Putting up with a pandemic

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Interpretation of this cover: It took weeks to paint the multiple layers, which symbolise the time-consuming process of creating this thesis; developing, contemplating and implementing ideas. It is also an expression of how the creation of this thesis covered several aspects of my life. With the support of the people around me it was shaped over time, like a diamond over time, under loads of pressure.

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Contents

Chapter 1

General introduction

Public health emergencies create a unique opportunity for health psychologists to examine the effects of real-life stressors on health. The outbreak of the SARS-CoV-2 virus (coronavirus) was declared a pandemic in the spring of 2020. Beyond the effects on those who could got severely ill or died from the coronavirus disease (COVID-19), the pandemic, including measures taken by the government to contain the virus, may have impacted mental and physical health of all people. Examining people during this pandemic could give us more insight into their worries, stress and ability to cope with more or less uncontrollable situations in daily life. Especially for those with a chronic illness, as disrupted medical treatment could have affected the management of their illness. Before giving the aim and outline of the thesis, this chapter introduces the two main themes. First, mental and physical health during the COVID-19 pandemic and, second, psychological flexibility as a means to put up with this pandemic.

1. Mental and physical health during the COVID-19 pandemic

1.1. COVID-19 as a public health emergency

Research in health psychology aims to promote health by examining health and disease with special attention to psychological determinants, lifestyle and effective interventions. To study these concepts, health psychologists use a variety of qualitative and quantitative research methods, including case studies, interviews, questionnaires, and experiments[1]. Experimental designs are often preferred, because of the possibility of inferring causal relationships among variables. However, the artificiality of manipulated variables and exclusion of relevant context variables may make such designs less suited as a model for real-life stressors. Public health emergencies and disasters are exceptional situations, in which health psychologists can use questionnaires to examine health and related matters in an ecological valid way. Exact causal links cannot be inferred from observational designs, but they give an opportunity to clarify how people are coping with or responding to naturally emerging challenges.

Results from studies into public health emergencies indicated that the estimated prevalence of mental illnesses almost doubled after exposure to disasters such as hurricanes[2,3,4], earthquakes and tsunamis[5] , or the 9/11 terrorist attacks[6]. The risk of developing an acute- or posttraumatic stress disorder seems higher for vulnerable people, such as those with a pre-existing psychiatric disorder[2,7], and for them, mental and physical health is likely to deteriorate more due to the separation or loss of a loved one during a disaster[8,9]. However, it has been observed that the frequency of suicides declines after an acute disaster, such as a hurricane or the 9/11 terrorist attacks[4,10], and the support from friends, neighbours and spiritual communities has been shown to grow stronger[11], which are indications that health emergencies may also have positive outcomes in people. Moreover, the experience of individuals' own resilience to withstand the negative effects of a health emergency might protect them against its detrimental effects[12].

1.2. COVID-19 pandemic as a disaster

Compared to the disasters mentioned above, the effects of the COVID-19 pandemic were perhaps more subtle for many people. Nevertheless, the geographical impact was extensive and affecting a lot of people. Getting infected with the coronavirus was a potential threat for every individual. Early results showed that especially elderly[13] and those with a pre-existing chronic illness[14,15] were more at risk of dying from COVID-19. However, young people and those without a chronic illness also could become severely ill or die. With the outbreak of the cononavirus in China, the immediate response among the general population was one of psychological distress: half of the Chinese participants rated the psychological impact of the COVID-19 pandemic as moderate to severe during its initial stage[16] and especially women and elderly reported elevated levels of psychological stress as a response to the outbreak[17]. Early research indicated that the pandemic increased depression and anxiety among the general population[17,18]. People feared for their own health and that of their loved ones, from whom they could be physically isolated or whom they might lose[19].

Besides the worry and risk of getting infected, measures taken by governments to prevent the spread of the coronavirus may have had detrimental effects on peoples' mental health[20]. Although seemingly effective against the spread of the virus[21], measures such as social distancing, lockdowns and personal quarantines, changed everyday life, and it was suggested that the reduction of social connections might lead to mental health problems, such as post-traumatic stress, anxiety and depression[22]. Thus, similar to other disasters[23], the COVID-19 pandemic may have affected peoples' physical and mental health[18]. The pandemic impacted the entire global population, as it was a 'threat' that could be everywhere and impact everyone[24]. This created a unique opportunity to examine effects of a global stressor and disrupted daily life on the general population, especially in specific vulnerable groups, such as those with a pre-existing chronic illness.

1.3. Impact on people with a chronic illness

The outbreak of the pandemic may have affected the mental and physical health of people with a pre-existing chronic illness even more than that of the general population. Their illness was already an adversity they had to deal with, and on top of that the mortality rate of elderly patients with a chronic illness was shown to be the highest[13,14,15,25]. When the novel virus outbreak became a pandemic, people with a chronic illness indicated to be more worried of getting infected, than those without a chronic illness[26]. Next to the increased worry and stress, the routinely medical treatments and other health care often was disrupted due to governmental measures[27]. This may have affected the effectiveness of management of chronic illnesses and, as a consequence, the severity of the symptoms and the physical and mental health of these patients[28].

People taking medicine that suppresses their immune system, to treat maladies such as autoimmune diseases, may be especially at risk of getting infected by the coronavirus[29]. Inflammatory Rheumatic Disease (IRD) is an umbrella term that is used in this thesis, to describe the whole spectrum of chronic rheumatic

diseases other than osteoarthritis and fibromyalgia. Thus, more diseases are included in the term IRD than the word inflammatory actually assumes. IRD mainly includes autoimmune diseases in which the individuals's own immune system attacks healthy cells of the body. As a consequence of immunosuppressive medication, that is given to modify this disease process, patients were considered more vulnerable for infection by the coronavirus. Moreover, the prevalence of an IRD increases with age. Thus, some governments considered these patients a high-risk group[29]. This risk could even be higher, because they faced disrupted illness management due to governmental measures[30]. All these consequences led to the hypothesis that, during the pandemic, people with an IRD were more worried, felt more stress and experienced a higher deterioration of their mental and physical health, than people without an IRD.

Also, people with a Central Sensitivity Syndrome[31] (CSS), such as fibromyalgia[32], chronic fatigue syndrome[33], or irritable bowel syndrome[34], may have experienced more severe consequences of the pandemic on their mental and physical health. Several studies suggest that, in these syndromes, a hypersensitive brain is responsible for augmentation of pain and other somatic symptoms, hence the term CSS. This augmentation might be stronger in response to stress[31,32,33,34]. The pandemic offered the possibility to examine whether also naturally occurring stress amplified symptoms in people with a CSS.

Another group that may have been especially vulnerable to the consequences of the COVID-19 pandemic, are young adults. Although it became quickly clear that this group was less at risk of getting severely ill and dying of a coronavirus infection, compared to elderly[35], this risk was higher than that of seasonal influenza[36]. Studies into the early stage of the pandemic indicated that being a young adult was associated with higher levels of stress, anxiety and depression[16,37]. Studies in the UK reported that right after governmental measures were instated in May 2020, just over one-fifth of the general population reported clinically relevant anxiety and depression symptoms[38]. While, as the pandemic progressed into the acute phase four weeks later, the dramatic observation was made that 63.3% of the young adults aged 18 to 24 years, reported clinically relevant depression and 59.2% clinically important anxiety, vs. 11.5% and 12.2%, respectively, in the group 65+ years of age[39]. These studies might indicate that consequences of the pandemic, such as uncertain working conditions and the restricted freedom of movement, could have impacted the life of young adults. Other studies reported that reduced physical activity due to lockdowns[40] and the tendency to collect information from social media[41], were associated with the worsening of mental health. First, studies like those of Pieh and co-workers[39] reported that the consequences of the pandemic for young adults were dramatic. This finding should, however, be replicated. Second, it was unclear what the physical and mental health status of young adults would be, as the pandemic progressed and new lockdowns of longer duration were instigated by the government. Mental and physical health of young adults could even be worse during the prolonged phase of the pandemic than during the acute phase. Finaly, special attention in research should be given to young adults with a chronic illness, who might experience larger disadvantages of the pandemic, than young adults without a chronic illness.

2. Putting up with a pandemic

As the COVID-19 pandemic impacted the health of the entire global population, examining people's ability to manage adversities in life, could give us more insight into whether and how people can preserve their health in potentially stressful times. Psychological flexibility may be a candidate fit to study, because it is thought to have a favorable effect when dealing with more or less uncontrollable challenges, such as those of a pandemic. This paragraph defines psychological flexibility and introduces the rationale for studying it during the pandemic.

2.1 Definition of health

In 1948, the WHO defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[42]. At that time, this definition was ground-breaking, as a disease was considered as more than just a pathological substrate that needed to be cured. However, the absoluteness of the word 'complete' in relation to well-being would leave most people unhealthy most of the time. In contrast with the situation in 1948, when acute diseases represented the main burden of illnesses and people did not live long with a chronic illness, people are now more likely to age with a chronic illness. The WHO definition of health declares these people as definitely ill, even though nowadays most of the people with a chronic illness can have the capacity to satisfyingly deal with the challenges they encounter and lead a fulfilling live. This asked for a reformulation of the definition of health. An international expert group formulated a new definition of health, as "the ability to adapt and self-manage in the face of social, physical, and emotional challenges"[43]. This definition expresses that not the health status per se, as seen by others, is essential in the definition of health, but one's skills to deal with health challenges.

2.2. Psychological flexibility

For health psychologists, adaptation to and (self-)management of health challenges are core topics in research and clinical practice. Within relational frame theory, mindful acceptance and being committed to pursue one's values, are considered important concepts underlying Acceptance and Commitment Therapy[44] (ACT). These skills are summarized under the label 'psychological flexibility', which is considered key to adapt to health challenges. While classical cognitive-behavioural approaches emphasize how a change of cognitions and behaviour may ameliorate the situation, psychological flexibility is also considered helpful when changes are difficult to establish. For instance, when one has persistent health symptoms. Also, adverse consequences of the pandemic, such as infection risk and governmental measures, might be difficult to control. Psychological flexibility could be an antidote to uncontrollable consequences of a crisis such as the pandemic.

Psychological flexibility is defined as contacting the present moment as a conscious human being, and, based on what that situation affords, acting in

accordance with one's chosen values[45]. Psychological flexibility comprises six core processes that are organized into a hexaflex model showing their mutual interrelatedness[44] (Figure 1):

Acceptance: the willingness to fully embrace unavoidable unwanted experiences.

Contact with the present moment: being in non-judgmental contact with one's thoughts, feelings and experiences.

Self as context: taking an observer perspective towards one's own experiences

Defusion: being able to step back from unavoidable unwanted experiences, without getting stuck in them.

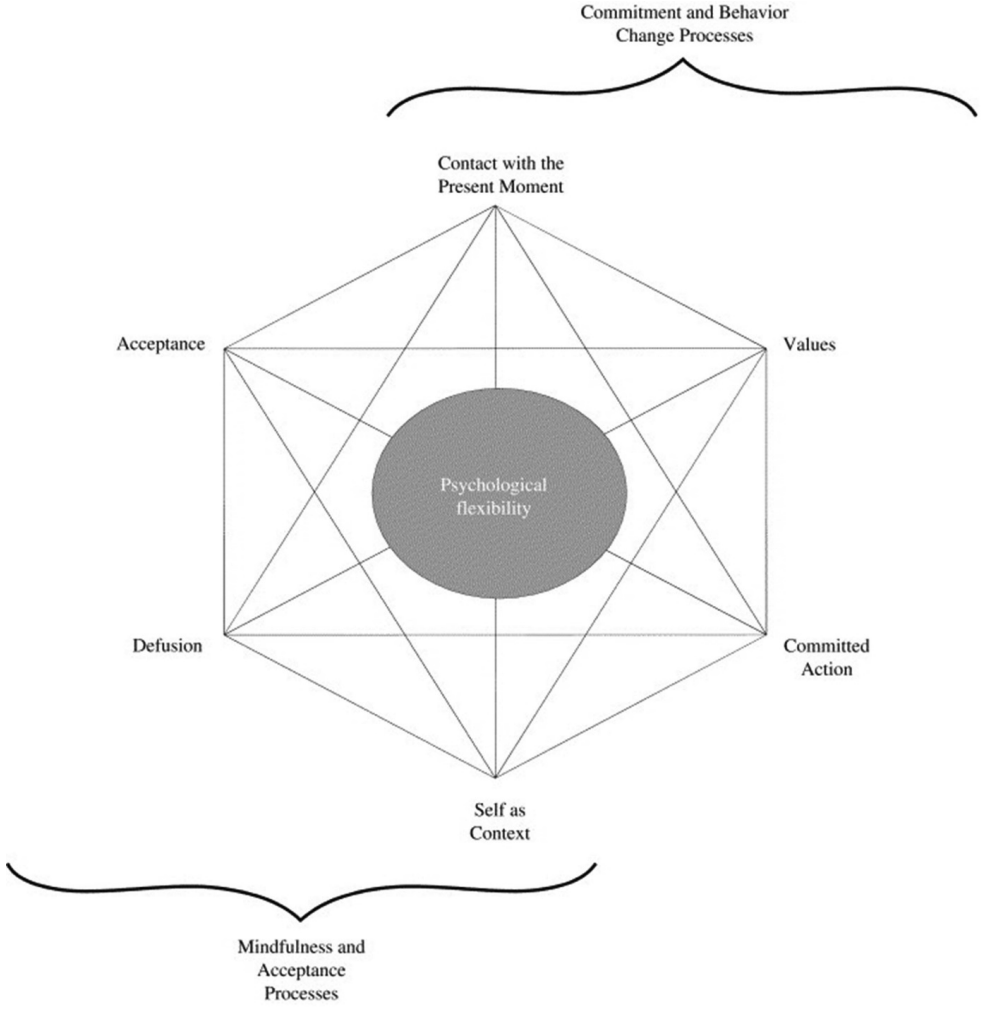
Committed action: engaging in value-based behaviour

Values: chosen life directions that are important and give direction to behaviour.

The six core processes are grouped into two overarching processes[44] (Figure 1). The core processes of "contact with the present moment" and "self as context" belong to both overarching processes, because it is argued that all psychological activity of conscious human beings involves the now as known. Besides these two, values and committed action are grouped under the *Commitment and Behaviour Change Processes*, while acceptance and defusion are assigned to the *Mindfulness and Acceptance Processes*.

Figure 1

A model of the six core and two overarching processes of psychological flexibility (adopted from Hayes et al., 2006, p. 8).



Psychological flexibility is indicated to be a resilience factor in patients with a chronic illness, protecting against the mental burden of the illness[46]. Systematic reviews and meta-analyses studying ACT (e.g. in patients with chronic pain, psychiatric, cardiac and paediatric illnesses) indicated that therapy enhancing psychological flexibility, is associated with improved chronic illness self-management, physical and social functioning and less medical visits, anxiety and depressive symptoms in patients[47,48,49,50]. Additionally, it is helpful in supporting relatives of patients and reducing their stress and anxiety levels[51,52]. Psychological flexibility is considered a fundamental aspect of health[53], not only for those with a (chronic) mental or physical illness, but for the entire population, as all people need to adapt to and self-manage the physical, emotional and social challenges of life.

In the Netherlands, the Flexibility Index Test[54] (FIT-60) was constructed based on literature review of psychological flexibility and on four existing questionnaires[55,56,57,58] (AAQ-2; CFQ-13; FFMQ; VLQ-2) The questionnaire includes all six core processes of psychological flexibility with ten questions for each process. Since these six processes are considered to be mutually interconnected, the questionnaire has been mostly used to assess overall psychological flexibility.

3. Thesis outline and aims

The aim of this thesis was to determine the mental and physical health in people with and without a chronic illness during the COVID-19 pandemic and whether psychological flexibility is a potential protective factor against a deterioration of health. To achieve this overall aim, at three time-points, data samples on mental and physical health, as well as psychological flexibility, were collected cross-sectionally in the Dutch speaking general population. The first dataset was obtained before the onset of the pandemic, in 2018, and the two other sets during the pandemic: one at the first major peak (2020; *acute phase*) and one year later, when the contamination rate and restrictive measures in the Netherlands were intensive and long-lasting (2021; *prolonged phase*).

Given that people with immunsuppressive medication were considered a high-risk group in the early stages of the pandemic, we aimed in **chapter 2** to determine the psychological impact of the pandemic on people with vs. without an inflammatory rheumatic disease and whether psychological flexibility buffered this impact. We examined in this chapter, whether people with an IRD were more worried and stressed and had lower mental well-being during the *acute phase* of the pandemic in 2020, compared to before the pandemic (in 2018) and to those without an IRD.

Stress is assumed to augment somatic symptoms in people with a central sensitivity syndrome (CSS) such as fibromyalgia, chronic fatigue syndrome, or irritable bowel syndrome. In **chapter 3** we examined the association between COVID-19 stress and somatic symptom severity, with the hypothesis that this association would be stronger in people with than without a CSS and that psychological flexibility would buffer the impact of this stress on symptom severity.

In people with fibromyalgia, symptoms, physical function and mental health may worsen in response to stress, delayed medical health care and other pandemic consequences. To obtain more insight into whether and which specific mental and physical health dimensions differed between pandemic phases, we compared in **chapter 4** eight health dimensions during the acute (2020) and prolonged phases (2021) of the pandemic, to before the pandemic (2018) in women with fibromyalgia.

Studies of young adults have reported poorer mental health during the pandemic, while the consequences for physical health, especially for those with a chronic illness remained unclear. Moreover, research typically analysed young adults' health only during the acute phase of the pandemic, whereas worsening of health during the prolonged pandemic phase was only assumed. In **Chapter 5** we aimed to better understand mental and physical health, in young adults with and without a chronic illness during the acute and prolonged phases of the pandemic, and whether psychological flexibility might have been a particularly useful ability to protect young adults' health under bad circumstances; that is, during (vs. before) the pandemic and in those with (vs. without) a chronic illness.

In the Netherlands, the Flexibility Index Test (FIT-60) was constructed to measure the six core processes of psychological flexibility. Separate assessments of these six processes are used in clinical practice, but not yet in research. When measured with a questionnaire, less than six dimensions representing these processes are found, possibly due to the the interconnectedness of the six processes. Therefore, perhaps a shorter questionnaire can be constructed to measure the processes represented in the FIT-60 questionnaire. Moreover, there are usability considerations to reduce the number of items of the FIT-60 questionnaire. The aim of **chapter 6** was to determine how many dimensions can be distinguished in this questionnaire and how many items are needed to reliably assess these dimensions.

The main findings of this thesis are summarized and discussed in **chapter 7**. It describes clinical implications and includes contemplations about what we can learn from this thesis for post-pandemic times, and gives future research directions.

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Chapter 2

The psychological impact of the COVID-19 pandemic on Dutch people with and without an inflammatory rheumatic disease

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ABSTRACT

Objectives: To determine the psychological impact of the COVID-19 pandemic on people with and without an inflammatory rheumatic disease and establish whether psychological flexibility buffers this impact.

Methods: From online surveys in the general Dutch population in 2018 and during the peak of the COVID-19 pandemic in 2020, we analysed data of people with (index group, n=239) and without (control group, n=1821) an inflammatory rheumatic disease. Worry, stress, mental well-being (SF-36) and psychological flexibility levels were subjected to covariate-adjusted analyses of variance or linear regression analyses.

Results: During the peak of the COVID-19 pandemic in 2020, as compared to the control group, the index group was more worried about getting infected with the virus (partial η^2=.098; medium effect) and more stressed (partial η^2= .040; small effect). However, as compared to data acquired in 2018, the level of mental well-being during the COVID-19 pandemic peak was not lower in both groups. Levels of psychological flexibility did not moderate associations of group or year with mental well-being.

Conclusions: Although patients with an inflammatory rheumatic disease were more worried and stressed during the peak of the COVID-19 pandemic, their level of mental well-being was not reduced, which may have prevented us from finding a buffering effect of psychological flexibility. Overall, our results suggest that the psychological impact of the COVID-19 pandemic in patients with inflammatory rheumatic disease is modest, which could imply that common education and health care will do for most patients.

Acknowledgement of author contributions

TYK and RG developed the design and collected and analysed the data, TYK drafted the paper and JWGJ and RG critically assessed, edited and revised the paper.

INTRODUCTION

During its peak months, the outbreak of the SARS-CoV-2 virus and measures that were taken to prevent the illness COVID-19 may have had a particularly high psychological impact on people with inflammatory rheumatic disease, who were considered a high risk group by some national governments[1] and who may have been worried that their disease or immunosuppressive medication increased the risk of getting infected by SARS-Cov-2[2,3]. After the peak period, some worry will have been taken away. Preliminary findings after the peak period showed there is little to no evidence that patients with rheumatic and musculoskeletal diseases (RMD) compared to people without RMD, face more risk of contracting COVID-19, nor that they have a worse prognosis when they contract it[4,5]. Besides the worry of getting infected, other consequences of the pandemic may have had a psychological impact on patients, such as social distance procedures, the lower accessibility of outpatient clinics and health care in some regions, and less outpatient visits because of concern for contagion that may have affected the management of their disease[6].

