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ALLOSTATIC OVERLOAD AND ITS MITIGATING FACTORS IN THE WHIRLWIND OF THE COVID-19 ERA

PhD thesis

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List of Abbreviations

AL	Allostatic Load
AO	Allostatic Overload
CBT	Cognitive Behavioural Therapy
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
DASS-21	Short version of Depression, Anxiety and Stress Scale
DCPR-SSI	Diagnostic Criteria for Psychosomatic Research Semi -Structured Interview
DIY	Do It Yourself
fPE	Practice of 3-1-2 meridian exercise at least 3-5 times a week
GAS	General Adaptation Syndrome
GPs	General Practitioners
HPA	Hypothalamic - Pituitary - Adrenal
HRQOL	Health-related quality of life
NCS	Non-Clinical Sample
PE	Practice of 3-1-2 meridian exercise 1-2 times a week
PHS-WB	Public Health Surveillance Well-Being Scale
PROMS	Patient-Reported Outcome Measures
PSI	Psychosocial Index
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SQ	Kellner's Symptom Questionnaire
WHO	World Health Organization

1. Introduction

1.1. Stress

1.1.1. An overview of the establishment of the concept and early research

The concept of stress and its role in health and disease stimulates continuously expanding research. It represents a diverse force or drive that is essential for the evolution of life [1]. The currently used definition was introduced by Hans Selye in 1936, who defined it as "the nonspecific response of the body to any demand made upon it, that is, the rate at which we live at any one moment" [2]. His scientific work has been decisive in further understanding of what stress is and what it does to living organisms. From early on, he suspected the existence of stress and its impact on the body and besides his own laboratory work, he investigated several researchers' work to support his concept by theirs.

Claude Bernard had developed his theory of the internal environment or in French "milieu intérieur", i.e.: "The constancy of the internal environment is the condition of a free and independent existence" and published it in 1865 [3]. Bernard explained the concept of necessity to maintain that internal milieu and described the features of bodily fluids. Replacing the ancient idea of life forces, Bernard based his concept on a mechanistic process in which physiology of the body was regulated by equilibrium adjustment feedbacks [4].

In 1932 Cannon further developed Bernard's concept of milieu intérieur and created his own theory of homeostasis [5]. He described it as "coordinated physiological processes, which maintain most of the steady states in the organism." He believed in a coordinated self-governing system, which reacts to changing external conditions through physiological mechanism to maintain internal consistency. He further detailed his theory by stating that neuroendocrine responses of the sympathoadrenal system play a pivotal role in preserving a stable internal environment and ensure survival. He described the acute changes in the secretion of the adrenal gland and the consequent activation of the sympathetic nervous system to noxious stimuli, and he named this phenomenon as "fight or flight" response [5]. Cannon's work was enriched by his contemporaries, Pavlov, discovering conditioned reflexes and realising the importance of them on homeostasis, and Barcroft as well, describing the central nervous system and

higher brain function being a mediator of many efferent mechanisms necessary for the stability of the internal environment [6].

Selye further analysed Cannon's concept in the 1940s. He recognised that the "fight or flight" response is only the first step in a complicated process, an initial "alarm reaction", and realised that arousal behaviour states occur under semichronic or chronic conditions as well. In that case, alarm reaction is followed by the so called "stage of resistance" which, under overexposure of stress, eventually converts into the "stage of exhaustion" and finally death. Selye termed this concept as the "General Adaptation Syndrome" (GAS) (see Figure 1.) [7].

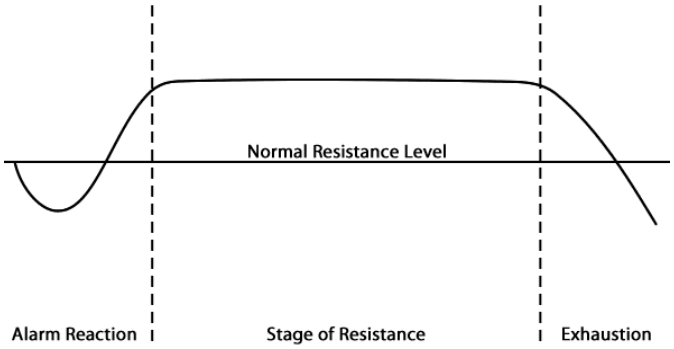

Figure 1. *General Adaptation Syndrome by Selye* [8]

Alarm reaction consists of several mechanisms like increased heart rate, cortisol secretion from the adrenal cortex, tissue catabolism, hypoglycaemia, or gastrointestinal erosions, which Selye observed in his animal experiments. Later he connected these changes to the activation of the sympathoadrenal system. After vanishing during the stage of resistance, these changes reappear in the stage of exhaustion. The released steroids are pivotal for the resistance, but they also cause pathological changes in the body. The adaptation energy of the living organism is only sustainable for a limited quantity. Therefore, in GAS, manifestations of damage and defence caused by stress are inseparably mixed [7, 9].

Selye stated that "all living beings are constantly under stress and anything, pleasant or unpleasant, that speeds up the intensity of life, causes a temporary increase in stress, the wear and tear exerted upon the body".

So, where is the line between "good" and "bad" stress? Distress is a kind of stress that negatively affects the body being associated with higher levels of oxidative damage, while eustress [10] is the manageable level of life stress that energizes and

motivates us to overcome difficulties and sickness and enhances psychobiological resilience to oxidative damage [11, 12].

Selye talked about the “disease of adaptation”, where diseases manifest by a faulty adaptive reaction to stress. Hereditary predisposition, diet, and environmental factors determine which organs are involved in this pathological process, that appears only under prolonged systemic stress [2]. As he recognised that both unpleasant stressors and pleasant stimuli drive the adrenal cortex to release the same glucocorticoids, he distinguished them by their nature. He encouraged to avoid distress that is noxious stress by “finding one’s own natural stress level”, practice “altruistic egoism” and “earn the neighbours’ love” (“avoid the stress of conflict, frustration, and hate, to achieve peace and happiness”) [2].

1.1.2. Stress from a functional network approach - allostasis, allostatic load, allostatic overload

In 1988 Sterling and Eyer introduced a new term called „allostasis” [13]. It reached beyond Cannon’s „homeostasis” concept as they reinterpreted internal consistency that Cannon had talked about. The new concept recognised that “to maintain stability an organism must vary all the parameters of its internal milieu and match them appropriately to environmental demands” [13]. They confirmed the necessity of the brain playing a pivotal part in keeping allostasis thus extend the concept of homeostasis that relies on local adjustment feedbacks. It is the complex system of the brain and the body that allows synchronization of resources and needs. While negative feedback mechanisms work with specific setpoints, in allostasis there is a continuous tracking of need and readjustment of setpoints [13].

In 1993 McEwen explained allostasis as „rather than maintaining constancy, the physiologic systems within the body fluctuate to meet demands from external forces” [14]. He also defined “allostatic state” later as “altered and sustained activity levels of the primary mediators, e.g., glucocorticosteroids, that integrate physiology and associated behaviours in response to changing environments and challenges such as social interactions, weather, disease, predators, pollution” [15]. He confirmed that there is no ideal set of conditions to maintain internal stability and different stressors cause the activation of different patterns of the sympathoadrenal systems. But he pointed out that the concept of allostasis does not include the effect of elongating chronic stress and

its potential pathological consequences on the body. So, he further analysed what happens to the body when external challenges increase the activity of the balancing mechanisms. The heavier the strain that burdens the body is, the more intense response the body needs to give to balance it out. The repeated load on the body, the elevated activity and changes of the physiological systems and the wear and tear on tissues and organs develop pathologies, thus, they cumulate and lead to disease. He called this "cumulative result of allostatic state" of the body as "allostatic load", which implies that "there is a steady state in which ongoing environmental challenge is balanced by a physiologic response that is elevated above the basal level". In other words, allostatic load (AL) is the cost of the adaptation to adversity. If stress does not resolve, the body remains on high alert, and eventually it learns how to cope with higher stress levels by continuous secretion of stress hormones [14].

If further loads accumulate in one's life such as unpredictable events, diseases, stressful social interactions, allostatic load may increase drastically, exceeds one's capacity to cope and allostatic overload (AO) occurs, and like in Selye's concept, the body arrives in the exhaustion stage [15, 16], a state in which stress-related mood-changes, sleep disruption, somatization, and interpersonal tensions occur [17]. McEwen differentiated two different types of AO. Type 1 AO occurs when energy demands exceed energy income, while Type 2 AO means that the body is overloaded with energy intake [15]. The cardiovascular, the metabolic, the immune and the nervous system all respond to external challenges. They are all involved in the body's coping mechanism and in an ideal state, they can be mobilized quickly, then "turned off" when not needed. When they become overactivated and cannot be switched off, that is when they develop diseases and lose their capability to be "turned on" when there is a need in restoring stability [18].

1.1.3. Neurobiological background of stress

It is now established that stress can cause ill health [19]. Individual vulnerability towards stress is determined by genetic, behavioural, and environmental factors, all interacting constantly throughout life to shape one's risk to and resilience against diseases [20]. These interactions happen through several neurobiological pathways. The brain is the central organ that coordinates stress reactivity and determines appropriate physiological responses to threatening stimuli [21, 22]. It constantly discriminates

harming inputs from benign ones and engages the body to respond to them using the available adapting coping mechanisms of the individual [20, 23]. It shows both structural (synaptic and dendritic remodelling, suppressed neurogenesis, atrophy) and functional plasticity and vulnerability to changing conditions [21, 24]. Stressful stimuli and triggered changes of stress hormones lead to both adaptive and maladaptive changes on the associated brain regions throughout life [20, 25]. These brain changes caused by chronic stress and AL holds the body back from being able to process stressors cognitively and respond to them physiologically [26]. If one is able to overcome stressful life events, beneficial adaptation can lead to future resilience, however other stressful experiences can lead to neural changes and pathophysiological states by overactivated mediators in a dysregulated manner, that contribute to compromised resilience and vulnerability to ill health [20, 25, 27].

Main brain structures that play an important part in regulating physiological and behavioural stress processes are part of the limbic system, the hypothalamus, the hippocampus, amygdala, and areas of the prefrontal cortex [20]. In the hypothalamus sympathetic nervous system is activated resulting in release of noradrenalin from the post-ganglionic fibres and adrenalin from the adrenal medulla (sympathetic–adrenal–medullary (SAM) axis) [28]. It is in the prefrontal cortex, where excitability of noradrenergic neurons maintain cortical vigility induced by stress [29] and the nucleus of tractus solitarius also receives projections from these brain centers [30]. Furthermore, the paraventricular nucleus of the hypothalamus is responsible for secretion of corticotropin-releasing hormone and vasopressin to further activate the release of corticotropin from the anterior pituitary, which then stimulates the adrenal cortex to release glucocorticoids (hypothalamic–pituitary–adrenal (HPA) axis) [28]. The fine-tuned functioning of these two axes play a pivotal role in providing proper distress-related response and their pathological dysregulation can potentially progress to stress-related disorders [31].

Body and brain are affected by mediators of allostasis simultaneously [24]. The biological model of AL, that McEwen and his colleges described, include a network of autonomic, endocrine, metabolic, and inflammatory mediators [18].

These mediators include hormones like the above mentioned adrenaline, noradrenaline, or dehydroepiandrosterone-sulphate produced by the sympathetic–

adrenal–medullary (SAM) axis, glucocorticoids (cortisol) induced by the hypothalamic–pituitary–adrenal (HPA) axis [30], but insulin, glucagon, and cytokines produced by immune cells, the brain, and the pancreas also play important parts in stress-response. Further biological markers of allostatic load and overload include systolic and diastolic blood pressure, body mass index, waist-hip ratio, high-density lipoprotein and low-density lipoprotein cholesterol, triglycerides, cholesterol, cholesterol/high-density lipoprotein ratio, glycosylated haemoglobin [HbA1c], fasting glucose, plasma C-reactive protein, fibrinogen, serum measures of interleukin-6, the soluble adhesion molecules E-selectin, intracellular adhesion molecule-1, and overnight urinary cortisol and catecholamines [18, 32–34].

Epigenetic dysregulation in the HPA axis and reward circuitry is associated with stress-induced and psychiatric disorders [24, 35–37].

Recent research has shown reciprocal communication between brain and body not just through neural pathways [7] but endocrine mechanisms as well [21]. These bidirectional mechanisms are important in short-term adaptation to stress, but can lead to maladaptive states on a long term [20].

Identifying allostatic load by its biological markers has been in the centre of research for many years [16, 18, 32]. Measuring various biomarkers, early detection of health consequences of AL is possible in high risk individuals [33, 38, 39]. But paying attention to identifying other measures as well, e.g., psychosocial, genotypes, and phenotypes is just as important in early prediction of co-morbid diseases as there is a non-linear interaction between mediators of AL and disease susceptibilities and therefore we cannot predict manifestation of diseases only based on these mediators [40].

The discovery of hippocampal adrenal steroid receptors transformed the meaning of “stress” in terms of the concepts of allostasis, AL and AO realizing the key importance of life style and health behaviors along stressful experiences [21]. Risk behaviours that increase the odds of pathological consequences have a reciprocal relationship with AL and are essential to evaluate when one attempts to predict and determine allostatic load and overload [33]. To measure the risk of allostatic load by biomarkers, a cumulative index has been developed, and even though it predicted clinical manifestations, pathology and mortality more sensitively than individual

parameters alone, it was too complex to easily be used in a clinical setting and only considered biomarkers ignoring other measures such as the utmost important health behaviour [32, 41].

1.1.4. Clinimetric definition of allostatic load and overload

As it is clear by now that stress along health behaviours leads to clinical manifestations of allostatic load and overload, thus, the clinical approach of allostatic states has become crucial in medical practice [17].

Clinical measurement of allostatic overload was introduced by Fava and colleagues in 2010 [17]. They developed clinimetric criteria to determine allostatic overload by assessing patients' life circumstances and clinical symptoms [42]. The term "clinimetrics" had been introduced by Alvan R. Feinstein in the 1980s [43]. Clinimetrics provides a frame for patient-reported outcome measures (PROMs) to measure clinical signs and physical symptoms by a set of rules. While psychometric criteria focus on the homogeneity of components and unidimensionality, clinimetrics do not require those (see Table 1. of Supplementary Material). Instead, sensitivity is the key, which was defined as "the ability of a rating or self-rating scale to discriminate between different groups of patients suffering from the same illness (e.g. depressed inpatients and outpatients) and to reflect changes in experiments in therapeutics such as drug trials" by Kellner [44]. Thus, psychometric guidelines do not consider the complexity of clinical challenges due to their request for homogeneity of components and lack of attention to sensitivity [44], while clinimetrics, being the science of clinical measurements, may offer conceptual base to assess a wide range of clinical issues [45].

AO may be evaluated by clinimetric tools, but proper exploration of the patient's history, life circumstances and symptoms is required [42]. The clinimetric definition of AO is found in the 2017 version of the Diagnostic Criteria for Psychosomatic Research Semi-Structured Interview (DCPR-SSI) [46]. Clinimetric evaluation of allostatic overload recognizes the importance of the individual's resources and cognition alongside of the influence of the physiological response, which was emphasised by Selye and Cannon in their stress-models. Even though stress activates a certain biological pattern, one's sensitivity to stress alters the physiological response, which is not considered by the above-mentioned models. Fava and colleges tried to overcome

this shortcoming by the clinimetric evaluation of allostatic overload and determining the "state that, by exceeding individual resources, may constitute a danger to health" [17].

In a rushing clinical practice, it is not always possible to use the DCPR-SSI due to its time-, and professional knowledge-consuming properties. Fava used a self-rating questionnaire, the Psychosocial Index (PSI), which holds its place in a clinical setting as well [47, 48]. When it comes to the evaluation of allostatic overload, the two measures overlap each other, thus, AO PSI items can be matched with the DCPR-SSI criteria [49]. The only item that PSI does not include is the allostatic-overload specific question to evaluate if stressors have exceeded one's capacity. During the Coronavirus disease 2019 (COVID-19) epidemic PSI has been used to evaluate allostatic overload without the above-mentioned question [50].

1.2. A positive approach to health

The positive aspects of mental health and improvement of well-being have been emphasized in recent research [51, 52]. Based on the 1948 WHO definition "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [53]. In the 1950s, Marie Jahoda Austrian-British social psychologist confirmed that it is wrong to determine health with the absence of disease and outlined the criteria for positive mental health:

- "autonomy (regulation of behaviour from within),
- mastering life situations ("environmental mastery"),
- satisfactory interactions with other people and the milieu,
- the individual's style and degree of growth,
- development and self-actualization,
- and the attitudes of the individual towards his/her own self (self-perception / acceptance)" [51, 54].

1.2.1. Well-being

According to Centers for Disease Control and Prevention (CDC) there is no consensus on a definition of well-being, but it can be explained as a dynamic and relative state where optimal experience with physical, mental, and social functioning are integrated in the context of a supportive environment with numerous benefits to health, social connections, work performance, and economic status [55–57]. ''Health-related

quality of life'' (HRQOL) is sometimes used to refer to the same concept, but while the evaluation of well-being focuses on the experience of the positive (contentment, satisfaction, autonomy, meaning, and relationship quality), HRQOL measures usually focus on the deficits (impact of illness, injury, pain, symptoms or life impairments) [58]. Altogether, the comprehensive definition of well-being includes all the physical, mental, and social domains. Individuals with higher levels of well-being are not only happier, but they are in better health with decreased risk of illnesses. Also they are more successful at work with higher salaries, have more meaningful relationships, and are more likely to actively contribute to their communities [56].

Tabibnia uses these three pillars of well-being in her tripartite model of building resilience. The mental domain can be identified as the cognitive and behavioural coping to down-regulate the negative. The physical domain appears in the enhancement of the physical health by exercise, sleep and dietary restrictions, while the social domain is listed under social connectedness, both to up-regulate the positive [59].

Defining figures of well-being and positive mental health researches include the earlier mentioned Marie Jahoda [54] and Carol Ryff [60]. Their approach to well-being considers human development and existential challenges of life as pre-requisites for thriving and root in a deep Greek historical background [60]. Ryff identifies with an eudaimonic approach toward well-being [61, 62], where meaning and self-realization and fully functioning are in focus in oppose to the hedonic approach, where the attention is on happiness, pleasure attainment and pain avoidance [60, 63]. It all goes back to Aristotle, who termed eudaimonia and defined it as a higher human good, which is not happiness, or satisfaction but it is about striving to achieve our best [64]. Eudaimonia captures the essence of awareness of one's self and talents, and becoming the best of one's self [65]. Eudaimonic approach to psychological well-being established the conceptions of self-realization and finding meaning in adversity. Ryff's theoretical model of psychological well-being determined 6 distinct dimensions of wellness:

- autonomy
- environmental mastery
- personal growth

- positive relation with others
- purpose in life
- self-acceptance [66–68].

In 1989 after analysing and summarizing literature on mental health, Ryff compiled a psychological well-being scale which consist of 84 questions (or in a shorter form of 54 questions). The items reflect on the six dimensions and can be answered on a 1 to 6 scale, 1 indicating strong disagreement, 6 indicating strong agreement. Ryff Scales of Psychological Well-Being is one of the prototypes of the patient-reported outcome measures (PROMS), and is an instrument that measures the theoretical core dimensions of psychological well-being [66].

However, there are other measurement tools to evaluate all aspects of well-being including physical and social aspects as well. One of them is the Public Health Surveillance Well-Being Scale (PHS-WB), which was created by Bann et al. in 2012. Their project included the review of comprehensive literature of the social, behavioural, health, policy and economic sciences, public health, and psychology fields to identify a well-being patient-reported outcome measure compatible for public health surveillance [58].

Kellner's Symptom Questionnaire (SQ) also provides a clinimetric evaluation [69] of well-being (contentment, relaxation, friendliness, and physical well-being) besides assessment of distress symptoms (depression, anxiety, hostility, and somatization). Focusing on physical well-being as well, it gives a broader insight on aspects of WB.

Moreover, not only PROMs are available, but interview formats and therapeutic modules have been recently developed to identify the domains of psychological well-being and enhance performance on each domain [70, 71].

1.2.2. Euthymia

When it comes to assess psychological health, it is important to concentrate on the positive besides the negative. In 1991, Garamoni described healthy functioning as an optimal balance of positive and negative perceptions and emotions and marked psychopathology by loss of this balance [72]. When patients with mood disorders, evaluated by rating scales, do not meet the diagnostic criteria for depression or mania,

their actual state is defined as “euthymic”. Numerous studies have examined the neurocognitive mechanisms, structural disorders, and neurotransmitter changes that cause the transition to acute manic or depressive episodes [73–76]. However, the significant fluctuation in psychological distress described in longitudinal studies [77, 78] suggests that the disease is always active, although its intensity may vary in line with the deterioration in the socioeconomic, psychosocial, and clinical status of patients. It is therefore questionable whether subthreshold periods actually represent euthymia or are simply part of the manifestations of bipolar disorder. Similar considerations apply to the use of the term euthymia in unipolar depression and dysthymia [79]. Therefore, euthymia is defined in a fundamentally negative sense in psychiatry as the absence of a certain intensity of mood symptoms and not as the presence of specific positive traits characterizing healing. But if these positive aspects are overlooked in remission, relapse may easily occur [51]. So, it is important to shift the goal of treatment, which Giovanni A. Fava did in the interpretation of Well-Being Therapy, a psychotherapeutic method developed by him [71]. The concept of euthymia approached by Fava is not identical to psychological well-being of all dimensions by positive psychology [72, 80–82]. In an individualized and balanced focus, as opposed to most positive interventions, his patients are encouraged to obtain a balanced functioning (euthymia) besides pursuing the highest possible levels of psychological well-being. A state of euthymia could vary in individuals, based on personality, cultural and social roles [83, 84].

Thus, the work of Fava is decisive in a value-driven presentation of the concept of euthymia. In the course of his work, he described the birth of the concept [51] and its clinical validity in detail [83], both of which are established by neurobiological background by Tabibnia et al. [59]. Fava defines euthymia as the optimal state of balanced positive and negative effects and determines three main pillars: lack of mood swings, occurrence of negative mood and emotional episodes only for a short time; the presence of positive effects, i.e. the individual feels cheerful, calm, active, interested, his sleep is relaxing; and achieving psychological well-being (flexibility, consistency, resilience) [84]. This last pillar is based on Marie Jahoda’ 1958 outlined characteristics related to the concept of euthymia, defined as integration:

- “individual’s balance of physic forces (flexibility),

- the unifying outlook on life, which guides actions and feelings to shape the future accordingly (consistency),
- and resistance to stress (resilience and anxiety or frustration tolerance)" [54].

The concept of euthymia reconnects to Selye by using the term "eustress" to state that stress should not be suppressed in all its forms, the goal is to reduce anxiety and achieve a psychological sense of well-being, thus to live with stress without it causing psychological distress [2].

