessary**."*

18) The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus.

Kang L., et al. The Lancet, 5. 2. 2020.

*"In the fight against the 2019 novel **coronavirus** (2019-nCoV**), medical workers in Wuhan have been facing enormous pressure**, including a high risk of infection and inadequate protection from contamination, overwork, frustration, discrimination, isolation, patients with negative emotions, a lack of contact with their families, and **exhaustion**. The severe situation **is causing mental health problems** such as stress, anxiety, depressive symptoms, insomnia, denial, anger, and fear. **These mental health problems not only affect the medical workers' attention, understanding, and decision-making ability, which might hinder the fight against 2019-nCoV**, but could also have a **lasting effect** on their overall wellbeing. Protecting the mental health of these medical workers is thus **important for control of the epidemic** and their **own long-term health**."*

*"Given more than 80% of patients are confirmed in Hubei province, **the hospitals and medical workers** in Hubei are facing and bearing **enormous pressure** and severe challenge, including a high risk of infection and inadequate protection, as well as **overwork, frustration and exhaustion**."*

19) Mental health services for older adults in China during the COVID-19 outbreak.

Yang Y., et al. The Lancet, 18. 2. 2020.

*"In addition, in most areas of China, clinically stable older adults with psychiatric disorders or their guardians usually **need to visit psychiatric outpatient clinics monthly** to obtain the maintenance medications. The current mass quarantines and restrictions to public transport have inevitably become **a major barrier to access maintenance treatments** for this group."*

20) Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China.

Wang C., et al. MDPI, 6. 3. 2020.

"Our findings suggest that with respect to the initial psychological responses of the general public from 31 January to 2 February 2020, ***just two weeks into the country's outbreak of COVID-19*** *and one day after WHO declared public health emergency of international concern,* ***53.8% of respondents*** *rated the* ***psychological impact*** *of outbreak as moderate or* ***severe****.*"

21) 2019-nCoV epidemic: address mental health care to empower society.

Bao Y., et al. The Lancet, 7. 2. 2020.

"The challenges and stress they experience could trigger common ***mental disorders****, including anxiety and depressive disorders, and posttraumatic stress disorder, which in turn could result in* ***hazards that exceed the consequences of the 2019-nCoV epidemic itself****."*

22) Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019.

Lai J., et al. Jama Network Open, 23. 3. 2020.

"Health care workers responding to the spread of COVID-19 reported high rates of symptoms of depression, anxiety, insomnia, and distress. Protecting ***health care workers*** *is an* ***important component of public health*** *measures for addressing the COVID-19 epidemic.* ***Special interventions*** *to promote mental well-being in health care workers exposed to COVID-19* ***need to be immediately implemented****, with women, nurses, and frontline workers requiring particular attention.*"

23) Generalized anxiety disorder, depressive symptoms and sleep quality during COVID-19 epidemic in China: a web-based cross-sectional survey.

Huang Y., et al. MedRxiv, 9. 3. 2020

"Our study identified ***a major mental health burden of the public during COVID-19 epidemic*** *in China.*"

"As mental health and public health ***professionals, we call for*** *adequate and* ***necessary*** *attention to people with* ***mental health disorders in the COVID-19 epidemic****.*"

24) Patients with mental health disorders in the COVID-19 epidemic.

Yao H., et al. ScienceDirect, 19. 3. 2020

"Third, the COVID-19 epidemic has caused a ***parallel epidemic of fear, anxiety, and depression****. People with mental health conditions could be more substantially influenced by the emotional responses brought on by the COVID-19 epidemic, resulting in* ***relapses or worsening*** *of an already existing* ***mental health condition*** *because of high susceptibility to stress compared with the general population.*"

*"****Few voices*** *of this large but vulnerable population of people with mental health disorders* ***have been heard during this epidemic****. Epidemics never affect all populations equally and inequalities can always* ***drive the spread of infections.***"

"As mental health and public health professionals, ***we call for adequate and necessary attention*** *to people with* ***mental health disorders*** *in the COVID-19 epidemic."*

25) Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement.

Shen K., et al. Springer Link, 7. 2. 2020.

"Psychological counseling plays an ***important*** *role in* ***disease recovery****."*

26) Mental health care for medical staff in China during the COVID-19 outbreak.

Chen Q., et al. The Lancet, 18. 2. 2020.

"The Second Xiangya Hospital, and the Institute of Mental Health, the Medical Psychology Research Center of the Second Xiangya Hospital, and the Chinese Medical and Psychological Disease Clinical Medicine Research Center ***responded rapidly to the psychological pressures on staff****."*

27) COVID-19 and the consequences of isolating the elderly.

Armitage R., et al. The Lancet, 19. 3. 2020.

"If health ministers instruct elderly people to remain home, have groceries and vital medications delivered, and avoid social contact with family and friends, ***urgent action is needed to mitigate the mental and physical health consequences****."*

28) Preparing for COVID-19: early experience from an intensive care unit in Singapore.

Liew F. M., et al. BMC (part of Springer Nature), 9. 3. 2020.

"Lastly, we realized ***staff morale took an early hit due to multiple factors,*** *including increased workload due to implementation of strict infection control measures, uncertainty over the effectiveness of personal protective equipment, anxiety over the lethality of any infection, concern for the well-being of their family members and stigmatization by members of the public."*

29) Psychological Effects of Quarantine: A Qualitative "Rapid Review".

Roy-Byrne P. NEJM Journal Watch, 26. 2. 2020.

"The five studies with nonquarantined control groups ***confirmed distressing impacts on both ordinary people and healthcare workers****, including anxiety, depression, anger, irritability, and post-traumatic stress disorder (PTSD)."*

30) The psychological impact of quarantine and how to reduce it: rapid review of the evidence.

S. K., et al. The Lancet, 14. 3. 2020.

"Overall, this Review suggests that the ***psychological impact of quarantine is wide-ranging, substantial, and can be long lasting****."*

"Review suggest there can be ***long-term consequences that affect*** *not just the people quarantined but also* ***the health-care system*** *that administered the quarantine and the* ***politicians and public health officials who mandated it.****"*