Researchers expected an increase of anxiety as a consequence of the COVID-19 pandemic among the general population[7]. Indeed, with the outbreak in China, about 50% of the respondents rated the psychological impact of the epidemic as moderate or severe[8]. Another study in China showed that almost 35% of the respondents experienced psychological distress, especially women and elderly[9]. However, psychological consequences will differ between people, because people differ in terms of personality and skills that help dealing with a mental setback[10].

Psychological flexibility[11] is considered key to adapt to challenging circumstances[12,13]. It refers to the ability to be open to adapt to new situational demands, while being committed to behaviour that is in line with one's own chosen values[10,11]. Longitudinal findings suggest that psychological flexibility impacts subsequent mental health, and not the reverse[11]. In patients with chronic diseases, psychological flexibility has been shown a resilience factor protecting against the mental burden of the disease[14]. A flexible attitude towards setbacks, like the consequences of a pandemic, aids in adapting to these new situational demands[15]. If psychological flexibility is also shown to buffer the impact of the pandemic, then training of psychological flexibility skills, with procedures derived from acceptance and commitment therapy, may be of use[12,16]. Therefore, the aim of our study was to determine the psychological impact of the peak of the COVID-19 pandemic on patients with chronic inflammatory rheumatic disease and establish whether psychological flexibility buffers this impact.

METHODS

Participants

Data from two online surveys in the general population were analysed. The first data collection was from November 2018 to May 2019 (year 2018). The second collection started on March, 24th 2020, one day after the Dutch government introduced strict

rules and regulations to prevent further spread of COVID-19, and ended at May, 2nd (year 2020). This latter period was the peak period in the Netherlands in terms of number of hospitalizations, patients on the intensive care, and deaths due to COVID-19[17]. In the questionnaire, respondents could indicate, among other diseases, whether they had a chronic rheumatic disease other than osteoarthritis or fibromyalgia. In the current study, we compared the last group (index group) to all other participants (control group). We use the label "inflammatory rheumatic disease" to describe the index group that includes the whole spectrum of chronic rheumatic diseases other than osteoarthritis and fibromyalgia. Many patients in this group will have an inflammatory rheumatic disease and use immunosuppressive medications. A patient having osteoarthritis or fibromyalgia next to another rheumatic disease (e.g., rheumatoid arthritis or systemic vasculitis) was also included in the group "inflammatory rheumatic disease". The control group consisted of participants who were healthy or had osteoarthritis, fibromyalgia or any other disease apart from index diseases.

Procedure

Participants were acquired via e-mail and social media, e.g. Facebook, Instagram, LinkedIn, local internet sites, and sites of associations including patient associations for rheumatic diseases and other diseases. The hyperlink to the online survey on individual and group sites was shared by other individuals and groups. Participants filled out the online survey at a secure university website. They self-reported their medical conditions and diseases. Before starting, all participants were informed on the content of the study and their voluntary participation, and signed an informed consent. Adult age (≥18) was the only inclusion criterion. Data collection was anonymous; it is theoretically possible that some persons participated both in 2018 and 2020. The online questionnaire studies in 2018 (FETC17-120) and 2020 (FETC20-190) were approved by the Ethics Committee of the Faculty of Social and Behavioural Sciences of Utrecht University.

Materials

Participants of the 2020 sample reported their current level of being worried about getting infected by the virus on a 4-point Likert scale (1 = 'not worried', 2 = 'a little worried', 3 = 'worried', 4 = 'very worried') and their current stress level compared to their normal stress level, on a 5-point Likert scale with the answering categories 1 = 'less stressed', 2 = 'just a little less stressed', 3 = 'not less nor more stressed', 4 = 'just a little more stressed' and 5 = 'more stressed'.

Mental well-being was assessed with the Dutch version of the RAND 36-Item Short Form Health Survey[18] (RAND SF-36). The SF-36 measures eight aspects of health, of which four reflect mental well-being: Mental health, Role emotional, Social functioning, and Vitality. The scoring method of Hays was used to derive a mental health composite score[19]. This is a normalized score with an average of 50 and a standard deviation of 10 in the general population, the theoretical range is from 11 to 60; a higher mental health composite score reflects better mental well-being[19]. The

internal reliability in the current sample was good; Cronbach's alphas of the four contributing scales was .81.

The FIT-60[20] was used to measure psychological flexibility, which consists of six processes that are presented in a *hexaflex* model[11]. The questionnaire is based on a literature review of psychological flexibility and on four existing questionnaires. The Acceptance and Action Questionnaire[21] (AAQ-II) and the Cognitive Fusion Questionnaire[22] (CFQ-13) were used to assess the committed action and diffusion scales of the hexaflex model, the Five Facet Mindfulness Questionnaire[23] (FFMQ) to assess the contact with the present moment subscale, and the Valued Living Questionnaire[24] (VLQ-2) to assess values. The FIT-60 comprises sixty statements, ten for each component of the hexaflex model. Participants can indicate to what extent this statement applies to them on a 7-point Likert scale, ranging from 0 ('totally disagree') to 6 ('totally agree'). The theoretical range is from 0 to 360[20]. Higher scores denote more flexibility. The initial psychometric qualities of the FIT-60 showed that the internal reliability was acceptable to good, with Cronbach's alphas ranging from .69 to .87 on the six subscales and an alpha of .95 for the total scale[20]. In the current study we use the total scale score with a Cronbach's alpha of .90.

Statistical analyses

We compared the psychological status of the index and control groups during the two peak months (March and April 2020) of COVID-19 in the Netherlands to examine the hypothesis that the index group was more worried about becoming infected with the virus as well as more stressed by the current situation. The hypothesis was tested using analysis of covariance, while controlling for gender, age, education level, and number of diseases other than an inflammatory rheumatic disease.

In the total population including both samples from 2018 and 2020, we examined whether higher levels of psychological flexibility protect against a reduction of mental well-being, especially in hard times. Four interaction hypotheses were studied. Mental well-being was hypothesized to be extra low 1) in the index group in 2020, because they were told at that time to have a higher risk of getting infected (group × year interaction), 2) in people with lower levels of psychological flexibility in the 2020 sample , because they probably have more difficulty dealing with the more stressful and uncontrollable current situation (psychological flexibility × year interaction), 3) in patients of the index group with lower levels of psychological flexibility, because they are disadvantaged in coping with their disease (group × psychological flexibility interaction), and 4) in patients from the index group having lower levels of psychological flexibility in 2020, because they probably have more difficulty coping with their disorder during a crisis (group × psychological flexibility × year interaction). To examine the associations of mental well-being with *group* (index and control), year of measurement (the years 2018 and 2020) and *psychological flexibility*, linear regression analyses with bootstrapping were performed. In the first model, gender, age, education, and number of diseases were entered as covariates, together with group, year, and psychological flexibility (i.e., total FIT-60 score). To the second model, the two-way interactions year × group, year × psychological

flexibility and group × psychological flexibility were added. In the final model, also the three-way interaction year × group × psychological flexibility was added. Statistical analyses were done using IBM SPSS statistics version 25.0. P-values <.05 were considered statistically significant; all tests were two-sided.

RESULTS

Description of the samples

The study data consisted of cross-sectional assessments in 2018 (n=531) and in 2020 (n=1529), in the index group (n=239) and the control group (n=1821). Only people with complete measurements of mental well-being and psychological flexibility were included. Table 1 shows the demographic characteristics of the samples. Marital status did not significantly differ between the index and control groups (p=.702), but the index group was older (p<.0001), included more women (p=.0002) and more people with lower education (p=.0002), and had a higher mean number of diseases (p<.0001); the occurrence of a skin disease was higher in the index group (p<.0001) and neurological disease (p=.050) and obesity had a higher occurrence in the control group (p=.035).

Table 1

Characteristics of the index and control groups of the two sample years

	Index group n = 239		**Control group n = 1821**		
Year	**2018 n = 74**	**2020 n = 165**	**2018 n = 457**	**2020 n = 1364**	**All n = 2060**
Age (years)					
Mean (SD)	52.3 (11.7)	51.8 (12.1)	38.8 (14.7)	45.8 (14.7)	45.6 (14.8)
Range	23 - 74	26 - 76	18 - 75	18 - 79	18 - 79
Gender, n (%)					
Men	5 (6.8)	21 (12.7)	86 (18.8)	300 (22.0)	412 (20.0)
Women	69 (93.2)	144 (87.3)	371 (81.2)	1064 (78.0)	1648 (80.0)
Education level[a], n (%)					
Low	32 (43.2)	82 (49.7)	159 (34.8)	489 (35.9)	762 (37.0)
High	41 (55.4)	81 (49.1)	295 (64.6)	870 (63.8)	1287 (62.5)
Missing	1 (1.4)	2 (1.2)	3 (0.7)	5 (0.4)	11 (0.5)
Marital status, n (%)					
Single	22 (29.7)	50 (30.3)	132 (28.9)	414 (30.4)	618 (30.0)
In a relation	52 (70.3)	111 (67.3)	303 (66.3)	920 (66.4)	1386 (67.3)
Unknown	0 (0.0)	4 (2.4)	22 (4.8)	30 (2.2)	56 (2.7)

Number of diseases other than an inflammatory rheumatic disease					
Mean (SD)	1.47 (1.45)	1.53 (1.67)	1.14 (1.24)	1.13 (1.22)	1.17 (1.27)
Range	0 - 7	0 - 6	0 - 6	0 - 7	0 - 7
Type of other disease, n (%)					
Osteoarthritis	11 (14.9)	26 (15.8)	58 (12.7)	146 (10.7)	241 (11.7)
Pulmonary	8 (10.8)	29 (17.6)	37 (8.1)	200 (14.7)	274 (13.3)
Skin	11 (14.9)	17 (10.3)	26 (5.7)	46 (3.4)	100 (4.9)
Cancer	2 (2.7)	7 (4.2)	6 (1.3)	31 (2.3)	46 (2.2)
Cardiovascular	13 (17.6)	27 (16.4)	35 (7.7)	211 (15.5)	286 (13.9)
Psychiatric	11 (14.9)	23 (13.9)	60 (13.1)	172 (1.6)	266 (12.9)
Persistent physical symptoms	27 (36.5)	52 (31.5)	167 (36.5)	376 (27.6)	622 (30.2)
Neurological	10 (13.5)	17 (10.3)	48 (10.5)	91 (6.7)	166 (8.1)
Obesity	11 (14.9)	21 (12.7)	36 (7.9)	13.0 (19.5)	198 (9.6)
One concomitant disease	7 (9.5)	20 (12.1)	48 (10.5)	125 (9.2)	200 (9.7)
Two or three concomitant diseases	1 (1.4)	1 (0.6)	0 (0.0)	3 (0.2)	5 (0.2)
Self-report measures, Mean (SD)					
Mental health	37.8 (11.0)	39.5 (10.9)	43.7 (11.4)	43.6 (11.7)	43.1 (11.6)
Psychological flexibility	220.1 (47.5)	220.7 (51.9)	227.1 (45.7)	230.5 (49.8)	228.6 (49.1)

[a]Education level: low: lower general secondary education or lower; high: higher general secondary education or higher.

As compared to the 2018 sample, the 2020 sample was older ($p<.0001$). The differences in gender was just not significant, with less women ($p=.056$) in 2020. There were no significant differences in education level ($p=.602$), marital status ($p=.198$) or number of diseases ($p=.619$).

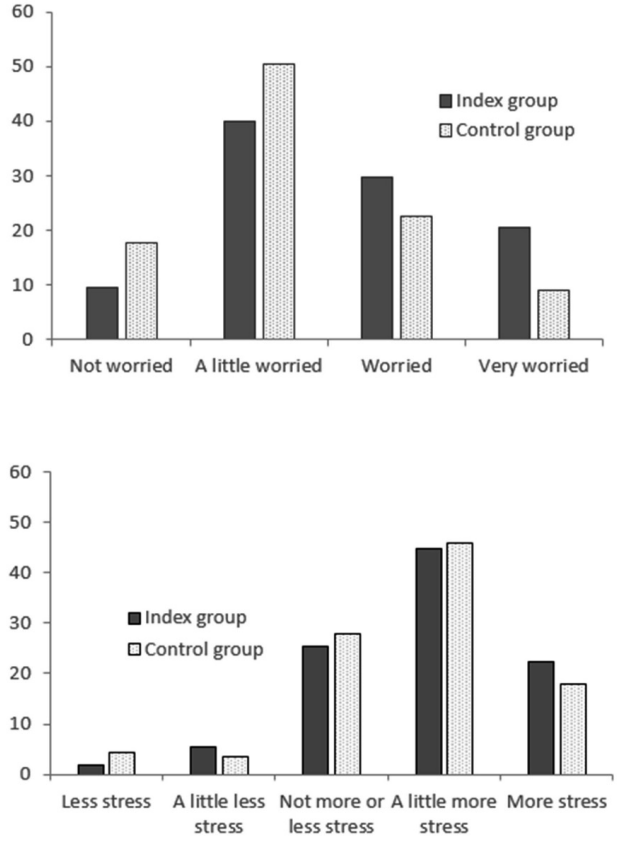
Levels of concern and stress about COVID-19

The top of figure 1 shows the levels of worry about getting infected by the virus in the index and control groups during the peak of COVID-19. About half of the participants in the index group and one third of the control group was worried or very worried. While controlling for gender, age, education and number of diseases, the levels of worrying differed between the index group (estimated marginal mean (M_e)=2.521, SE=.065) and the control group (M_e =2.244, SE=.022, $p<.0001$), the effect size was

medium (partial η^2=.098). Also, the stress levels (Figure 1, bottom) differed between the groups with somewhat more patients of the index group reporting to experience more stress (Figure 2). The covariate-adjusted levels of stress differed between the index (M_e=3.757, SE=.074) and the control groups (M_e=3.703, p<.0001), the effect size was small (partial η^2=.040).

Figure 1

Percentages (y-axis) of levels of worry about contracting COVID-19 (top) and stress (bottom) during the peak period of COVID-19 for people with (index group, n=165) and without (control group, n=1364) an inflammatory rheumatic disease.



Levels of mental well-being

The covariate-adjusted mean scores of mental well-being per group and year are shown in supplementary file Table S1. The differences with the unadjusted mean scores (table 1) were small. In the first regression model, female gender (p<.0001), higher age (p=.041), having more concomitant diseases (p<.0001), having an inflammatory rheumatic disease (p<.0001), and having a lower level of psychological flexibility (p < .0001) were associated with lower mental well-being (F=367.258,

p<.0001, Adjusted R^2=.556). In the second multiple regression model (table 2), the two-way interactions added significant variance to the model (F-change = 2.885, p=.034, Adjusted R^2=.557). The year × psychological flexibility interaction (p=.023) indicated that the group with high psychological flexibility scored somewhat higher on mental well-being in 2018 than in 2020. Having an inflammatory rheumatic disease approximated significance in this model (p=.079). In the third model (not shown), the added three-way interaction year × group × psychological flexibility was not significant (F-change = 2.456, p=.117, Adjusted R^2=.557).

Table 2

Linear regression analysis of mental well-being associated with demographics, group[a], year[b] and psychological flexibility[c]

	B	(SE)	β	t	*P*-value	95% CI
Constant	10.648	(2.056)		5.650	<.0001	[7.297, 15.578]
Demographics						
Gender	-2.658	(.412)	-.092	-6.063	<.0001	[-3.742, -1.662]
Age	.028	(.012)	.035	2.211	.027	[0.005, 0.045]
Education	-.378	(.388)	-.016	-1.010	.313	[-1.105, 0.416]
Disease number	-2.109	(.161)	-.230	-14.374	<.0001	[-2.443, -1.728]
Group	-4.500	(2.382)	-.124	-1.755	.079	[-9.695, 1.165]
Year	3.426	(1.821)	.129	1.753	.080	[-0.955, 6.645]
FIT-60[†]	.162	(.008)	.685	21.115	<.0001	[0.143, 0.176]
Year × Group	1.995	(1.044)	.047	1.704	.089	[-0.007, 3.454]
Year × FIT-60	-.019	(.008)	-.180	-2.282	.023	[-0.033, 0.000]
Group × FIT-60	.003	(.010)	.016	.236	.813	[-0.014, 0.021]

[a]0 = control group, 1 = index group (people with an inflammatory rheumatic disease).
[b]0 = 2018, 1 = 2020. [c]FIT-60, Flexibility Index Test.
B: unstandardized beta; β: standardized beta; t: t test statistic.

DISCUSSION

During the two peak months of the COVID-19 outbreak in the Netherlands in 2020, people with an inflammatory rheumatic disease were more worried about getting infected (large effect) and more stressed (small effect) than people without an inflammatory rheumatic disease. However, as compared to scores collected in 2018, the level of mental well-being during the peak of COVID-19 was neither lower for patients with an inflammatory rheumatic disease, nor for those without. Moreover, all analyses rejected the hypothesis that higher levels of psychological flexibility protect against a reduction of mental well-being in hard times and in the group with an inflammatory rheumatic disease that was considered to be more at risk.

About half of the group with an inflammatory rheumatic disease and one quarter of the control group was worried or very worried about the risk of getting infected. For the first group, this could be considered an adaptive reaction to a realistic threat at that time, because it was communicated that people with an inflammatory rheumatic disease had an overall higher risk of getting infected due to their drug-induced suppressed immune system[2,3]. Worry makes people more cautious, which may cause them to pay more attention to hygienic behaviour including social distancing. In line with earlier findings during the COVID-19 outbreak in China[8,9], both groups were more stressed than usual, but the index group was only a little bit more stressed than the control group. In the current study, mental well-being of no group was clearly reduced during the COVID-19 peak as compared to the sample of 2018. Thus, it appears that patients with an inflammatory rheumatic disease, on average, show a realistic level of concern without being overly stressed or distressed.

Based on previous studies[11,15], we hypothesized that psychological flexibility skills would protect against a reduction of mental well-being, especially in hard times (2020 vs. 2018) and in groups that are more at risk, and that particularly the index group in 2020 would have lower mental well-being, because of the consequences of the COVID-19 pandemic. However, not one of these hypotheses was confirmed and one interaction even showed a small, but statistically significant opposite pattern. Overall, our findings do not confirm the notion that psychological flexibility acts as a buffer against impeding consequences of COVID-19 in patients with an inflammatory rheumatic disease.

During the initial outbreak of the coronavirus, people with inflammatory rheumatic disease were considered to be at high risk for getting COVID-19. They should, even more than other people, be aware of the risks and should stay home as much as possible, avoid contact with people with a cold or fever and should contact their general practitioner when showing viral symptoms[25]. Worry is a normal reaction to the threat of contamination. It makes people cautious and prevents them from getting infected. However, in some (very) worried people, the worry may become excessive and lead to an anxiety disorder. For them a doctor can help in finding appropriate professional help, such as cognitive-behavioural therapy[26]. To prevent excessive worry, people are advised to read and watch trustworthy, fact-based information in the media, instead of the much more common anxiety-provoking information[27]. It is also important to seek and cherish positive social contacts, because it may protect against anxiety[28], to try to adapt to the new situation and to accept it and seek professional help when needed, e.g., by going to the doctor when the disease changes.

A strength of the current study is the time frame in which data were collected. People participated during the two peak months (March and April) of the virus outbreak in the Netherlands. At that time strict safety measurements were set by the government, many people got infected and died, and there was uncertainty about the development of the virus outbreak. Our sample size was large enough to have small margins of error and quite evenly distributed on age and various regions in the

Netherlands. It is a limitation that diseases were self-reported and that we did not ask to specify the inflammatory rheumatic diseases. Moreover, instead of a representative sample, our sample was a convenience sample with an overrepresentation of highly educated women. Therefore, caution is needed in generalizing these results. However, analyses were adjusted for differences in demographic variables and number of diseases. Finally, our study only targeted the first peak period of the pandemic in the Netherlands. A third data collection will could give us more information about the long-term effects of the pandemic.

This is perhaps the first and only study that examined the psychological impact of the peak of the COVID-19 crisis on people with an inflammatory rheumatic disease. In the media and professional literature, we often hear that the psychological impact of the crisis is huge. We indeed observed that respondents, and especially those with inflammatory rheumatic disease, are worried about getting infected by the coronavirus, and we also observed that respondents experienced more stress than usual at the time of the COVID-19 outbreak. However, we did not observe a lower mental well-being during this peak period of the outbreak of the virus, neither in the index group nor in controls, which may also have prevented us from finding a buffering effect of psychological flexibility, contrary to our expectation. Overall, our results suggest that the psychological impact of the COVID-19 pandemic in patients with inflammatory rheumatic disease is modest, which might imply that common education and health care will do for most patients.