1.2.3. Resilience

The issue of flexibility and resilience has been in focus of research in recent years [85–91]. Mental health and psychological resilience has been defined as a state of well-being where one is able to recognize their abilities and needs to cope with stress of life adaptively, work productively, and make a contribution to their communities during acute or chronic adverse circumstances or to return quickly to a pre-crisis state [92–94]. The lack of this ability is likely to lead to depression, anxiety, and the experience of negative emotions more frequently or intensively [51]. Vulnerability and resilience to stress is highly unique, gender-specific, and depends on individual adaptive stress responses and behaviors defined by the genetically encoded biological structure, as well as environmental effects [14]. Psychological, social and behavioural factors throughout a lifespan can build resilience, which then facilitates resistance to disease, thus, resilience is linked to well-being, e.i. one's quality of life depends on their mental toughness [53, 59, 93].

Thus, building resilience as a part of one's well-being may lead to the ability to avoid stress to become toxic [95]. In Tabibnia's tripartite neurobiological model, inhibition or down-regulation of the "negative" through anxiety networks (responses of the HPA and SMA axes) by behavioural and cognitive coping, the stimulation of the "positive" through reward networks by optimism, active attention to physical health, socializing, and, as a third pillar, transcending the self through the "default" networks by mindfulness, exposure to nature, "flow" [96, 97] or religious engagement are essential to achieve optimal balance [59].

An unexpected stressful adversity like COVID-19 may counteract with possible distress-reduction like exposure, active coping, stress inoculation, and cognitive

behavioural therapy (CBT) due to confinements. It becomes almost impossible to avoid the stressor as it surrounds all individuals, and it brings such a new way of inexperienced and locked down lifestyle that active coping becomes hindered. Thus, a world epidemic may shift the focus to working on the positive instead of trying to block out the negative [98–100]. The first wave of the COVID-19 pandemic especially meant an excessive stressor for all, that brought fear, health-damaging consequences and superimposed on other life stressors, potentially causing allostatic overload. Against such a diverse strain, one needs to find ways to coping.

Active health-prevention activities like physical exercise may play a pivotal part in building resilience and avoidance of negative consequences of a phenomena like COVID-19 [101, 102]. 3-1-2 Meridian Exercise being a Chinese 30-minute medium-strength aerobic formula physical exercise, which can be easily performed without equipment by the older generations as well with the purpose of health preservation, offers an opportunity to include physical exercise in one's daily life even during adverse circumstances. Besides physical activity, recreational activities being rewarding experiences that are personally meaningful, can help the individual find purpose and fight against acute or chronic adversity by adopting positive coping strategies.

Achieving and maintaining the status of euthymia is a key health prevention tool. Increasing resilience also plays a major role in the fight against everyday stress. It is most important today to offset the negative with the positive, especially during the increasing challenges of everyday life with regard of the pandemic or the war around us. There is a need to consciously find the means to reach the state of well-being and thereby strive to maintain health and resist overloading stress [103] by finding meaning in adversity or an absurd world.

2. Objectives

Clinimetric evaluation expands the customary taxonomy by evaluating patterns of symptoms, severity and progression of illness, effects of comorbid conditions, functional capacity. It is to distinguish prognostic and therapeutic differences among seemingly similar patients with the same diagnosis and lab results [43]. We intended to measure allostatic load from a clinimetric perspective, specifically focusing on the first wave of COVID-19. The ongoing pandemic and the related restrictions have appeared as strong stressors for many people. Not only it could be considered as a universal stressor resulting in significant change of socioeconomic and work conditions, but it also specifically puts a burden on the health care system affecting professionals and patients as well [104]. We took two specific groups into consideration for research purposes.

We explored allostatic overload and well-being in an aging general population sample, who practiced regular, uniform, moderately intensive aerobic exercise (3-1-2 meridian exercise).

Hungarian general practitioners were exposed professionally not only by means of change in daily work (acute infectious cases and their communities), but through the interruption of patients' way in the healthcare system (disrupted care of chronic patients) beside their own fears as aging humans. We evaluated the prevalence of allostatic overload among them as well and defined its most important predictors. We measured their well-being, forms, and regularity of recreational activity they practiced to increase mental and physical health, as well as resilience against stress load.

Our hypotheses were the followings:

I. The infection itself and the health care confinements both might have contributed to the stress burden of an aging population, but we postulated that among those, who practice regular 3-1-2 meridian exercise with the aim of active health preservation, the prevalence of AO would be lower than in those who practice it irregularly or do not at all.
II. Our further hypothesis was that due to the active health-preserving activity – those who regularly practiced 3-1-2 meridian exercise, had better physical well-being than those who did not.

III. Working in the frontline, GPs were exposed to the infection while having had to provide adequate care to their patients in adverse circumstances. We assumed that these aspects accumulated in high prevalence of AO.
IV. Among GPs we aimed to assess individual habit of recreation and postulated that regular recreation was associated with lower prevalence of AO.

3. Methods

3.1. Study design and sample recruitment

3.1.1. Sample of a non-clinical aging population

We conducted cross-sectional research after the first wave of the COVID-19 pandemic. We performed a voluntary and anonymous online survey on platform Google Forms between 21 May and 1 September 2020 among certified 3-1-2 meridian exercise instructors and their communities. All participants were recruited via email, using the official mailing list of certified instructors. Additionally, control cases were recruited through personal contacts as well. In our invitation letter we clarified that the Family Medicine Department at Semmelweis University conducted the survey. We defined the length of completing the survey and our aim. We set out to explore the effects of the first wave of the pandemic during the previous six months on them. We did not offer monetary or non-monetary incentives and sent out one reminder after two weeks.

3.1.1.1 Physical exercise in the form of 3-1-2 Meridian Exercise

It was our intention to target a group of non-clinical adults who, with the intention of health prevention, practice formula exercise within controlled circumstances to secure homogeneity of the sample. 3-1-2 Meridian Exercise is a Chinese 30-minute medium-strength aerobic physical exercise introduced by Prof. Zhu Zong-Xiang. This is a uniformed identically performed exercise sequence in all areas of Hungary coordinated by hundreds of certified instructors and practiced by thousands of exercisers. “Three” refers to the massage of three acupoints (LI-4 (Hegu), PC-6 (Neiguan) and St-36 (Zusanli)). “One” stands for abdominal breathing and “two” is for squatting. It is known and practiced worldwide with the purpose of health preservation, has no contraindications, and can be easily performed by the older generations as well. It has been widely practiced in Hungary as well after being naturalized in the country by Prof. Ajándok Előry in 1985. Its characteristics meet the WHO recommendations of physical activity, which is defined as a “bodily movement produced by skeletal muscles that requires energy expenditure” [105]. All movement done during leisure time is considered physical activity, and regardless its intensity, it is proven to improve health and help prevent diseases such as cardiovascular diseases, diabetes, cancer,

hypertension. It also has beneficial effects on mental health, quality of life and well-being [105].

WHO specifies the recommended amount of physical exercise a week: "Adults aged 18–64 years should do at least 150–300 minutes of moderate-intensity aerobic physical activity; or at least 75–150 minutes of vigorous-intensity aerobic physical activity; or an equivalent combination of moderate- and vigorous-intensity activity throughout the week." [105].

In our sample, the frequency of the meridian exercise was specified, as well as how long it has been practiced. We grouped our participants based on the frequency of meridian exercise practice to match WHO recommendation, to those who practiced exercise frequently as recommended (at least 30 minutes 3-5 times weekly) (fPE), those who practiced regularly but the frequency did not reach the recommendation (1-2 times weekly) (PE) and those who did not practice at all or practice irregularly. Latter meant our control group.

3.1.2. Sample of Hungarian general practitioners

We collected data among Hungarian general practitioners (GPs) between 28 August and 16 October 2020. Our sample was homogeneous since we only included general practitioners. Participants were recruited via institutional sources (1,262 registered email addresses of GP surgeries or family physicians throughout Hungary), and again, we named the Family Medicine Department at Semmelweis University as conductor of the survey and claimed the necessary time frame to complete it (15-20 minutes). We stated the aim of the survey and did not offer any monetary or non-monetary compensation. After the initial email, one reminder was sent out to all available email addresses between 8-10 September.

3.1.2.1. Recreational resources

While in our non-clinical sample we had a hypothetic protecting factor against allostatic overload, we needed a mitigating factor against AO to measure in our GP sample as well. Additionally, to the items of the first investigation among non-clinical adults, here we offered multiple possibilities for recreation to choose from besides providing option for individual answers. Recreational activities are rewarding experiences that are personally meaningful and help the individual arrive in the present,

disengage from the burdening self-oriented default mode and thus boost resilience, the ability to face acute or chronic adversity by adopting positive coping strategies [59]. Active recreation facilitates coping mechanisms and well-being, it is easily accessible and by all that, it helps counteract chronic stress [106]. The inspiration behind monitoring recreational activities among GPs came from UK's Coach Magazine article, where the importance of 30-minute-a-day-recreation in the light of mental health is emphasised [107]. Easily achievable lifestyle interventions play a pivotal role in boosting resilience since isolation and increased workload limit the opportunities of external help. When creating categories of stress releasing recreational activities, we selected the Mental Health Foundation (UK) 'How to manage and reduce stress' booklet [108] as well as the American Counseling Association's article '100 Ways to Reduce Stress: Making the Balancing Act More Manageable' [109] to support our choices. Thus, we offered multiple recreational categories for our participants (connection with nature, reading or watching movies, physical exercise, meeting friends and acquaintances, cooking, praying or meditation, creative manual and Do It Yourself (DIY) activities, or beautification and cosmetics) and they could mark any of them they practice, also they were able to provide their own individual answers on their sources of recreation as well.

They were asked about the number of days when they chose to take time to do recreational activities for at least 30 minutes during a week. We grouped them based on the number of days they take at least 30 minutes for recreation: 5-7 days, 3-4 days, and 0-2 days were determined for frequency. Latter meant our control group.

3.1.3. Data collection

Personal data was not collected in either case and accordingly we performed data analysis anonymously, but we generated an ID code for each participant in both data collection for a possible follow up. Online consent was given by all participants. Both surveys were constructed in a way that all answers had to be given to the items of the measurement tools to continue with the survey; therefore, we did not need to exclude anyone due to incomplete reply to any questions.

Inclusion criteria were above 18 years of age and understanding of Hungarian language. Participants needed to be willing to complete the survey.

Exclusion criteria were under 18 years of age, no access of the online platform, and insufficient understanding of Hungarian language.

Research Ethics Clearance was applied and granted for both studies. Both were conducted by the Declaration of Helsinki and was approved by the review board of the Medical Research Council (IV/5657-2/2020/EKU).

3.2. Measurements

3.2.1. Sociodemographic, health and work-related characteristics

Basic sociodemographic variables like age, gender, place of living, and working conditions were collected. Number of acute diseases, number of chronic diseases and self-reported psychiatric conditions were also registered, as well as drug consuming habits, like number of prescribed and over-the-counter medicines taken daily. We also inquired about need of health care services during restrictions in both studies. Among GPs working conditions were specifically detailed including whether they had actively worked during the pandemic and their method of working (personal, phone consultations, other).

3.2.2. Measurement tools

3.2.2.1. Allostatic overload

In both studies we measured COVID-related allostatic overload according to Fava's definition [17] based on the Diagnostic Criteria for Psychosomatic Research Semi-Structured Interview (DCPR-SSI). It measures allostatic overload via items related to stress factors (A1 criterion), the perceived burden of these factors (A2 criterion) with stressor-related distress symptoms (B1 criterion), social (B2 criterion) or environmental inadequacies (B3 criterion) [46]. We used the Psychosocial Index (PSI), which is a self-rating questionnaire to cover each criterion [47]. PSI was introduced by Sonino and Fava in 1998 including 55 items. It is a self-rated scale used to evaluate stress, well-being, distress, illness behaviour, and quality of life [47]. PSI items can be found in detail in Table 1.

Stress: this scale contains 17 items (13-20, 22-30) with yes/no answers. From 13-20 and 23-30, "yes" is worth 1 point and indicates stress, while "no" is worth 0 points and shows the absence of stress. Item 22 is reverse scored, with "yes" worth 0

and "no" worth 1. The total score can vary between 0 (no stress) and 17 (maximum stress).

Well-being: this scale consists of six items (31-36) with two possible choices (yes/no). A "yes" answer to items 31-32 is worth 1 point, while a "no" is worth 0. On the other hand, the scoring is reversed for items 33-36: the answer "yes" is worth 0 points, while the answer "no" is worth 1. The total score can scale between 0-6.

Distress: this scale consists of 15 items (37-51), four possible choices ranging from no distress to severe distress ("not at all", "only a little", "somewhat", "a great deal"). The answer for each item can range from 0 to 3, with higher values indicating more severe distress. The total score may vary between 0 and 45. Items 37-40 refer to sleep disorders, they can be evaluated separately (from 0-12).

Abnormal illness behaviour: this scale consists of three items (52-54) with four choices from none to maximum abnormal illness behaviour ("not at all", "only a little", "somewhat", "a great deal"). The score to each items range from 0 to 3, total score from 0 to 9.

Quality of life: this scale consists of item 55: "How do you rate the quality of life?" five choices of answer are provided ("excellent" "good" "fair" "poor" "awful"). The maximum possible rating is 4, minimum is 0, where 4 is "excellent" and 0 is "awful". Psychological well-being (0-6) and quality of life (0-4) may be summed to obtain a global well-being score [48].

We matched items of PSI to criteria of DCPR-SSI to be able to conduct the studies online due to lack of personal contact with our participants due to COVID.

We specifically aimed to measure COVID-19 as a stressor, however, we listed other possible personal stressors (A1 criterion) as well. To focus on stress caused by the pandemic, we tailored A2 criterion asking if it has been exceeding one's coping strategies: 'During the time of the restrictions, did you feel that the changes caused by the coronavirus epidemic were testing or exceeding your capacity?'. B1 criterion (at least two distress symptoms) was covered by PSI items 37-51, while B2 criterion (deterioration of work, home, or human relationships) met PSI items 23-30 and B3 (everyday challenges) PSI items 33-34. According to DCPR-SSI instructions, allostatic overload was diagnosed if A1 and A2, and additionally either one or more of the B criteria were realized. We measured stress load independent of COVID-19 (A1) as well

with PSI items 13-20 and 22-30. We excluded the first 12 questions of PSI covering socio-demographic characteristics.

Clinimetric criteria of allostatic overload based on the Diagnostic Criteria for Psychosomatic Research Semi Structured Interview (DCPR-SSI) which was applied via the Psychosocial Index (PSI) is demonstrated in Table 1.

Table 1. Clinimetric criteria of allostatic overload by the Diagnostic Criteria for Psychosomatic Research Semi Structured Interview (DCPR-SSI) and the Psychosocial Index (PSI) [49].

ALLOSTATIC OVERLOAD		
	DCPR-SSI [46]	**PSI** [47]
Criterion A	***A1***	***items***
	the presence of a current identifiable source of distress in the form of recent life events and/or chronic stress	• death of a family member • separation from spouse or long-time partner • recent change of job • financial difficulties • moving within the same city • moving to another city • legal problems • beginning of a new relationship • seriously ill close relative
	A2	***COVID-specific question***
	the stressor is judged to tax or exceed the individual coping skills when its full nature and full circumstances are evaluated	*'During the time of the restrictions, did you feel that the changes caused by the coronavirus epidemic were testing or exceeding your capacity?'*
Criterion B	***B1***	***items***
the stressor is associated with 1 or more of the following 3 features which have occurred within 6 months after the onset of the stressor	at least two symptoms • difficulty falling asleep • restless sleep • early morning awakening • lack of energy • dizziness • generalized anxiety • irritability • sadness • demoralization	• long time to fall asleep/restless sleep/waking up too early/feeling tired waking up • stomach, bowel pains • heart beating quickly or strongly without any reason • pressure or tightness in head or body/ dizziness • breathing difficulties • tired, lack of energy • irritable/sad/tense/lost interest • panic attacks

	B2	***items***
	significant impairment in social or occupational functioning	• work-related: satisfying/under pressure/problems with colleagues/unemployed • serious arguments with close relatives/others • tension at home • living alone/feeling lonely • anyone to trust and confide in • getting along well with people
	B3	***items***
	significant impairments in environmental mastery (feeling overwhelmed by the demands of everyday life)	• Do you often feel overwhelmed by the demands of everyday life? • Do you often feel you cannot make it?

3.2.2.2. Distress symptoms

Short version of Depression, Anxiety and Stress Scale (DASS-21) has been developed for assessment of depression, anxiety, and stress. In a rushing clinical setting, the short version of the scale (DASS-21) is usually used, so that is what we used in our online survey as well. We added up the specified item scores to assess depression (3, 5, 10, 13, 16, 17, 21), anxiety (2, 4, 7, 9, 15, 19, 20), and stress (1, 6, 8, 11, 12, 14, 18) [108, 109] in our samples. For evaluation the final score is interpreted based on the following range:

Stress: normal: 0-10; mild: 11-18; moderate: 19-26; severe: 27-34; extremely severe: 35-42.

Anxiety: normal: 0-6; mild: 7-9; moderate: 10-14; severe: 15-19; extremely severe: 20-42.

Depression: normal: 0-9; mild: 10-12; moderate: 13-20; severe: 21-27; extremely severe: 28-42 [110].

Kellner Symptom Questionnaire (SQ) is also a self-rated scale developed by Robert Kellner in 1976 [107]. The questionnaire includes 92 items, 68 on clinical symptoms, and 24 assessing well-being. Participants check YES/NO or TRUE/FALSE for each item.

The tool consists of 4 scales: depression, anxiety, somatization, and hostility. Each are divided into 2 subscales, adding up to 8 subscales: depression – contentment, anxiety – relaxation, somatization – physical well-being and hostility – friendliness

[102]. To receive a final score for each scale, we summed the symptom subscales with the reverse of each corresponding wellbeing subscale:

ANXIETY: Anxiety + Relaxation (reverse score)

DEPRESSION: Depression + Contentment (reverse score)

SOMATIZATION: Somatic Symptoms + Physical Well-Being (reverse score)

HOSTILITY: Hostility + Friendliness (reverse score)

A total psychological distress score can be calculated by adding up the four scales (ANXIETY + DEPRESSION + SOMATIZATION + HOSTILITY).

A total well-being score can be calculated by adding up the four well-being scales (Relaxation + Contentment + Physical Well-Being + Friendliness)

3.2.2.3. Well-being

We used Kellner's Symptom Questionnaire (see above) and the Public Health Surveillance Well-being Scale (PHS-WB) to measure well-being. PHS-WB was developed by Bann and colleagues in 2012 to measure mental, social and physical well-being [58]. Three different aspects of well-being are differentiated by this questionnaire using 10 items.

The first 3 items:

1a: I am satisfied with my life.,

1b. My life has a clear sense of purpose.

and

1c. Most days I feel a sense of accomplishment from what I do.

can be answered on a scale from 0 to 5, 0 indicating total disagreement with the statement, while 5 being complete agreement.

Items

2a. How much of the time during the past 30 days have you felt cheerful?

and

2b. How much of the time during the past 30 days have you felt hopeless?

can be answered on the same scale 0 indicating none of the time, 3 indicating some of the time, while 5 indication all of the time. Total of those 5 answers result in a score of mental well-being.

The next 2 items:

3a. How satisfied are you with your family life?

and

3b. How satisfied are you with your friends and social life?

provide scales from 0 to 10, 0 indicating total dissatisfaction, while 10 being total satisfaction, and they are converted into a 0 to 5 scale to be evaluated. The sum of those gives a final score of social well-being.

Items

3c. How satisfied are you with your energy level? (on scale 0-10),

4. In general, would you say your health is? (on scale 0-5: excellent – very good – good – fair – poor),

and

5. During the past 30 days, for about how many days have you felt very healthy and full of energy? (on scale 0-30)

provide the score of physical well-being after their scales are unified [93].

3.2.2.4. Hungarian validation of the measurement tools

The Hungarian validation of the above-described questionnaires (PSI, DASS-21, PHS-WB and Kellner SQ) is currently in progress based on the scientific studies of this thesis. Publications on the validation are expected in the near future (see further details in section 5.6 Future directions / 5.6.3. Process of validation of assessment tools in Hungarian language).

3.3. Statistical analyses

3.3.1. Qualitative methods

To identify the most burdening challenges during the pandemic, we asked for free-text answers in both surveys to the question: ‘What was the biggest challenge for you during the epidemic and the quarantine?’ Participants’ answers ranged from single-word answers to paragraphs. Following qualitative analytical guidelines all free text responses were systematically read by all members of our research group, blocks of text that reported factors contributing to allostatic overload were identified, and provisional code names were assigned to them. We then compared our codes and agreed on common ones, which were then re-examined. We then identified themes to organise coded answers into higher-level concepts that explained the origins of overload, while

constantly checking their interpretation with the original data, and agreeing on a final list of categories.

3.3.2. Quantitative methods

In both studies we used Chi square tests in case of categorical data, two-tailed t-test for normally-, and Kruskal-Wallis test for non-normally distributed continuous variables. Post hoc we applied Dunn's pairwise tests with Bonferroni adjustment for multiple comparisons of the three pairs of groups (fPE: practice exercise at least 3-5 times a week, PE: practice exercise at least 3 times a week, controls: do not practice at all or practice irregularly; 30 minutes of recreation done on 5-7 days, 3-4 days and 0-2 days). Normality of data was assessed by Kolmogorov-Smirnov test. In both cases step forward likelihood ratio logistic regression was applied to identify predictors, like age, sex, place of living, the number of chronic diseases, the number of stressors of AO.

In the case of our non-clinical sample general linear model was applied to measure the effect of the regularity of physical exercise on SQ total well-being adjusting for sex, age, and chronic diseases, while in the case of GPs, step forward likelihood ratio logistic regression was also used to measure the effect of the number of days when at least 30-minute recreation was practiced by the respondents on allostatic overload. We applied 95% confidence intervals (CI). In all cases a p value < 0.05 was considered statistically significant. We applied SPSS-24.0 software (SPSS Inc., Armonk, NY, USA).

4. Results

4.1. Sample characteristics

4.1.1. Sample of a non-clinical aging population

Altogether 442 adults completed the survey, 406 (92%) were women (mean age: 62 years ± 10.6; males: 63.5 years ± 11.5). 276 of them (62%) were retired. 89 (20%) went to their workplace and 52 (12%) worked in home office (25 participants (6%) did not provide information on their work circumstances). 213 (48%) had no chronic diseases, 184 (42%) had one or two, 31 (7%) had 3-5 and 14 of them (3%) had more than five. During the quarantine period 45 persons (10%) developed one, 6 persons (1%) developed two acute conditions. The proportion of acute and chronic conditions distributed equally in this group. Altogether 20 persons (5%) reported to have psychiatric disease. 99 of them (22%) needed the healthcare system in some way and 66 of them (15%) could use it despite the aggravating circumstances.