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Chapter 3

The impact of COVID-19 stress on pain and fatigue in people with and without a central sensitivity syndrome

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ABSTRACT

Objectives: Stress may augment somatic symptoms in central sensitivity syndromes (CSS) such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome. To test this hypothesis, we examined whether the association between COVID-19 stress and somatic symptom severity would be stronger in people with than without CSS and whether psychological flexibility would buffer the impact of this stress on symptom severity.

Methods: In a 2-sample, repeated cross-sectional design, we analysed questionnaire data from Dutch people with and without CSS, collected in two independent surveys: before the COVID-19 pandemic (2018; CSS: n=194, non-CSS: n=337) and at the peak of the pandemic (2020; CSS: n=428, non-CSS: n=1101). Somatic symptom severity, worry and stress due to the pandemic, and psychological flexibility were examined in regression analyses. Two stress operationalisations were analysed: stress levels during the peak of the pandemic, and a comparison of measurements in 2020 and 2018 (assuming higher stress levels in 2020).

Results: Higher worry and stress during the pandemic (standardized β=.14), the presence of a CSS (β=.40), and lower psychological flexibility (β =-.33) were all (p<.0001) associated with more severe somatic symptoms, but the associations of each stress operationalisation with somatic symptoms was not particularly strong in people with CSS (β=-.026, p=.27; β=-.037, p=.22), and psychological flexibility (β=-.025, p=.18; β=.076, p=.35) did not buffer this association.

Conclusions: Findings do not support the hypotheses that COVID-19 stress augments somatic symptoms, particularly in CSS, or that psychological flexibility buffers this impact. Rather, COVID-19-related stress appears to have an uncertain impact on somatic symptoms.

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TYK and RG developed the design and collected and analysed the data, TYK drafted the paper and JWGJ, MAL and RG critically assessed, edited and revised the paper.

INTRODUCTION

Conditions such as fibromyalgia, chronic fatigue syndrome (CFS), and irritable bowel syndrome (IBS) are described with various labels, such as medically unexplained symptoms[1], persistent physical symptoms[2], functional somatic syndromes[3], bodily distress syndromes[4], and central sensitivity syndromes[5] (CSS). In this paper, we will use the label CSS. The CSS nosology is based on mutual associations among syndromes with overlapping clinical features, and central sensitization as a presumed common pathophysiological mechanism. In this nosology, the term "sensitivity" rather than "sensitization" is used, to emphasize that it is a biopsychological rather than neuropathophysiological phenomenon[5]. Several studies suggest that a sensitive brain may augment pain and other somatic symptoms in response to stress, such as in people with fibromyalgia and widespread pain[6,7], CFS[8] or IBS[9]. The COVID-19 pandemic offers a unique context to study the impact of stress on somatic symptom severity in people with CSS.

The outbreak of the SARS-CoV-2 virus and the measures taken by governments to prevent the spread of COVID-19 have impacted the entire global population[10,11,12]. Stress during the pandemic may be caused by worry of getting infected, changes in daily routines and caregiving, decreased opportunities for social and leisure activities, the illness or death of family members or friends, loss of work, and financial concerns[13,14,15,16]. Furthermore, for people with chronic conditions, somatic symptoms may also be enhanced by delayed medical evaluations[17,18], reduced access to health services, and disrupted treatment[7,19,20]. These psychological and health care challenges suggest that pain and other somatic symptoms in people with CSS may be more severe during than before the stressful peak months of the COVID-19 pandemic.

People differ in their ability to deal with stress. Symptom exacerbation may be less likely among people who are able to accept what cannot be changed and find other ways to pursue their goals in life. Psychological flexibility[21] refers to the ability to be open to adapt to new situational demands, while being committed to behaviour that is in line with one's own chosen values[21,22], and is considered key to adapt to challenging circumstances[23,24]. Longitudinal findings suggest that psychological flexibility impacts subsequent mental health, and not the reverse[21]. In people with chronic pain, CFS, or IBS, psychological flexibility is a resilience factor, protecting against and reducing the burden and severity of somatic symptoms[25,26,27,28,29,30]. If psychological flexibility is also shown to buffer the impact of stress of the COVID-19 pandemic, then enhancing psychological flexibility by acceptance- and mindfulness-based education or interventions, for example, may be of value.

The aim of our study was to determine the impact of stress due to the COVID-19 pandemic on the severity of somatic symptoms in people with CSS, as compared to people without CSS, and as compared to an earlier pandemic-free period. Given that the stress-somatic symptom link may be especially strong in people with CSS, we hypothesized that people with CSS (vs. non-CSS) would show more severe somatic

symptoms in response to stress of the pandemic, and that psychological flexibility would buffer the impact of stress on somatic symptoms.

METHODS

Participants

Data from two separate online surveys in the general, Dutch-speaking population were analysed. The first data collection was from November 2018 to May 2019 (*year* 2018). The second collection started on March 24, 2020, one day after the Dutch government introduced strict rules and regulations to prevent further spread of COVID-19 and ended on May 2, 2020 (*year* 2020). This latter period was the first serious pandemic peak period in the Netherlands in terms of number of hospitalizations, patients on the intensive care, and deaths due to COVID-19 (Dutch National Institute for Public Health and the Environment). In the online questionnaires, respondents could indicate with "Yes" or "No" on a list with a variety of diseases, if they had fibromyalgia, chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), somatoform disorder/somatic symptom disorder, chronic headache (not migraine), or chronic pain elsewhere in the body (not the head). We classified participants reporting any of these syndromes into a CSS group and all other participants into a non-CSS group. Note that someone with, for instance, rheumatoid arthritis or a cardiovascular disorder would be allocated to the CSS group if the person also had fibromyalgia, whereas a person with rheumatoid arthritis or a cardiovascular disorder without any of the CSS disorders was allocated to the non-CSS group. In both samples, all participants with complete assessments on worry, stress, pain, fatigue, and psychological flexibility were retained and analysed. Figure S1 (supplementary material) shows the flowchart comprising the 2018 and 2020 samples.

Procedure

For each of the two samples, participants were recruited via social media (e.g., Facebook, Instagram, LinkedIn, local internet sites) and websites of associations including the Dutch national patient associations for fibromyalgia, CFS, and IBS. A hyperlink to the online survey (housed on a secure university website) was provided, where participants were informed about the study and could provide informed consent, after which they were allowed to participate. They were not compensated for their participation. Approval was given by the Ethics Committee of the Faculty of Social and Behavioural Sciences of Utrecht University, the Netherlands for the 2018 (FETC17-120) and 2020 (FETC20-190) data collections.

Instruments

Somatic symptom severity

In both the 2018 and 2020 samples, the severity of somatic symptoms was measured with the *bodily pain* and *energy/fatigue* scales of the Dutch version of the RAND 36-Item Short Form Health Survey[31] (RAND SF-36). The bodily pain scale consists of

two items assessing the level of bodily pain and its interference with daily activities during the past 4 weeks, on 6- and 5-point Likert scales, respectively. The vitality scale consists of two items assessing the level of fatigue and two items on the energy level during the past 4 weeks, all on 6-point Likert scales. After reversing scores, higher scores on the SF-36 reflect more severe pain and fatigue. We used the standardized mean deviation from the norm scores[31] of these pain and energy/fatigue scales as a measure of somatic symptom severity.

Psychological flexibility

Also in both samples, the Flexibility Index Test-60 (FIT-60) was used to measure psychological flexibility[32]. This questionnaire assesses six processes: acceptance, cognitive defusion, contact with the present moment, self as context, values, and committed action[21]. The 60-item questionnaire (10 items for each process) is based on a literature review of psychological flexibility and on four existing questionnaires. Participants rate the extent to which each item applies to them from 0 ('totally disagree') to 6 ('totally agree'). The theoretical range of the total score is from 0 to 360, and higher scores indicate more flexibility. The initial psychometric analyses of the FIT-60 showed that the internal consistency was high, with a Cronbach's alpha of .95 for the total scale[32].

COVID-19 stress

The participants of the 2020 sample reported their current level of being worried about getting infected by the virus on a 4-point scale (1 = 'not worried', 2 = 'a little worried', 3 = 'worried', 4 = 'very worried') and their current stress compared to their normal stress level, on a 5-point scale (1 = 'less stressed', 2 = 'a little less stressed', 3 = 'neither less nor more stressed', 4 = 'a little more stressed' and 5 = 'more stressed'). The z-scores of each participant on these two items were averaged; the resulting score was labelled "COVID-19 stress".

Statistical analyses

The CSS and non-CSS groups were compared using parametric or nonparametric tests, where appropriate. Pearson correlations were calculated to examine associations between independent variables and the dependent variable somatic symptom severity.

Our main analyses consisted of two linear regression, the first in the sample of 2020 only (analysis 1), and the second in the samples of 2018 and 2020 (analysis 2). Two operationalisations of stress were used. In analysis 1, stress was operationalized as the mean of standardized self-reported worry and stress levels during the first peak of the COVID-19 pandemic ('COVID-19 stress'). In analysis 2, it was assumed that participants during the 2020 pandemic were more stressed than the participants two years earlier. Thus, in this analysis, 'year' was the operationalization of stress, with scores in the sample of 2020 representing COVID-19 stress circumstances and scores in the sample of 2018 default circumstances.

In both analyses, linear regressions with bootstrapping (1000 samples) examined the associations of somatic symptom severity (dependent variable) with *group* (CSS vs. non-CSS), *stress* ('COVID-19 stress' in analysis 1 and 'year' in analysis 2), and *psychological flexibility* (total score of FIT-60) as independent variables (COVID-19 stress and the FIT-60 score were centred in analysis 1). Gender, age, education, and number of (comorbid) diseases were entered as covariates. The 2-way interactions (COVID-19 stress × group, COVID-19 stress × psychological flexibility, and group × psychological flexibility) were included to examine whether belonging to the CSS group was associated with higher somatic symptom levels in response to stress and whether higher levels of psychological flexibility protected against increased stress-related somatic symptom severity. To interpret significant interactions, regression lines for individuals with low (−1 SD) and high (+1 SD) scores on the two interacting variables were plotted[33]. The magnitude of the interaction was indicated with Cohen's *d* effect sizes, with values of 0.20, 0.50 and 0.80 representing small, medium, and large effects, respectively[34].

To examine, whether findings might be due to the diagnostic overlap of CSS with osteoarthritis or an inflammatory rheumatic disease, we performed ad hoc regression analyses excluding people with osteoarthritis or an inflammatory rheumatic disease. For all analyses, p-values <.05 were considered statistically significant, with all tests being 2-sided. Statistical analyses were done using IBM SPSS statistics version 25.0.

RESULTS

Participants

Table 1 shows the characteristics of the CSS and non-CSS groups in the samples of 2018 (n = 531) and 2020 (n = 1529). The CSS and non-CSS groups did not differ in age in 2018 ($F(1, 530)$ = 3.09, p = .079) and 2020 ($F(1, 1528)$ = 1.71, p = .191). In 2020, groups did not differ on marital status ($\chi^2(2)$ = 1.37, p = .505), but in 2018, more people in the CSS than the non-CSS group were in a relationship ($\chi^2(2)$ = 8.18, p = .017). In both samples, the CSS groups included more women (2018: $\chi^2(1)$ = 36.46; 2020: $\chi^2(1)$ = 90.07, p < .0001), people with a lower education level (2018: $\chi^2(2)$ = 21.13; 2020: χ^2 (2) = 79.50, p < .0001) and a higher number of (comorbid) diseases (2018: $F(1, 530)$ = 60.78; 2020: $F(1,1528)$ = 94.86, p < .0001). More specifically, the prevalence of osteoarthritis (2018: $\chi^2(1)$ = 47.49; 2020: $\chi^2(1)$ = 49.06,p < .0001), skin diseases (2018: $\chi^2(1)$ = 15.52; 2020: $\chi^2(1)$ = 16.95, p < .0001), neurological diseases (2018: $\chi^2(1)$ = 11.64, p = .001; 2020: $\chi^2(1)$ = 19.32, p < .0001) and obesity (2018: $\chi^2(1)$ = 7.85, p = .005, 2020: $\chi^2(1)$ = 30.01, p < .0001) was higher in the CSS groups in both samples, whereas in the CSS group pulmonary disease was more prevalent in 2020 ($\chi^2(1)$ = 17.09, p < .0001) and cardiovascular disease in 2018 ($\chi^2(1)$ = 7.08, p = .008). Table S1 (supplementary material) shows the comorbid conditions for each CSS. Analyses comparing the overall samples from 2018 and 2020, showed a significant age difference (2018: M = 40.3; 2020: M = 47.7; F(1, 2059) = 54.90, p < .0001), whereas gender, education, and marital status did not

significantly differ between the two overall samples. Ten out of 1529 people reported having COVID-19 during the first peak: 3 in the CSS group and 7 in the non-CSS group. This may be an underestimate because widespread testing was rare in the Netherlands at that time.

Table 1

Characteristics of the groups with a central sensitivity syndrome (CSS) and without (non-CSS) before (2018) and during (2020) the first peak of the COVID-19 outbreak in the Netherlands

Year	**2018** ***n* = 531**		**2020** ***n* = 1529**		
Group	**CSS** ***n* = 194**	**non-CSS** ***n* = 337**	**CSS** ***n* = 428**	**non-CSS** ***n* = 1101**	**All** ***n* = 2060**
Age (years)					
Mean (SD)	45.2 (12.1)	42.8 (16.2)	48.3 (12.6)	49.4 (15.2)	47.7 (14.8)
Range	18 - 69	18 - 87	20 - 80	18 - 91	18 - 91
Gender, *n* (%)					
Women	186 (95.9)	254 (75.4)	406 (94.9)	802 (72.8)	1648 (80.0)
Education level*, *n* (%)					
Low	94 (48.5)	97 (28.8)	235 (54.9)	336 (30.5)	762 (37.0)
High	98 (50.5)	238 (70.6)	190 (44.4)	761 (69.1)	1287 (62.5)
Missing	2 (1.0)	2 (0.6)	3 (0.7)	4 (0.4)	11 (0.5)
Marital status, *n* (%)					
Single	42 (21.6)	112 (33.2)	139 (32.5)	325 (29.5)	618 (30.0)
In a relation	144 (74.2)	211 (62.6)	279 (65.2)	752 (68.3)	1386 (67.3)
Unknown	8 (4.1)	14 (4.2)	10 (2.3)	24 (2.2)	56 (2.7)
Number of diseases other than a central sensitivity syndrome					
Mean (SD)	1.46 (1.41)	0.69 (0.87)	1.43 (1.35)	0.82 (0.98)	0.98 (1.14)
Range	0 - 7	0 - 5	0 - 6	0 - 6	0 - 7
Type of other disease, *n* (%)					
Inflammatory rheumatic disease†	27 (13.9)	47 (13.9)	52 (12.1)	113 (10.3)	239 (11.6)
Osteoarthritis	51 (26.3)	18 (5.3)	87 (20.3)	85 (7.7)	241 (11.7)
Pulmonary	20 (10.3)	25 (7.4)	90 (21.0)	139 (12.6)	274 (13.3)
Skin	25 (12.9)	12 (3.6)	32 (7.5)	31 (2.8)	100 (4.9)
Cancer	4 (2.1)	4 (1.2)	7 (4.2)	29 (2.6)	46 (2.2)
Cardiovascular	26 (13.4)	22 (6.5)	79 (18.5)	159 (14.4)	286 (13.9)

Psychiatric	47 (24.2)	24 (7.1)	91 (21.3)	104 (9.4)	266 (12.9)
Neurological	33 (17.0)	25 (7.4)	50 (11.7)	58 (5.3)	166 (8.1)
Obesity	26 (13.4)	21 (6.2)	71 (16.6)	80 (7.3)	198 (9.6)
One other non-listed disease	24 (12.4)	31 (9.2)	48 (11.2)	97 (8.8)	200 (9.7)
Two or three other non-listed diseases	0 (0.0)	1 (0.3)	1 (0.2)	3 (0.3)	5 (0.2)
Self-report measures, Mean (SD)					
Somatic symptom severity (RAND SF-36)‡	1.56 (0.78)	0.28 (0.83)	1.27 (0.79)	0.08 (0.76)	0.50 (0.97)
Psychological flexibility (FIT-60) §	213.3 (48.3)	233.6 (42.9)	210.3 (53.3)	236.8 (46.8)	228.6 (49.1)

*Education level: low: lower general secondary education or lower; high: higher general secondary education or higher.
†These participants reported to have a chronic rheumatic disease other than osteoarthritis or fibromyalgia.
‡This score is the mean of standardized deviation scores from the general adult population norm for pain and fatigue/vitality[31]. Scores were reversed: higher scores reflect more pain and fatigue.
§This total score ranges from 0 to 360, with higher scores reflecting more flexibility.

Stress levels during the first peak of the COVID-19 outbreak in the Netherlands

During this peak in 2020, 80.5% of the people in the non-CSS group and 90.0% in the CSS group reported being "a little" to "very worried" about getting infected by the SARS-CoV-2 virus. When asked about their current stress level compared to their normal stress level, 61.7% of the non-CSS group reported being "a little more stressed" or "more stressed", versus 71.5% of the CSS-group. The mean standardized worry and stress levels for the CSS and non-CSS groups were 0.21 (SD=0.86) and -0.08 (SD=0.83), respectively. Figure S2 (supplementary material) shows the distribution of worry and stress levels for the CSS and non-CSS groups. Overall, people indicated that they perceived themselves, on average, to be more worried and stressed than normal during the peak of the pandemic.

Analysis 1. COVID-19 stress and somatic symptom severity (sample of 2020)

This analysis involved the prediction of the severity of somatic symptoms from all other concurrent variables during the peak of the COVID-19 crisis in 2020 (see Table 2). The linear regression model was significant and explained 56% of the variance in

somatic symptom severity (F = 199.62, p < .0001, Adjusted R^2 = .56). Higher levels of COVID-19 stress were significantly associated with more severe somatic symptoms (r = .35, p < .0001), also when taking account of all other variables in the model (β = .14, p < .0001). All other variables were also significantly and independently associated with higher levels of somatic symptom severity; in order of strength (β): having a central sensitivity syndrome (β = .40, p < .0001), a lower level of psychological flexibility (β = -.33, p < .0001), more (comorbid) diseases (β = .23, p < .0001), female gender (β = .05, p = .004), lower age (β = -.05, p = .010), and lower education (β = -.04, p = .026). The two-way interactions were not significant, indicating that the relationship between COVID-19 stress and symptom severity was statistically not different in people with versus without CSS or in people with lower versus higher psychological flexibility.

Table 2

COVID-19 stress and other associations with somatic symptom severity in the sample of 2020 (n = 1522)

	r	*b*	*SE*	β	*t*	*p*	*95% CI*
Constant		.103	.070		1.32	.19	-.047 to .214
Demographics							
Gender	.24‡	.117	.038	.051	2.85	.004	.052 to .202
Age	-.05	-.003	.001	-.047	-2.57	.01	-.005 to -.001
Education*	-.26‡	-.079	.038	-.041	-2.23	.03	-.152 to .001
Number of (comorbid) diseases	.42‡	.186	.014	.226	12.13	<.0001	.151 to .212
Group†	.57‡	.836	.045	.401	21.08	<.0001	.743 to .899
COVID-19 stress	.35‡	.157	.026	.142	6.48	<.0001	.109 to .201
Psychological flexibility	-.53‡	-.006	.000	-.330	-14.17	<.0001	-.007 to -.005
COVID-19 stress × Group	.25‡	-.052	.056	-.026	-1.10	.27	-.144 to .063
COVID-19 stress × Psychological flexibility	-.15‡	-.001	.000	-.025	-1.34	.18	-.001 to .000
Group × Psychological flexibility	-.37‡	.001	.001	.032	1.31	.19	-.001 to .002

Pearson correlations (*r*) and results of the linear regression analysis with bootstrapping examining the association of somatic symptom severity (SF-36) with gender (0=men, 1=women), age, education level, number of (comorbid) diseases, group, COVID-19 stress and psychological flexibility and two-way interactions.

*Education level: 0=low: lower general secondary education or lower; 1=high: higher general secondary education or higher.

†Group: 0=non-CSS; 1=CSS: people with a central sensitivity syndrome

‡Pearson correlation with somatic symptom severity was significant at the 0.01 level (2-tailed testing)

b, unstandardized regression coefficient, *SE*, Standard Error; β, standardized beta; *t*, t-test statistic; *CI*, confidence interval of unstandardized regression coefficient.

Analysis 2. Associations with somatic severity during the peak of the COVID-19 pandemic in 2020 compared to 2018

In this analysis, the severity of somatic symptoms was predicted from year and all other concurrent variables (see Table 3); more stress was assumed in 2020 during the peak of the COVID-19 pandemic than before (2018).