The sample was not representative due to gender disproportion. According to sex we did not find any statistically significant differences in health-related and sociodemographic characteristics.

4.1.2. Sample of Hungarian general practitioners

We successfully reached 228 GPs, among whose 155 (68%) were females (mean age (range): 57 years ± 25; males: 56 years ± 32. 222 GP colleagues (97%) worked actively throughout the first wave of the pandemic. 155 of them (68%) worked in person in their surgeries. All of them used mixed — personal, phone calls/video calls and online —consultation forms. This sample was not representative either due to gender disproportion. According to sex we did not find any statistically significant differences in health-related and sociodemographic characteristics in this sample either.
Table 2. sums up the number of chronic diseases, psychiatric disease, and drug prescriptions among GPs and NCS.

Table 2. Number of chronic diseases, psychiatric disease, and drug prescriptions among NCS and GPs.

	NCS (n=442)	GPs (n=228)
Number of chronic diseases n (%) 0 (%) 1-2 (%) 3-5 (%) 5< (%)	 213 (48%) 184 (42%) 31 (7%) 14 (3%)	 71 (31%) 122 (54%) 32 (14%) 3 (1%)
Self-reported psychiatric disorders n (%)	20 (5%)	6 (3%)
Drug prescriptions n (%) 0 (%) 1-5 (%) 5< (%)	 217 (49%) 210 (48%) 15 (3%)	 76 (33%) 133 (58%) 19 (8%)

Note: NCS: non-clinical sample, GP: general practitioners

4.2. Allostatic overload

4.2.1. Sample of a non-clinical aging population

Allostatic overload with physical symptoms of distress, impaired social and occupational functioning or declined psychological well-being was experienced by 29% (n=128) of the normative sample, although 33.5% (n=148) of the NCS reported that COVID-related changes exceeded their coping abilities. Those who did 3-1-2 meridian exercise regularly (fPE) were statistically significant less likely to develop allostatic overload comparing to controls ($\chi^2(1) = 5.6$; $p=0.018$).

After adjusting for age, sex, and the number of chronic diseases, each individual life stressor (PSI items of A1 criterion – see in Table 1.) increased the likelihood of allostatic overload by 20% (OR:1.19, CI [1.06 -1.36], $p=0.005$) and anxiety symptoms measured by the Kellner's Symptom Questionnaire by 18% (OR: 1.18, CI [1.13-1.24], $p<0.001$).

4.2.2. Sample of Hungarian General Practitioners

Allostatic overload with physical symptoms of distress, impaired social and occupational functioning or declined psychological well-being was experienced by 57% (n=131) of the GPs, although 60% (n=139) of the GPs reported that COVID-related changes exceeded their coping abilities. Female sex (OR: 1.99, CI [1.06 - 3.74], $p<0.032$) increasing number of individual life stressors (PSI items of A1 criterion – see in Table 1.) (OR: 1.4, CI [1.2 - 1.6], $p<0.001$) increased the likelihood of allostatic overload.

Additionally, we found that each more day, when time was spared for recreation, lowered the odds of AO by 20% (OR: 0.838, CI [0.72 - 0.97], $p=0.020$) after adjusting for age, place of living and chronic diseases.

4.3. Well-being

4.3.1. Physical exercise

337 out of 442 (76%) adults reported to do 3-1-2 meridian exercise, 217 (64%) of them practice it at least 3-5 times a week (fPE), while 120 (36%) find time for it only 1-2 times a week (PE). Our control group consist of the remaining 105 (24%) participants.

Doing 3-1-2 meridian exercise at least 3-5 times a week (fPE) was found to be associated with decreased symptoms of anxiety, and depression as well (see Table 3.). While somatization symptoms proved to be non-significant between exercise groups and controls, the final somatization scale showed better results in the fPE group due to higher scoring on Kellner's QS subscale of physical well-being. Total well-being reached higher scores in the exercising groups and the same good results were shown on both mental and physical aspects of it (see Table 3.).

After adjusting for age, sex and chronic diseases, a significant effect of exercise on well-being outlined ($F(2, 435)=225.0$, $p<0.001$). Planned contrasts revealed that both fPE ($p<0.001$, 95% CI [1.4-3.9]) and PE ($p=0.043$, 95% CI [0.04 -2.83]) associated with significantly higher well-being, compared to control group.

Table 3. Health-, and stress-related characteristics of an adult community sample (n=442) who practice 3-1-2 meridian exercise frequently (fPE) or less frequently (PE) and controls

	fPE (n=217) Mdn (IQR)	PE (n=120) Mdn (IQR)	controls (n=105) Mdn (IQR)	p	p (adj)	p n.s.
Sociodemographic and health-related characteristics						
Sex (female)	196 (90%)	116 (97%)	94 (90%)	n.s.		
Age (SD)	65 (9.1)	64 (9.8)	57 (12.5)	<0.0001		
Stress-related parameters						
Allostatic overload (A1+A2+B1/B2/B3)	53.0 (24.0)	36.0 (30.0)	39.0 (37.0)	0.059		
DCPR A2 criterion	62.0 (29.0)	39.0 (32.0)	47.0 (45.0)	0.015		
Individual life stressors (PSI – A1 criterion)	1.0 (0.0, 3.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	0.001	0.001*	0.669; 0.082$^{\S n.s}$
PSI distress	4.0 (1.0, 9.0)	6.0 (2.0, 11.0)	8.0 (3.0, 14.0)	0.002	0.002*	0.310; 0.284$^{\S n.s}$
Stress (DASS)	2.00 (0.0, 5.0)	3.5 (1.0, 6.2)	4.0 (1.0, 7.0)	0.006	0.012*	1.000; 0.064$^{\S n.s}$
Distress-related characteristics						
Depression (DASS)	2.0 (0.0, 4.0)	3.0 (1.0, 6.0)	2.0 (0.0, 7.2)	0.020	0.017§	0.704; 0.570*$^{n.s}$
Anxiety (DASS)	1.0 (0.0, 2.0)	1.0 (0.0, 3.0)	1.0 (0.0, 5.0)	n.s.		
ANXIETY (SQ)	2.0 (0, 8.0)	4.0 (1.0, 9.0)	5.0 (2.0, 11.5)	<0.001	<0.001*; 0.022§	0.386
Anxiety (SQ subscale)	1.0 (0.0, 5.5)	3.0 (1.0, 6.0)	3.0 (1.0, 8.5)	0.001	<0.001*	0.268; 0.142$^{\S n.s}$
DEPRESSION (SQ)	3.0 (1.0, 6.0)	4.0 (2.0, 7.0)	5.0 (2.0, 9.5)	<0.001	<0.001*	0.270; 0.119$^{\S n.s}$
Depression (SQ subscale)	1.0 (0.0, 4.0)	2.0 (0.0, 4.0)	3.0 (1.0, 6.5)	<0.001	<0.001*	0.135; 0.201$^{\S n.s}$

SOMATIZATION (SQ)	4.0 (2.0, 9.0)	5.0 (2.0, 8.0)	6.0 (3.0, 10.0)	0.008	0.006*	0.226; 0.733$^{\S n.s}$
Somatization (SQ subscale)	1.0 (0.0, 4.0)	2.0 (0.0, 4.0)	3.0 (0.0, 6.0)	n.s.		
HOSTILITY (SQ)	1.0 (0, 5.0)	3.0 (1.0, 5.0)	3.0 (1.0, 9.0)	<0.001	<0.001*; 0.032§	0.554
Hostility (SQ subscale)	0.0 (0.0, 4.0)	2.0 (0.0, 4.0)	2.0 (0.0, 8.0)	<0.001	<0.001*; 0.041§	0.578
TOTAL DISTRESS (SQ)	11.0 (4.5, 25.0)	17.0 (8.0, 28.7)	21.0 (11.0, 39.0)	<0.001	<0.001*	0.153; 0.062$^{\S n.s}$
Well-being-related characteristics						
Relaxation (SQ subscale)	6.0 (4.0, 6.0)	5.0 (3.0, 6.0)	5.0 (2.5, 6.0)	<0.001	0.001*; 0.014§	1.000
Contentment (SQ subscale)	5.0 (3.0, 6.0)	4.0 (2.2, 5.0)	4.0 (2.0, 5.0)	0.039	0.059*	1.000; 0.231$^{\S n.s}$
Physical well-being (SQ subscale)	4.0 (2.0, 5.0)	3.0 (2.0, 5.0)	2.0 (1.0, 4.0)	<0.001	<0.001*	0.150; 0.232$^{\S n.s}$
Friendliness (SQ subscale)	6.0 (5.0, 6.0)	5.0 (5.0, 6.0)	5.0 (4.0, 6.0)	n.s.		
TOTAL WELL-BEING (SQ)	19.0 (15.0, 22.0)	17.0 (13.0, 20.0)	17.0 (11.0, 20.0)	<0.001	<0.001*; 0.024§	0.476
Mental well-being (PHS-WB)	4.4 (3.8, 4.8)	4.1 (3.6, 4.6)	4.2 (3.6, 4.6)	0.004	0.006§	1.000; 0.081*$^{n.s}$
Social well-being (PHS-WB)	4.5 (4.0, 5.0)	4.0 (3.5, 5.0)	4.0 (3.5, 5)	n.s.		
Physical well-being (PHS-WB)	4.3 (3.3, 4.7)	4.0 (3.3, 4.7)	4.0 (3, 4.3)	0.003	0.006*; 0.042§	1.000
Total well-being (PHS-WB)	4.3 (3.7, 4.7)	4.0 (3.4, 4.5)	4.1 (3.5, 4.4)	0.004	0.033*; 0.011§	1.000

*Note: fPE: practice 3-1-2 meridian exercise at least 30 minutes 3-5 times a week, PE: practice 3-1-2 meridian exercise 30 minutes 1-2 times a week, controls: does not practice 3-1-2 meridian exercise at all or do it irregularly; Kruskal-Wallis tests were applied with Dunn's pairwise tests with Bonferroni corrections [p (adj); *=significance between fPE - controls; §=between fPE - PE; p n.s.: non-significant p levels between PE - controls; *$^{n.s.}$: non-significant difference between fPE - controls; §$^{n.s.}$: non-*

significant difference between fPE - PE] to continuous non-normally distributed variables; Mdn: Median, IQR: Interquartile Range.

4.3.2. Recreation

All together large percent of GPs turned out to do actively for their health. 217 (95%) GPs reported they do recreational activities with the purpose of conscious health prevention out of 228. 98 (43%) of them even spare 30 minutes for recreation at least on 5 days a week. The median number of different marked recreation types was 4 (IQR: 3, 5). We found that being involved in 30 minutes of recreation at least 5 days a week was associated with lower scores on symptoms of anxiety, depression, somatisation, and hostility**,** while 30-minute recreation on 3-4 days weekly was associated with elevated mental and physical well-being scores (Table 4.).

Table 4. Mental health parameters of general practitioners according to the number of days they spent at least 30 minutes for recreation during the week (n=228).

	30 mins / 5-7 days (n=98) Mdn (IQR)	30 mins / 3-4 days (n=75) Mdn (IQR)	30 mins / 0-2 days (n=55) Mdn (IQR)	p	p (adj)	p n. s.
Distress-related characteristics						
ANXIETY (SQ)	3.0 (1.0;7.2)	6.0 (2.0;8.0)	6.0 (3.0;12.0)	<0.001	<0.001*; 0.049§	0.325
DEPRESSION (SQ)	3.5 (1.0;7.0)	3.0 (2.0;7.0)	6.0 (3.0;11.0)	<0.001	<0.001*; 0.002§	1.000
SOMATIZATION (SQ)	3.5 (1.0;7.0)	4.0 (2.0;8.0)	6.0 (4.0;12.0)	0.001	0.001*; 0.031§	0.984
HOSTILITY (SQ)	3.5 (1.0;9.0)	5.0 (1.0;10.0)	7.0 (2.0;12.0)	0.005	0.003*	0.559; 0.148§n.s.

Well-being-related characteristics						
Mental well-being (PHS-WB)	4.4 (4;4.8.0)	4.4 (4.0;4.8)	4.4 (3.2;4.6)	0.017	0.032*; 0.030§	1.000
Social well-being (PHS-WB)	4.5 (3.6;5.0)	4.5 (4.0;5.0)	4.5 (3.5;4.5)	n.s.		
Physical well-being (PHS-WB)	4.3 (3.3;4.6)	4.0 (3.3;4.5)	3.3 (2.3;4.0)	<0.001	<0.001*; 0.005§	0.480
Total well-being (PHS-WB)	4.2 (3.6;4.7)	4.2 (3.8;4.6)	3.7 (2.9;4.3)	0.002	0.002*; 0.007§	1.000

Note: SQ: Kellner Symptom Questionnaire; PHS-WB: Public Health Surveillance Well-being Scale; Kruskal-Wallis tests were applied with Dunn's pairwise tests and with Bonferroni adjustment for multiple comparisons [: significant difference between 0-2 days - 5-7 days; §: significant difference between 0-2 days - 3-4 days; p n.s.: non-significant p levels between 3-4 days - 5-7 days; $§^{n.s.}$: non-significant difference between 0-2 days - 3-4 days]. Mdn: Median, IQR: Interquartile Range.*

4.4. Qualitative results

4.4.1. Challenges of COVID-19

According to our qualitative data analysis, the most disturbing issue people faced during the lock-down was the obligatory quarantine resulting in lack of personal contacts and loneliness. This challenge appeared among GPs' answers as well, but most of them reported professional issues like work-related conditions and increased workload as most challenging. Interestingly both groups suffered from unavailability of specialist care. GPs were unable to refer their patients to necessary specialist care, thus, lack of professional help due to the burden of COVID-19 that afflicted specialized health institutions tormented both populations we examined. Besides decreased availability for outpatient specialty care, undeveloped proceeding rules and structural changes in delivering care (online and phone consultation) stood as most bothering circumstances for our GPs. Among personal challenges both samples reported wearing a mask and sanitizing, increased home workload, organization, online education, curfew, travelling restrictions, opening restrictions, misleading information, uncertainty, financial problems, loss of loved ones and last but not least loss of mental balance as challenging (Figure 2., Figure 3.).

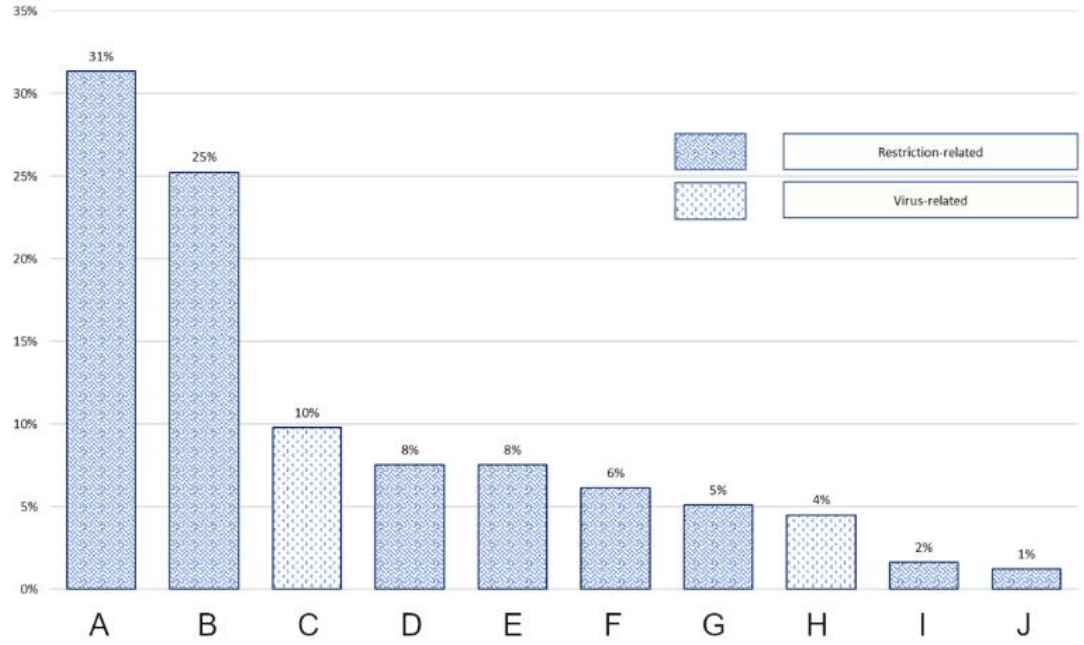

Figure 2. Percentage distribution of restriction-, and virus-related challenges non-clinical sample reported during COVID-19 [111]

A) Lack of personal contact, B) Confinement, vulnerability, C) Panic, fear, worry, unreliable information, D) Increased home workload, organization, online education, E), Opening hours restrictions, F) Nothing, G) Work, financial problems, H) Wearing mask, sanitizing, I) Unavailability of health care, J) Loss of mental balance

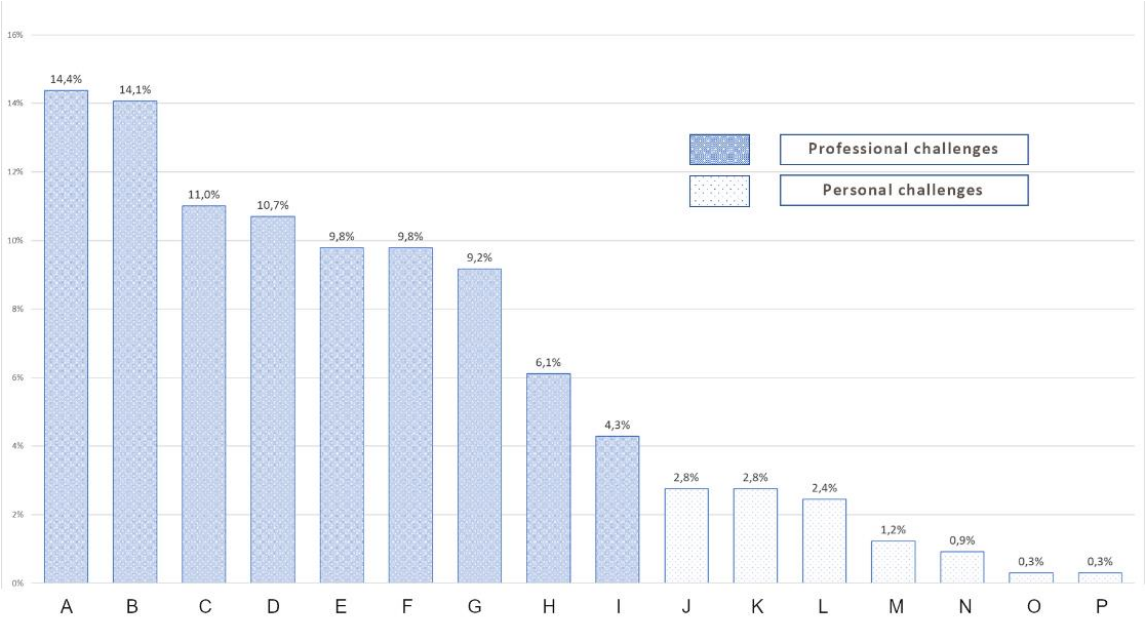

Figure 3. Percentage distribution of professional and personal challenges GPs reported related to COVID-19 [49]

A) Changes in means of consultation (phone, online), B) Discontinuation of patient care, patient observations, thus difficulties of diagnosing, C) Undeveloped proceeding rules and lack of information on them, disorganization, D) Increased work-, thus stress load and responsibility due to COVID-19 and unavailability of specialist care, E) Fear, worry, unreliable information, uncertainty, F) Panic and worry of patients and to calm and inform them, G) Lack of protective equipment, H) Protecting own health, wearing mask, sanitizing, I) Lack of professional contact and help, incompetence of professionals, J) Lack of personal contact, K) Increased home workload, organization, online education, L) Curfew, travelling restrictions, M) Opening restrictions, N) Loss of mental balance, need of psychological help, O) Financial problems, P) Loss of loved ones

4.4.2. Health-prevention activities

While in our non-clinical sample, the health-prevention activity was given by 3-1-2 meridian exercise, we investigated recreational activities among GPs that might boost their resilience, and thus, prevent suffering from allostatic overload. The most popular categories turned out to be connection with nature, reading, watching movies and not surprisingly physical exercise (Figure 4.).

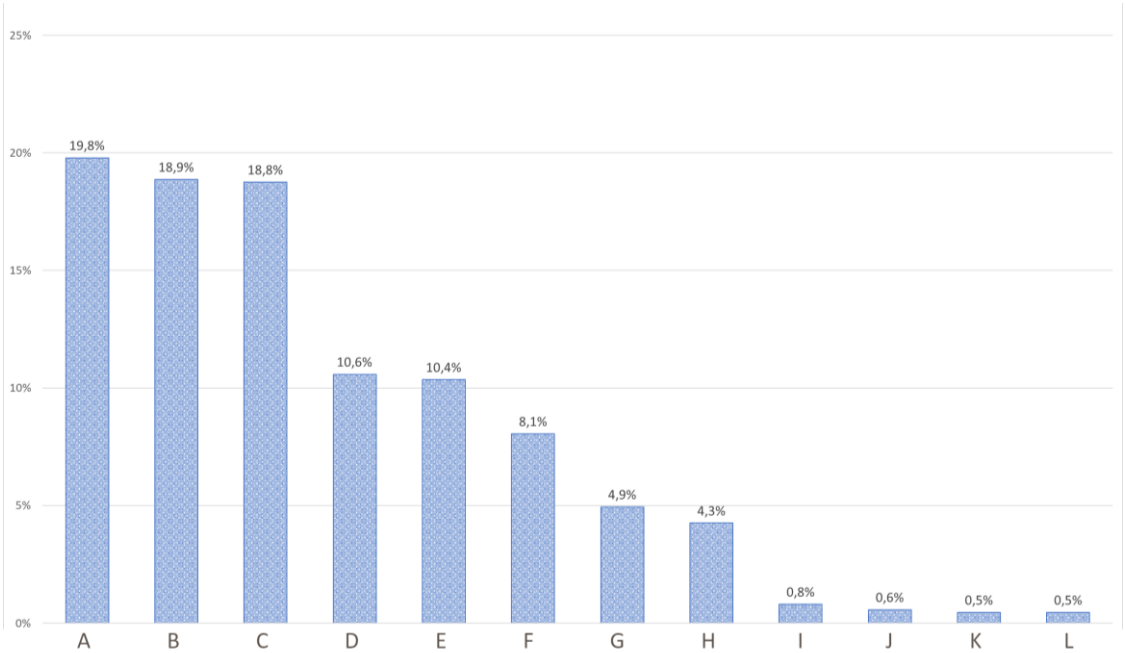

Figure 4. Percentage distribution of recreational activities reported by Hungarian GPs [49]

A) Connection with nature, B) Reading, watching movies, C) Physical exercise, D) Meeting friends and acquaintances, E) Cooking, F) Praying, meditation, G) Creative manual activities, DIY, H) Beautification, cosmetics, I) Spending time with children, grandchildren, J) Making and listening to music, K) Gardening, L) Training, learning, educational tasks

5. Discussion

5.1. Coronavirus disease 2019 (COVID-19) as a stressor

The outbreak of the global pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China caused a whirlwind all over the world back in December 2019. The World Health Organization (WHO) declared COVID-19 as a public health emergency on 30 January 2020 and a pandemic on 11 March 2020. As of August 2020, around 24 million cases have been reported worldwide, resulting in more than 800,000 deaths.