The bootstrap regression model was highly significant and explained 56% of the variance in somatic symptom severity (F = 259.33, p < .0001, Adjusted R^2 = .56). Contrary to our hypothesis, the 2018 sample reported more severe somatic symptoms (r = -.15, p < .0001) than the 2020 sample, and this difference remained significant at including all other variables in the model (β = -.16, p = .040). All other variables but age were significantly and independently associated with higher levels of somatic symptom severity; in order of strength (β): lower levels of psychological flexibility (β = -.40, p < .0001), having a CSS (β = .29, p < .0001), more (comorbid) diseases (β = .24, p < .0001), female gender (β = .07, p < .0001), and lower education (β = -.04, p = .010). Also contrary to expectation, the significant group × psychological flexibility interaction (β = .001, p = .029) indicated that in the non-CSS group, higher psychological flexibility buffered somatic symptom severity more, compared to in the CSS group (Figure 1). However, as Figure 1 shows the regression lines are nearly parallel, indicating a very small interaction; the effect size difference between the two groups for lower (-1 SD) flexibility was 1.01, while it was 1.18 for higher (+1 SD) psychological flexibility; a trivial difference of d = 0.17. All other interactions were not significant, indicating that at the first peak of the COVID-19 outbreak in the Netherlands, the level of symptom severity was not higher for people with CSS or with lower psychological flexibility.

Ad hoc analyses

The two hypotheses of our study were also rejected in ad hoc analyses excluding people with osteoarthritis or an inflammatory rheumatic disease; none of the interactions were significant.

Table 3

Year 2020 (during the first peak of the COVID-19) versus year 2018 and other associations with somatic symptom severity (n = 2049)

	r	*b*	*SE*	β	*t*	*p*	*95%* CI
Constant		1.901	.179		11.13	<.0001	1.565 to 2.202
Demographics							
Gender	.26‡	.165	.037	.069	4.48	<.0001	.095 to .242
Age	-.02	.000	.001	-.004	-.27	.79	-.002 to .001
Education*	-.25‡	-.081	.034	-.040	-2.58	.01	-.167 to .011
Number of (comorbid) diseases	.43‡	.206	.013	.243	15.12	<.0001	.177 to .236
Group†	.58‡	.612	.154	.291	4.04	<.0001	.317 to .999
Year	-.15‡	-.354	.181	-.160	-2.06	.04	-.772 to .079
Psychological flexibility	-.51‡	-.008	.001	-.395	-11.37	<.0001	-.010 to -.006
Year × Group	.41‡	-.087	.070	-.037	-1.24	.22	-.246 to .029
Year × Psychological flexibility	-.31‡	.001	.001	.076	.94	.35	-.001 to .002
Group × Psychological flexibility	.50‡	.001	.001	.143	2.19	.03	.000 to .003

Pearson correlations (*r*) and results of the linear regression analysis with bootstrapping examining the association of somatic symptom severity (SF-36) with gender (0=men, 1=women), age, education level, number of (comorbid) diseases, group, year (0=2018, 1=2020), psychological flexibility and two-way interactions.

*Education level: 0=low: lower general secondary education or lower; 1=high: higher general secondary education or higher.

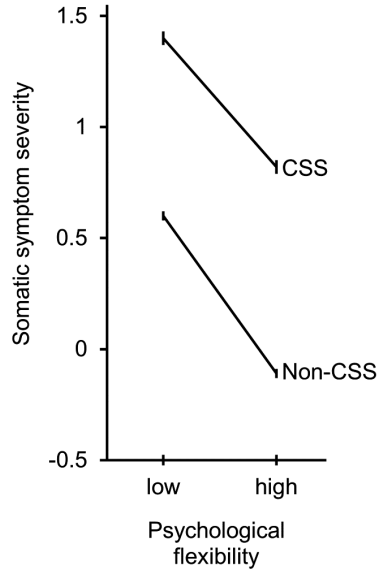
†Group: 0=non-CSS; 1=CSS: people with a central sensitivity syndrome

‡Pearson correlation with somatic symptom severity significant at the 0.01 level (2-tailed)

b, unstandardized regression coefficient; *SE*, Standard Error; β, standardized beta; *t*, t-test statistic; *CI*, confidence interval of unstandardized regression coefficient.

Figure 1

Somatic symptom severity (standard deviation from the norm) on y-axis as a function of low (-1 SD) and high (+1 SD) psychological flexibility (x-axis) for having a central sensitivity syndrome disorder (CSS) or not having it (non-CSS), while controlling for gender, age, education level, number of diseases and year (2020 vs. 2018). The error bars show the standard error of measurement.



DISCUSSION

During the first peak of the COVID-19 pandemic in the Netherlands, people perceived themselves to be, on average, more stressed than normal, and these stress levels were associated with more severe somatic symptoms. In contrast, based on another operationalization of stress—comparing the peak period of the pandemic to a previous year—there was no link between stress and more severe somatic symptoms. Also, both moderator hypotheses were rejected: the link between stress and somatic symptom severity was not stronger in people with CSS than those without CSS, and psychological flexibility did not act as a buffer against an increase of somatic symptoms severity in response to stress.

Our cross-sectional analysis during the pandemic peak showed an association between self-reported COVID-19 stress levels and self-reported somatic symptom severity, which is consistent with the larger literature showing correlations between self-reported scores reflecting negative experiences. A 10-day online survey, of people with fibromyalgia during the pandemic, found such an association between intra-individual levels of in anxiety and chronic pain[35]. Such concurrent inter-individual and intra-individual associations may reflect mutual influences on a negative affect dimension instead of a specific somatic symptom reaction to stress[36]. Guided by the hypothesis that a sensitized brain may augment somatic symptoms in response to stress in people with CSS[6,7,8,9], we expected a stronger correlation between COVID-stress and somatic symptoms in people with CSS, compared to people without CSS. Our data did not support this hypothesis. A study that was conducted in parallel to our study showed that longitudinal assessments of pain symptoms measured pre- and post-lockdown did not change significantly on average[37]. Our results showed even a small but statistically significant lower level of symptom severity in the pandemic year (2020), compared to that in the pre-pandemic year (2018). Thus, overall, there is no indication of a COVID-19 stress-somatic symptom link, nor that such a link is stronger in people with CSS.

Several previous studies have examined the effects on people with CSS before and after a major environmental stressor. Pain in people with fibromyalgia was assessed before and after the September 11 attacks[38,39]. Both studies found no increase in symptoms from before to after the attack. Another two studies did not find lower levels of mental well-being during the COVID-19 pandemic in patients with inflammatory rheumatic diseases[40] or patients with systemic lupus erythematosus[41], although both groups were considered at increased risk for acquiring COVID-19 infection and for a more severe course and outcome of this infection. Several other studies compared mental well-being during the pandemic, with data collected before the pandemic. One study in the UK observed a higher prevalence of depressive-, anxiety-, and insomnia symptoms during the pandemic as compared to general population norms[11], whereas two other studies in the Netherlands reported that mental health remained stable as compared to pre-pandemic measurements from one year earlier[42,43]. A prospective study in people with systemic sclerosis from four countries showed that levels of anxiety symptoms

increased during the COVID-19 pandemic, whereas the change in depression symptoms was negligible[44]. Together, these studies suggest that somatic symptoms do not reliably increase in response to major environmental stressors. Regarding mental health, the results of all but one study are in agreement by showing that, although increased levels of self-reported worry, anxiety and stress were present during the first peak of the COVID-19 pandemic, there was no clear increase of depressive mood.

There is another possible explanation for the lack of change in somatic symptom severity during the pandemic. The pandemic forced people to focus on external stressors and behaviour changes. This could have had a positive impact in some people with CSS, shifting their focus from internal somatosensory processes and psychological conflicts to environmental issues, which may have positively modulated their pain perception[45]. It is also possible that the impact of the COVID-19 pandemic on people with CSS is, on average, weaker than assumed. Some persons with CSS may have experienced a positive mental impact, for instance, because they felt less pressure from work, more social connectedness, or more recognition for their symptoms and situation during the pandemic.

Studies during the COVID-19 pandemic consistently show that higher scores on psychological flexibility or related constructs such as resilience are associated with *mental well-being*[14,46,47,48,49,50,51]. We also found that higher psychological flexibility was associated with less severe *somatic symptoms*. One study observed that positive personality traits (i.e., optimism, mindfulness, and resilience) served as protective factors in the association between fear of the virus and mental distress[52]. In line with the authors of this study, we hypothesized that psychological flexibility would protect against an increase of somatic symptom severity due to COVID-19 stress, particularly in people with CSS. Our findings do not support this specific hypothesis, although one analysis indicated that psychological flexibility might buffer against somatic symptom severity in people without CSS. Thus, although in both groups higher levels of psychological flexibility were strongly related to lower symptom severity, we did not find evidence that this buffer is particularly strong in people with higher COVID-19 stress or in people with CSS. One possible explanation could be that there was little effect to buffer, because COVID-19 stress did not increase this burden in people with CSS, maybe also because they were already experienced in coping with multiple adversities of life.

A strength of the current study is the time frame in which data were collected. People participated during the first two peak months (March and April of 2020) of the virus outbreak in the Netherlands, when strict safety measurements to limit the spread of the virus were in place, and during which many people got infected and died, and a lot of uncertainty existed on the development of the virus outbreak. Our sample size was large enough to have small margins of error and quite evenly distributed on age and various regions in the Netherlands. However, somatic symptom severity as measured with the RAND SF-36 may be less sensitive to stress as it referred to the past 4 weeks. Another limitation is that CSS conditions were not confirmed by clinical assessment, which may have underestimated CSS in, for

instance, rheumatic diseases[53]. A questionnaire for assessing central sensitivity[54,55] would have given insight into the perceived general disability and physical symptoms, central sensitivity features, urological and dermatological problems and emotional distress of our CSS group as compared to the non-CSS group. Our samples were convenience rather than representative, and, importantly, the samples at the two time points were different; obtaining data from the same people at similar periods in the year, rather than from two separate samples, would have yielded a more valid test of intra-individual changes in somatic symptoms between the two sample periods. Results showed an overrepresentation of highly educated women, especially in the non-CSS group, and an association of lower education level with more severe somatic symptoms. Although analyses were adjusted for relevant covariates, including education level and number of comorbid diseases, other uncontrolled variables may be relevant. Finally, our study only targeted the first peak period of the pandemic in the Netherlands, so stress was measured in the acute phase, rather than after a more prolonged experience of stress. A third data collection would give more information about the long-term stress effects of the pandemic.

To our knowledge, this is the only study that has examined the impact of the peak of the COVID-19 crisis on somatic symptom severity in people with CSS. We hypothesized that stress might augment somatic symptoms in people with CSS, but we did not find evidence for this hypothesis; nor did we find a buffering effect of psychological flexibility. Overall, our results suggest that the impact of the COVID-19 pandemic on somatic symptoms in people with CSS is uncertain.

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Chapter 4

A better but persistently low health status in women with fibromyalgia during the COVID-19 pandemic: a repeated cross-sectional data analysis

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ABSTRACT
Objectives: Multiple overlapping and complementary theoretical arguments suggest that the COVID-19 pandemic could worsen health in fibromyalgia. The aim of this study was to determine mental and physical health in women with fibromyalgia before and during the pandemic.
Methods: In a 3-sample, repeated cross-sectional design, we analyzed questionnaire data from Dutch women with fibromyalgia, collected in three independent samples: before the COVID-19 pandemic (2018; n=142) and during the first acute (2020; n=304) and prolonged (2021; n=95) phases of the pandemic. Eight dimensions of mental and physical health were assessed using The RAND 36-Item Short Form Health Survey (RAND SF-36).
Results: Compared to norm group data, both before and during the pandemic, women with fibromyalgia showed high levels of fatigue and pain and low levels of general health, social functioning, physical functioning, role physical functioning (d>1.2, very large effect sizes), role emotional functioning, and mental health (0.71<d<1.2, medium to large effect sizes). Contrary to theoretical expectation, levels at five health variables before vs. during the pandemic did not differ (p>.05), and levels of pain (p<.001), role physical functioning (p<.001), and physical functioning (p=.03) (0.014≤pη^2≤0.042, small effect sizes) reflected a healthier status during than before the pandemic.
Conclusions: These findings indicate a somewhat better but persistently low health status in women with fibromyalgia during the pandemic. This suggests that the pandemic may include changed circumstances that are favorable for some women with fibromyalgia.

Acknowledgment of author contributions
TYK and RG developed the design and drafted the paper, TYK, HvM and RG collected and analysed the data, HvM and RG critically assessed, edited and revised the paper.

INTRODUCTION

For healthy and unhealthy people, the COVID-19 pandemic may cause stress and distress by worry of getting infected, changes in daily routines and caregiving, decreased opportunities for social and leisure activities, the illness or death of family members or friends, loss of work, or financial concerns[1] .In addition, for people with a chronic condition, the disease may get worse because of delayed medical evaluations, reduced access to health services, and disrupted treatment[2]. Furthermore, symptoms such as pain and fatigue encompass mutually interacting biological, psychological and social factors[3], which suggests that they may be amplified by stress of the pandemic. Specifically in fibromyalgia, central nervous system processes such as central sensitization and loss of descending analgesic activity[4], may augment pain and other somatic symptoms in response to stress[5,6]. All in all, there are multiple overlapping and complementary theoretical arguments to expect that COVID-19 stress may worsen mental and physical health in people with fibromyalgia.

However, this expectation that the COVID-19 pandemic might lead to lower health in people with fibromyalgia, is not consistently confirmed by research. In a qualitative study, next to exacerbation of pain and fatigue, patients also reported better quality of life[7]. In longitudinal studies[8,9,10,11] with assessments before and during the pandemic or comparing a sample during the pandemic with a historic pre-pandemic sample[12], self-reported health of patients with fibromyalgia did not differ before, during or after the lockdown[8,10,11] . In one study, worse health during the lockdown[9] was indicated, but in another study, health improved[12]. Also, in our study including people with fibromyalgia among other groups with persistent physical symptoms, somatic symptom severity was suggested to be lower during than before the pandemic[13].

The studies analyzing quantitative data commonly analyzed the first acute phase of the corona pandemic, were conducted in small samples ($31<N<80$), and reported mainly composite health scores comprising mental health, physical functioning, and symptom severity without distinguishing between these dimensions. Novel aspects of our study are that (1) it was conducted in large samples, (2) included both the acute and a later phase of the pandemic, (3) evaluated distinct dimensions of health instead of only one composite measure, and (4) evaluated health as compared to a general population norm reference group. We collected data in three separate samples of people with fibromyalgia before (2018) and at two times during the pandemic: during the first major peak (2020; acute phase) and one year later when the contamination rate and restrictive measures were again high in the Netherlands (2021; prolonged phase). The aim of the current study was to determine levels at eight dimensions of mental and physical health in people with fibromyalgia before the pandemic and during two pandemic periods. Based on theoretical grounds, worse scores during the pandemic were expected, but observations of composite scores in previous studies appear to refute this expectation. Our study might give an indication

about the specific dimensions of fibromyalgia health that do and do not change during the pandemic.

MATERIALS AND METHODS

Participants

This repeated cross-sectional design included three separate online surveys in the general Dutch population. The first data collection was from November 2018 to May 2019 (year 2018, pre-pandemic). The second and third collections were from March to May during the acute (year 2020) and prolonged (year 2021) phases of the COVID-19 pandemic; these were peak periods in terms of number of (intensive care) hospitalizations and deaths due to COVID-19, and in terms of strict regulations to prevent further spread of COVID-19. In the questionnaire, respondents indicated their chronic health condition(s), including fibromyalgia. For this study, only data of women with fibromyalgia were analyzed, because the number of men was too low for reliable analyses.

Procedure

Participants were acquired via e-mail and social media, e.g., Facebook, Instagram, LinkedIn, local internet sites, and sites of associations including patient associations for fibromyalgia. The hyperlink to the online survey on individual and group sites was shared by other individuals and groups. Participants filled out the online survey at a secure university website. They self-reported their medical conditions and diseases. Participants gave informed consent prior to inclusion in the study. An inclusion criterion for the study was adult age (≥18 yrs.). An inclusion criterion for the current analysis was a self-reported diagnosis of fibromyalgia. There were no other inclusion criteria. Data collection was anonymous; it is theoretically possible that some persons participated in more than one of the surveys. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The online questionnaire studies in 2018 (FETC17-120, December 5, 2017) and 2020 (FETC20-190, March 23, 2020) were approved by the Ethics Committee at Utrecht University and the study in 2021 (2021-02-16-Henriet van Middendorp-V2-2959, February 16, 2021) by the Psychology Research Ethics Committee at Leiden University, the Netherlands.

Materials

To assess mental and physical health, we used the Dutch version[14] of the RAND 36-Item Short Form Health Survey (RAND SF-36), which measures eight dimensions of health: physical functioning, social functioning, role limitations due to physical problems (role physical), role limitations due to emotional problems (role emotional), mental health, fatigue, pain and general health perception. High scores define more favorable health. The internal consistency reliability of these dimensions was good: Cronbach's alphas ranged from .79 for social functioning to .94 for the physical functioning dimension.

Statistical analyses

To get an indication of the health of women with fibromyalgia as compared to normal, we calculated for each dimension the standardized mean deviation from the norm score[14]. Levels on the eight health dimensions before (2018) and during the two peak phases (2020, 2021) of the COVID-19 pandemic were compared in analyses of covariance. Age, education level and having a comorbid disease, were correlated with (at least one of) the eight scales and included as covariate in analyses. Post hoc estimated marginal means were compared between the three years using Bonferroni correction.

Although score distributions hardly deviated from normal [15], with no skewness values exceeding |1| and only the kurtosis of role emotional (-1.7) exceeding |1|, we performed bootstrap analyses to verify the validity of the results.

RESULTS

Table 1 shows the characteristics of women with fibromyalgia in the pre-pandemic (2018) and pandemic (2020 and 2021) samples. Age differed between the three years: $F(2,538)$ = 3.36, p = .035; these differences were marginally or not significant in post hoc tests: 2018 vs. 2020, p = .10; 2018 vs. 2021, p = .06; 2020 vs. 2021, p = 1.00. Neither education level ($\chi2(2)$ = 4.51, p = .11), nor having a comorbid disease ($\chi2(2)$ = 1.43, p = .49) differed between the three samples.

Table 1

Characteristics of women with fibromyalgia before (2018) and during the first acute (2020) and prolonged (2021) phases of the COVID-19 pandemic in the Netherlands

Year	2018 (*n* = 142)	2020 (*n* = 304)	2021 (*n* = 95)	All (*n* = 541)
Age (years)				
Mean (SD)	46.6 (10.7)	49.0 (11.5)	50.1 (10.9)	48.6 (11.3)
Range	19 – 69	20 - 80	21 - 79	19 - 80
Education level[a], *n* (%)				
Lower	76 (54.3)	190 (62.9)	50 (53.2)	316 (59.0)
Higher	64 (45.7)	112 (37.1)	44 (46.8)	220 (41.0)
Comorbid disease, *n* (%)				
None	36 (25.4)	79 (26.0)	19 (20.0)	134 (24.8)
One or more[b]	106 (74.6)	225 (74.0)	76 (80.0)	407 (75.2)

[a]lower: lower general secondary education (48.2%) or lower (10.8%); higher: higher general secondary education (7.4%) or higher (33.6%).

[b]having a comorbid disease other than (overlapping) chronic fatigue syndrome, irritable bowel syndrome, somatoform disorder/somatic symptom disorder, chronic headache (not migraine), or chronic pain elsewhere in the body (not the head)

Physical and mental health scores before and during the pandemic are shown in Table 2. Both before and during the pandemic, women with fibromyalgia had medium to large mean deviation scores from the norm on role emotional functioning and mental health and, with only one exception (physical functioning in 2021), and very large deviation scores on all other health dimensions, all scores indicated worse health than norm reference values.

Comparison of scores before and during the pandemic, showed less favorable scores pre-pandemic (2018) on pain (95% confidence interval *[CI]* of the standardized regression coefficient [-.567, -.188], p <.001) and role physical (*95% CI* [-.748, -.234], p <.001) compared to the acute pandemic phase (2020), and on pain (*95% CI* [-.541, -.047], p = .01) and physical functioning (*95% CI* [-.640, -.033], p =

.02) compared to the prolonged pandemic phase (2021). Effect sizes for these differences between years were small (in between .014 and .042). No differences between the three samples were shown for the other five health dimensions.

In bootstrap analyses, differences were more pronounced and other aspects of health also showed differences between samples. The sample from 2018 reported lower physical functioning (95% confidence interval *[CI]* of the standardized regression coefficient [-.360, -.001], p = .048) and role physical (*95% CI* [-.682, -.303], p = .001) and higher fatigue (*95% CI* [.021, .369], p = .04) and pain (*95% CI* [.230, .524], p = .001) compared to the sample from 2020 and, apart from fatigue, also compared to the 2021 sample (*95% CI* [-.576, -.104], p = .009; *95% CI* [-.583, -.054], p = .02; *95% CI* [.107, .485], p = .001, respectively). In contrast, mental wellbeing was higher in 2018 compared to 2020 (95% CI [.021, .431], p = .03).