To prepare for the emergency, the Hungarian government has introduced a special legal order into force and the Operational Group responsible for the prevention of the epidemic was formed. National emergency was announced on 11 March 2020 after the first registered case in Hungary was confirmed on 4 March. Despite the many confinements that have been applied to prevent the spread of the infection, the case numbers rapidly increased. Restrictions were eased when the numbers improved, but people's daily lives were certainly affected by them. Entertainment and sport facilities closed down, people were forbidden to leave their homes, or visit their families. The economy has declined significantly, with tens of thousands losing their jobs. Opening hours restrictions also put a huge burden on every generation, so did the responsibility of the younger to take care of their elderly loved ones' needs. Thus, the first wave of the pandemic of COVID-19 turned out to be a strong diversified stressor for all [112–115]. Facing such diverse difficulties and adverse circumstances has resulted in declining physical and mental well-being, impaired resilience, and burdensome health consequences [116–122].

Medical doctors especially were confronting difficulties not only by worrying about their own personal health but also by dealing with professional challenges in their practice resulting in psychological distress and mental health problems [123–126]. The pandemic demanded hospitals and specialist care to transform into pandemic centres, forcing hospital care and the intensive care units to focus on treating patients of COVID-19. This has increased the responsibility of general practitioners (GPs) working in primary care. They were and still are the first and last contact of infected patients and were expected to adjust quickly to altered consultation ways without physical examination and were not sufficiently equipped for physically contacting patients when

needed [104, 127]. But their tasks did not end with treating those in need, GPs were managing the consequences of the pandemic and the related damage caused by reallocated resources [104, 128]. The COVID-19 pandemic transformed the way health care operates, more emphasis has been put on preventive and remote care, the number of hospital beds has decreased, chronic patients have been less likely to receive secondary care treatment [129, 130]. This further increases the need of competence of primary care givers and the expectation towards them, not to mention the shortage of family physicians [131], while there is extended literature on their strains and burn-out [127, 132, 133]. Extreme workload and expectations may increase their work-related stress to an unbearable extent, which – in many cases – could result in allostatic overload [42, 134, 135]. Scientific literature concerning GPs' health focuses primarily on mental ill-health [136], but such an exceptional situation like the pandemic and its consequences, however, should also lead to explore sources of recreation and resilience beside identifying distress. Increasing well-being contributes to reaching optimal health and euthymia, thus, it improves resistance against and help adapt to adverse circumstances [83, 84].

5.2. Stress and allostatic overload in terms of COVID-19

Stress is a diverse force that drives us and is essential for the evolution of life [2]. Stress can be labelled as good, tolerable, or toxic. It all depends on the individual's control and adaptive mechanisms whether stress becomes intolerable. Vulnerability to and resilience against toxic stress is determined by the combination of genetic, behavioural, and environmental factors [20]. The brain is an essential coordinator when it comes to individual reaction to stress, and it discriminates threatening stimuli from benign ones [21, 22]. When the brain and the body are able to keep stability throughout environmental changes, a balanced state called allostasis is maintained. The threshold of stimuli that tips out this balance differs in individuals. But it is universal that the heavier the strain is the body has to respond to, the more chance there is for loss of balance due to cumulative load. The clinical definition of allostatic overload identifies a state where accumulation of life events exceeds individual resources and may endanger one's health [17]. It is associated with increased level of depression and anxiety as well as somatization and hostility symptoms [50]. Individuals with AO also reported statistically significant lower levels of well-being [137].

With COVID-19 we were facing an excessive stressor that superimposed on other life events. It proved to be a trigger that can push individuals into the state of AO [138]. Our results verified that COVID-related acute stress was more likely to cause allostatic overload when added to individual life stressors. In our non-clinical sample 29% of our participants experienced AO. The most stressful challenges they reported were the lack of personal contact and the pandemic-related confinements that put them in a vulnerable state. Social interaction is essential for mental and physical health [139] and mandatory isolation can lead to significant negative consequences in relation with psychological well-being [140].

The pandemic especially put a tremendous burden on health care professionals, who were now facing a professional challenge on top of a personal one [50, 138, 141]. Several studies show that allostatic load is correlated with work-related stress [142, 134, 135]. Our results show that Hungarian general practitioners experienced the professional challenges over the first wave of the pandemic more demanding than the personal ones. The changes in means of consultation and the discontinuation of patient care in person were reported amongst the most arising problems besides undeveloped proceeding ways due to the lack of information and increased workload and responsibility and unavailability of specialist care. All together our qualitative analysis supports the results of the international literature on this topic [128]. Our research group implemented a pandemic specific version of the DCPR-SSI A2 criterion of allostatic overload: “During the time of the restrictions, did you feel that the changes caused by the coronavirus epidemic were testing or exceeding your capacity?” [49, 111]. We found that 57% of the participating primary physicians experienced allostatic overload in relation to adverse experiences during the first wave of pandemic. Female sex and additional individual life stressors were associated with increased vulnerability to AO. Although our sample was not representative because of higher proportion of females, our results add to the international findings on correlation between sex and allostatic load [143].

One would expect GPs to score higher on negative distress domains of Kellner’s SQ and lower on the positive well-being ones. However, even though elevated stress levels were seen amongst GPs, they did better on the well-being subscales and only scored higher on the hostility subscale. This can be explained with their ability to adopt

quickly to altered circumstances and adverse life events as shown by Hoff et al. [144]. Still it is utmost important to find ways that effectively help build resilience on the individual level besides finding ways to support them on an organization level [129].

5.3. Protecting role of regular physical exercise and recreational activities

It is widely known that sedentary lifestyle increases the risk of modern life illnesses like cardiovascular diseases, obesity, diabetes, and depression [145]. Unfortunately, COVID-19 enhanced sedentary lifestyle and unhealthy behavioural patterns [146, 147]. The two most important interventions to prevent these from happening are physical activity and social integration [20]. Voluntary physical activity has been proven to enhance adaptive changes in regions of the brain that can be associated with stress management [20]. Based on the recommendation on physical activity of the WHO, 3-1-2 meridian exercise, which is a 30-minute moderate intensity aerobic training, is an adequate form of physical activity for health-preventing purposes [105]. We recruited our non-clinical sample from groups of people who practice this form of exercise. As COVID-19 forced sport facilities to close down, many individuals stopped their physical activities, so we aimed to present a form of movement that does not need equipment or large room, is easily done at home, has no contraindications for the elderly and has been practiced by large groups of people nationwide. We found this form of physical exercise to be effective and beneficial during the pandemic in relation to allostatic overload, mental and physical health. Those who exercised regularly (30 minute routine 3-5 times a week) were statistically significant less likely to suffer from allostatic overload compared to controls. Regularly practiced exercise has also proved to be associated with improved well-being [148, 149], and lesser depressive and anxiety symptoms [149, 150]. In sync of the WHO recommendation of heath preventing exercising, based on our univariate analysis we found that 3-1-2 meridian exercise practiced at least 3-5 times a week was associated with better well-being, especially having a positive effect on the physical aspect of it. Therefore, practicing 3-1-2 meridian exercise 3-5 time a week can be expected to bring beneficial changes in well-being and can be used to achieve exercise-related prevention goals of the WHO. Multivariate analysis showed that practicing only 1-2 times a week can also be associated with better well-being. Our findings extend the knowledge on health-

preventing exercise by exploring the beneficial effects on the physical health domain of well-being and somatization as well.

Although we asked about the physical activity among our general practitioners as well, we could not standardize it, thus, our main focus was on general recreational sources. Based on the recommendations [108, 109] we mapped individual recreational habits GPs have with conscious purpose of health-prevention. 95.2% of primary physicians reported doing actively and regularly for their health in general. The most popular forms of recreation activities were connection with nature, reading or watching movies, and physical exercise, but meeting friends and acquaintances was also frequently mentioned. Therefore, the two most important interventions were confirmed by our sample [20]. We found that being involved in 30 minutes of recreation on 3-4 days weekly was associated with lower scores on symptoms of anxiety, depression, somatisation and with elevated mental and physical well-being scores. Results also show that taking 30 minutes to engage in recreational activities at least 5 days a week was further associated with lower scores on symptoms of hostility besides lower anxiety, depression, somatisation scores and elevated well-being scores. Based on our findings, we can claim that 30 minutes of recreation 3-4 times a week is sufficient to achieve a positive effect. Also, each additional day when time was taken for 30-minute recreation was associated with almost 20% of decrease in the odds of vulnerability to allostatic overload. There is little scientific information on primary care [151] and state or potential improvement of GPs' mental health [152], and we could extend the existing literature with our findings.

5.4. Implications of practice

The ultimate goal is to be able to prevent overwhelming stress or to decrease the negative impact of it on health [17, 153]. Diagnosing allostatic overload helps identify the need of psychotherapeutic interventions or lifestyle modifications to improve coping mechanisms with stress and reach emotional well-being [154]. Physical exercise and recreational activities are easily accessible examples of the latter that can be applied to everyday life to consciously take care of one's self [49, 111]. There is a need for change of perspective prioritizing health and prevention. Scientific community should reach out to the general population to urge them to apply practical scientific findings to

their daily lives. Thus, we recorded an educational video of the correct execution of the 3-1-2 meridian exercise, which is available free of charge for everyone on the following link (Figure 5.).

Figure 5. QR code to the link of educational video of the correct execution of the 3-1-2 meridian exercise

5.5. Limitations

We conducted a cross-sectional research, thus, causality could not be estimated. Nonetheless, using statistical models we could predict the role of physical exercise and recreational activities in lowering the odds of allostatic overload. Further research should confirm our results. Defining a true causal relationship could only be achieved by a longitudinal study, the data collection for which has been undergoing since 2021/22 by our research group.

In both of our samples the proportion of females was higher (92% vs 52.5% in the general population and 68% vs 53% in the GP population). A possible case could be that the proportion of women are generally higher in the 3-1-2 meridian community in comparison to the average population, also it is known that females are more likely to spend time on health-related topics, than males. Nevertheless, our sample is not representable due to gender inequality.

In our data-collection phase we used an online platform to reach the targeted population, which limited our participants to regular internet users. So that lack of internet access was an exclusion criterion.

As we had no personal contact with the participants, and all questions were self-reported through an online platform, credibility of answers on the frequency of 3-1-2 meridian exercise and recreational activities may be questioned. Among the non-clinical sample, we reached out to leaders of 3-1-2 meridian communities to ensure reliability,

as they registered active exercisers, they lead and organize their communities and participate in trainings twice a year. Still, further prospective study is needed to follow up habits of meridian exercising, which we have been conducting since 2021.

Among GPs the response rate reached 18%, however, compared to other online GP surveys, and considering that medical doctors are more willing to complete paper-based surveys than online questionnaires [155], 18% seems to be adequate.

Also it was not a personal database we had, which certainly influenced the response rate. Surgery email addresses might have been handled by assistants and did not reach GPs directly.

We could not differentiate unwillingness to complete the survey from invalid email addresses or mistargeted GPs though. Former can be also related to high workload during the assessed period. But in general, it is also possible that GP population receives lots of surveys daily therefore are not willing to spend extra time to do more. Computer illiteracy might be another cause among the aging GP population for non-responsiveness. This as well can be the reason that the average age of our GP sample was slightly lower than that of the Hungarian GP population.

Allostatic overload should be evaluated by a personal form of a semi-structured interview. Due to lack of personal contact during COVID-19, we investigated AO by a self-rating form, which can be considered a limitation. Though DCPR criteria were paired with PSI items and the two measurement tools were developed by the same research group, the lack of personal help from the interviewer may have resulted in misinterpretation in our participants at certain questions. Though it is important to note, that in a personal interview it is the interviewer who judges the answers based on the conversation, which due to its subjectivity can be misleading. Also, participants may give a more honest answer when not afraid to be judged by the interviewer.

For our study we have used questionnaires that have not been validated in Hungarian language yet, however, we have started the validation process and it is in our future plans to proceed (see details on process in chapter 5.6.2.).

5.6. Future directions

5.6.1. Stress and well-being among medical students

We have three simultaneously running projects that are organically connected to our recent research, thus we would like to further extend and continue our work. When

we look at the Hungarian GPs it is unmistakable to notice the aging feature of the population. These middle-aged or still working retired medical doctors are not only overwhelmed with their surgeries but have had to deal with a great amount of pressure COVID-19 put on them, which was followed by other adversities such as war, energy crisis and shortage of medical doctors in the health care system. All these result in constant changes and consequent challenges. They need the younger generations to take their work on and successfully meet the expectations this new era brings. But there is lack of interest in primary care for young doctors and there is shortage when it comes to this profession [131]. We need to investigate their capacities and whether they need help to build or maintain their resilience against stress and ensure their well-being.

We found that the more regular GPs spent time on recreation, the better they could manage allostatic load and ensure well-being. We aim to measure stress load as well as well-being dimensions in younger medical doctor populations even in medical students to guide them improving resilience through staying in a euthymic state even facing adversities.

5.6.2. Longitudinal study on the effects of 3-1-2 meridian exercise

Having found promising results in our cross-sectional study on 3-1-2 meridian exercisers we wanted to establish the true relationship between exercise and psychosocial background. And therefore, we conducted a longitudinal study in 2021-2022, in which we measured allostatic load simultaneously with biomarkers as well as our clinimetric toolkit. Regarding biomarkers, we measured cortisol and norepinephrine from morning urine (cortisol was titrated to urine creatinine, it was not from collected urine). In addition, we looked at CRP, cholesterol, TSH, and HbA1c, liver and kidney function from blood count. This was followed by 3-1-2 meridian exercising, blood pressure measurement, weight-, body height-, and waist-hip ratio measurement, and the described questionnaires were completed.

The examination itself took half a year, we went through the whole session three times during the semester: first at the very beginning when participants entered the study, then after the first three months, and finally at the end after six months from the start. In the meantime, they had to constantly perform 3-1-2 meridian exercise, which they sent a written report on every week.

Although the study itself ended in October, the data analyses are still ongoing, so we cannot yet report results.

5.6.3. Process of validation of assessment tools in Hungarian language

Having used meticulously developed questionnaires, it is utmost important to us to validate them in Hungarian language. Becoming available for the Hungarian clinical and scientific practice, these measurements may provide insights to the importance and usefulness of clinimetrics.

5.6.3.1. DCPR-SSI

We considered Diagnostic Criteria of Psychosomatic Research Semi-Structured Interview the framework of our research as we started our work aiming to investigate psychosomatic background of chronic diseases. DCPR targets four main domains: stress, personality, illness behaviour and psychological manifestations. Stress meaning allostatic overload then shifted into our focus point.

We started the adaptation of the interview into Hungarian language in 2018, when we translated, then back-translated it and received the approval for the Hungarian translation from the creator of the interview, Giovanni Andrea Fava.

We organized an 8-hour workshop attended by an experienced psychologist, who was our statistical analyst as well, an experienced general practitioner, and medical doctors and students with the aim of learning to use the interview. Each item was explained by the psychologist in detail, which was then supported by the general practitioner and other attendees with clinical examples. We continued clarification of the items until no further questions remained in any of the participants. The full text of the interview was then discussed, and all attendees performed the interview on each other. Questions were listed which were answered by Professor Fava later on, and alterations were made to the translation.

We then started to use the Hungarian DCPR-SSI in clinical setting and discussed further arisen questions. From the beginning we were interested in the usefulness of a self-rating form and therefore simultaneously we applied the Psychosocial Index, which was developed by the same authors and is a self-rating instrument. More than 100 cases were investigated by these measurement tools.

5.6.3.2. PSI

The Psychosocial Index is an older assessment tool than DCPR, it is a self-rating questionnaire and was developed by a psychiatrist (G. A. Fava) and an endocrinologist (N. Sonino) together [47]. It aims to assess psychosomatic background information that is not mapped in either a psychiatric or a medical history.

Created by the same group of clinicians, PSI measures very similar domains as DCPR, but due to its self-rating characteristics, it can be easily used online. As the items for allostatic overload in the two tools match, we applied PSI to assess DCPR AO. As it was not validated at that point, we used other questionnaires as well (DASS, PHSWB), which were suggested by our statistical analyst, dr. Sándor Rózsa. He then performed analysis for validation, the results of which are convincing on the assessed Hungarian population (awaiting for publication).

5.6.3.3. Kellner's SQ

Kellner's Symptom Questionnaire raised our attention due to its clinimetric characteristics and the fact that it assesses distress and well-being together - giving a sight on the positive domains as well - which were the two focus points of our research.

Kellner's SQ uses one-word items and meaning of some of them fall very close to each other. During testing, participants gave feedback on the possible difficulties of interpreting the meaning of each word, and simultaneously a group of senior experts in validational translations (led by S. Rózsa) compared our translated words with already existing validated questionnaires using the same original words and suggested corrections, which were then discussed by our research group and accepted. After using its revised translation, the results were then analysed by our statistical analyst (S. Rózsa), who found the results satisfactory and promising. Kellner's SQ is a classical clinimetric tool, thus we plan to perform its validation by clinimetric methods (see Table 1. of Supplementary Material).

6. Conclusions

COVID-19 pandemic has brought new challenges into everyday life in the form of continuous uncertainty. As our brain seeks to maintain balance, uncertainty results in increasing stress load consequently rising distress symptoms like depression with greater prevalence of allostatic overload. To identify factors that potentially increase vulnerability to allostatic overload is of utmost importance to prevent the formulation of stress-related - mainly non-communicable - diseases and the overload of the healthcare system. With this regard, increasing awareness on well-being and pointing out to those areas that work dysfunctionally in the individual level has great impact not only on individual, but on a social level as well.

The pandemic not only impacted the general population but burdened medical professionals cumulatively. To resist the weighing pressure, one must be conscious about mechanisms that help balance out external effects. Examining a non-clinical regularly exercising aging population we were able to monitor the positive influence of moderate intensity aerobic exercise on mental and physical health as well as its potential protecting effect against allostatic overload. Investigating Hungarian general practitioners, we could find correlations between their recreational habits and their well-being as well as reduced levels of depressive and anxiety symptoms, somatization, and hostility. In conclusion, we confirmed that physical exercise and recreational activities have beneficial effects on individuals' well-being.

6.1. Main findings

I. We found that among the non-clinical participants the lack of personal contact, the confinements, and the panic and fear due to uncertainty were the most challenging aspects of the pandemic. 29% of the participants met the criteria of allostatic overload.

II. Those who practiced 3-1-2 meridian exercise regularly (at least 3-5 times a week) with the aim of health preservation presented statistically significant less depressive and anxiety symptoms, than those who did not. They also maintained better mental and physical health as compared to the control group and were statistically significant less likely to develop allostatic overload. Somatization symptoms differed statistically not significant between exercise groups and

controls, however, the final somatization scale showed better results in the fPE group due to the increased physical well-being.

III. The pandemic and the related confinements of proceeding rules resulted in significantly increased stress load of health care professionals. General practitioners – as frontline workers – faced doubled challenges, personal and professional, and the latter was not only related to the increasing number of infections and consequent life-threatening conditions, but – through the disrupted communication and facilities – to the care for their chronically ill patients. Additionally, they suffered from communication pressure and psychological burden of their own and patient-related fears. Facing all these challenges simultaneously, 57% of the Hungarian general practitioners experienced allostatic overload during the first wave of the COVID-19 pandemic in our study.

I. Ninety five percent of the general practitioners reported to do actively for their health by spending at least 30 mins on recreation on average 4 days a week. 30 minutes of recreation 3-4 days a week was associated with increased mental, and physical well-being, while 30 mins of recreation 5-7 days a week was associated with reduced levels of depressive and anxiety symptoms, somatization, and hostility besides increased well-being.

7. Summary

Extensive knowledge has become available about specific biological mechanisms generated by physical and psychological stress that affect the body negatively and lead to disease. Thus, stress should be in focus of a medical research and taken seriously when diagnosing and treating diseases.

We therefore applied clinimetric measurement tools to identify the psychosocial background that leads to allostatic overload (AO) on the individual level. Simultaneously we explored the effect of standardised physical exercise and regular recreational activities to counteract stressful life events.

AO refers to a state when the stressors exceed the individual's coping capacity causing wear and tear on the physiological regulatory network system leading to diseases. We used the clinimetric criteria introduced by Fava to evaluate the prevalence of AO among a cohort of Hungarian community adults who regularly practiced a standardised physical exercise (3-1-2 Meridian exercise). We also measured their distress and well-being. The other cohort of our interest was Hungarian general practitioners during the first wave of COVID-19. In their case, individually chosen recreational activities were registered to assess the association with AO and mental and physical health. Our results show that COVID-related changes have had a prominent role in causing allostatic overload as 57% of the general practitioners and 29% of the non-clinical sample met the diagnostic criteria of COVID-related AO with lacking coping abilities and signs of distress as a consequence. GPs suffered from professional aspects of the pandemic besides a personal health aspect that the general population was facing. Regular physical exercise (at least 30 minutes 3-5 times a week) as well as personally chosen recreational activities (at least 30 minutes 5-7 days a week) were shown to be associated with decreased symptoms of anxiety, depression and with increased mental and physical well-being.

We found that regular physical exercise and regular recreational activities were able to act positively on well-being and decrease the prevalence of AO. They therefore can be used to ensure resilience on an individual level. However, it is clear that we have to expand our therapeutic tool kit with effective measurement tools for stress load and consequent medical symptoms to increase therapeutic effectiveness.

8. Összefoglalás

Egyre szélesebb tudományos rálátásunk van a fizikai és pszichológiai stressz által kiváltott specifikus biológiai mechanizmusokra, amelyek negatívan hatnak a szervezetre és betegségekhez vezetnek. Így a stresszt komolyan mérlegelni kell a betegségek diagnosztizálása és kezelése során.

Kutatásunk során ezért olyan klinimetriai mérőeszközöket alkalmaztunk, melyekkel lehetővé válik az allosztatikus túlterheléshez (AO) vezető pszichoszociális háttértényezők beazonosítása. Ezzel egyidőben a standardizált testmozgás és az egyéni szinten alkalmazott rekreációs tevékenységek hatását vizsgáltuk stresszhelyzetben.
Az AO olyan állapotot jelent, melyben a stresszorok meghaladják az egyén megküzdési kapacitását, és az élettani szabályozórendszerek felőrlésével betegséghez vezetnek. Fava diagnosztikus kritériumrendszerét alkalmazva felmértük az AO prevalenciáját magyar átlagnépesség egy kohorszában, mely rendszeresen végzett egy standardizált testmozgást (3-1-2 meridián torna). Emellett mértük diszstresszüket és jóllétüket is. Az érdeklődésünk fókuszában álló másik kohorszt magyar háziorvosok alkották a COVID-19 első hulláma alatt. Az ő esetükben az egyéni rekreációs aktivitást térképeztük fel, hogy megbecsüljük ennek összefüggését az AO-val, valamint mentális és fizikai egészségükkel. Eredményeink azt mutatják, hogy a COVID-19-hez kapcsolódó változások kiemelkedő szerepet játszottak az AO kialakulásában, hiszen a háziorvosok 57%-a és a nem-klinikai minta 29%-a megfelelt a COVID-hoz köthető AO diagnosztikai kritériumainak, megküzdési képességeik lecsökkenésével és distressz tünetekkel. A háziorvosok a pandémia által szakmai életükben előidézett változásoktól is szenvedtek, az átlagnépességet érintő személyes egészségi aspektusok mellett. A rendszeres testmozgás (30 perc legalább heti 3-5 alkalommal), valamint a személyesen választott rekreációs tevékenységek (30 perc hetente 5-7 napon) együtt jártak a szorongás és a depresszió tüneteinek csökkenésével, valamint a mentális és fizikai jóllét javulásával.

Eredményeink tehát azt mutatják, hogy a rendszeres testmozgás és a rendszeres személyes rekreációs aktivitás egyaránt pozitív összefüggést mutat a jólléttel és az AO csökkent prevalenciájával az egyén szintjén. Azonban terápiás eszköztárunkat ki kell bővítsük a stressz-terhelés és a következményesen jelentkező testi tünetek hatékony mérőeszközeivel, hogy terápiás hatékonyságunkat növelni tudjuk.

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2021 JOURNAL IMPACT FACTOR: 3.636

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12. Appendix

12.1. Measurement tools in English and Hungarian language

12.1.1.1. Diagnostic Criteria for Psychosomatic Research Semi -Structured Interview (DCPR-SSI) allostatic overload in English language

ALLOSTATIC OVERLOAD			
Criteria		**Answer**	
Criterion A: The presence of at least one current identifiable source of distress in the form of recent life events and/or chronic stress; the stressor is judged to tax or exceed the individual coping skills when its full nature and full circumstances are evaluated	**A1.** In the last 12 months, ☐ Did a family member or a close friend die? ☐ Did you separate or divorce from your partner? ☐ Did you change job? ☐ Did you move? ☐ Did you have severe economic difficulties? ☐ Did you have legal problems? ☐ Did you start a new relationship? ☐ Did you feel under pressure at work? ☐ Did you not get along with co-workers? ☐ Have you been a victim of bullying, stalking or severe interpersonal pressure? ☐ Did you not get along with your spouse / partner or other family members? ☐ Did you feel tension at home? ☐ Has at least one family member been seriously ill? ☐ OTHER _____ _____ _____	YES	NO
		IF NO, SKIP TO *HEALTH ANXIETY*	
	A2. Have you had the feeling that life is asking you too much?	YES	NO
Criterion B: The stressor is associated with one or more of the following 3 features, which have occurred within 6 months after the onset of the stressor: (1) At least 2 of the following symptoms: difficulty falling asleep, restless sleep, early morning awakening, lack of energy, dizziness, generalized anxiety, irritability, sadness, demoralization	**B1.** Within 6 months after the onset of the (NAME OF THE STRESSOR), ☐ Did it happen to take a long time to fall asleep? ☐ Did you wake up many times during the night? ☐ Did you wake up too early and could not get back to sleep? ☐ Did you feel tired, without energy? ☐ Did you feel a sense of instability, dizziness? ☐ Did you feel nervous or anxious? ☐ Did you feel irritable? ☐ Did you feel sad or depressed? ☐ Did you feel demoralized?	YES	NO
(2) Significant impairment in social or occupational functioning	**B2.** Did you have problems or difficulties at work, at home or in relationships with other people?	YES	NO
(3) Significant impairment in environmental mastery (feeling overwhelmed by the demands of everyday life)	**B3.** Did you feel overwhelmed by the demands of everyday life?	YES	NO

12.1.1.2. Diagnostic Criteria for Psychosomatic Research Semi -Structured Interview (DCPR-SSI) allostatic overload in Hungaraian language

ALLOSZTATIKUS TÚLTERHELÉS			
Kritériumok		**Válasz**	
A Kritérium: Legalább egy beazonosítható distressz forrás, közeli életesemény és/vagy krónikus stressz formájában jelentkezik melyben a stresszor próbára teszi vagy meghaladja az egyén megküzdési képességét, ha teljes mélységében és minden körülményével együtt értékeljük.	**A1.** Az elmúlt 12 hónapban, □ Elhalálozott-e családtagja vagy közeli ismerőse? □ Elvált-e vagy ért-e véget párkapcsolata? □ Váltott-e munkahelyet? □ Költözött? □ Voltak-e komoly pénzügyi gondjai? □ került-e összeütközésbe a törvénnyel? □ Lett-e új párkapcsolata? □ Nyomás alatt érezte-e magát a munkahelyén? □ Voltak-e személyes konfliktusai a munkatársaival? □ Előfordult-e, hogy bántalmazták, zaklatták, vagy rá akarták kényszeríteni valamire? □ Volt-e olyan, hogy nem jött jól ki a párjával vagy más családtagjával? □ Feszültnek érezte-e magát otthon? □ Megbetegedett-e súlyosan valamelyik családtagja? □ EGYÉB _____	IGEN	NEM
		HA NEM, UGRÁS AZ *EGÉSZSÉGSZORONGÁSRA*	
	A2. Volt-e olyan érzése, hogy az élet túl sokat követel Öntől?	IGEN	NEM
B kritérium: A stresszor összefüggésbe hozható legalább egyel az alábbi 3 jellemző közül, amelyek a stresszor megjelenése utáni 6 hónapban léptek fel: (1) Legalább 2 az alábbi tünetek közül: elalvási nehézség, nyugtalan alvás, kora reggeli ébredés, energia hiány, szédülés, generalizált szorongás, ingerlékenység, szomorúság, demoralizáció (2) A szociális funkciók vagy munkaképesség jelentős romlása (3) Jelentős romlás az élethelyzetek kezelésében (a hétköznapi teendők is túlterhelőek)	**B1.** Az elmúlt 6 hónapban, a ... (STRESSZOR NEVE) megjelenését követően, □ Előfordult-e, hogy sok időbe telt, míg el tudott aludni? □ Felébredt-e sokszor éjszaka? □ Volt-e olyan, hogy túl korán ébredt és nem tudott visszaaludni? □ Érezte-e magát fáradtnak, erőtlennek? □ Fordult-e elő Önnel, hogy instabilnak érezte magát, szédült? □ Érezte-e magát idegesnek, nyugtalannak? □ Érezte-e magát ingerlékenynek? □ Érezte-e magát szomorúnak, depressziósnak? □ Érezte-e magát úgy, hogy nem tudja uralni az életét vagy nem kap elég segítséget ehhez?	IGEN	NEM
	B2. Voltak-e problémái vagy nehézségei a munkavégzésben, otthoni feladataival kapcsolataiban vagy személyes kapcsolataiban? B3. Érezte-e úgy, hogy elborítják a hétköznapi teendők?	IGEN	NEM

12.1.2.1. Psychosocial Index (PSI) in English language

Appendix 1. PSI, revised version (modified from Sonino and Fava [1])

Self-rating items

NAME_____SURNAME_____

1.	Date of birth:_____day_____month_____year_____		
2.	Sex:	Male	☐
		Female	☐
3.	Marital status:	Single	☐
		Married	☐
		Divorced	☐
		Separated	☐
		Widowed	☐
4.	Occupation_____		
	How many hours do you work per week?_____		
	Occupation of spouse:_____		
5.	Have you ever been hospitalized?	YES	NO
6.	Please list illnesses, surgical operations and other treatments and give dates		
	_____		
7.	Are you allergic to any drug or substances?	YES	NO
	If yes, specify_____		
8.	What medication are you taking at present?_____		
9.	Do you drink alcohol?	YES	NO
10.	Do you smoke?	YES	NO
11.	Do you take recreational drugs?	YES	NO
12.	Do you drink coffee or tea?	YES	NO
	If yes, how many per day?_____		
Did any of the following happen to you in the past year? (YES/NO)			
13.	Death of a family member	YES	NO
14.	Separation from spouse or long-time partner	YES	NO
15.	Recent change of job	YES	NO
16.	Financial difficulties	YES	NO
17.	Moving within the same city	YES	NO
18.	Moving to another city	YES	NO
19.	Legal problems	YES	NO
20.	Beginning of a new relationship	YES	NO
Please answer the following questions (YES/NO)			
21	Do you have a job?	YES	NO
If you have a job:			
22.	Are you satisfied with your work?	YES	NO
23.	Do you feel under pressure at work?	YES	NO
24.	Do you have problems with your colleagues at work?	YES	NO
If you do not have a job:			
22.	Are you retired or student?	YES	NO
23.	Do you feel under pressure during the day?	YES	NO
24.	Are you unable to find a job?	YES	NO
25.	Do you have serious arguments with close relatives?	YES	NO
26.	Do you have serious arguments with other people?	YES	NO
27.	Has any close relative been seriously ill in the past year?	YES	NO
	If yes, specify:_____		
28.	Do you feel tension at home?	YES	NO

29.	Do you live by yourself?	YES	NO
30.	Do you feel lonely?	YES	NO
31.	Do you have anyone whom you can trust and confide in?	YES	NO
32.	Do you get along well with people?	YES	NO
33.	Do you often feel overwhelmed by the demands of everyday life?	YES	NO
34.	Do you often feel you cannot make it?	YES	NO
35.	Do you tend to be influenced by people with strong opinions?	YES	NO
36.	Do you tend to worry about what other people think of you?	YES	NO

Please describe any problems or difficulties you have had recently and indicate how much they have troubled you by marking the appropriate column

		Not at all	Only a little	Some-what	A great deal	
37.	It takes a long time to fall asleep	☐	☐	☐	☐	
38.	Restless sleep	☐	☐	☐	☐	
39.	Waking too early and not being able to fall asleep again	☐	☐	☐	☐	
40.	Feeling tired on waking up	☐	☐	☐	☐	
41.	Stomach, bowel pains	☐	☐	☐	☐	
42.	Heart beating quickly or strongly without a reason	☐	☐	☐	☐	
43.	Feeling dizzy or faint	☐	☐	☐	☐	
44.	Feelings of pressure or tightness in head or body	☐	☐	☐	☐	
45.	Breathing difficulties or feeling of not having enough air	☐	☐	☐	☐	
46.	Feeling tired or lack of energy	☐	☐	☐	☐	
47.	Irritable	☐	☐	☐	☐	
48.	Sad or depressed	☐	☐	☐	☐	
49.	Feeling tense or 'wound up'	☐	☐	☐	☐	
50.	Lost interests in most things	☐	☐	☐	☐	
51.	Attacks of panic	☐	☐	☐	☐	
52.	Do you believe you have a physical disease but that doctors have not diagnosed it correctly?	☐	☐	☐	☐	
53.	When you read or hear about an illness, do you get similar symptoms?	☐	☐	☐	☐	
54.	When you notice a sensation in your body, do you find it difficult to think of something else?	☐	☐	☐	☐	
55.	How do you rate the quality of your life?	Excellent	Good	Fair	Poor	Awful

Appendix 2. PSI, revised version (modified by Sonino and Fava [1])

Observer-rating scores

	Highly stressful life		Stressful life		Non-stressful life
Stress	5	4	3	2	1
	Excellent	Good	Fair	Poor	Absent
Well-being	5	4	3	2	1
	Incapacitating	Severe	Moderate	Slight	Absent
Psychological distress	5	4	3	2	1
	Incapacitating	Severe	Moderate	Slight	Absent
Abnormal illness behavior	5	4	3	2	1

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12.1.2.2. Psychosocial Index (PSI) in Hungarian language

Pszichoszociális Index (PSI revised, Sonino & Fava 2016) - Önjellemző tételek

KÓD: ……..

1. Születési dátum:…….. év ……hónap ……nap
2. Nem: Férfi ☐
   Nő ☐
3. Családi állapot: Egyedülálló ☐
   Házas/párkapcsolatban él ☐
   Elvált ☐
   Különélő ☐
   Özvegy ☐
4. Foglalkozás ……..
   Hány órát dolgozik egy héten? ……..
   Partnere foglalkozása: ……..
5. Volt-e valaha kórházban? Igen ☐ Nem ☐
6. Kérem, sorolja fel a betegségeit, a műtéteit és a kapott kezeléseket dátummal:
   ……
   ……
   ……
   ……
   ……..
7. Van-e valamilyen allergiája (gyógyszer, vegyszer)? Igen ☐ Nem ☐
   Ha igen, kérem nevezze meg, hogy mire:
   ……
8. Milyen gyógyszereket szed jelenleg?
   ……..
9. Fogyaszt-e rendszeresen alkoholt? Igen ☐ Nem ☐
10. Dohányzik-e? Igen ☐ Nem ☐
11. Használ-e kábítószert? Igen ☐ Nem ☐
12. Fogyaszt-e kávét vagy teát? Igen ☐ Nem ☐
    Ha igen, hányat naponta?.....

Az elmúlt egy évben történt-e valamelyik Önnel az alább felsoroltak közül? (Igen/Nem)

13. Egy családtag halála Igen ☐ Nem ☐
14. Különválás a házastársától/élettársától Igen ☐ Nem ☐
15. Munkahelyváltás a közelmúltban Igen ☐ Nem ☐
16. Anyagi nehézségek Igen ☐ Nem ☐
17. Költözés a településen belül Igen ☐ Nem ☐
18. Költözés másik településre Igen ☐ Nem ☐
19. Jogi problémák Igen ☐ Nem ☐
20. Új párkapcsolat kezdete Igen ☐ Nem ☐

Kérjük, válaszoljon az alábbi kérdésekre (Igen/Nem)

21. Van-e állása? Igen ☐ Nem ☐
    Ha van állása:

22. Elégedett a munkájával? Igen [ ] Nem [ ]
23. Nyomás alatt van-e a munkahelyén? Igen [ ] Nem [ ]
24. Vannak-e problémái a munkatársaival? Igen [ ] Nem [ ]

Ha nincs állása:

22. Ön nyugdíjas vagy tanuló? Igen [ ] Nem [ ]
23. Nyomás alatt érzi-e magát a mindennapokban? Igen [ ] Nem [ ]
24. Képtelen munkát találni? Igen [ ] Nem [ ]
25. Vannak komoly vitái közeli hozzátartozóival? Igen [ ] Nem [ ]
26. Vannak komoly vitái másokkal? Igen [ ] Nem [ ]
27. Volt-e közeli rokona súlyos beteg az elmúlt évben? Igen [ ] Nem [ ]

Ha igen, kérem írja le mi volt az:

……

28. Feszültnek érzi magát otthon? Igen [ ] Nem [ ]
29. Egyedül él? Igen [ ] Nem [ ]
30. Magányosnak érzi magát? Igen [ ] Nem [ ]
31. Van olyan ember, akiben megbízhat? Igen [ ] Nem [ ]
32. Jól kijön másokkal? Igen [ ] Nem [ ]
33. Gyakran érzi úgy, hogy túl sok hárul Önre a mindennapokban? Igen [ ] Nem [ ]
34. Gyakran érzi úgy, hogy képtelen megbirkózni ezzel? Igen [ ] Nem [ ]
35. Hajlamos arra, hogy befolyásolja mások erős véleménye? Igen [ ] Nem [ ]
36. Hajlamos arra, hogy aggódjon amiatt, amit mások gondolnak Önről? Igen [ ] Nem [ ]

Kérem, jelezze, ha a felsoroltak közül mostanában bármelyiket észlelte, és jelölje a probléma súlyosságát a megfelelő négyzetbe helyezett X-szel

	Nem	Kicsit	Eléggé	Nagyon
37. Hosszú időbe telik, míg el tudok aludni	[ ]	[ ]	[ ]	[ ]
38. Nyugtalanul alszom	[ ]	[ ]	[ ]	[ ]
39. Túl korán ébredek és nem tudok visszaaludni	[ ]	[ ]	[ ]	[ ]
40. Fáradtan ébredek	[ ]	[ ]	[ ]	[ ]
41. Gyomor-, bélfájdalmak	[ ]	[ ]	[ ]	[ ]
42. Ok nélküli gyors vagy erős szívverés	[ ]	[ ]	[ ]	[ ]
43. Szédelgés vagy ájulás érzet	[ ]	[ ]	[ ]	[ ]
44. Nyomás vagy feszülés érzet a fejben vagy a testben	[ ]	[ ]	[ ]	[ ]
45. Nehézlégzés vagy légszomj	[ ]	[ ]	[ ]	[ ]
46. Fáradtság vagy energia hiány	[ ]	[ ]	[ ]	[ ]
47. Ingerlékenység	[ ]	[ ]	[ ]	[ ]
48. Szomorúság vagy nyomott hangulat	[ ]	[ ]	[ ]	[ ]
49. Feszültség vagy felhangoltság	[ ]	[ ]	[ ]	[ ]
50. Elvesztettem az érdeklődésemet a dolgok iránt	[ ]	[ ]	[ ]	[ ]
51. Pánik rohamok	[ ]	[ ]	[ ]	[ ]
52. Azt hiszem, hogy testi betegségem van, de az orvos nem ismerte fel	[ ]	[ ]	[ ]	[ ]

53. Ha olvasok, vagy hallok egy betegségről, észlelem magamon a tüneteit [ ] [ ] [ ] [ ]
54. Ha érzek valamit a testemben, nehéz az, hogy másra gondoljak [ ] [ ] [ ] [ ]
55. Hogyan értékeli az életminőségét?

Kiváló [ ] Jó [ ] Átlagos [ ] Rossz [ ] Szörnyű [ ]

12.1.3.1. Kellner's Symptom Questionnaire (SQ) in English language

1. Kellner's Symptom Questionnaire

Please describe how you have felt DURING THE PAST WEEK TO DAY and make a small check mark like this √ .
For example the word NERVOUS is on the first line: if you have felt nervous check YES like this √YES NO
If you have not felt nervous check NO like this YES √NO
A few times you have the choice of checking either TRUE or FALSE.
Do not think long before answering. Work quickly!

1	Nervous	YES	NO
2	Weary	YES	NO
3	Irritable	YES	NO
4	Cheerful	YES	NO
5	Tense, tensed up	YES	NO
6	Sad, blue	YES	NO
7	Happy	YES	NO
8	Frightened	YES	NO
9	Feeling Calm	YES	NO
10	Feeling healthy	YES	NO
11	Loosing temper easily	YES	NO
12	Feeling of not enough air	TRUE	FALSE
13	Feeling kind toward people	YES	NO
14	Feeling fit	YES	NO
15	Heavy arms or legs	YES	NO
16	Feeling confident	YES	NO
17	Feeling warm toward people	YES	NO
18	Shaky	YES	NO
19	No pain anywhere	TRUE	FALSE
20	Angry	YES	NO
21	Arms and legs feel strong	YES	NO
22	Appetite poor	YES	NO
23	Feeling peaceful	YES	NO
24	Feeling unworthy	YES	NO
25	Annoyed	YES	NO
26	Feeling of rage	YES	NO
27	Cannot enjoy yourself	YES	NO
28	Tight head or neck	YES	NO
29	Relaxed	YES	NO
30	Restless	YES	NO
31	Feeling friendly	YES	NO
32	Feeling of hate	YES	NO
33	Choking feeling	YES	NO
34	Afraid	YES	NO
35	Patient	YES	NO
36	Scared	YES	NO
37	Furious	YES	NO
38	Feeling charitable, forgiving	YES	NO
39	Feeling guilty	YES	NO
40	Feeing well	YES	NO
41	Feeling of pressure in head or body	YES	NO
42	Worried	YES	NO
43	Contented	YES	NO
44	Weak arms or legs	YES	NO
45	Feeling desperate, terrible	YES	NO

46	No aches anywhere	TRUE	FALSE
47	Thinking of death or dying	YES	NO
48	Hot tempered	YES	NO
49	Terrified	YES	NO
50	Feeling of courage	YES	NO
51	Enjoying yourself	YES	NO
52	Breathing difficult	YES	NO
53	Parts of the body feel numb or tingling	YES	NO
54	Takes a long time to fall asleep	YES	NO
55	Feeling hostile	YES	NO
56	Infuriated	YES	NO
57	Heart beating fast or pounding	YES	NO
58	Depressed	YES	NO
59	Jumpy	YES	NO
60	Feeling a failure	YES	NO
61	Not interested in things	TRUE	FALSE
62	Highly strung	YES	NO
63	Cannot relax	TRUE	FALSE
64	Panicky	YES	NO
65	Pressure on head	YES	NO
66	Blaming yourself	YES	NO
67	Thoughts of ending your life	YES	NO
68	Frightening thoughts	YES	NO
69	Enraged	YES	NO
70	Irritated by other people	YES	NO
71	Looking forward toward the future	YES	NO
72	Nauseated, sick to stomach	YES	NO
73	Feeling that life is bad	YES	NO
74	Upset bowels or stomach	YES	NO
75	Feeling inferior to others	YES	NO
76	Feeling useless	YES	NO
77	Muscle pains	YES	NO
78	No unpleasant feeling s in head or body	TRUE	FALSE
79	Headaches	YES	NO
80	Feel like attacking people	YES	NO
81	Shaking with anger	YES	NO
82	Mad	YES	NO
83	Feeling goodwill	YES	NO
84	Feel like crying	YES	NO
85	Cramps	YES	NO
86	Feeling that something bad will happen	YES	NO
87	Wound up, uptight	YES	NO
88	Get angry quickly	YES	NO
89	Self-confident	YES	NO
90	Resentful	YES	NO
91	Feeling of hopelessness	YES	NO
92	Head pains	YES	NO

12.1.3.2. Kellner’s Symptom Questionnaire (SQ) in Hungarian language

R. Kellner-féle TÜNET kérdőív

Kérjük, gondolja végig, hogy érezte magát az elmúlt héten / mai napon, és x-elje be a megfelelő választ. Vegyük például az első pontban az „Ideges” szót. Ha idegesnek érezte magát, x-elje be az IGEN választ. Ha nem érezte magát idegesnek, akkor a NEM választ jelölje x-szel. Néhány állításnál IGAZ vagy HAMIS közül kell választania. Például, vegyük a „”Nem kaptam elég levegőt”-érzés” kifejezést: ha valóban úgy érezte, hogy nincs elég levegője, akkor jelölje be az IGAZ választ, de ha nem volt ilyen érzése, akkor a HAMIS választ x-elje. Ugyanígy a „Nincsenek sehol fájdalmaim” állításnál: IGAZ, ha nem voltak fájdalmai, és éppen ellenkezőleg, HAMIS, ha voltak fájdalmai. Ne gondolkodjon sokat, mielőtt válaszol. Köszönjük a kitöltést!