Table 2

Estimated marginal means (standard error) of mental and physical health in women with fibromyalgia before (2018) and during the acute (2020) and prolonged phases (2021) of the COVID-19 pandemic in the Netherlands

	2018 (*n*=140)	2020 (*n*=302)	2021 (*n*=99)	Comparison of Years			Post hoc pairwise comparisons
Variable	***M(SE)***	***M(SE)***	***M(SE)***	***F***	***p***	**pη²**	
Physical functioning	-1.38(.08)	-1.20(.05)	-1.05(.10)	3.70	.03	.014	2018<2021
Social functioning	-1.90(.11)	-1.80(.07)	-1.78(.13)	0.34	.71	.001	
Role physical	-1.74(.09)	-1.25(.06)	-1.42(.11)	10.52	<.001	.038	2018<2020
Role emotional	-0.79(.12)	-0.78(.08)	-0.75(.14)	.03	.97	.000	
Mental health	-0.71(.09)	-0.94(.06)	-0.89(.11)	2.21	.11	.008	
Fatigue (reverse score)	-1.69(.08)	-1.50(.05)	-1.67(.09)	2.75	.07	.010	
Pain (reverse score)	-1.74(.07)	-1.37(.04)	-1.45(.08)	11.50	<.001	.042	2018<2020,2021
General health	-1.61(.07)	-1.52(.05)	-1.47(.08)	0.94	.39	.004	

Estimated marginal means are standardized deviation scores from the general adult population norm[14]. Lower scores indicate a worse health status.

Effect sizes for estimated marginal means: |0.5|–|0.8| medium, |0.8|–|1.2| large, |1.2|–|2.0| very large[16].

Effect sizes for partial eta-squared (pη²): small = 0.01–0.06.

Variables were compared while controlling for age, education level and having a comorbid disorder.

DISCUSSION

Both before and during the pandemic, the health of women with fibromyalgia was shown to be worse as compared to the Dutch population reference group with very large deviating scores for fatigue, pain, general health, social functioning, and (role) physical functioning, and medium to large deviating scores for role emotional functioning and mental health. Contrary to theoretical expectation, levels at five health variables before and during the pandemic did not differ, and levels of pain, role physical, and physical functioning (small differences) reflected even a healthier status in samples during than before the pandemic.

There were earlier studies indicating that mental and physical health, such as reflected in fibromyalgia severity scores, was not worse[8,10,11] and perhaps even better[12] during than before the pandemic. Only one study observed a lower health during the pandemic[9]. Our study was the first with a larger (>80) sample size and the first study that differentiated between health dimensions instead of using a generic health or disease severity score. Our results clearly indicate that the health of women with fibromyalgia, on average, remains low during the pandemic, with perhaps somewhat better scores for somatic symptoms and physical functioning. The only exception was the mean mental health score that appeared lower during than before the pandemic. However, the effect size was very small and only significant in the bootstrap analysis.

Although during the pandemic the severity of fibromyalgia was also observed to worsen in a considerable part of the participants[7,10,11,12], from a theoretical point of view it is unexpected that, on a group level, there was no mean change or even a positive change. This suggests that the negative impact of the COVID-19 pandemic on people with fibromyalgia is weaker than assumed. In a previous publication, we considered that some people with persistent somatic symptoms may have experienced a positive impact, for instance, because they felt less pressure from work, more social connectedness, or more recognition for their symptoms and situation during the pandemic[13]. In one study, people with fibromyalgia during the pandemic thought that their improvement was caused by beneficial effects of smart working and the opportunity to exercise more regularly[10]. In another study, some interviewed people with fibromyalgia reported that reduced social constraints allowed them to adjust the rhythms of their life to fluctuations of symptoms and that fibromyalgia stopped being a main priority in their lives[7]. These authors concluded that reducing social constraints could be a key for fibromyalgia management, where symptoms seemed to take less space in everyday life.

A strength of the current study is its time frame. People participated during the first two peak months of the virus outbreak in 2020, when COVID-19 had the most invasive consequences and during the prolonged lockdown in 2021 when many people became inpatient. Our samples did not include an equal number of participants in each year, but in every year the sample size was large enough to have small margins of error. Our study included self-reported data from people with fibromyalgia in the general population. A limitation is that we did not collect clinical data, such as current interventions (pharmacological, physical exercise,

psychological) and whether treatment, such as regular physical exercise was promoted or hindered during the pandemic, which likely both may occur[10]. The results of our study do not generalize beyond the report of self-perceived health. A limitation is that our samples were convenience rather than representative. Moreover, some persons may have participated in more than one of the surveys. Because data collection was anonymous, we do not know how many. Obtaining repeated data from the same people at similar periods in the year would have yielded insight into how many people deteriorated and ameliorated. However, our results are not inconsistent with most studies measuring intra-individual changes in smaller samples of people with fibromyalgia[10,11,12]. We did not have perfect norm data, because the norm group is from 25 years ago and included 35% men, which may have yielded somewhat lower scores in our sample of women with fibromyalgia. Another limitation is that fibromyalgia was not confirmed by clinical assessment. Finally, considering that during the pandemic similar findings were found in European studies[10,11,12] and that our results deviated from deterioration observed in Mexican people with fibromyalgia[9], suggests that our data are at best generalizable to women with fibromyalgia in Western European countries.

CONCLUSIONS

Women with fibromyalgia have, on average, a low level of mental and physical health irrespective of the COVID-19 pandemic. Our findings tentatively indicate that mean health levels do not further deteriorate during the pandemic and that somatic symptoms and physical functioning may even be better. This suggests that the pandemic may include changed circumstances that are favorable for at least part of the women with fibromyalgia.

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Chapter 5

Mental and physical health during the COVID-19 pandemic in young adults with and without a chronic illness

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ABSTRACT

Objectives: We sought to better understand mental and physical health among young (18-32 years old) adults with and without a chronic illness during the COVID-19 pandemic, and to establish whether psychological flexibility preserved better health.
Methods: In a repeated cross-sectional design, questionnaire data were collected in three samples: pre-pandemic (2018, *n*=155) and during the acute (2020, *n*=270) and prolonged (2021, *n*=588) phases of the COVID-19 pandemic in the Netherlands.
Results: Especially during the prolonged phase of the pandemic young adults' mental and physical health was low, with one exception: in young adults with a chronic illness and low psychological flexibility, physical health was indicated to be better during the prolonged phase than other phases.
Conclusions: Thus, although being psychological flexible may be, in general, beneficial for young adults' health, this appears not the case specifically during the pandemic or among those with a chronic illness and low levels of psychological flexibility. Future research should clarify this unexpected finding and, for instance, whether creating less demanding and calmer circumstances may enhance physical health in young adults with a chronic illness and low psychological flexibility.

Acknowledgment of author contributions
TYK and RG developed the design of the study and analysed the data, which was collected by TYK, HvM and RG. TYK drafted the paper and JWGJ, MAL, HvM and RG critically assessed, edited and revised the paper.

INTRODUCTION

Many studies of young adults have reported elevated levels of anxiety, depression, and mental distress during the COVID-19 pandemic compared to pre-pandemic or norm group levels (Cielo et al., 2021; Hawes, 2021; Kwong et al., 2021; Varma et al., 2021; Watkins-Martin et al., 2021). The results are mixed, however, as other studies reported only more depression (Lee et al., 2020) or more anxiety (Kwong et al., 2021), or showed that mental health symptoms remained relatively stable (Robinson et al., 2022; Shanahan et al., 2022). These studies typically analyzed mental health only during the initial, acute phase of the pandemic, whereas a few longitudinal studies suggest more concern about the effects of the prolonged pandemic on youth and young adults' mental health (Chadi et al., 2022; Lee et al., 2020; Shanahan et al., 2022).

There is less research on the consequences of the pandemic for young adults' physical health. Some young adults became more physically active, while others became less so, especially with the progression of the pandemic (Huber et al., 2020; Schwartz et al., 2021;), but it is unclear whether the physical health of young adults was poorer during than before the pandemic. Clinicians and researchers anticipated that health would be especially threatened during the pandemic for people with a chronic illness, due to delayed medical evaluations, reduced access to health services, and disrupted treatment (Ligus et al., 2021; Neelam et al., 2021; Shanthanna et al., 2020), but pandemic-related studies in young adults have generally not distinguished between those with or without a chronic illness.

Longitudinal research and a systematic review of cross-sectional studies in adults generally found poorer mental health during the pandemic in people with pre-existing illnesses (Andersen et al., 2021; Xiong et al., 2020). Two "rapid reviews" reported worsening of mental health symptoms for youth with pre-existing conditions (Hards et al., 2021; Zolopa et al., 2022); however, results for physical health might differ from those for mental health. During the pandemic, physical health decreased in adults with osteoarthritis (Endstrasser, 2020) or a psychiatric disorder (Hao et al., 2020), but remained stable for young adults with chronic pain (Tham et al., 2022) and adults with cancer (Baffert et al., 2021) or fibromyalgia (Schweiger et al., 2022; Cavalli et al., 2021; Rivera et al., 2021); physical health may even have improved in adults with fibromyalgia (Iannuccelli et al., 2021; Koppert et al., 2022). Thus, it remains unclear what might be expected for young adults with a chronic illness; even though one might anticipate worsening of physical health during the pandemic, observations in both younger and older adults do not consistently support this hypothesis. A study of young adults with and without a chronic illness before and during the pandemic is needed to clarify changes in their physical health during the pandemic.

Being psychological flexible may protect individuals against negative consequences of the COVID-19 pandemic and a chronic illness. Psychological flexibility refers to the tendency to approach difficult or challenging internal states in a non-judgmental, mindful way, and being committed to pursue one's values (Hayes

et al., 2006; Kashdan & Rottenberg, 2010). Both better mental and physical health are associated with greater psychological flexibility in general (Hayes et al., 2006, 2012) and during the pandemic specifically (Arslan & Allen 2021; Barzilay et al., 2020; Conversano et al., 2020; Dawson & Golijani-Moghaddam, 2020; Koppert et al., 2021; Kroska et al., 2020; Landi et al., 2022; McCracken et al., 2022; Pakenham et al., 2020). As yet, to our knowledge, no study has examined whether psychological flexibility can protect against the impact of the pandemic on both mental and physical health of young adults, let alone for those people with a chronic illness. Psychological flexibility might be a particularly useful ability to protect health under bad circumstances; that is, during (vs. before) the pandemic and in young adults with (vs. without) chronic illness.

The aim of this study was to better understand mental and physical health of young adults with and without a chronic illness during the acute and prolonged phases of the COVID-19 pandemic. To achieve that aim, cross-sectional health data collected during the acute (2020) and prolonged (2021) phases of the pandemic were compared to data collected before the pandemic (2018). Mental health, especially during the prolonged phase, was expected to be poorer during than before the pandemic, regardless of whether or not one has a chronic illness. We anticipated that physical health would not significantly differ among the three phases for young adults without a chronic illness, but because the literature does not give a clear indication about the physical health during the pandemic in people with a chronic illness, we explored physical health specifically in this group. We also tested the hypothesis that psychological flexibility would protect both mental and physical health, particularly during the pandemic and for young adults with a chronic illness.

MATERIALS AND METHODS

Participants

The repeated cross-sectional design included three independent, anonymous data collections through online questionnaires. Participants for each of the three separate samples were recruited in the Dutch general population via e-mail and social media (e.g., Facebook, Instagram, LinkedIn), local internet sites, and sites of patient associations. The only selection criterion for the current analyses was an age of 18-32 yrs., which is similar to the Dutch reference group of health assessment in young adults (VanderZee, 1996); there were no exclusion criteria. A flow chart comprising the participants is found in Figure S1 of the supplementary file.

Procedure

Data were collected at three phases, in different samples: The first collection was from November 2018 to May 2019 (sample "2018"), which we labeled *pre-pandemic phase*. The second was from March to May 2020, during the *acute phase* (sample "2020") of the pandemic. The third was from March to May 2021, during the *prolonged phase* of the COVID-19 pandemic (sample "2021"). Data in both pandemic samples were collected during peak periods in the Netherlands with respect to the

number of hospitalizations and deaths due to COVID-19, and the implementation of strict regulations to prevent further spread of COVID-19. A hyperlink in an e-mail and social media sites brought participants to the online survey. This hyperlink was shared by other individuals and groups. Participants filled out the online survey at a secure university website.

The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The three online questionnaire studies were approved by the Ethics Committee at Utrecht University, and by the Psychology Research Ethics Committee at Leiden University, the Netherlands. Participants gave informed consent prior to inclusion in the online survey by clicking a "Yes" button after having read the consent information.

Measures

Participant Characteristics

Participants reported their age, gender, and education level. They could indicate male, female, or 'other' for gender. With education level, they could report one of seven levels, ranging from lower education to university. Participants further indicated whether they had one or more of 21 listed chronic illnesses (e.g., cardiovascular, cancer, osteoarthritis, psychiatric), or whether they had a chronic illness that was not specified in this predetermined list. Based on their answer they were assigned to a "group" with or without a chronic illness.

Health

Mental and physical health were assessed with the Dutch version of the RAND 36-Item Short Form Health Survey (RAND SF-36; Vanderzee, 1996). The SF-36 measures eight domains of health, four of which reflect mental health: Emotional wellbeing, role limitations due to emotional problems (Role emotional), Social functioning, and Fatigue; and four reflect physical health: Physical functioning, role limitations due to physical problems (Role physical), Pain, and General health. The scoring method of Hays was used to derive *mental health composite* and *physical health composite* scores (Hays, 1998). These are normalized scores with an average of 50 and a standard deviation of 10 in the general population. The mental health composite ranges from 11 to 60 and the physical health composite from 15 to 61; a higher score reflects more favorable health. The internal reliability was consistently good across the three samples; Cronbach's alphas for the eight domains ranged from .75 for social functioning to .93 for physical functioning, from .82 to .89 for the mental health composite, and .79 to .90 for the physical health composite.

Psychological Flexibility

The Flexibility Index Test-60 (FIT-60) was used to measure psychological flexibility (Batink et al., 2012). This 60-item questionnaire was developed from a literature review of psychological flexibility and four existing questionnaires and assesses six processes of psychological flexibility (10 items each): acceptance, cognitive defusion, contact with the present moment, self as context, values, and committed action

(Hayes, 2006). Participants rate the extent to which each item applies to them, from 0 ('totally disagree') to 6 ('totally agree'). The total score ranges theoretically from 0 to 360, and higher scores indicate more flexibility. The initial psychometric analyses of the FIT-60 found high internal consistency (Cronbach's alpha = .95; Batink et al., 2012). Cronbach's alphas in the current three samples were: .88 (2018), .90 (2020), and .89 (2021).

Data Analysis

Main Analyses

Analyses of covariance, with Bonferroni-corrected post-hoc tests, were used to test for significance differences in mental and physical health between participants with and without a chronic illness (*Group* effect), differences between samples acquired before (2018) and during the two peak phases (2020, 2021) of the COVID-19 pandemic (*Phase* effect), and the interaction of these variables (*Group* × *Phase* interaction). Effect sizes for differences between groups (presence or absence of a chronic illness) and phases (three samples) were expressed using partial eta squared (η_p^2), where values of 0.01, 0.06 and 0.14 represent small, medium, and large effects, respectively (Tabachnick & Fidell, 2013).

To examine the moderator role of psychological flexibility, linear regression analyses were performed with mental health composite and physical health composite scores as dependent variables, and group, phase (prolonged vs. pre-pandemic), and psychological flexibility as independent variables. The two-way interactions (Phase × Psychological flexibility and Group × Psychological flexibility) were included to determine whether higher levels of psychological flexibility might preserve good health, especially when having to deal with a chronic illness or during health challenges, such as the pandemic. To interpret significant interactions, regression lines for individuals with low (−1 SD) and high (+1 SD) scores on the two interacting variables were plotted (Aiken & West, 1991); the magnitude of differences was indicated with Cohen's d effect sizes, with values of 0.20, 0.50 and 0.80 representing small, medium, and large effects, respectively (Cohen, 1992).

In analyses, to restrict the number of covariates, we transformed gender into a dichotomous variable: "men" vs. "women and others" as well as education level: "at or below lower general secondary education" and "at or above higher general secondary education". In all analyses, variables that were significantly associated with the mental or physical health composite in at least one group or during one phase were added as covariates: gender, age, and education level. For all analyses, 2-tailed *p*-values <.05 were considered statistically significant. Statistical analyses were done using IBM SPSS statistics version 25.

Ancillary Analyses

We performed ancillary analyses to gain insight into which of the eight domains of mental and physical health contributed to the effects and to learn whether findings were due to the group with or without a chronic illness.

RESULTS

Participant Characteristics

Table 1 shows the participant characteristics. A total of 1,013 young adults participated; 419 with and 594 without a chronic illness. The mean age of all participants was 24.4 yrs.; participants in the group with a chronic illness were older than those in the group without: $\chi^2 = 24.79$, $p = .037$. Age also significantly differed among the three samples ($\chi^2 = 254.03$, $p < .001$), with older participants in the acute phase compared to the pre-pandemic and prolonged phase of the pandemic (all p-values< .001). The minority of the participants was men (24.8%), with a lower percentage of men in the group with a chronic illness compared to the group without ($\chi^2 = 38.19$, $p < .001$). The majority of participants had a higher education level (85.1%), and participants without a chronic illness more often had a higher education level than those with a chronic illness ($\chi^2 = 28.96$, $p < .001$). Gender and education level did not significantly differ among the three samples.

Table 1

Characteristics of the samples from before and during the COVID-19 pandemic in the Netherlands

Phase	**Pre-pandemic (2018)** ***n*** **= 155**		**Acute (2020)** ***n*** **= 270**		**Prolonged (2021)** ***n*** **= 588**		
	Chronic Illness		**Chronic Illness**		**Chronic Illness**		
Group	Yes	No	Yes	No	Yes	No	All
	n = 73	*n* = 82	*n* = 127	*n* = 143	*n* = 219	*n* = 369	*N* = 1,013
Age (years, range: 18 – 32)							
Mean (SD)	25.3 (3.8)	25.3 (3.4)	27.0 (3.4)	27.1 (3.3)	23.7 (4.1)	22.4 (3.3)	24.4 (4.0)
Gender[a], *n* (%)							
Men	9 (12.3)	31 (37.8)	10 (7.9)	48 (33.6)	43 (19.6)	110 (29.8)	251 (24.8)
Education level[b], *n* (%)							
Lower	21 (28.8)	10 (12.1)	30 (23.6)	11 (7.7)	41 (18.9)	37 (10.1)	150 (14.9)
Higher	52 (71.2)	72 (87.8)	97 (76.4)	132 (92.3)	176 (81.1)	329 (89.9)	857 (85.1)
Missing	0	0	0	0	2 (0.9)	3 (0.8)	5(0.5)
Type of illness[c], *n* (%)							
Psychiatric	20 (27.4)	-	45 (35.4)	-	106 (48.4)	-	171 (16.9)
Inflammatory arthritis	5 (6.8)	-	16 (12.6)	-	11 (5)	-	32 (3.2)
CSS[d]	31 (43.7)	-	59 (46.5)	-	63 (28.8)	-	153 (15.1)
Pulmonary	9 (12.3)	-	26 (20.5)	-	34 (15.5)	-	69 (6.8)
Skin	4 (5.5)	-	6 (4.7)	-	14 (6.4)	-	24 (2.4)
Neurological	15 (20.5)	-	21 (16.5)	-	50 (22.8)	-	86 (8.5)
Other illnesses[e]	37 (50.7)	-	63 (49.6)	-	116 (53.0)	-	216 (21.3)

[a]Gender: categorized as men vs. not-men (viz., 756 women and 6 participants answering 'other' than male or female).

[b]Education level: low: lower general secondary education or lower; high: higher general secondary education or higher.

[c]Percentage within the group of people with a chronic illness.

[d]Central Sensitivity Syndrome: Overarching classification for people with fibromyalgia (5.1%), chronic fatigue syndrome (CFS, 2.1%), irritable bowel syndrome (IBS, 8.2%).

[e]One or more other non-listed illness(es), with frequency in the sample <1%.

Mental Health

Analyses of covariance examined mental health for Groups and Phases on mental health (Figure 1, left panel). As expected, there was a Group effect: the mental health composite was significantly lower in participants with than without a chronic illness: $F(1,8) = 108.91$, $p < .001$, $\eta_p^2 = .098$. There was also a significant Phase effect ($F(2,8) = 20.87$, $p < .001$, $\eta_p^2 = .04$), with worse mental health in the prolonged phase, compared to both the acute and pre-pandemic phase (both $p < .001$). The Group × Phase interaction for mental health was significant: $F(2,8) = 4.47$, $p = .010$, $\eta_p^2 = .009$. This interaction especially reflects poor mental health during the prolonged phase for participants without a chronic illness.

In ancillary analyses, it was examined which of the four mental health variables accounted for the Group × Phase interaction. Both social functioning and fatigue showed lower scores in the participants without a chronic illness during the prolonged phase, but emotional wellbeing and role emotional did not (Supplementary table S1 and figure S2).