1.	Ideges	IGEN	NEM
2.	Fáradt	IGEN	NEM
3.	Irritábilis	IGEN	NEM
4.	Vidám	IGEN	NEM
5.	Feszült	IGEN	NEM
6.	Szomorú	IGEN	NEM
7.	Boldog	IGEN	NEM
8.	Rémült	IGEN	NEM
9.	Nyugodt	IGEN	NEM
10.	Egészséges	IGEN	NEM
11.	Könnyen elvesztettem a nyugalmam	IGEN	NEM
12.	“ Nem kaptam elég levegőt”-érzés	IGAZ	HAMIS
13.	Kedvesség érzés mások iránt	IGEN	NEM
14.	Fitt érzés	IGEN	NEM
15.	“Nehéz” végtagok	IGEN	NEM
16.	Magabiztosság érzése	IGEN	NEM
17.	Melegség érzés mások iránt	IGEN	NEM
18.	Remegő	IGEN	NEM
19.	Nincsenek sehol fájdalmaim	IGAZ	HAMIS
20.	Mérges	IGEN	NEM
21.	Karjaim, lábaim erősnek éreztem	IGEN	NEM
22.	Kis étvágy	IGEN	NEM
23.	Békés	IGEN	NEM
24.	Értéktelen	IGEN	NEM
25.	Bosszús	IGEN	NEM
26.	Düh érzése	IGEN	NEM
27.	Nem tudtam jól érezni magam	IGAZ	HAMIS
28.	Merev nyak vagy fej	IGEN	NEM
29.	Nyugodt	IGEN	NEM

30.	Nyugtalan	IGEN	NEM
31.	Barátságos	IGEN	NEM
32.	Utálatot éreztem	IGEN	NEM
33.	Fuldokló érzés	IGEN	NEM
34.	Félelem	IGEN	NEM
35.	Türelmes	IGEN	NEM
36.	Ijedt	IGEN	NEM
37.	Dühös	IGEN	NEM
38.	Adakozó, adományozó	IGEN	NEM
39.	Lelkiismeretfurdalás	IGEN	NEM
40.	Jó közérzet	IGEN	NEM
41.	Nyomásérzés a fejben vagy a testben	IGEN	NEM
42.	Aggódó	IGEN	NEM
43.	Elégedett	IGEN	NEM
44.	Gyenge karok és lábak	IGEN	NEM
45.	Kétségbeesett, szörnyű érzés	IGEN	NEM
46.	Semmi fájdalom sehol	IGAZ	HAMIS
47.	Halálról vagy a haldoklásról gondolkodtam	IGEN	NEM
48.	Fűtött temperamentum	IGEN	NEM
49.	Rémült	IGEN	NEM
50.	Bátorság érzése	IGEN	NEM
51.	Jól éreztem magam	IGEN	NEM
52.	Nehezen lélegeztem	IGEN	NEM
53.	Egyes testrészeim zsibbadtak vagy bizseregtek	IGEN	NEM
54.	Sok időbe telt elaludni	IGEN	NEM
55.	Rosszindulat érzése	IGEN	NEM
56.	Feldühödöttség érzése	IGEN	NEM
57.	Heves, gyors szívdobogás érzés	IGEN	NEM
58.	Depresszió	IGEN	NEM
59.	Izgatott	IGEN	NEM
60.	Kudarc érzése	IGEN	NEM
61.	Nem érdekelnek a dolgok	IGAZ	HAMIS
62.	Erősen feszült	IGEN	NEM
63.	Nem tudtam ellazulni	IGAZ	HAMIS
64.	Pánikolás	IGEN	NEM
65.	Nyomás érzés a fejen	IGEN	NEM
66.	Saját magam okolása	IGEN	NEM
67.	Öngyilkossági gondolatok	IGEN	NEM
68.	Ijesztő gondolatok	IGEN	NEM
69.	Feldühítettség érzése	IGEN	NEM
70.	Mások által irritált	IGEN	NEM
71.	Alig vártam, mit hoz a jövő	IGEN	NEM

72.	Hányinger	IGEN	NEM
73.	Úgy éreztem, rossz az élet	IGEN	NEM
74.	Felfordult gyomor, belek	IGEN	NEM
75.	Alárendelt érzés másokkal szemben	IGEN	NEM
76.	Haszontalan érzés	IGEN	NEM
77.	Izomfájdalmak	IGEN	NEM
78.	Semmi kellemetlen érzés a fejben vagy a testben	IGAZ	HAMIS
79.	Fejfájás	IGEN	NEM
80.	Ahhoz volt kedvem, hogy megtámadjak másokat	IGEN	NEM
81.	Remegtem a dühtől, dühöngtem	IGEN	NEM
82.	Megőrülés érzése	IGEN	NEM
83.	Jóakarat érzése	IGEN	NEM
84.	Sírhatnékom volt	IGEN	NEM
85.	Görcsök	IGEN	NEM
86.	Úgy éreztem, valami rossz fog történni	IGEN	NEM
87.	Felhúztam magma, feszült voltam	IGEN	NEM
88.	Gyorsan mérges lettem	IGEN	NEM
89.	Önbizalom érzése	IGEN	NEM
90.	Bánatos	IGEN	NEM
91.	Reménytelenség érzése	IGEN	NEM
92.	Fej tájéki fájdalmak	IGEN	NEM

12.1.4.1. Short version of Depression, Anxiety and Stress Scale (DASS-21) in English language

DASS21

Name: *Date:*

Please read each statement and circle a number 0, 1, 2 or 3 that indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1	I found it hard to wind down	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5	I found it difficult to work up the initiative to do things	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I experienced trembling (eg, in the hands)	0	1	2	3
8	I felt that I was using a lot of nervous energy	0	1	2	3
9	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting agitated	0	1	2	3
12	I found it difficult to relax	0	1	2	3
13	I felt down-hearted and blue	0	1	2	3
14	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
15	I felt I was close to panic	0	1	2	3
16	I was unable to become enthusiastic about anything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3
18	I felt that I was rather touchy	0	1	2	3
19	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
20	I felt scared without any good reason	0	1	2	3
21	I felt that life was meaningless	0	1	2	3

12.1.4.2. Short version of Depression, Anxiety and Stress Scale (DASS-21) in Hungarian language

DASS21

Név: ***Dátum:***

Kérjük, olvassa el az alábbi kijelentéseket és karikázza be a 0, 1, 2 vagy 3 számot, attól függően hogy *az* ***elmúlt hétre vonatkozóan*** az adott kijelentés mennyire volt jellemző Önre. Nincs jó vagy rossz válasz. Ne töltsön túl sok időt a válaszadással!

A válaszadás fokozatainak jelentése a következő:

0 Egyáltalán nem volt rám jellemző
1 Egy kicsit, vagy időnként jellemző volt rám
2 Elég jelentősen, vagy gyakran volt rám jellemző
3 Igen tekintélyes mértékben, vagy nagyon gyakran jellemző volt rám

1	Nehezemre esett, hogy ellazuljak	0	1	2	3
2	Azt vettem észre, hogy kiszáradt a szám	0	1	2	3
3	Egyáltalán nem voltam képes pozitív érzelmekre	0	1	2	3
4	Úgy éreztem mintha valami baj lenne a lélegzésemmel (pl. nagyon gyorsan kapkodtam a levegőt, vagy alig kaptam levegőt, pedig nem voltam fizikailag megterhelve)	0	1	2	3
5	Nehezemre esett bármibe is belekezdeni	0	1	2	3
6	Indulatosan reagáltam sok mindenre	0	1	2	3
7	Észrevettem, hogy reszketek (pl. a kezem)	0	1	2	3
8	Úgy éreztem, hogy a feszültségből származó energia hajt	0	1	2	3
9	Aggódtam amiatt, hogy egyszer olyan helyzetbe kerülök, ahol elfog a pánik és bolondot csinálok magamból	0	1	2	3
10	Úgy éreztem, hogy az életben semmi jó nem vár rám	0	1	2	3
11	Zaklatottnak éreztem magam	0	1	2	3
12	Nehezemre esett a pihenés és a kikapcsolódás	0	1	2	3
13	Csüggedtnek és lehangoltnak éreztem magam	0	1	2	3
14	Nehezen tudtam elviselni, ha mások feltartottak a dolgokban	0	1	2	3
15	A rémület érzése fogott el	0	1	2	3
16	Semmi sem tudott lelkesíteni	0	1	2	3
17	Nem éreztem úgy, hogy értékes ember vagyok	0	1	2	3
18	Feszült, ideges voltam	0	1	2	3
19	Észrevehető volt a szívműködésem (pl. gyorsan vagy furcsán vert a szívem), pedig nem voltam fizikailag megterhelve	0	1	2	3
20	Minden ok nélkül félelemérzés fogott el	0	1	2	3
21	Értelmetlennek láttam az életet	0	1	2	3

12.1.5.1. Public Health Surveillance Well-being Scale (PHS-WB) in English language

Appendix

APPENDIX A. PUBLIC HEALTH SURVEILLANCE WELL-BEING (PHS-WB) SCALE

1. In this section, there are a number of statements with which you may or may not agree. For each statement listed, please indicate whether you personally agree or disagree with it using a scale where 1 means "strongly disagree," 2 means "somewhat disagree," 3 means "neither agree nor disagree," 4 means "somewhat agree," and 5 means "strongly agree." If you don't understand a statement or it is not applicable to you, please let that row blank.

	Strongly disagree				Strongly agree
a. I am satisfied with my life	1☐	2☐	3☐	4☐	5☐
b. My life has a clear sense of purpose.....	1☐	2☐	3☐	4☐	5☐
c. Most days I feel a sense of accomplishment from what I do	1☐	2☐	3☐	4☐	5☐

2. How much of the time during the past 30 days have you felt…?

	None of the time		Some of the time		All of the time
a. Cheerful	1☐	2☐	3☐	4☐	5☐
b. Hopeless	1☐	2☐	3☐	4☐	5☐

3. Please tell me on a scale of 1 to 10 how satisfied you are with each of the following items, where 1 means "very dissatisfied" and 10 means "very satisfied."

	1	2	3	4	5	6	7	8	9	10
a. Your family life	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐	9☐	10☐
b. Your friends and social life	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐	9☐	10☐
c. Your energy level	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐	9☐	10☐

	Excellent	Very good	Good	Fair	Poor
4. In general, would you say your health is…?	1☐	2☐	3☐	4☐	5☐

	Number of days	None/zero days	Don't know/ Not sure
5. During the past 30 days, for about how many days have you felt very healthy and full of energy?	___	1☐	2☐

12.1.5.2. Public Health Surveillance Well-being Scale (PHS-WB) in Hungarian language

Általános Elégedettség Skála (PHS-WB)

1. Kérjük, értékelje 5 fokozatú skálán, hogy mennyire ért egyet az alábbi állításokkal.

	Egyáltalán nem értek egyet	*Nem értek egyet*	*Igaz is, nem is*	*Egyetértek*	*Teljesen egyetértek*
a. Elégedett vagyok az életemmel.	①	②	③	④	⑤
b. Az életemnek egyértelmű célja van.	①	②	③	④	⑤
c. A legtöbbször értelmét látom annak, amit véghez viszek.	①	②	③	④	⑤

2. Az elmúlt 30 napban milyen gyakran érezte az alábbiakat?

	Soha	Néha	Többször	Sokszor	Mindig
a. Vidám	①	②	③	④	⑤
b. Reménytelen	①	②	③	④	⑤

3. Kérjük, értékelje 10 fokozatú skálán, hogy mennyire elégedett az alábbi jellemzőkkel. Az **1-es** végpont a **teljes elégedetlenség**et jelenti, míg a **10-es** a **teljes elégedettség**et.

	Nagyon elégedetlen									*Nagyon elégedett*
a. A családi életével.	①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩
b. Barátaival és egyéb társas kapcsolataival.	①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩
c. Az energia-szintjével.	①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩

4. Kérjük, értékelje 5 fokozatú skála segítségével, hogy összességében hogyan minősíti saját egészségi állapotát.

	Rossz	*Türhető*	*Jó*	*Nagyon jó*	*Kitűnő*

a. Az egészégi állapotom…	①	②	③	④	⑤

5. Az **elmúlt 30 napban**, kb. hány napon érezte magát **nagyon egészségesnek** és **energikusnak**? Kérjük, hogy 0-30 közötti számmal válaszoljon. Ha egyetlen egy ilyen nap sem volt, akkor írjon 0-át, ha az egész hónapban egészségesnek és energikusnak érezte magát, akkor írjon 30-at. ☐☐ nap

13. Supplementary Material

Table 1. Methodological approaches for the assessment of patient-reported outcome measures (PROMs) [44]

	CLINIMETRIC APPROACH	PSYCHOMETRIC APPROACH
RELIABILITY	Homogeneity not required Multidimensionality	Homogeneity Unidimensionality
SENSITIVITY	Ability to discriminate between: • different groups of patients • patients from healthy controls • changes in clinical trials • wanted and unwanted effects of treatments • active treatment from placebo	Ability to detect meaningful changes
VALIDITY	**Construct validity:** the items provide distinctive clinical information and belong to underlying clinical dimensions (Rasch and Mokken analysis) **Predictive validity:** the ability to predict response to treatment and clinical outcomes **Incremental validity:** distinctive contribution or increase in predictive ability associated with the inclusion of a particular instrument in the clinical decision process (Regression analysis)	**Construct validity:** psychometric evidence of the unidimensionality of the rating scale under examination (Factoranalysis) **Content validity:** moderate to strong correlations between evaluated rating scale and already commonly used and accepted PROMs

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ORIGINAL ARTICLE

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To prevent being stressed-out: Allostatic overload and resilience of general practitioners in the era of COVID-19. A cross-sectional observational study

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KEY MESSAGES

- Allostatic overload refers to the dysregulation of stress-related responses leading to disease.
- High-risk and high-gain: the higher the complexity, the higher the potential impact.
- It arises when acute or chronic stress-load exceeds individual coping ability.
- COVID-19 – related allostatic overload caused a huge burden on healthcare professionals, including GPs.
- Active recreation might help staying balanced with elevated well-being.

ABSTRACT

Background: Responsibility of general practitioners (GPs) in delivering safe and effective care is always high but during the COVID-19 pandemic they face even growing pressure that might result in unbearable stress load (allostatic overload, AO) leading to disease.

Objectives: We aimed to measure AO of Hungarian GPs during the COVID-19 pandemic and explore their recreational resources to identify potential protective factors against stress load.

Methods: In a mixed-method design, Fava's clinimetric approach to AO was applied alongside the Psychosocial Index (PSI); Kellner's symptom questionnaire (SQ) to measure depression, anxiety, hostility and somatisation and the Public Health Surveillance Well-being Scale (PHS-WB) to determine mental, social, and physical well-being. Recreational resources were mapped. Besides Chi-square and Kruskal-Wallis tests, regression analysis was applied to identify explanatory variables of AO.

Results: Data of 228 GPs (68% females) were analysed. Work-related changes caused the biggest challenges leading to AO in 60% of the sample. While female sex (OR: 1.99; CI: 1.06; 3.74, $p = 0.032$) and other life stresses (OR: 1.4; CI: 1.2; 1.6, $p < 0.001$) associated with increased odds of AO, each additional day with 30 min for recreation purposes associated with 20% decreased odds (OR: 0.838; CI: 0.72; 0.97, $p = 0.020$). 3–4 days a week when time was ensured for recreation associated with elevated mental and physical well-being, while 5–7 days associated with lower depressive and anxiety symptoms, somatisation, and hostility.

Conclusion: Under changing circumstances, resilience improvement through increasing time spent on recreation should be emphasised to prevent GPs from the adverse health consequences of stress load.

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KEYWORDS
Allostatic overload; resilience; general practitioners; COVID-19; recreational resources

Introduction

The ongoing pandemic of COVID-19 turned out to be a strong stressor for all medical doctors, causing psychological distress and mental health problems [1]. It demanded hospitals and specialist care to transform into pandemic centres. This has increased the responsibility of family physicians working in primary care to screen and treat serious cases requiring skills specific to other specialities. They were also expected to run their consultations online without physical examination, and were not sufficiently equipped to contact patients when needed [2]. In the last decades, general practitioners' physical and mental health has come into focus [3,4]. Besides extreme workload, moral

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implications for 'good doctoring' increased their work-related stress. Major events, but subtle, chronic daily experiences as well – which an individual perceives as stressful – activate regulatory systems (the autonomic, neuroendocrine, metabolic, and immune system) to change a set point and operate at elevated or reduced levels [5,6]. This is called allostasis, the process to achieve stability through change [7]. Increased catecholamine, cytokine and HPA hormone levels are the mediators of this adaptational process resulting in elevated heart rate, blood pressure or inflammation [5]. However, long-term activation of the regulatory systems by repeated stress will lead to overuse and dysregulation of the mediators of allostasis, causing allostatic load, manifesting in anger, fatigue, frustration and feeling out of control ('stressed-out') [8]. When challenges exceed the individual's coping ability, allostatic overload will be the result, a condition with consequent diseases (e.g. hypertension, depression, arthritis, metabolic syndrome or tumorous diseases) [9–11]. To understand the role of allostatic overload in the background of ill-health [12], identification of individual stressors, clinical signs and symptoms directly related to stress sources and the individual's response to the stressors give the cue [10,13]. Scientific literature concerning GPs' health focuses primarily on mental ill-health [14]. This is even more essential with the burden of the pandemic on the health care system worldwide. Such an exceptional situation, however, should also lead to exploring sources of resilience beside identifying distress. Increasing well-being will contribute to reaching optimum health through positive affect, personal relationships, and a meaningful and optimistic life [14–16]. Besides, cognitive-behavioural stress-management techniques and mindfulness-based education programmes [14], recreation has recently come into focus as a positive coping response to stress [15,17].

Study objectives

We targeted to define the prevalence of allostatic overload among Hungarian general practitioners during the first wave of COVID-19 and define the most important factors associated with it. We postulated that the infection and the related confinements and proceeding rules concerning primary health care resulted in significantly increased stress load of professionals. Additionally, we aimed to measure their well-being, regularity, and forms of recreational activity they attain and – consequently – if these might associate with increased mental and physical health or increased resilience against stress load.

Methods

Study design and sample recruitment

We performed a voluntary online survey among Hungarian GPs between 28th August and 16th October 2020. Participants were recruited between 28th and 30th August *via* institutional sources (1,262 registered email addresses of surgeries or doctors throughout Hungary) and then one reminder was sent between 8th and 10th September. Our invitation letter contained that the Family Medicine Department at Semmelweis University conducted the survey, the time frame for completing the survey (15–20 min) and we defined our aim as to explore the effects of the previous 6 months (the first wave of the pandemic) on them as family physicians and as persons. We did not offer monetary or non-monetary incentives. Personal data was not collected, but – to allow possible follow up – we generated an ID code for each participant. We constructed our survey so that all answers had to be given to continue with the survey; therefore, participants answered all questions, and we did not need to exclude anyone due to incomplete questionnaire reply.

Ethics

Online consent was secured by all participants. The study was conducted by the Declaration of Helsinki and was approved by the review board of the Medical Research Council (IV/5657-2/2020/EKU).

Measurements

Sociodemographic and health-related characteristics of the sample. We collected data on participants' age, gender, and place of living (capital, county seat, town or village); on working conditions (actively working during the pandemic; method of working (personal, phone consultations, other), uncertainty about coronavirus in comparison to the first wave (no change, decreased, increased)). We asked if they took an active role in maintaining their health and the number of days they did recreational activities for at least 30 min. We also asked for the number of chronic diseases, any diagnosed psychiatric disease, the number of prescribed and over-the-counter medicines taken daily.

Allostatic overload. We measured COVID-related allostatic overload according to Fava's definition based on

Table 1. Clinimetric criteria of allostatic overload based on the Diagnostic Criteria for Psychosomatic Research Revised Semi Structured Interview (DCPR-R-SSI) and the Psychosocial Index (PSI).

Allostatic overload	DCPR-R-SSI	PSI
Criterion A	A1 The presence of a current identifiable source of distress in the form of recent life events and/ or chronic stress	Items • Death of a family member • Separation from spouse or long-time partner • Recent change of job • Financial difficulties • Moving within the same city • Moving to another city • Legal problems • Beginning of a new relationship • Seriously ill close relative
	A2 The stressor is judged to tax or exceed the individual coping skills when its full nature and full circumstances are evaluated	COVID-specific question *'During the time of the restrictions, did you feel that the changes caused by the coronavirus epidemic were testing or exceeding your capacity?'**
Criterion B *The stressor is associated with 1 or more of the following 3 features which have occurred within 6 months after the onset of the stressor*	B1 At least two symptoms • Difficulty falling asleep • Restless sleep • Early morning awakening • Lack of energy • Dizziness • Generalised anxiety • Irritability • Sadness • Demoralisation	Items • Long time to fall asleep/restless sleep/ waking up too early/feeling tired waking up • Stomach, bowel pains • Heart beating quickly or strongly without any reason • Pressure or tightness in head or body/ dizziness • Breathing difficulties • Tired, lack of energy • Irritable/sad/tense/lost interest • Panic attacks
	B2 Significant impairment in social or occupational functioning	Items • Work-related: satisfying/under pressure/ problems with colleagues/unemployed • Serious arguments with close relatives/others • Tension at home • Living alone/feeling lonely • Anyone to trust and confide in • Getting along well with people
	B3 Significant impairments in environmental mastery (feeling overwhelmed by the demands of everyday life)	Items • Do you often feel overwhelmed by the demands of everyday life? • Do you often feel you cannot make it?

DCPR-R criteria defined allostatic overload with related items from the Psychosocial Index self-rated questionnaire. Text in italics (fulfilling A2 criterion) was formulated to be specific to COVID epidemic as a stressor. PSI does not contain A2 criterion [19,20].

the Diagnostic Criteria for Psychosomatic Research-Revised (DCPR-R) and used the Psychosocial Index (PSI) self-rating questionnaire by the same authors to measure each criterion [13,18,19]. The PSI includes 55 items. Sociodemographic and clinical data are measured from 1 to 12, perceived and objective stress by items 13–20 and 22–30 in a YES/NO format with a maximum score of 17, and well-being by items 31–36 with a score ranging from 0 to 6. Psychological distress is measured by items 37–51 addressing symptoms of sleep disturbances, somatisation, anxiety, depression, and irritability on a 0–3 Likert scale with a maximum score of 45. Abnormal illness behaviour contains items 52–54, concerning bodily preoccupations and hypochondriac beliefs on a 0–3 Likert scale with a range from 0 to 9. Quality of life is measured by one direct question (item 55) with 5 possible choices from excellent to awful [19].

We applied these tools – in accordance with previous research [20,21] – to measure COVID-related allostatic overload (Table 1). Besides measuring individual stressors, our primary focus was on COVID-related allostatic overload. Therefore, we tailored A2 criterion of DCPR-R to COVID as a particular stressor. According to the instructions provided in the DCPR-R allostatic overload is diagnosed when A1 + A2 + B1 or B2 or B3 is present. To measure stress load independent of COVID-19, we applied PSI questions 13–20 and 22–30 [19].

Mental health and somatisation

Mental health was measured with the Kellner Symptom Questionnaire (SQ) and the Public Health Surveillance Well-being Scale (PHS-WB) [22,23]. SQ consists of four scales: depression, anxiety, somatisation, and hostility, each divided into two subscales, one for the symptoms

Table 2. Categories of COVID-related professional challenges of GPs with description and example responses.

Category	Description of category	Example response
Changes in means of consultation (phone, online)	Responses related to changing proceeding rules to continue consultation with telemedicine	*'Manage a lot of phone calls and emails'; 'telephone consultations during physical patient care'*
Discontinuation of patient care, patient observations, thus difficulties of diagnosing	Responses related to lack of personal contact with patients due to online consultations	*'It was difficult to decide whether there was an urgent and serious condition requiring immediate intervention – based on phone consultation and without physical examination'*
Undeveloped proceeding rules and lack of information on them, disorganisation	Responses related to chaos in regulations of primary health care and lack of information update considering proceeding rules	*'An inextricable, ever-changing set of proceeding rules'; 'not being informed and updated on time'*
Increased work-, thus stress load and responsibility due to COVID and unavailability of specialist care	Responses related to shot down of specialist care, thus having increased workload and responsibility	*'Unavailable specialist care'; 'I felt helpless that hospital and clinic care had actually ceased'*
Fear, worry, unreliable information, uncertainty	Responses related to uncertainty, lack of reliable information and predictability	*'Uncertainty, daily changing rules, chaos;' 'fear, ignorance'*
Panic and concern of patients and to calm and inform them	Responses related to the burden of calming panicking patients and giving them reliable information	*'Reassuring patients'; 'the dread that the patients pounded on me'*
Lack of protective equipment	Responses related to not having access to protective equipment when possibly being exposed to the virus	*'Lack of protective equipment;' 'the impossibility of obtaining protective equipment'*
Protecting own health, wearing mask, sanitising	Responses related to anxiety about own safety	*'protecting my assistant's and my health;' 'take care of the patient while I stay healthy'*
Lack of professional contact and help, incompetence of professionals	Responses related to unavailability of consultation with colleges of other specialties because of increased workload	*'Lack of both professional and political support;' 'unavailable specialist clinics;' 'tolerate the incompetence of epidemiologists'*

(depression, anxiety, somatisation and hostility) and the other for well-being (contentment, relaxation, physical well-being and friendliness) [22]. The 10-item shortened version of PHS-WB was used to measure physical, mental, and social well-being. The first five items (on scale 0–5) result in a score of mental well-being. The following two items measure social well-being with scales from 0 to 10. The last three items provide the score of physical well-being after their scales being unified. Total well-being is then calculated from all converted scores [23].

Qualitative methods

To identify the most burdening challenges Hungarian GPs had dealt with in relation to the pandemic, we included the following question in our survey: 'What was the biggest challenge for you during the epidemic and the quarantine?' Participants gave free-text answers, which ranged from single-word answers to paragraphs. Following standard qualitative analytical procedures, each researcher read all free-text responses systematically, identified blocks of text that reported factors contributing to allostatic overload, and assigned provisional code names. They compared their coding schemas and agreed on a common one. They then examined the codes, identified themes that organised them into higher-level concepts that explained the origins of overload, constantly comparing their interpretation with the original data, and agreeing on a final interpretation (Tables 2 and 3; Figure 1).

To create categories of stress releasing recreational activities, we selected the Mental Health Foundation (UK) 'How to manage and reduce stress' booklet as well as the American Counselling Association's article '100 Ways to Reduce Stress: Making the Balancing Act More Manageable' to base our choices. We offered multiple possibilities for recreation (connection with nature, reading or watching movies, physical exercise, meeting friends and acquaintances, cooking, praying or meditation, creative manual activities and DIY, or beautification and cosmetics) and participants were able to provide their answers on their sources of recreation as well. Their answers were then sorted and counted and presented in Figure 2.

Statistical analyses

Chi square tests were used in case of the categorical data, two-tailed *t*-test for normally and Kruskal-Wallis test for non-normally distributed continuous variables. Dunn's pairwise tests with Bonferroni adjustment for multiple comparisons were carried out for the three pairs of groups. Normality of data was assessed using the Kolmogorov-Smirnov test. In our cross-sectional study, we applied step forward likelihood ratio logistic regression analysis to estimate the role of age, sex, place of living, the number of chronic diseases, the number of stressors and the number of days the respondents applied at least 30-min recreation in the exposure to allostatic overload.

Table 3. Categories of COVID-related personal challenges of GPs with description and example responses.

Category	Description of category	Example response
Lack of personal contact	Responses related to being separated from loved ones and acquaintances	*'Lack of personal encounter;' 'lack of personal communication'*
Increased home workload, organisation, online education	Responses related to pressure at home to manage work, housekeeping, online education of children at the same time	*'Doing my work and taking care of the children in parallel, mainly studying with my school-age children;' 'helping my children learn at home'*
Curfew, travelling restrictions	Responses related to lack of freedom and curfew	*'My trip abroad had to be cancelled;' 'the confinement'*
Opening restrictions	Responses related to difficulties to run errands due to restrictions of opening hours	*'The time limit of shopping because my wife and I couldn't shop at the same time'*
Loss of mental balance, need of psychological help	Responses related to mental health problems and needing psychological help	*'To face my state of mind, my limits, my need for help'; 'psychic tension'*
Financial problems	Responses related to losing job and facing a financial crisis	*'The financial deficit due to the loss of side jobs'*
Loss of loved ones	Responses related to mourning passing loved ones	*'death of my husband'*

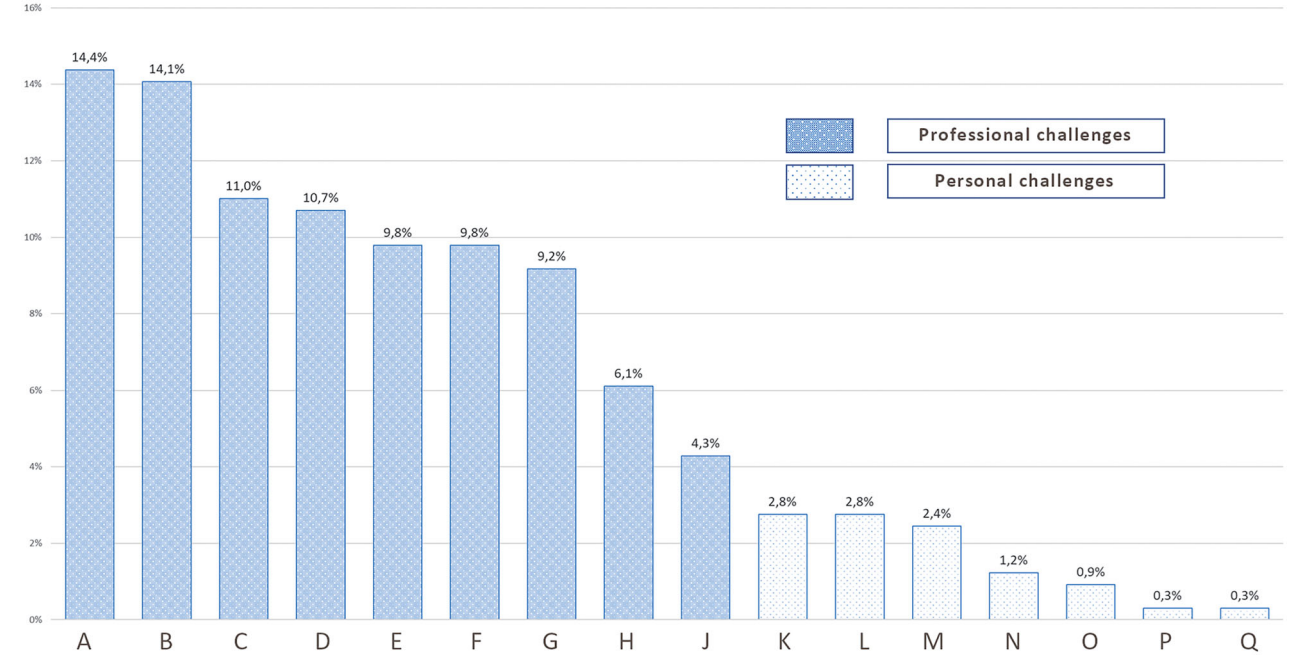

Figure 1. Percentage distribution of professional and personal challenges Hungarian GPs reported related to COVID ($n = 228$). (A) Changes in means of consultation (phone, online), (B) Discontinuation of patient care, patient observations, thus difficulties of diagnosing, (C) Undeveloped proceeding rules and lack of information on them, disorganisation, (D) Increased work-, thus stress load and responsibility due to COVID and unavailability of specialist care, (E) Fear, worry, unreliable information, uncertainty, (F) Panic and worry of patients and to calm and inform them, (G) Lack of protective equipment, (H) Protecting own health, wearing mask, sanitising, (I) Lack of professional contact and help, incompetence of professionals, (J) Lack of personal contact, (K) Increased home workload, organisation, online education, (L) Curfew, travelling restrictions, (M) Opening restrictions, (N) Loss of mental balance, need of psychological help, (O) Financial problems, (P) Loss of loved ones, (Q) Nothing.

We applied 95% confidence intervals (CI). In all cases, a p value < 0.05 was considered statistically significant. We used SPSS-24.0 software (SPSS Inc., Armonk, NY, USA).

Results

Sociodemographic and COVID-related characteristics

After excluding 13 double fill-outs, we analysed the data of 228 GPs, 155 of whom were females. The youngest doctor was 32 years old while the oldest was 88. We did not find any statistically significant differences in health-related and sociodemographic characteristics according to sex (Table 4).

We found that 222 colleagues worked during the first wave of the pandemic. Two-thirds of them (155) worked in person in the surgery during the pandemic. They all used mixed – personal, phone calls/video calls and online – possibilities for consultation.

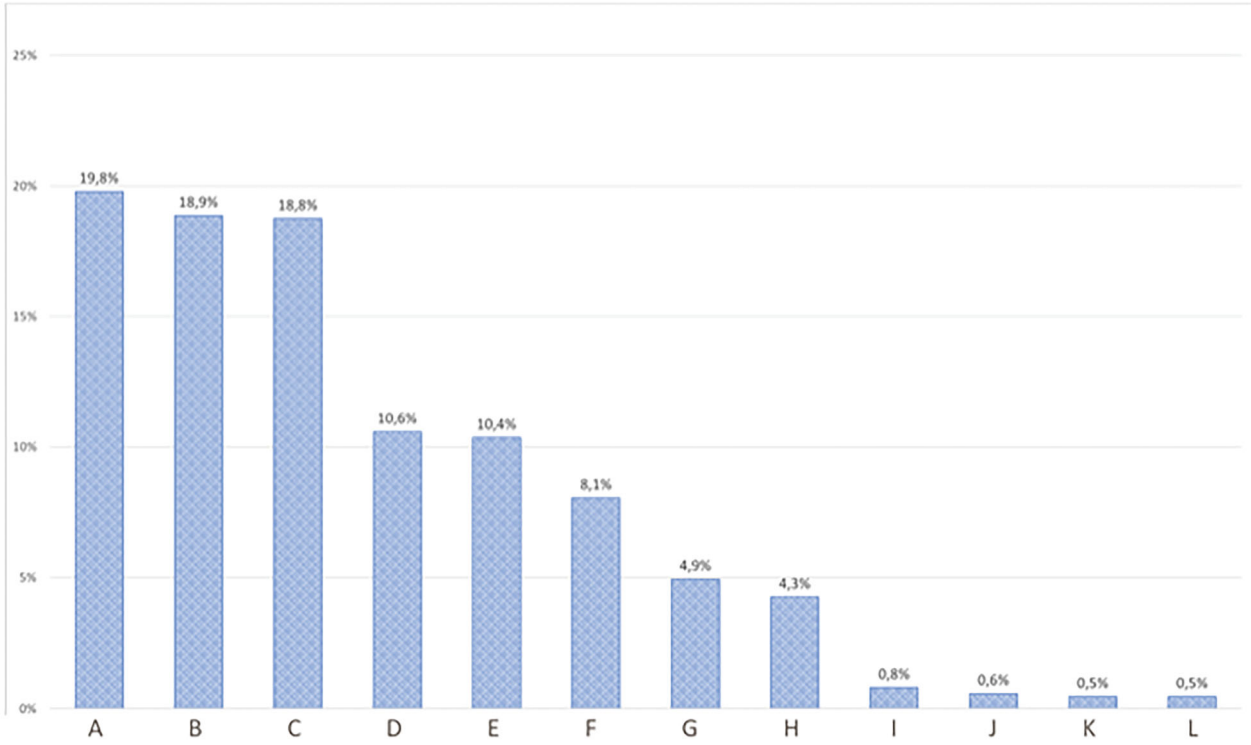

Figure 2. Percentage distribution of recreational activities reported by Hungarian GPs ($n = 228$). (A) Connection with nature, (B) Reading, watching movies, (C) Physical exercise, (D) Meeting friends and acquaintances, (E) Cooking, (F) Praying, meditation, (G) Creative manual activities, DIY, (H) Beautification, cosmetics, (I) Spending time with children, grandchildren, (J) Making and listening to music, (K) Gardening, (L) Training, learning, educational tasks.

Table 4. Sociodemographic and health-related characteristics of a Hungarian general practitioner sample during the COVID-19 pandemic ($N = 228$).

	Males ($N = 73$)	Females ($N = 155$)
Variables	Mean (SD)	Mean (SD)
Age	56 (12)	57 (10)
	N (%)	*N (%)*
Place of living, *n* (%)		
capital	22 (30)	67 (43)
county seat	12 (16)	20 (13)
town	30 (41)	48 (31)
village	9 (12)	20 (13)
Number of chronic diseases participating doctors had		
0	23 (32)	48 (31)
1–2	38 (52)	84 (54)
3–5	12 (16)	20 (13)
5<	0 (0)	3 (2)
Psychiatric disease (yes)		
	1 (1)	5 (3)
Number of medications participating doctors were taking themselves		
0	25 (34)	51 (33)
1–5	40 (55)	93 (60)
6≤	8 (11)	11 (7)

No significant difference was found between the two groups on any of the variables.

Sources of stress

According to GPs' answers on the most challenging aspects of the pandemic and the related quarantine, qualitative data showed that work-related conditions and increased workload were the most challenging for the majority of GPs (Figure 1). Electronic prescription and the use of virtual health service space increased dramatically, causing challenge for less frequent users. Structural changes in delivering care (from personal to online and phone consultation) as well as decreased possibility for outpatient specialty care, stood as the most essential points. Additionally, they dealt with increased responsibility of calming and informing patients while also in fear and uncertainty (Figure 1 and Table 2).

As shown in Figure 1, general practitioners mainly reported professional challenges as most burdening but personal difficulties yield important as well (Table 3).

Prevalence of allostatic overload and factors associated with it

Allostatic overload with somatic symptoms of distress or impaired social and occupational functioning was experienced by 60% ($N = 131$) of the sample. Female sex (OR: 1.99; CI: 1.06; 3.74, $p = 0.032$) and the increasing number of chronic daily stressors (OR: 1.4; CI: 1.2; 1.6, $p < 0.001$) both associated with increased odds of allostatic overload while each more day with time for recreation associated with 20% lower odds (OR: 0.838;

Table 5. Mental health parameters of general practitioners according to the number of days they spent at least 30 min for recreation during the week ($N = 228$).

	30 min/0–2 days ($N = 55$)	30 min/3–4 days ($N = 75$)	30 min/5–7 days ($N = 98$)
Anxiety (SQ)	6.00 (3.00;12.00)	6.00 (2.00;8.00)	3.00 (1.00;7.25)*
Depression (SQ)	6.00 (3.00;11.00)	3.00 (2.00;7.00)§	3.50 (1.00;7.00)*
Somatisation (SQ)	6.00 (4.00;12.00)	4.00 (2.00;8.00)	3.50 (1.00;7.00)*
Hostility (SQ)	7.00 (2.00;12.00)	5.00 (1.00;10.00)	3.50 (1.00;9.00)*
Mental health well-being (PHS-WB)	4.40 (3.20;4.60)	4.40 (4.00;4.80)§	4.40 (4.00;4.80)*
Social well-being (PHS-WB)	4.50 (3.50;4.50)	4.50 (4.00;5.00)	4.50 (3.63;5.00)
Physical well-being (PHS-WB)	3.30 (2.30;4.00)	4.00 (3.33;4.50)§	4.33 (3.33;4.66)*
Total well-being (PHS-WB)	3.77 (2.94;4.33)	4.24 (3.80;4.65)§	4.26 (3.67;4.71)*

SQ: Kellner Symptom Questionnaire; PHS-WB: Public Health Surveillance Well-being Scale; Medians and (IQRs) can be seen in cells. *Significant difference between 0–2 days and 5–7 days; §: significant difference between 0–2 days and 3–4 days.

CI: 0.72; 0.97, $p = 0.020$) after adjusting for age, place of living and chronic diseases.

Recreation and well-being

Two hundred and seventeen (95.2%) out of 228 family physicians reported doing something actively for their health in general. They reported spending at least 30 minutes on recreation an average of 4 days a week. We offered multiple possibilities for recreation to choose from besides individual answers. The median number of different recreation types chosen was 4 (IQR: 3, 5). The most popular forms were connection with nature, reading or watching movies and physical exercise (Figure 2). When grouping family physicians according to the number of days they recreated, we found that being involved in recreation at least 5 days a week associated with lower point scores on symptoms of anxiety, depression, somatisation, and hostility while just 3 days weekly associated with elevated scores on mental and physical well-being (Table 5).

Discussion

Main findings

We found that 60% of participating Hungarian family physicians suffered from allostatic overload in relation to adverse life events during the first wave of COVID-19 pandemic. Females and those experiencing more stressors in their lives were more vulnerable. Each additional day when time was ensured for 30-min recreation associated with 19% decreased odds of this vulnerability. Elevated mental and physical well-being associated with at least 3 days; lower symptoms of depression, anxiety, somatisation, and hostility, with 5–7 days recreation weekly.

Strengths and limitations

There is insufficient literature mapping general practitioners' mental health, but even those few concentrate mostly on negative aspects of it [14]. It is a rarity to find studies on resources to promote well-being which also support the ability to cope and perform under extreme stress circumstances. The strength of our research is to explore distress symptoms (depression, anxiety, hostility, and somatisation) as well as well-being (mental, physical, and social) under an acute stressor (COVID-19) amongst GPs. We defined the association of regular recreation with lower distress levels alongside with higher level of mental and physical well-being.

Our online survey reached an 18% response rate. Since response rates of 70% or higher are considered good, our response rate is low. Compared to other web-based GP surveys [24], however, our response rate did not seem inferior to others with similar constructions. One shortcoming of our data collection was that we could not separate non-respondents who did not receive the invitation (invalid email addresses) from those who did not provide a fill-in. Approximately one-third of the email addresses belonged to the surgery and not the doctor. High workload and administrative workload are main sources of GPs' nonresponse to surveys. Our results show that the COVID pandemic put extraordinary burden on GPs (increased workload was the fourth most important source of stress). This might increase the possibility of nonresponse, especially when the request arrived at surgery-related email address. Online surveys are less preferred than paper-based among family physicians. Computer illiteracy might be one cause for that. The finding supports that participant GPs found the changes in consultations most challenging. We found that our respondents were slightly younger than the average age of Hungarian general practitioners (57 years in the sample vs 64 years in the total population) and consisted of more female general practitioners (68% vs 53%). Similarly, French and Swiss GP respondents of a web-based survey were younger and contained fewer males than the community-based GP population [24]. COVID-19 related changes in

professional and personal life or emotional or psychological discomfort related to this topic could also influence participation. Recreational sources are individual sets of interests, relations, values, and goals developing throughout life, and practising them is advised by experts to prevent 'corona phobia' [25]. Although we could predict their role in lowering the odds of allostatic overload, defining a true causal relationship will be achievable by longitudinal research.

Allostatic overload and the most important factors associated with it in GPs during the first wave of COVID-19

The first wave of the ongoing pandemic shed light on the psychosocial burden health workers faced [26,27]. Job strain, social isolation, fears of stigmatisation and uncertainty about the future added to stress, exhaustion, and depressive mood nurses and doctors had experienced [27]. While most studies focus on those in close contact with COVID-19 patients [20,26,27], quantitative data about the types and levels of COVID-19 related stress among family physicians are scarce, even though they are first contact to most patients. Recent research in a hospital environment has confirmed that job strain and uncertainty about the future were the most common causes of higher levels of stress and depressive mood healthcare workers experienced [28]. Our results are in line with these findings, showing that in primary health care settings changes in working conditions, uncertainty and emotional issues multiplied the burden of the pandemic on them. Females and those who experienced additional stressors simultaneously to the pandemic were at higher risk. Exploring mental ill-health and constituents of GPs' well-being enhance the knowledge in the field.

Mental health and well-being of GPs and regularity and forms of recreational activity

According to literature, general practitioners are more depressed than white-collar workers [29] and experience higher patient-related stress than other medical specialists while their self-estimated health and workability is lower [30]. However, the well-being of British general practitioners was comparable to the local population, and GPs above 55 years showed higher hope and optimism than their younger counterparts [31]. Our sample showed comparable levels of mental and social well-being during the COVID-19 pandemic to a community sample [21]; however, anxiety and hostility scored higher, probably referring to the high level of additional professional stress load. Most of the GPs ensured time regularly for recreation. According to our results, higher frequency of weekly recreation associated with higher mental and physical well-being and lower distress symptoms. A recent review article on interventions highlights that besides psychotherapeutic programmes [14], increasing awareness on thoughts, beliefs, self-care, personal health and self-care boundaries improved mental health. Our results strengthen these findings because individually chosen types of recreation were equally able to improve mental health. This is even more important during the burdening time of the pandemic, when besides psychosocial support and a better infrastructure adjustment, leisure time is the second biggest resource following interpersonal connectedness [28].

Implications for practice

Besides providing eminent care for patients, it is of utmost importance to take conscious care of ourselves. Recreational activity can be easily achieved and is provenly effective in maintaining better mental and physical health and significantly reducing distress symptoms. Actively applying 30 minutes of recreation 5–7 days a week might dramatically improve our ability to succeed.

Conclusion

Our study demonstrates that Hungarian general practitioners were burdened by the first wave of COVID-19, with 60% of the participating physicians presenting allostatic overload. Professional challenges were most demanding, and females and those experiencing additional life stresses were more vulnerable. Regular recreation associated with elevated mental and physical well-being, lower distress symptoms and lowered odds of AO. Longitudinal research is needed to support our results further.