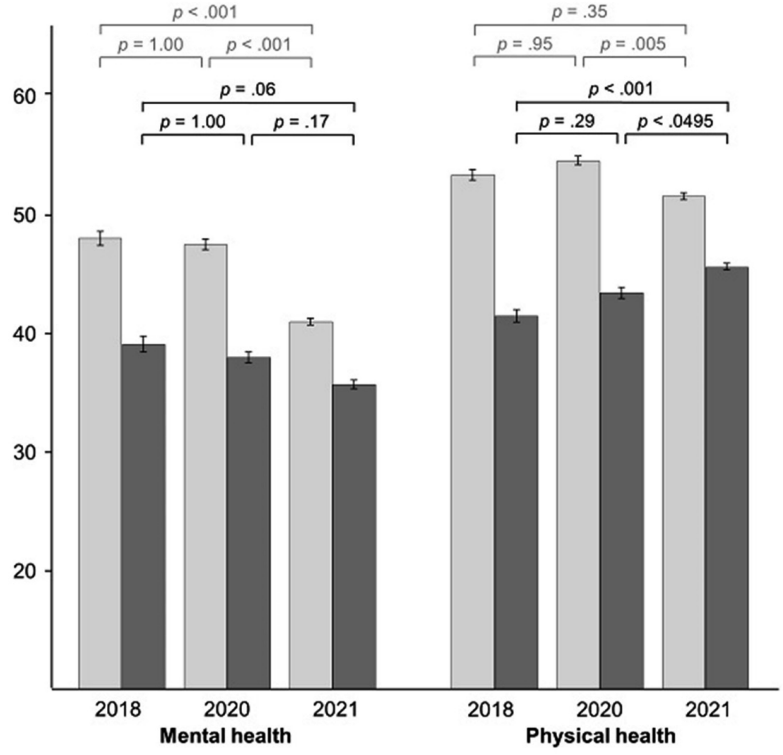
Physical Health

For the physical health composite (Figure 1, right panel), the Group effect was significant, with worse scores for those with a chronic illness compared to those without: ($F(1,8) = 229.58$, $p < .001$, $\eta_p^2 = .187$). A significant effect of Phase was not found ($p = .14$). Again, the Group × Phase interaction was significant: $F(2,8) = 12.28$, $p < .001$, $\eta_p^2 = .024$. This interaction reflects that in the group with a chronic illness, the best physical health was observed during the prolonged phase of the pandemic. In contrast, in the group without a chronic illness, the worst physical health was observed during the prolonged phase.

Ancillary analyses showed that the Group × Phase interactions for all four variables of physical health were significant: in people with a chronic illness, *healthier* physical functioning, role physical, and pain scores were observed in the prolonged phase. In contrast, in people without a chronic illness, *worse* physical functioning and general health were observed in the prolonged phase (Supplementary table S1 and figure S3).

Figure 1

Mental health composite and physical health composite scores for groups without (light gray bars) and with a chronic illness (dark gray bars) during the pre-pandemic (2018), acute (2020) and prolonged (2021) phases (n = 1,008)



The Role of Psychological Flexibility

The possible role of psychological flexibility for mental and physical health was examined for the prolonged phase of the pandemic (2021) as compared to the pre-pandemic phase (2018), because a difference in health between these two phases was shown in the prior analyses of covariance. Results of the regression analyses are shown in Table 2.

Mental Health

The linear regression model (Table 2) showed 54.5% shared variance between the set of predictor variables and the mental health composite. Psychological flexibility (β = .803), Group (β = -.119), and Phase (β = -.105) were significant (all *p*-values < .001): worse mental health was observed with lower psychological flexibility, having a chronic illness, and during the prolonged phase. None of the covariates was associated with the mental health composite (*p*-values > .11). The Phase × Psychological flexibility interaction was significant (β = -.145, *p* = .02); see Figure 2. This interaction indicates that mental health was lower in the prolonged than pre-pandemic phase among participants with high psychological flexibility (*d* = 0.46), whereas mental health in the two phases was about similar in participants with low psychological flexibility (*d* = 0.10).

Table 2

Results of the linear regression analysis examining the association of the Mental Health Composite (SF-36) with demographic variables, Group, Phase, Psychological flexibility (FIT-60), and two-way interactions including psychological flexibility (n=738)

	B	**(*SE*)**	**β**	***t***	***p***
Constant	42.848	(2.134)		20.079	<.0001
Demographics					
Gender[a]	-.517	(.635)	-.021	-.814	.42
Age	.074	(.077)	.025	.959	.34
Education level[b]	-1.252	(.790)	-.040	-1.586	.11
Group[c]	-2.667	(.599)	-.119	-4.467	<.0001
Phase[d]	-2.821	(.712)	-.105	-3.964	<.0001
Psychological flexibility	.189	(.016)	.803	11.773	<.0001
Phase × Psychological flexibility	-.038	(.016)	-.145	-2.347	.019
Group × Psychological flexibility	.004	(.012)	.012	.340	.73

[a]Gender: 0 = men, 1 = women and other. [b]Education level: 0 = lower general secondary education or lower; 1 = higher general secondary education or higher. [c]Group: 0 = without a chronic illness; 1 = with a chronic illness. [d]Phase: 0 = pre-pandemic, 2018, 1 = prolonged, 2021. *B*, unstandardized regression coefficient, *SE*, Standard Error; β, standardized regression coefficient.

Physical Health

The set of predictor variables accounted for 29.9% of the variance in physical health (Table 3). In addition to lower psychological flexibility (β = .481, $p < .001$) and having a chronic illness (β = -.297, $p < .001$), the pre-pandemic phase (β = .090, $p = .006$) was, unexpectedly, associated with lower physical health; as were higher age (β = -.131, $p < .001$), lower education level (β = .084, $p = .009$), and female gender (β = -.081, $p = .011$). The Phase × Psychological flexibility interaction was significant (β = -.235, $p = .002$); see Figure 2. In contrast to expectation, participants with low psychological flexibility were doing physically better in the prolonged phase as compared to those in the pre-pandemic phase ($d = 0.45$), whereas physical health in those with high psychological flexibility in these two phases was about similar ($d = 0.04$).

Table 3

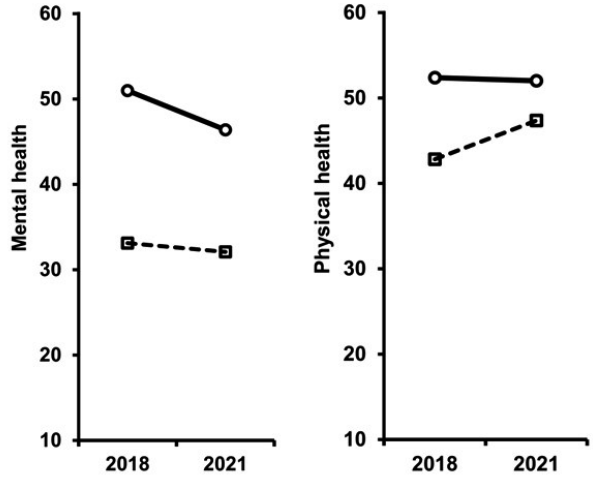
Results of the linear regression analysis examining the association of the Physical Health Composite (SF-36) with demographic variables, Group, Phase, Psychological flexibility (FIT-60), and two-way interactions including psychological flexibility (N=738)

	B	***(SE)***	**β**	***t***	***p***
Constant	56.838	(2.243)		25.341	<.0001
Demographics					
Gender[a]	-1.706	(.668)	-.081	-2.555	.011
Age	-.324	(.081)	-131	-4.028	<.0001
Education level[b]	2.188	(.830)	.084	2.636	.009
Group[c]	-5.662	(.630)	-.297	-8.991	<.0001
Phase[d]	2.061	(.748)	.090	2.755	.006
Psychological flexibility	.096	(.017)	.481	15.684	<.0001
Phase × Psychological flexibility	-.051	(.017)	-.235	-3.057	.002
Group × Psychological flexibility	.014	(.013)	.047	1.093	.28

[a]Gender: 0 = men, 1 = women and other. [b]Education level: 0 = lower general secondary education or lower; 1 = higher general secondary education or higher. [c]Group: 0 = without a chronic illness; 1 = with a chronic illness. [d]Phase: 0 = pre-pandemic, 2018, 1 = prolonged, 2021. *B*, unstandardized regression coefficient, *SE*, Standard Error; β, standardized regression coefficient.

Figure 2

Regression scores on mental and physical health composite scores as a function of low (-1 SD, dashed line) and high (+1 SD, solid line) psychological flexibility, in the samples comprising participants at the pre-pandemic (2018) versus prolonged (2021) phases, while controlling for gender, age, education level and the presence of a chronic illness (n = 738)

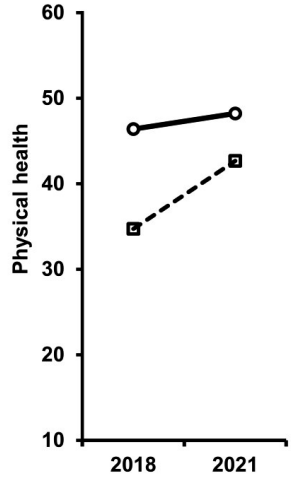


Ancillary Analyses

Regression analyses were also run separately within the groups with and without a chronic illness to examine whether the results applied to one of these groups. In both groups no significant Phase × Psychological flexibility interaction was found for the mental health composite ($p > .15$). However, the Phase × Psychological flexibility interaction was significant for the physical health composite in the group with ($\beta = -.260$, $p = .03$), but not in the group without a chronic illness ($p = .49$). The interaction is shown in Figure 3: participants with a chronic illness and *low* levels of psychological flexibility were doing better during the prolonged phase of the pandemic, in presumed worse times, as compared to before the pandemic ($d = 0.80$), while physical health in those with an illness and high psychological flexibility was about similar during the two phases ($d = 0.18$).

Figure 3

Regression scores on the physical health composite as a function of low (-1 SD, dashed line) and high (+1 SD, solid line) psychological flexibility, in the sample comprising solely participants with a chronic illness during the pre-pandemic (2018) versus prolonged (2021) phases, while controlling for gender, age, and education level (n = 290)



DISCUSSION

For young adults, either with or without a chronic illness, mental health was poorer during the prolonged phase of the pandemic, compared to the pre-pandemic phase. Compared to the acute phase, also physical health was worse during the prolonged phase for those *without* a chronic illness. However, unexpectedly physical health for those *with* a chronic illness was better during the prolonged than pre-pandemic and acute phases. High levels of psychological flexibility were found to be associated with better health, but not particularly during the pandemic or among participants with a chronic illness. Contrary to our expectation, those *with* a chronic illness and *low* levels of psychological flexibility reported *better* physical health during the prolonged phase of the pandemic, as compared to the pre-pandemic phase.

In confirmation of earlier concerns about more detrimental effects on mental health with a longer duration of the pandemic (Watkins-Martin et al., 2021), our study observed poorer mental health, particularly on the two domains reflecting emotional well-being, during the prolonged phase of the pandemic. Similar to previous studies in children and young adults (Kauhanen et al., 2022) and adults

(Prati & Mancini, 2021), this effect was small in magnitude. Variable results across studies suggest that the pandemic did not have a uniformly detrimental effect on mental health, and that many people were able to deal with the adversities. Of note, there has been progressive increase in psychological distress from the middle of the last century (Twenge, 2000) to recent years (Twenge et al., 2019). Still, in our ancillary analyses, we used norm scores from 1996 as reference values and observed a larger decline in mental health from 2018 to 2021 than from 1996 to 2018. This indicates that the pandemic caused an additional decline of mental health over and above the historical decline. The observed progressive decline of mental health may imply that enhancement of mental health in young adults should be a priority in research and health policy, and the indicated larger decline during the pandemic suggests that this is especially important during a public health crisis.

With respect to physical health, different results were observed for participants with versus those without a chronic illness. Those without an illness had poorer health in the prolonged phase, compared to those in the acute phase. During this first acute phase of the pandemic, physical health may have improved in some people, because of enhanced physical activity (Füzéki et al., 2020; Maugeri et al., 2020), sleep quality (Socarras et al., 2021) and work flexibility (Dassieu et al., 2021; Margolies et al., 2021). But, perhaps in the prolonged phase, reduced motivation to exercise in combination with the ongoing closure of fitness centers and sports facilities caused a reduction of physical health. The results might indicate that, in addition to mental health, preservation of physical health should get attention in healthy young adults during a pandemic.

Contrary to the pattern found in the healthy group, but in line with some findings in the general adult population (Iannuccelli et al., 2021; Koppert et al., 2022), physical health of the participants with a chronic illness was better in the prolonged phase than pre-pandemic. This result seems surprising; one might expect that people's physical health would worsen due to reduced or delayed health care (Ligus et al., 2021; Neelam et al., 2021; Shanthanna et al., 2020) and increased stress. However, young adults with chronic illnesses during the pandemic might have benefited from their past development of skills in managing adversities. Still, this does not explain why participants in the prolonged phase had a better physical health than those before the pandemic.

Consistent with our results, studies during the pandemic have shown that psychological flexibility and related constructs such as resilience are positively associated with mental (Barzilay et al., 2020; Conversano et al., 2020; Kroska et al., 2020) and physical health (McCracken et al., 2022; Ran et al., 2020), which may suggest a health-protective role of psychological flexibility and related skills. However, other interpretations are possible. The association between psychological flexibility and mental health may reflect construct overlap, an impact of mental health on psychological flexibility, as well as influences of third factors such as a trait-like affectivity dimension (e.g., neuroticism) or a response tendency (e.g., acquiescence or social desirability) on both psychological flexibility and mental health. A protecting role would have been clearer if psychological flexibility was

shown to be particularly useful in terms of protecting health under bad circumstances, such as the pandemic or when having a chronic illness. However, our interaction analyses did not show this. On the contrary, it was observed that participants with a chronic illness and *low* levels of psychological flexibility reported better physical health during the pandemic; that is, in presumed worse times.

Perhaps our results reflect that the 'lockdown society', on average, better, fits young adults with a chronic illness and low psychological flexibility than common modern (pre-pandemic) society. They may have experienced the pandemic as less demanding. Because of remote working and less traveling (Cavalli et al., 2021), the impact of their illness on their work decreased. In addition, they may have felt more recognition for their symptoms and situation. The less demanding and calmer life (Cornell et al., 2021) in the prolonged phase of the pandemic may have allowed people with a chronic illness and low flexibility to better adjust the rhythms of their life to fluctuations of their symptoms (Colas et al., 2021). For people with a chronic illness and high psychological flexibility, physical health in the pre-pandemic and prolonged phases was about similar. Some of the high flexible people may be able to adapt, accept and stay mindful during pre-pandemic life with its daily challenges and social obligations despite having a chronic illness. Psychological flexibility can be promoted through mindfulness and acceptance-based therapy, such as Acceptance and Commitment Therapy (ACT; Hayes et al., 2006/2012), which has been proven to be effective in treating mental and physical health problems (e.g., A-Tjak et al., 2015; Veehof et al., 2011; Graham et al., 2016). The results of our study might indicate that it is useful to examine in future research in common modern society, whether management focused on creating less demanding and calmer circumstances would be an effective way of enhancing physical health of people with a chronic illness and low psychological flexibility.

A strength of the current study is its time frame including data collected before (2018) and during the acute (2020) and prolonged (2021) phases of the pandemic in a population including both people with and without a chronic illness. Although our three samples did not have similar numbers of participants, the samples at each phase were large enough to have small margins of error. A primary limitation is that the data were obtained from different samples across the three pandemic phases, and the samples were convenience rather than representative of the young adult population. Obtaining repeated data from the same people over time would have yielded better insight into the number of people with deteriorated or ameliorated health. Also, the data were collected through self-report questionnaires, which can reflect trait-like aspects and do not reflect processes that are intended by the psychological flexibility construct. Finally, the results of our study do not generalize beyond the report of self-perceived health and the selected populations in the Netherlands.

Several studies and the media have reported a substantial negative impact of the pandemic on young adults. We indeed observed poorer health during the prolonged phase compared to pre-pandemic and acute phases. However, among those with a chronic illness, physical health was better during the prolonged than the

pre-pandemic phase. Future research should clarify the treatment implications of this unexpected finding, in particular, whether management focused on creating less demanding and calmer circumstances enhances physical health in this specific group. Although being psychological flexible may be, in general, beneficial for young adults' health, this appears not to hold specifically during the pandemic or among those with a chronic illness. Our results indicate that during a stressful situation such as a pandemic, health implications should be understood as a function of duration of the adverse situation as well as pre-existing health problems and psychological flexibility.

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Chapter 6

Dimensions of psychological flexibility and their significance in people with somatic symptoms: The 18-item Flexibility Index Test (FIT-18)

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ABSTRACT
Objective: To reduce the length of a 60-item psychological flexibility questionnaire and to get insight into the applicability of this abbreviated questionnaire by examining whether psychological flexibility might preserve mental and physical health when having somatic symptoms.
Methods: Participants were 2060 Dutch people with and without persistent somatic symptoms. The Flexibility Index Test (FIT-60) was subjected to principal axis factoring. Resulting dimensions were analyzed in linear regression analyses.
Results: A 2-factor structure best represented the 60 items with 18 resulting items representing a 'mindfulness and acceptance' dimension and a 'commitment and behavior change' dimension. These two dimensions and symptom severity were additively associated with mental well-being, and 'mindfulness and acceptance' was indicated to protect mental well-being when having more severe somatic symptoms.
Conclusion: Our study yielded a succinct FIT-18 questionnaire with two dimensions of psychological flexibility. Differential associations of these dimensions with health, suggest applicability of the FIT-18.

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TYK, RvH and RG developed the design and drafted the paper and collected and analysed the data. TYK and RG finalized the paper and RvH critically assessed the paper.

INTRODUCTION

Psychological flexibility refers to approaching difficult or challenging internal states in a non-judgmental, mindful way, and being committed to pursue one's values (Hayes et al., 2006; Kashdan & Rottenberg, 2010). It is considered key to adapt to circumstances (Hayes et al., 2012; Presti et al., 2020) and to preserve well-being and functioning when confronted with adversities such as persistent somatic symptoms.
Psychological flexibility includes six mutually interconnected processes that depend on each other and are difficult to entangle (Hayes, 2006): 'acceptance' (willingness to experience uncomfortable thoughts and feelings without attempts to change or avoid them), 'cognitive defusion' (distancing oneself from unhelpful thoughts and noticing they are not facts that need to be acted upon), 'contact with the present moment' (ongoing non-judgmental contact with thoughts, feelings and other private events as they occur), 'self-as-context' (taking an observer perspective towards one's own experiences), 'values' (chosen life directions that guide behavior), and 'committed action' (engaging in value-based behavior). These six processes have been further organized into two overarching processes (Hayes, 2006): 'acceptance' and 'cognitive defusion' into a 'mindfulness and acceptance' process, 'values' and 'committed action' into a 'commitment and behavior change' process. 'Contact with the present moment' and 'self-as-context' are represented in both processes, but when a dichotomy is created in research, they are usually grouped under the 'mindfulness and acceptance' process (Morin et al., 2021).

In clinical practice (Hayes, Pistorello & Levin, 2012) and the workplace (Bond et al., 2015), each of the six processes, as supplemented by traditional functional analysis, and applied to the specific cognitive, behavioral, emotional, and social content, can be linked to intervention methods and clinical targets (Hayes et al., 2012). This is one of the reasons why researchers have tried to assess psychological flexibility and its processes using dimensions reflecting more enduring traits or skills. These assessments may be useful to screen whether a person may need a more mindfulness and acceptance-based or value-based therapeutic approach, to examine moderation and mediation by these processes, or to monitor and evaluate the outcome of therapy. Self-report questionnaires have been developed to measure a single process (Gillanders et al., 2014) and two to five processes (Baer et al., 2006; Gámez et al., 2011) of psychological flexibility, or a single overarching dimension (Bond et al., 2011). In the Netherlands, the Flexibility Index Test (FIT-60; Batink et al., 2012) was developed to measure all six processes using 10 items for each process.

The initial study into the psychometric qualities of the FIT-60 indicated acceptable to good internal consistencies and sensitivity to change of the six dimensions (Batink et al., 2012). Later studies observed associations of psychological flexibility with personality traits, mental well-being, and somatic symptoms (Steenhaut et al., 2020; Koppert et al., 2020, Koppert et al., 2021). However, these later studies only examined the overarching dimension of psychological flexibility, not the six separate processes. Quantitative assessment of all six processes in clinical practice and research using dimensions on self-report questionnaires requires high

inter-item correlations within a process and low correlations between processes. This can be determined in factor analysis. If factor analysis shows that less than six dimensions are reflected by the FIT-60 questionnaire, then the number of items of this questionnaire can be reduced. There are also practical considerations to reduce the number of items of the FIT-60: respondents commented that the questionnaire is too long and that several items are difficult to understand.