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Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Physical Exercise as a Resilience Factor to Mitigate COVID-Related Allostatic Overload

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Keywords
Physical exercise · 312 meridian exercise · Allostatic overload · Resilience · Well-being

Abstract
Introduction: The long-lasting threat of COVID-19 makes it necessary to explore strategies to improve coping skills which enable us to master a balanced life in the face of adversity. ***Objective:*** To unravel the most challenging aspects of COVID-19 in a nonclinical adult population and identify predictors of lost balance and consequent allostatic overload (AO). We examined the role of regular, moderate-intensity formula aerobic exercise (312 meridian exercise) in preventing allostatic overload through increasing well-being. ***Methods:*** An online survey was conducted to measure COVID-related allostatic overload according to clinimetric criteria. The Psychosocial Index (PSI), Kellner's Symptom Questionnaire (KSQ), short Depression Anxiety Stress Scales (DASS-21), Public Health Surveillance Well-Being Scale (PHS-WB), and Whiteley-7 were used to explore mental health characteristics. Univariate statistics logistic regression analysis and a general linear model were used. ***Results:*** According to 442 valid answers, 217 adults practiced physical exercise (PE) frequently (fPE, 3–5 times/every day) while 120 did it less regularly (1–2 times/week), and 105 did not exercise/practiced irregularly (controls). Restriction-related stressors were most challenging, resulting in AO in 29% (n = 128) of the sample. The main predictors were additional stressors (p = 0.005) and anxiety symptoms (p < 0.001). The prevalence of AO was lower (p = 0.018) in the fPE group when compared to controls. KSQ distress symptoms were also lower in fPE (p < 0.0001), while total well-being was increased (p < 0.001) after adjusting for sex, age, and number of chronic diseases. According to the PHS-WB, both physical and mental well-being were higher (p = 0.003 and p = 0.004, respectively) in fPE. ***Conclusions:*** Frequent moderate exercise is associated with better mental and physical well-being and a lower prevalence of AO.

Introduction

The ongoing pandemic of COVID-19 and the related confinements (online suppl. material [OSM]; see www.karger.com/doi/10.1159/000514331 for all online suppl. material) appear as strong stressors result-

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ing in significant changes in socioeconomic and work conditions for many. Additionally, family life has been restructured, with isolation of the elderly, and managing home-office and home-schooling simultaneously. These changes are becoming permanent with the second wave of the epidemic and people need to develop strategies to fight the threat and health consequences of the infection, cope successfully with long-lasting changes, and work up a lifestyle which results in improved resilience and well-being under trying circumstances.

Allostatic Load and Overload

The term allostatic load was coined by McEwen and Stellar [1] in 1993, with the aim of reinterpreting Selye's concept of stress [2]. It stems from the term allostasis [3], which refers to the ability of the human body to sustain homeostasis (to allow pH, blood glucose levels, body temperature, and oxygen supply to remain constant) via changes in other parameters [4, 5]. Elements of the neuroendocrine, autonomic, metabolic, and immune systems act as "mediators" in the process, resulting in adaptations to the physical and psychosocial stressors of everyday life [1, 4, 5]. However, when daily stressors sustain an alarm response, with increased catecholamine, cytokine, and HPA hormone levels for weeks or months, the resulting allostatic load will lead to lost balance and disorganization [5, 6]. The additional load of unpredictable events increases the allostatic load dramatically and can cause allostatic overload (AO), with overuse of mediators in a dysregulated manner [4]. Consequent wear and tear on the regulatory systems of the body leads to the exacerbation of pathophysiologic changes, resulting in myocardial infarction, tumor metastases, metabolic diseases, or health-damaging behaviour [1, 4, 5]. Stressful lifestyle-related unhealthy eating, a lack of physical activity, poor sleep, smoking, and alcohol or drug consumption all act through these same "mediators" to cause lifestyle-diseases [6].

Individual Vulnerability

Vulnerability to stress, or resilience against it, however, are highly individual, differ according to sex [1, 2, 4], and depend on the unique adaptive stress response and behavior determined by an individual's genetically encoded biological constitution as well as the environmental exposures during their lifespan [5, 7, 8]. While biomarkers express the state of the body, underlying individual experiential causes can be explored in clinical settings through structured measures of symptoms, physical signs, and other clinical phenomena [9, 10]. The clinical measurement of allostatic load and AO was established by Fava et al. [11, 12] in 2010 and refined in 2017. The clinimetric assessment defines stressors in social and family circles and at work [8, 12], and measures if the stressor has exceeded individual coping skills, when its full nature and all circumstances have been evaluated [8, 12]. This is followed by an evaluation of physiological and cognitive components of the individual stress response including psychosocial and physical symptoms [8, 12].

Stress Resilience

Resilience may reflect the state of heightened adaptability in the face of acute or chronic adversity [13, 14]. According to the concept of euthymia [15], it can be achieved through an optimal balance of positive and negative cognitions and affects [16]; this notion is supported by novel neurobiological research [14].

The Role of Physical Exercise in Boosting Resilience

To adapt to ongoing stress and promote well-being and resilience, especially when facing chronic stressors, lifestyle interventions play a pivotal role [17, 18]. Physical exercise (PE) has been obtaining attention for decades as a tangible and highly effective nonpharmacological tool to boost resilience by preventing chronic diseases, enhancing cognitive functioning and mental health, delaying the gradual loss of functional reserve associated with the aging process, improving immunity, reducing inflammation, and positively affecting mood states like anxiety and depression [19–24]. Exercise is a planned, structured, and repetitive physical activity targeted at improving health- or skill-related attributes [25]. Regular, moderate-intensity exercise [26] promotes stress coping mechanisms, and has antidepressant-like effects by buffering of the HPA axis response to novel stress and increasing dopamine levels of the medial prefrontal cortex via elevated basal cortisol levels [20]. Moreover, PE modulates the epigenetic processes, positively influencing the development and course of inflammatory and cancer diseases as well as the aging process [23]. COVID-19-related stress and isolation easily result in decreased physical activity, thereby increasing the burden of chronic stress on coping strategies and the capacity of the immune system [27]. According to expert opinion, moderate-intensity exercise is recommended to improve the immune response and mitigate the negative effects of stress, anxiety, and sedentarism [28].

Factors for COVID-19-Related AO and Stress Resilience

Medical health workers in China and worldwide developed mental health problems (anxiety, depression, and obsessive-compulsive symptoms) as well as insomnia during the first wave of the pandemic [29, 30]. Organic disease was an independent risk factor [29]. COVID-19-related physical and psychological support was deemed effective in keeping emotional distress and burnout at a tolerable level [31]. Recent research into the factors of stress resistance showed that a higher preoutbreak sense of coherence predicted fewer psychopathological symptoms during the first outbreak of the pandemic [32].

We aimed to explore the role of regular, moderate-intensity formula aerobic exercise in coping with COVID-19-related stress and resilience in a general population sample. We postulate that the infection itself and the related confinements contribute equally to stress, in addition to increased age-related chronic diseases and the consequent reliance on the health care system. We examined if those who practice regular PE, with the aim of health preservation, maintain better mental and physical health than those who do not. Additionally, we aimed to explore if PE might contribute to a more effective coping style, thereby reducing allostatic load and increasing well-being.

Materials and Methods

Study Design and Sample Recruitment

We performed a voluntary and anonymous online survey between 21 May and 1 September 2020, enrolling 750 certified 312 meridian exercise [33] instructors and their (n = 7–30) member communities. The instructors' contacts who had never practiced meridian exercise served as controls. This 30-min aerobic medium-strength exercise series has no contraindications and can be easily performed by the elderly. Its moderate intensity and duration meet the recommendations of the WHO [34] (see OSM).

Measures

We applied a mixed-method design. By using qualitative content analysis [35], we specified the most challenging life-situations our participants had dealt with in relation to the pandemic to code free-text answers and arranged them into categories (see OSM).

Stress Load

COVID-19-related AO was measured according to Fava's definition based on the Diagnostic Criteria for Psychosomatic Research (DCPR) [8] and the Psychosocial Index (PSI) [36, 37]: A1 (stressor – COVID-19) + A2 (stressor exceeding coping strategies: "During the time of the restrictions, did you feel that the changes caused by the coronavirus epidemic were testing or exceeding your capacity?") + B1 (at least 2 distress symptoms – PSI 37–51)/B2 (deterioration of work, home, or human relationships – PSI 23–30)/B3 (everyday challenges – PSI 33–34). AO was diagnosed in case of A1, A2, and, additionally, either one of the B criteria were realized. To measure stress load independent of COVID-19, we applied PSI items 13–20 and 22–30.

Mental Health and Somatization

Mental health was measured with Kellner's Symptom Questionnaire (KSQ) [38], the short Depression Anxiety Stress Scales (DASS-21) [39–41], and the Public Health Surveillance Well-Being Scale (PHS-WB) [42], and somatization was measured with Whiteley-7 [43] (see OSM).

Statistical Analyses

The χ^2 test was used for categorical data, and the two-tailed t test and Kruskal-Wallis test for normally and nonnormally distributed continuous variables, respectively. Dunn's pairwise tests with Bonferroni adjustment for multiple comparisons were carried out for the 3 pairs of groups. Normality of data was assessed using the Kolmogorov-Smirnov test. Step forward likelihood ratio logistic regression was applied to identify predictors of AO and a general linear model was used to measure the effect of PE groups on KSQ total well-being by adjusting for sex, age, and the number of chronic diseases. In all cases, $p < 0.05$ was considered statistically significant. We applied SPSS v24.0 software (SPSS Inc., Armonk, NY, USA).

Results

Sample Characteristics

Altogether, 442 people completed the survey, 406 of whom were women with a mean age of 62 ± 10.6 years (males were aged 63.5 ± 11.5 years); 267 (55%) were retired, 77 (16%) went to their workplace, and 51 (11%) worked in home-office. Regarding chronic diseases, 213 (48%) had none, 184 (41.6%) had 1–2, 31 (7.0%) had 3–5, and 14 (3.2%) had >5. During the quarantine period, 45 people (10.2%) developed 1 acute condition and 6 (1.4%) developed 2 acute conditions. Ninety-nine people (22.4%) needed the health care system and 66 of these could use it. The proportion of acute and chronic conditions were distributed equally in this group. Altogether 20 persons (4.6%) reported having psychiatric disease.

COVID-19-Related Stressors

Among the participants, 23 (5%) indicated no challenges related to the pandemic and quarantine, while 419 (95%) specified ≥1 stressors (Fig. 1). Details of the qualitative analysis are reported in the OSM.

Allostatic Overload

Altogether 148 people (33.5%) reported that COVID-19-related changes exceeded their coping resources. AO,

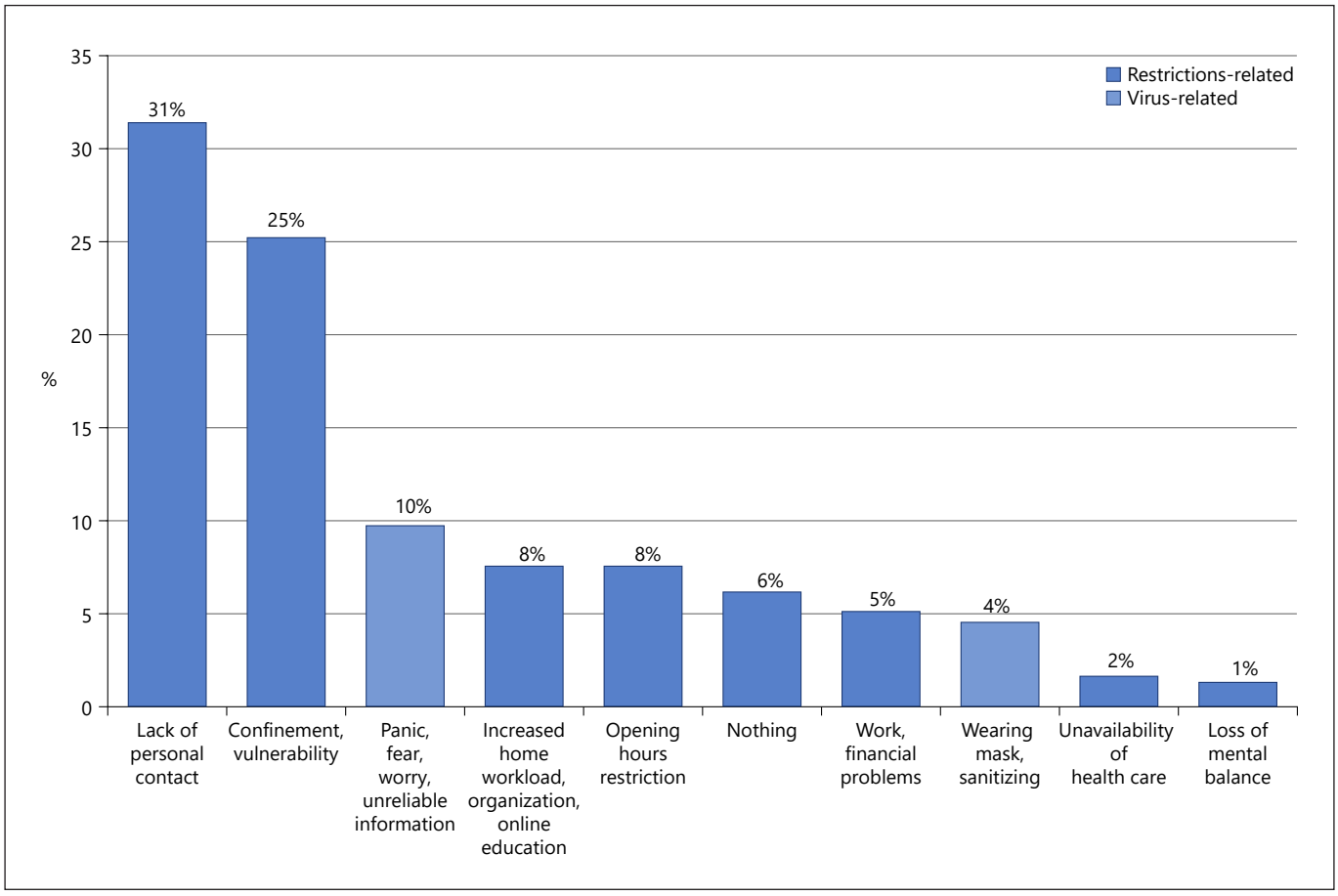

Fig. 1. Categories of participants' challenges and percentage distribution.

with stressor-related physical symptoms and impairment of social and occupational functioning as well as psychological well-being, was present in 128 people (29%). After adjusting for age, sex, and the number of chronic diseases, each additional life stress increased the likelihood of AO by 20% (OR 1.19; 95% CI 1.06–1.36, $p = 0.005$) and anxiety symptoms (on the KSQ) by 18% (OR 1.18; 95% CI 1.13–1.24, $p < 0.001$).

PE and Physical and Mental Health during the First Wave of the Pandemic

Median number of years practicing PE 3–5 times weekly or regularly every day (i.e., frequent PE [fPE]) was 5 years in our sample (IQR 2.5–7 and 3–6.5, respectively; Table 1). AO was less prevalent in the fPE group compared to controls ($\chi^2[1] = 5.6$; $p = 0.018$). fPE was also associated with significantly fewer depressive, stress, and anxiety symptoms (KSQ; Table 1). Although somatization symptoms proved to be nonsignificant on the subscale between the exercise groups and the controls, well-being was markedly higher in those who were exercising, so that the final somatization scale was better in the fPE group (Table 1). Total well-being reached higher scores in the exercising groups, and the same good results were shown for both mental and physical aspects (Table 1). After controlling for the effect of age, sex, and chronic diseases, we found a significant effect of exercise on well-being ($F[2, 435] = 225.0$, $p < 0.001$). Planned contrasts revealed that both fPE ($p < 0.001$, 95% CI 1.4–3.9) and PE ($p = 0.043$, 95% CI 0.04–2.83) was associated with significantly higher well-being than in the controls.

Discussion

We found that AO was less prevalent in those exercising frequently than those who lived a sedentary life during the first wave of COVID-19 pandemic. Moreover, fPE

Table 1. Health-related characteristics of an adult community sample (n = 442) who practiced 312 meridian exercise frequently (fPE) or less frequently (PE) and controls

	fPE (n = 217)	PE (n = 120)	Controls (n = 105)	p value	p (adjusted)
Sociodemographic and health-related characteristics					
Female sex	196 (90)	116 (97)	94 (90)	ns	
Age, years	65 (9.1)	64 (9.8)	57 (12.5)	<0.001	
Need of healthcare system (n = 99)	45 (21)	26 (22)	28 (27)	ns	
Chronic diseases, n (0/1–2/3–4/>5)	109/87/16/5	52/58/4/6	52/39/11/3	ns	
Acute diseases, n (0/1/2/>2)	195/19/3/0	108/10/1/1	87/16/2/0	ns	
ICD-10 diagnosed psychiatric disease	9 (4.2)	5 (4.3)	6 (5.7)	ns	
Years practicing 312 meridian exercise	5 (3–7)	3 (1.8–5)	1 (0–4)	–	
Stress-related parameters					
AO/A2	62 (29)	39 (32)	47 (45)	0.015	
AO	53 (24)	36 (30)	39 (37)	0.059	0.018*
PSI_stress_total	1 (0–3)	2 (1–4)	2 (1–4)	0.001	0.001*
PSI_psychological_distress	4 (1–9)	6 (2–11)	8 (3–14)	0.002	0.002*
Mental health characteristics					
DASS_depression	2 (0–4)	3 (1–6)	2 (0–7.25)	0.02	0.017§
DASS_anxiety	1 (0–2)	1 (0–3)	1 (0–5)	ns	
DASS_stress	2 (0–5)	3.5 (1–6.25)	4 (1–7)	0.006	0.012*
Kellner_anxiety	1 (0–5.5)	3 (1–6)	3 (1–8.5)	0.001	<0.001*
Kellner_depression	1 (0–4)	2 (0–4)	3 (1–6.5)	<0.001	<0.001*
Kellner_somatic symptoms	1 (0–4)	2 (0–4)	3 (0–6)	ns	
Kellner_hostility	0 (0–4)	2 (0–4)	2 (0–8)	<0.001	<0.001*; 0.041§
Kellner_anxiety	2 (0–8)	4 (1–9)	5 (2–11.5)	<0.001	<0.001*; 0.022§
Kellner_depression	3 (1–6)	4 (2–7)	5 (2–9.5)	<0.001	<0.001*
Kellner_somatization	4 (2–9)	5 (2–8)	6 (3–10)	0.008	0.006*
Kellner_hostility	1 (0–5)	3 (1–5)	3 (1–9)	<0.001	<0.001*; 0.032§
Kellner_psychological_distress	11 (4.5–25)	17 (8–28.75)	21 (11–39)	<0.001	<0.001*
Whiteley-7	3 (1–8)	5 (2–9.25)	6 (3–11)	0.002	0.002*
Well-being characteristics					
PHS_mental well-being	4.4 (3.8–4.8)	4.1 (3.6–4.6)	4.2 (3.6–4.6)	0.004	0.006§
PHS_social well-being	4.5 (4–5)	4 (3.5–5)	4 (3.5–5)	ns	
PHS_physical well-being	4.3 (3.3–4.7)	4 (3.3–4.7)	4 (3–4.3)	0.003	0.006*; 0.042§
PHS_well-being_total	4.3 (3.7–4.7)	4.0 (3.4–4.5)	4.1 (3.5–4.4)	0.004	0.033*; 0.011§
Kellner_relaxation	6 (4–6)	5 (3–6)	5 (2.5–6)	<0.001	0.001*; 0.014§
Kellner_contentment	5 (3–6)	4 (2.25–5)	4 (2–5)	0.039	0.059*
Kellner_physical well-being	4 (2–5)	3 (2–5)	2 (1–4)	<0.001	<0.001*
Kellner_friendliness	6 (5–6)	5 (5–6)	5 (4–6)	ns	
Kellner_well-being	19 (15–22)	17 (13–20)	17 (11–20)	<0.001	<0.001*; 0.024§

Values express n (%) or median (IQR), unless otherwise indicated. The fPE group practiced 312 meridian exercise at least 3–5 times weekly, the PE group practiced 312 meridian exercise 1–2 times weekly, and the controls did not practice 312 meridian exercise at all or irregularly. Kellner capital letter scales indicate the total score (clinical symptoms added up with the inverse of related well-being scores; see OSM); χ^2 tests were applied in case of categorical variables and Kruskal-Wallis tests with Dunn's pairwise tests with Bonferroni corrections. AO/A2, stressor exceeded coping resources of participants; AO, allostatic overload.

* Significance between fPE and controls; § significance between fPE and PE.

was associated with lower depressive, anxiety, and stress symptoms and greater mental and physical well-being. Interestingly, the beneficial effects of increased physical well-being compensated for somatization, resulting in significantly fewer symptoms when measured with the KSQ.

According to the clinimetric definition, AO serves as a global distress index of the interaction between chron-

ic life-stresses and life events [2, 8, 11, 12, 44, 45]. Its prevalence in healthy populations ranges between 15.8 and 43% [46–48], and it is associated with increased symptoms of depression, anxiety [47], somatization, and hostility [46] as well as with impaired well-being [47]. We found that pandemic-related acute stress was more likely to cause AO when combined with chronic life-stresses, and its prevalence was significantly lower in those who exercised regularly. The beneficial effects of regular exercise on inflammation and stress-related diseases are widely known [5, 49–51], and mental health and well-being indices can also be improved [24, 28]. Regular exercise has proved to be beneficial during the pandemic in increasing resilience [52], improving mental well-being [53, 54], and easing symptoms of depression [52, 54] and anxiety [54]. Our research adds to this knowledge by exploring the beneficial effects of exercise on the physical health domain of well-being as well. Somatizing patients burden the health care system with excessive utilization of medical care [55]. According to our results, fPE is associated with increased physical well-being, resulting in improved subjective physical health and significantly decreased somatization. Thus, PE may indirectly contribute to unencumbering the health care system.

Our study had several limitations. Although exposure to fPE preceded the pandemic, the cross-sectional nature of the study hindered drawing causal relationships. The significantly higher proportion of females made our sample nonrepresentative.

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Statements of Ethics

Online consent was secured by all participants. The study was conducted according to the Declaration of Helsinki and approved by the review board of the Medical Research Council (IV/5657–2/2020/EKU).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Ajandek Eöry, Ajandok Eöry, and D. Békési designed and planned the study. D. Békési collected the data. Ajandek Eöry and S. Rózsa analyzed the data and interpreted the results. All authors drafted and revised the intellectual content of the manuscript. We sadly report that Ajandok Eöry, who established 312 meridian exercise in Hungary and played a fundamental role in the scientific and practical aspects of our research, died during the data collection period.

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