Having a brief measure of psychological flexibility is useful from a practical point of view, but its development should not be at the cost of its contents. Psychological flexibility is considered particularly useful when challenges arise that produce distress and hamper goal pursuit (Doorley et al., 2020). This implies that more psychological flexibility is expected to be associated with better mental well-being and physical functioning (Hayes et al., 2006). Moreover, as indicated in previous studies examining a moderator role of psychological flexibility (Gloster et al., 2017; Leonidou et al., 2019), in case of adversities such as having persistent somatic symptoms, psychological flexibility is expected to protect mental well-being and perhaps also physical functioning.

The aim of our study was to clarify whether the length of the Flexibility Index Test (FIT-60) questionnaire can be reduced and to get insight into the applicability of the resulting questionnaire in health research. To that aim, we first examined how many dimensions can be distinguished with the FIT-60, and second, whether the resulting dimensions of psychological flexibility indicated that psychological flexibility might preserve mental well-being and physical functioning when having somatic symptoms.

METHODS

Participants

This study involves a new analysis of data that have been described previously (Koppert et al., 2021). Data from two separate online surveys in the general, Dutch-speaking adult (≥18 yrs.) population were analyzed. The first data collection was from November 2018 to May 2019 and the second from March to May 2020. In both samples, we retained all participants with complete assessments on psychological flexibility as well as on the questionnaire that assessed somatic symptom severity, mental well-being, and physical functioning. Figure S1 (supplementary material) shows the flowchart comprising both samples. A total of 2739 participants started to fill out the online questionnaire. Of this group, 679 (24.8%) participants did not complete the entire survey. The dropouts differed from the completers (n=2060), in terms of age (mean age [SD] for dropouts 45.0 [15.8] and for completers 47.7 [14.8], gender (n=121 [17.8%] men vs. 558 [82.2%] women and n=412 [20.0%] men vs. 1648 [80.0%] women, χ^2=7.54, p=.02) and education level (n=311 [46.5%] lower vs. n=358 [53.5%] higher and n=762 [37.2%] lower vs. n=1287 [62.8%] higher, χ^2=18.25, p<.001).

Procedure

Participants were recruited through social media (e.g., Facebook, Instagram, LinkedIn, local internet sites) and websites of patient associations with a focus on associations for people with persistent somatic symptoms. This recruitment note was shared by other individuals and groups. Participants filled out the online survey at a secure university website. A hyperlink to the online survey (housed on a secure university website) was provided, where participants were informed about the study and could provide informed consent, after which they were allowed to participate. They were not compensated for their participation. Approval for the two data collections was given by the Ethics Committee of the Faculty of Social and Behavioral Sciences of Utrecht University, the Netherlands (FETC17-120 and FETC20-190).

Instruments

Psychological flexibility

The FIT-60 was used to measure psychological flexibility (Batink et al., 2012). This instrument includes 10 items for each of the six processes of psychological flexibility (Hayes et al., 2006). Items are based on a literature review of psychological flexibility and on four existing questionnaires. The Acceptance and Action Questionnaire (AAQ-II, Bond et al., 2011) was used to measure 'acceptance', the Cognitive Fusion Questionnaire (CFQ-13, Gillanders et al., 2014) to assess 'cognitive defusion', the Five Facet Mindfulness Questionnaire (FFMQ, Baer et al., 2006) to assess 'contact with the present moment', and the Value Living Questionnaire (VLQ-2, Wilson et al., 2010) to assess 'values.' Participants indicated to what extent an item applies to them on a 7-point Likert scale, ranging from 0 ('totally disagree') to 6 ('totally agree'). The range of the total score is from 0 to 360 (Batink et al., 2012). Higher scores denote more flexibility. The initial psychometric qualities of the FIT-60 showed acceptable to good internal consistencies, with Cronbach's alphas ranging from .69 to .87 on the dimensions reflecting the six processes and Cronbach's alpha of .95 for the total dimension (Batink & Delespaul, 2015). In the current study, Cronbach's alpha of the 60-item total dimension was also .95.

Somatic symptom severity

The severity of somatic symptoms was measured with the pain and fatigue scales of the Dutch version of the 36-item RAND Short Form Health Survey (RAND SF-36, VanderZee et al., 1996). The pain scale consists of 4 items assessing the level of bodily pain and its interference with daily activities during the past 4 weeks, on 6- and 5-point Likert scales. The fatigue scale consists of 4 items assessing the level of fatigue and energy during the past 4 weeks on 6-point Likert scales. After reversing the scores, higher scores on the SF-36 reflect more severe pain and fatigue. We will use the standardized mean deviation from the norm scores (VanderZee et al., 1996) of these pain and fatigue scales as a measure of somatic symptom severity. In this study, Cronbach's alpha of this 2-scale composite score was .76.

Mental well-being and physical functioning

Also, mental well-being and physical functioning were measured with the RAND SF-36. As an indicator of mental well-being, we used the mean of the standardized mean deviation from the norm scores (VanderZee et al., 1996) of three subscales: emotional well-being, role limitations due to emotional problems, and social functioning. Physical functioning was derived in the same way using three subscales: physical functioning, role limitations due to physical problems, and general health. Higher mental well-being and physical functioning scores reflect better health. In the current study, Cronbach's alpha of these 3-scale composite scores were .76 for mental well-being and .82 for physical functioning.

Statistical analyses

Statistical analyses were performed using IBM SPSS statistics version 29.0.0.0. Tests were two-tailed and statistical significance was considered for $p < .05$. Exploratory factor analysis was used to get insight into the number of dimensions of psychological flexibility as measured with the FIT-60. Principal Axis Factoring (PAF) with direct oblimin rotation was used because the items were expected to correlate (Hayes et al., 2006). The number of factors was determined based on the scree-plot, the pattern of factor loadings, internal consistency of the items within a factor, the number of items included in a factor (a minimum of 3), and the content of the items. Criteria for excluding an item from further analysis were a factor loading below .45 on any factor (Comrey & Lee, 1992) or a factor loading above .32 on two or more factors (Costello & Osborne, 2005). Cronbach's alpha was used to analyze the internal consistency.

In constructing a shorter version of the FIT-60, to preserve diversity of the items, we wanted to include at least three items of each process in a dimension reflecting that process. In selecting items, we first took account of the factor loadings (high on the primary factor and low on other factors). Items that had a too large conceptual overlap with other items were not chosen. Also, items that were difficult to understand for respondents were not chosen. Pearson's correlations were calculated to assess the univariate associations between the resulting psychological flexibility dimensions of the shortened FIT-60 with demographic variables, symptom severity, mental well-being and physical functioning. Moderator analyses were done to examine whether and which dimensions of psychological flexibility were indicated to preserve mental well-being and physical functioning in case of somatic symptoms. Continuous predictor variables were centered and interactions were computed from these centered variables. In linear regression analysis, mental well-being and physical functioning were associated with symptom severity, the psychological flexibility dimensions, and the interaction between symptom severity and the psychological flexibility dimensions; age, gender, and education level were added to the model as covariates. To interpret significant interactions, regression lines for individuals with low (−1SD) and high (+1SD) scores on the interacting variables were plotted (Aiken & West, 1991). The magnitude of the interaction was indicated with Cohen's *d* effect sizes, with values of 0.20, 0.50 and 0.80 as cutoffs for small, medium, and large effects, respectively (Cohen, 1992).

RESULTS

Participant characteristics

Table 1 shows the characteristics of participants. The sample that included 2060 participants showed a predominance of women and a large representation of people with persistent somatic symptoms, such as people with an inflammatory rheumatic disease (11.6%), central sensitivity syndrome (30.2%), and osteoarthritis (11.7%). These chronic illnesses often have a concurrent other disease.

Table 1
Characteristics of participants (N=2060)

Variable	Statistic	
Age (years)		
Mean (SD)	47.7	(14.8)
Range	18	- 91
Gender, *n* (%)		
Men	412	(20.0)
Women	1648	(80.0)
Education level, *n* (%)*		
Low	762	(37.0)
High	1287	(62.5)
Missing	11	(0.5)
Marital status, *n* (%)		
Single	618	(30.0)
In a relation	1386	(67.3)
Unknow	56	(2.7)
Type of illness, *n* (%)		
Not any illness	583	(28.3)
Inflammatory rheumatic disease†	239	(11.6)
Central sensitivity syndrome‡	622	(30.2)
Osteoarthritis	241	(11.7)
Pulmonary	274	(13.3)
Skin	100	(4.9)
Cancer	46	(2.2)
Cardiovascular	286	(13.9)
Psychiatric	266	(12.9)
Neurological	166	(8.1)
Obesity	198	(9.6)
One or more other non-listed diseases	205	(9.9)
Health (RAND SF-36), Mean (SD) §		
Mental well-being	-0.58	(1.01)
Physical functioning	-0.46	(0.96)
Somatic symptom severity	0.50	(0.97)
Psychological flexibility (FIT-60), Mean (SD)‖	228.6	(49.1)

*Education level: low: lower general secondary education or lower; high: higher general secondary education or higher.

†These participants reported to have a chronic rheumatic disease other than osteoarthritis or fibromyalgia.

‡This group comprises participants with fibromyalgia, chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), somatoform disorder/somatic symptom disorder, chronic headache (not migraine), or chronic pain elsewhere in the body (not the head).

§These scores are the mean of standardized deviation scores from the general adult population norm (VanderZee et al., 1996). Scores for somatic symptom severity were reversed: higher scores reflect more pain and fatigue.

‖This total score ranges from 0 to 360, with higher scores reflecting more psychological flexibility.

Reduction of the size of the questionnaire

Six-factor solution

Although the scree plot of factor analysis clearly indicated a 2-factor solution, we explored whether factor analysis would show the six processes of psychological flexibility when forcing a 6-factor solution. The total variance explained by the six factors after principal axis factoring with oblique rotation was 42.1%. Table S1 in the supplementary file shows the pattern matrix after principal axis factoring. In the 6-factor solution, there were only four factors in which at least three items with a high enough factor loading (>.45) representing one process were included: Factor 1 included items representing three processes: 'Contact with the present moment' (all items had a negative formulation), 'Acceptance', and 'Cognitive defusion'. Also Factor 3 included four 'Contact with the present moment' items, but three of those four items had a positive formulation. Factor 2 was clearly a 'Committed action' factor and factor 5 was clearly a 'Values' factor. As the six processes were neither clearly represented in the six factors solution, nor in 3 to 5-factor solutions, we tried a 2-factor solution.

Two-factor solution

Principal axis factoring yielded a clearly interpretable two-factor solution (see Table S2 in the supplementary file). The eigenvalues of the two factors were 16.8 (28.0%) and 3.6 (6.0%) with a total explained variance of 34.0%. The first factor included 25 items with high (>.45) loadings and low (<.32) cross-loadings; item 3 showed a significant but negative loading on factor 1 and was therefore not included in this factor. The resulting 24 items comprised four processes. These are 'acceptance' and 'cognitive defusion', that were described in the theoretical model (Hayes, 2006) under the 'mindfulness and acceptance' label as well as 'contact with the present moment' and 'self-as-context' that have been grouped under this label in empirical research (Morin et al., 2021). We call this factor 'mindfulness and acceptance'. The second factor included 14 items with high (>.45) loadings and low (<.32; .316 for item 6) cross-loadings that were described in the theoretical model (Hayes, 2006) under the 'commitment and behavior change' label, which we will also use to denote factor 2.

FIT-18 questionnaire

Because the FIT-60 questionnaire included only two dimensions reflecting internally consistent individual differences that were distinguished from the other factor, we examined whether this would still be the case if we would select three items from each process included in the two dimensions. The selection process is described in the supplementary file.

A new principal axis factoring was done with the 18 resulting items (Table 2). With this large sample size, both the Kaiser–Meyer–Olkin measure of sampling adequacy of 0.95 and Bartlett's test of sphericity ($\chi 2=16646$, $p<.001$) indicated that factor analysis was appropriate. The eigenvalues of the two factors were 6.9 (38.5%)

and 1.3 (7.4%) with a total explained variance of 45.9%. The Pearson correlation between the two factors was .59.

Cronbach's alphas of the 'mindfulness and acceptance' and 'commitment and behavior change' factors were .92 and .78. The means (SD, range) of the scores on factor 1, factor 2, and the total score were 44.0 (15.5, 0-72), 26.7 (5.7, 0-36), and 70.7 (19.0, 11-108), respectively. Their score distributions were normal (skewness and kurtosis <|.66|).

Table 2
Pattern matrix with factor loadings of the FIT-18 questionnaire (N=2060)

	Factor	
	1	**2**
Items factor 1: Mindfulness and acceptance		
42R. I tend to react very strongly to my negative thoughts (Defusion)	**.82**	-.07
58R. I get upset with myself for having certain thoughts (Defusion)	**.78**	-.04
57R. It's such a struggle to let go of upsetting thoughts even when I know that letting go would be helpful (Defusion)	**.77**	.01
43R. I disapprove of myself when I have irrational ideas (Present)	**.76**	-.11
60R. I think some of my emotions are bad or inappropriate and I shouldn't feel them (Present)	**.72**	.00
38R. I believe some of my thoughts are abnormal or bad and I shouldn't think that way (Present)	**.69**	.02
53R. I'm afraid of my feelings (Acceptance)	**.67**	.14
45R. Emotions cause problems in my life (Acceptance)	**.65**	.10
26R. If I allow painful feelings to arise, I am afraid they will not go away (Acceptance)	**.63**	.11
23R. I suffer from a negative self-image (Self)	**.59**	.19
2R. I often feel limited by all that I feel I must do (Self)	**.50**	.15
24R. When I'm doing something wrong, I blame myself (Self)	**.49**	-.07
Items factor 2: Commitment and behavior change		
40. I am on my way to fulfill my goals and dreams (Commitment)	-.09	**.72**
48. I enjoy taking on new challenges (Commitment)	.01	**.66**
37. I find my life valuable (Values)	.15	**.66**
12. If I'm failing at something, I push through and try to tackle it in a different way (Commitment)	-.01	**.62**
50. I find support in the people around me (Values)	.08	**.47**
27. There are some things I do that are important to me (Values)	.02	**.46**

Note. Extraction Method: Principal Axis Factoring; Rotation Method: Oblimin with Kaiser Normalization.
Factor loading larger than |.45| are indicated in bold.
Processes: Acceptance, Defusion (cognitive defusion), Present (contact with the present moment), Self (self-as-context), Values, Commitment (committed action).
R behind the item number indicates that item scores were reversed before they were entered in factor analysis

Preservation of health in case of somatic symptoms

Linear regression analyses were done to examine whether the two dimensions of psychological flexibility might preserve mental well-being and physical functioning when having somatic symptoms. The Pearson correlations between all variables of the regression analyses are shown in Table 3. The correlations between the three health variables (mental well-being, physical functioning, and symptom severity) and the correlations between mental well-being and the two dimensions of psychological flexibility were large. Correlations of physical functioning and symptom severity with the two dimensions of psychological flexibility were medium. Correlations of demographic variables with the other variables were mostly small.

Table 3

Pearson correlations between mental well-being, physical functioning, and symptom severity, the 'Mindfulness and acceptance' and 'commitment and behavior change' dimensions of psychological flexibility, and demographic variables (N=2060)

Variables	1	2	3	4	5
1. Mental well-being (SF-36)					
2. Physical functioning (SF-36)	.58***				
3. Symptom severity(SF-36)	-.68***	-.82***			
4. Mindfulness and acceptance (FIT-18)	.59***	.28***	-.40***		
5. Commitment and behavior change (FIT-18)	.51***	.37***	-.46***	.51***	
6. Gender †	-.20***	.20***	.26***	-.16***	-.07**
7. Age	.05*	-.16***	-.02	.17***	.01
8. Education level‡	.16***	.28***	-.25***	.16***	.19***

*p<.05, **p<.01, ***p<.001

SF-36=Rand Short form-36, FIT-18= Flexibility index test-18

†Gender: 0 = men, 1 = women.

‡Education level: 0 = lower general secondary education or lower; 1 = higher general secondary education or higher

Mental well-being

Results of the regression analyses are shown in Table 4 and Figure 1. The linear regression model showed 60.3% shared variance between the set of predictor variables and mental well-being (F = 386.9, p < .001). All main variables were associated with mental well-being (all p-values < .001): Symptom severity (β = -.498), 'mindfulness and acceptance' (β = .330), and 'commitment and behavioral change' (β = .091). Thus, while taking account of the symptom severity and the other psychological flexibility dimension, 'mindfulness and acceptance' as well as ''commitment and behavioral change' were additively associated with better mental health.

The interaction of symptom severity with 'mindfulness and acceptance' was significantly associated with mental well-being (β = .133, p < .001). As shown by the

regression lines in figure 1, for respondents with high levels of 'mindfulness and acceptance' the association between symptom severity and mental well-being was less strong than for those with low levels. The effects size difference on mental well-being for 'mindfulness and acceptance' between respondents with low (-1 SD) symptom severity was small (d = .45), while it was large (d = .87) for those with high symptom severity. The effect size difference for respondents with low vs. high 'mindfulness and acceptance' was small (d = .42).

Physical functioning

The linear regression model showed 71.4% shared variance between the set of predictor variables and physical functioning (F = 635.3, p < .001). As shown in Table 4 and Figure 1, symptom severity accounted for virtually all variance in physical functioning. Thus, while taking account of the symptom severity and the other psychological flexibility dimension, neither 'mindfulness and acceptance' nor 'commitment and behavioral change' were associated with physical functioning.

The interaction of symptom severity with 'commitment and behavior change' was significantly associated with physical functioning (β = .047, p = .002). The effects size difference on physical functioning for 'commitment and behavior change' between respondents with low (d = .12) and high (d = .04) symptom severity was trivial. Thus, also the effect size difference for respondents with low vs. high 'commitment and behavior change' was trivial (d = .08).

Table 4

Results of linear regression analysis examining the association of mental well-being and physical functioning (SF-36) with demographic variables, symptom severity (pain & fatigue, SF-36), the 'mindfulness and acceptance' (M&A) and 'commitment and behavior change' (C&BC) dimensions of psychological flexibility (FIT-18), and the two-way interaction of symptom severity with the two psychological flexibility dimensions (N=2049)

Mental well-being	***b***	**(SE)**	**β**	***t***	***p***
Constant	-.378	.066		-5.76	<.001
Gender*	-.044	.037	-.017	-1.19	.24
Age	-.001	.001	-.019	-1.29	.20
Education level†	-.092	.031	-.044	-2.99	.003
Symptom severity	-.518	.018	-.498	-39.62	<.001
M&A	.022	.001	.330	19.16	<.001
C&BC	.016	.003	.091	5.02	<.001
Symptom severity x M&A	.007	.001	.113	6.73	<.001
Symptom severity x C&BC	.003	.003	.016	.90	.37
Physical functioning	***b***	**(SE)**	**β**	***t***	***p***
Constant	-.040	.053		-.76	.45
Gender*	.010	.030	.004	.34	.74
Age	-.010	.001	-.156	-.12.60	<.001
Education level†	.108	.025	.054	4.32	<.001
Symptom severity	-.825	.014	-.828	-58.04	<.001
M&A	-.002	.001	-.027	-1.82	.07
C&BC	-.004	.003	-.023	-1.47	.14
Symptom severity x M&A	-.001	.001	-.019	-1.34	.18
Symptom severity x C&BC	.007	.002	.047	3.16	.002

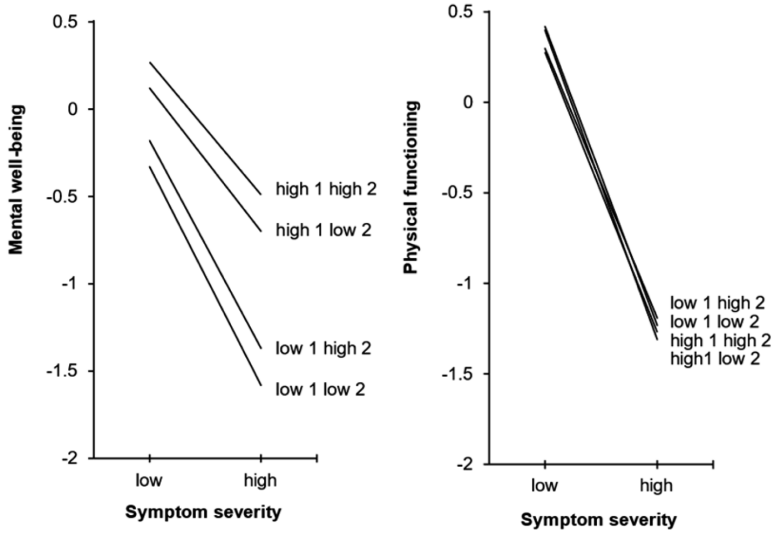
*Gender: 0 = men, 1 = women.

†Education level: 0 = lower general secondary education or lower; 1 = higher general secondary education or higher

b, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient

Figure 1

Mental well-being and physical functioning (standard deviation from the norm) on y-axis as a function of low (-1 SD) and high (+1 SD) symptom severity (x-axis) for people with low (-1 SD) or high (+1 SD) 'mindfulness and acceptance' (1) and low or high 'commitment and behavior change' (2), while controlling for gender, age, and education level



Note. Standard errors of measurement were .022 for mental well-being and .021 for physical functioning.

DISCUSSION

This study yielded the FIT-18 questionnaire, a brief 18-item version of the FIT-60 questionnaire. Factor-analysis generated two factors. Items belonging to the two predefined overarching dimensions of psychological flexibility were allocated to these factors: 'mindfulness and acceptance' and 'commitment and behavior change'. The internal consistency of the two dimensions (Cronbach's alpha of .92 and .78) was good. While taking account of all variables in the model, symptom severity, 'mindfulness and acceptance' and 'commitment and behavior change' were additively associated with mental well-being. Furthermore, moderator analysis showed that the association between symptom severity and mental well-being was higher in people with low than high 'mindfulness and acceptance'. The dimensions of psychological flexibility were not associated with physical functioning.

The six intended dimensions of the FIT-60 could not be derived in factor analysis. Perhaps the interdependence of the processes prevented us from finding all six processes. Ideally, an exhaustive database of items should be used to derive items that are correlated with other items of the same dimension, but not with items of other dimensions. After the start of data collection in our study, such a method was adopted when developing the 60-item Multidimensional Psychological Flexibility Inventory (MPFI, Rolffs et al., 2018). That study even derived twelve independent dimensions, that represented both the positive and the negative version of each of the six processes comprising psychological flexibility; for instance, 'acceptance' as well as the opposite construct 'experiential avoidance', or 'committed action' as well as 'inaction.' Of note, the pattern matrix with factor loadings of the MPFI clearly showed that these six negative versions are not simply the opposite poles of the six positive psychological flexibility versions. Moreover, it was shown that variables could vary independently, that is, patients could show improvement on specific dimensions of flexibility without showing improvement on all dimensions of flexibility, and without showing similar improvements on the corresponding dimensions of inflexibility (Rogge et al., 2019; Rolffs et al., 2018). Thus, the validity tests supported a 12-factor solution instead of a 6-factor solution. Therefore, the MPFI appears a better instrument than the FIT-60 for a researcher or clinician who wants to assess all processes of psychological flexibility and psychological inflexibility.

The FIT-18 includes items of the two overarching dimensions of psychological flexibility. The first factor included only negatively worded items representing the four processes of 'mindfulness and acceptance' and the second factor included only positively worded items of the two processes of 'commitment and behavior change'. Thus, the first factor includes only psychological *in*flexibility items and the second factor only psychological *flexibility* items. However, while the grouping of items factor analysis clearly discriminated between the two predefined overarching factors of psychological flexibility, there are challenges for interpretation. Three somewhat overlapping challenges are discussed: response bias, approach-avoidance and affect.

First, response bias may hamper interpretation. Besides in terms of content, the two dimensions showed a semantic difference. The first dimension includes

exclusively negatively worded items and the second positively worded items. This wording may cue the respondent to give specific answers such as agreeing with positive worded items and disagreeing with negatively worded items (acquiescence), which could be the cause of getting two factors (e.g., Lindwall et al., 2012). The development of the MPFI showed that negatively and positively worded items of the same processes were included in distinct factors (Rolffs 2018). This can suggest that the content of the construct changes when the wording changes as well as that the changed wording triggers response bias. Ideally, it should be tried to include an equal amount of positively and negatively worded items in each dimension such as has been done with the Big Five Inventory-2 (Soto 2017). This cannot be done with the FIT-60, because too few positively worded items were included.

Second, 2-factor solutions of questionnaires often differentiate between what Pribram (1981) called "out of motion" (e-motion) and motivation (in-motion) processes and what has been described as avoidance and approach temperaments (Elliot 2002) or behavioral inhibition vs. behavioral activation systems (Carver & White 1994). These emotional "stop" and motivational "go" processes have been linked to differential neurological systems. To a certain extent, experiential avoidance is reflected in the items of the 'mindfulness and acceptance' dimension and motivational approach behavior in the items of the 'commitment and behavior change' dimension.

Third, and related to the other two interpretations, two-factor solutions of questionnaires often differentiate negative and positive affectivity (Tellegen, 1999) or the personality factors neuroticism and extraversion. The first questionnaire to measure psychological flexibility was the Acceptance and Action Questionnaire (AAQ-II; Bond 2011). This questionnaire assessed a single dimension called experiential avoidance or psychological inflexibility. Critiques indicated at the overlap between this questionnaire and psychological distress (Tyndall 2019; Wolgast 2014). The ambition of questionnaires of psychological (in)flexibility is to assess processes and skills that may influence mood, but it is an inherent problem of self-report measures that they contain a substantial pervasive mood disposition of negative affectivity (Watson & Pennebaker, 1989). Therefore, to get insight in what FIT-18 actually measures, future research of construct validity should assess associations of the two FIT-18 dimensions with self-reports of approach-avoidance (e.g., the BIS/BAS scales, Carver & White 1994) and positive and negative affectivity (e.g., The Positive and Negative Affect Schedule (Watson, Clark and Tellegen, 1988a) to test divergent validity. Moreover, it should be examined whether the FIT-18 dimensions are more sensitive to change in response to interventions that target psychological flexibility, than these other self-report measures.

In examining the potential applicability of the FIT-18, we observed that physical functioning was strongly associated with symptom severity, but not with the psychological flexibility dimensions. The interaction between symptom severity and 'commitment & behavior change' was significantly associated with physical functioning, but the effect size was trivial. In contrast, the association with mental well-being indicated a role for psychological flexibility. While adjusting for symptom

severity, both psychological flexibility dimensions were additively associated with mental well-being. Although such associations have sometimes been presented as showing that psychological flexibility preserves mental well-being (Dawson et al., 2020; McCracken et al., 2021), this inference from a cross-sectional observation is too strong. Other mechanism may explain the observations; for instance, that mental well-being influences psychological flexibility, a third variable influences both mental well-being and psychological flexibility, or that the associations reflect mutual influences, overlap between items, or confounding by answer tendencies. Our interaction of symptom severity with the 'mindfulness and acceptance' dimension gave a stronger indication. In agreement with previous observations of moderation (Gloster et al., 2017; Leonidou et al., 2019; Pleman et al., 2019), the significant interaction suggested that psychological flexibility had a stronger role in preserving mental well-being in case of high than low symptom severity. Overall, the patterns of associations with health variables indicate that the two dimensions of psychological flexibility have a different meaning. Longitudinal and clinical experimental research is needed to get a more thorough understanding of the directionality of associations and the changeability of variables.

A strength of the current study is the large sample including many people with severe pain and fatigue for whom psychological flexibility might be relevant. Furthermore, whereas in other studies measurement of psychological flexibility was often limited to one or a few processes underlying psychological flexibility, this study used items encompassing all six processes. In this stage of questionnaire development, the collected data were cross-sectional and the first analysis of validity was restricted to one aspect of construct validity. An indication of applicability of the FIT-18 questionnaire was not yet obtained using repeated measures within persons. Future validation studies could also employ other self-report measures to examine convergent and divergent validity and other than self-report questionnaires, which might better reflect dynamic processes that are intended by the psychological flexibility construct. The differences between demographic variables of completers and dropouts were significant but small. The results of our study do not generalize beyond the report of self-perceived health, the participating Dutch sample, and the employed cross-sectional design.

An asset of the FIT-18 questionnaire as compared to other questionnaires is that it includes only 18 items which will have positive effects on the burden for respondents, the response rate, and the possibility to take repeated assessments across time. After and as part of more validation research, the FIT-18 might be used to (further) examine associations with existing questionnaires, measurement invariance, moderation and mediation, and sensitivity to change. It should also be examined whether the questionnaire can inform treatment by using it to screen whether a mindfulness and acceptance-based or value-based therapeutic approach is indicated for a person or both, and to monitor and evaluate the outcome of therapy. If further research confirms its validity, the FIT-18 is a succinct questionnaire that can be easily and quickly applied in research and clinical practice to get insight into the

'mindfulness and acceptance' dimension of psychological inflexibility and the 'commitment and behavior change' dimension of psychological flexibility.

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Chapter 7

Summary and general discussion

The COVID-19 pandemic created a unique opportunity to examine health as a function of multiple real-life stressors, especially in people with a chronic disease. Early studies indicated that the pandemic had an impact on social, physical and emotional aspects of life[1,2,3,4]. This thesis examined mental and physical health during the COVID-19 pandemic in people with and without a chronic illness and whether psychological flexibility is a potential protective factor againt the deterioration of health. The main findings of the thesis are presented in Box 1. This chapter gives a summary of each study, including its implications and suggestions for further research, followed by a general discussion with overarching recommendations beyond this pandemic.

Box 1. Main findings

The five studies of this thesis yielded the following main findings:

- Although patients with an Inflammatory Rheumatic Disease (IRD) were more worried and stressed during the acute peak of the COVID-19 pandemic in 2020 compared to those without an IRD, their level of mental well-being was not lower compared to that of patients before the pandemic in 2018. There was no indication that psychological flexibility was a protective factor against a deterioration of health (chapter 2).

- Higher worry and stress during the pandemic, having a Central Sensitivity Syndrome (CSS) and lower psychological flexibility were all associated with more severe somatic symptoms. However, the association of stress with somatic symptoms was not particularly strong in people with a CSS and psychological flexibility did not buffer this association. The hypothesis that COVID-19 stress augments somatic symptoms particularly in people with a CSS, was not confirmed by our research (chapter 3).

- Although health of women with fibromyalgia was persistently low, mental health was not lower and pain and physical functioning were even better during, compared to before the COVID-19 pandemic (chapter 4).

- Especially during the prolonged phase of the pandemic in 2021, young adults' mental and physical health was low, with one exception: in young adults with a chronic illness and low psychological flexibility, physical health was found to be better during the prolonged phase, compared to the acute and pre-pandemic phases (chapter 5).

- Factor analysis on the sixty items of the FIT-60 yielded a 2-factor solution, representing items of the 'mindfulness and acceptance' dimension of psychological *in*flexibility and of the 'commitment and behavior change' dimension of psychological flexibility, which were also represented in a succinct 18 item questionnaire: the FIT-18 (chapter 6).

1. Mental and physical health during the COVID-19 pandemic

In the early stage of the pandemic, it was expected that the pandemic might affect the mental and physical health of people and especially of those with a chronic illness[5,6,7]. One aim of this thesis was to determine the mental and physical health in people with and without a chronic illness during the COVID-19 pandemic. To achieve this overall aim, at three time-points, data samples on mental and physical health, as well as psychological flexibility, were collected cross-sectionally in the Dutch speaking general population. The first dataset was obtained before the onset of the pandemic, in 2018, and the two other sets during the pandemic: one at the first major peak (2020; *acute phase*) and one year later, when the contamination rate and restrictive measures in the Netherlands were intensive and long-lasting (2021; *prolonged phase*). Both studies in chapter 2 and 3 made use of data from the acute and pre-pandemic phases of the pandemic, while chapter 4 and 5 also included data from the prolonged phase.

1.1. The pandemic may be more dangerous for people with an autoimmune disease.
In the early stage of the pandemic, people with an inflammatory rheumatic disease (IRD) were considered a high-risk group to aquire COVID-19, to face disrupted treatment for their illness due to governmental measures, and to have a worse disease outcome. **Chapter 2** examined whether people with an IRD, compared to those without were more worried and stressed during the acute phase of the pandemic in 2020 and whether they had lower mental health than a reference sample before the pandemic.

We found that those with an IRD were more worried about getting infected by the virus (medium effect) and more stressed (small effect), than those without an IRD. About half of the group with an IRD and one quarter of those without an IRD were worried or very worried about the risk of getting infected. For the first group, worry could be considered an adaptive reaction to a realistic threat at that time, because it was communicated that people with an IRD had an overall higher risk of getting infected due to their drug-induced suppressed immune system. Moreover, in either group mental wellbeing was not clearly reduced during, compared to before the pandemic. Thus, it appears that patients with an IRD, on average, show a realistic level of concern without being overly stressed or distressed. Nonetheless, even though worry is a normal reaction to the threat of contamination as it makes people cautious and prevents them from getting infected, in some (very) worried people, the worry may become excessive and lead to an anxiety disorder. For them, it can help to seek and cherish positive social contacts in a safe way, because this may protect against anxiety[8]. Finding appropriate professional help may aid people with an IRD in getting more resilient when facing severe worry and stress, depression or anxiety[9].

During the early stages of the pandemic, (social) media and professional literature often reported that the psychological impact of the pandemic was huge. We observed that respondents, and especially those with an IRD, were indeed worried

about getting infected by the coronavirus. However, we did not observe a lower mental health, as compared to before the pandemic. Overall, this indicates that the psychological impact of the COVID-19 pandemic in patients with an IRD was modest, which might imply that common education and health care will suffice for most patients, and additional interventions are not needed.

1.2. Augmentation of somatic symptoms by pandemic stress

It is assumed that a hypersensitive brain is a core pathophysiological mechanism in people with fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome. Therefore, these illnesses have been grouped using the label Central Sensitivity Syndromes[10] (CSS). Part of the pathology is that stressful or threatful circumstances may augment somatic symptoms in CSS. Guided by this theory, we examined in **chapter 3** whether the association between COVID-19 stress and somatic symptom severity would be stronger in people with, than in those without CSS.

Two operationalizations of stress were used. First, the mean standardized self-reported worry and stress levels during the acute phase of the pandemic in 2020. Second, a comparison between time periods: the acute phase of the pandemic was assumed to be more stressful than pre-pandemic (2018). Results indicated that during the acute phase, people perceived themselves to be, on average, more stressed than normal, and that these stress levels were associated with more severe somatic symptoms. In contrast, based on the second operationalization of stress, there was no link between stress and more severe somatic symptoms. Our results showed even a small but statistically significant lower level of symptom severity in the acute phase, compared to before the pandemic. Thus, overall, this study neither yield a convincing indication of a stress-somatic symptom link, nor of a stronger link in people with CSS.

In line with our results, previous studies in people with CSS suggested that somatic symptoms do not reliably increase in response to major environmental stressors[11,12]. A possible explanation for the lack of change in somatic symptom severity is that the pandemic forced people to focus on external stressors and behavior changes. This could have had a positive impact in some people with CSS, shifting their focus from internal somatosensory processes and psychological conflicts to environmental issues, which may have positively modulated their symptom perception[13]. It is also possible that the impact of the COVID-19 pandemic on people with CSS is, on average, weaker than assumed. Some people with CSS may have experienced less stress, for instance, because they felt less pressure from work, more social connectedness, or more recognition for their symptoms and situation during the pandemic. Overall, our results suggest that it is uncertain whether there is an impact of the COVID-19 pandemic on somatic symptoms in people with CSS. This study included assessment only during the first peak period of the pandemic in the Netherlands. Perhaps this phase did, on average, not yield enough stress to activate the sensitized brain.

1.3. *Fibromyalgia during the pandemic: for better or worse*

Research from the initial acute phase of the pandemic did not consistently confirm the expectation that health was worse in people with fibromyalgia during the COVID-19 pandemic. These studies commonly analyzed the first acute phase of the pandemic, were conducted in small samples and reported mainly composite health scores comprising mental health, physical functioning, and symptom severity without distinguishing between these dimensions. Our study in **chapter 4** made use of a large data sample, included both the acute and a prolonged phase of the pandemic, evaluated distinct dimensions of health and compared health to a norm reference group.

Results showed that, both before and during the pandemic, the health of women with fibromyalgia was worse as compared to Dutch norm reference values for the general population. With very large deviating scores for fatigue, pain, general health, social functioning, and (role) physical functioning, and medium to large deviating scores for role emotional functioning and mental health. However, contrary to the expectation, results indicated that the pandemic did, on average, not negatively impact women with fibromyalgia and even suggest a positive impact on physical health. Qualitative studies investigated improvement in people with fibromyalgia during the pandemic[14,15], and observed that some patients thought that their improvement was caused by beneficial effects of smart working and the opportunity to exercise more regularly[14]. Also reduced social constraints might have allowed them to adjust the rhythms of their life to fluctuations of symptoms, which might have caused that fibromyalgia stopped being the main priority in their lives[15]. This suggests that reducing social obligations might be a therapeutic modality in the management of fibromyalgia.

In conclusion, our findings tentatively indicate that mean health levels do not further deteriorate during a pandemic and that somatic symptoms and physical functioning may even be better in women with fibromyalgia during a pandemic. This suggests that the consequences of a pandemic, may include favorable ones for at least part of women with fibromyalgia.

1.4. Young adults' disrupted possibilities to pursue a valued life.

Multiple studies reported on the detrimental effects the pandemic on young adults' health and indicated that levels of anxiety, depression, and mental distress were elevated during the COVID-19 pandemic compared to pre-pandemic or norm group levels[16,17,18,19,20]. These studies typically analyzed mental health and not physical health and only during the initial, acute phase of the pandemic. Moreover, due to the limited amount of research, mental and physical health status of young adults with a chronic illness during the pandemic was unclear. **Chapter 5** showed that in young adults, either with or without a chronic illness, mental health was poorer during the prolonged compared to the pre-pandemic phase. This observation confirmed earlier concerns about more detrimental effects on mental health with a longer duration of the pandemic[21,22]. With respect to physical health, different results were observed for

participants with versus those without a chronic illness. Those without an illness had poorer health in the prolonged phase, compared to the acute phase, while it was unexpectedly better for those with a chronic illness.

A possible explanation of the results found in the group without a chronic illness is that during this first acute phase of the pandemic, physical health did not deteriorate on average, because the young adults could still walk or cycle outside and perform workouts at home[23,24]. While perhaps in the prolonged phase, reduced motivation to exercise alone, in combination with the ongoing closure of fitness centers and sports facilities, caused a reduction of physical health.

For the young adults with a chronic illness, one might expect that physical health would worsen due to reduced or delayed health care and increased stress[25,26,27]. However, in line with some findings in studies of people with fibromyalgia[28,29], physical health of young adults with a chronic illness was better during the prolonged phase than during the pre-pandemic phase. A possible explanation is that during the pandemic they have benefited from their past development of skills in managing adversities. Still, their overall health was observed to be lower than that of those without a chronic illness.

Taken together, our results and results of other studies suggest that enhancement of mental and physical health of both young adults with and without a chronic illness should be a priority in research and health policy.

2. Psychological flexibility

Psychological flexibility is assumed to help dealing with adverse circumstances. This part of the chapter discusses whether and to what extend psychological flexibility played a health-protecting role during the pandemic and whether the questionnaire that was used to assess psychological flexibility might be shortened.

2.1. The protecting role of psychological flexibility

People differ in the way they deal with challenging circumstances. We expected that psychological flexibility might be an antidote to situations that are difficult to control, like those of a pandemic and when having severe pain, fatigue or other adverse consequences of a chronic illness. Our results indicated that psychological flexibility is, in general, associated with favorable mental and physical health. However, there were hardly indications of a moderating – protective – role of psychological flexibility in our studies. With exception of the analyses in chapter 6, small but significant opposite patterns were observed: high psychological flexibility was associated with better health, in what were presumed as propitious circumstances, e.g., *before* the pandemic (chapter 2) and in people *without* a chronic illness (chapter 3). Moreover, young adults *with* a chronic illness and *low* levels of psychological flexibility reported even better physical health during the pandemic, in presumed worse times (chapter 4).

Consistently with results from this thesis, other studies during the pandemic showed that psychological flexibility and related constructs such as resilience are

positively associated with mental[30,31,32] and physical health[33,34]. This may indeed suggest a health-protective role of psychological flexibility and related skills[35], but it is a tentative inference. Some authors deduce a protective role of psychological flexibility based on cross-sectional data examining concurrent associations[33,36]. It is, however, not possible to verify a protective role of psychological flexibility in cross-sectional studies. The association between psychological flexibility and health, may reflect construct overlap; health might impact psychological flexibility and vice versa, or the influence of third factors, such as a trait-like affectivity dimension (e.g., neuroticism) or a response tendency (e.g., acquiescence or social desirability) might impact both constructs. A protective role would have been clearer, if psychological flexibility was shown to be particularly useful in terms of protecting health under bad circumstances, such as during the pandemic or when having a chronic illness. In this thesis, only one interaction analysis (**Chapter 6**) confirmed this conjecture.

Within our studies that examined the initial acute phase of the pandemic (**chapters 2 and 3**), it is possible that a moderating role of psychological flexibility could not be found because mental and physical health were not lower in this acute phase, than before the pandemic. In other words: because, on average, there was nothing to protect. The reported increased worry and stress is perhaps a natural and healthy reaction to an actual threat that did not have consequences for mental and physical health.

However, our study among young adults (**chapter 5**) included data from the prolonged phase, which did show that mental and physical health were worse then, compared to in the acute phase. Thus, a protective role of psychological flexibility would be detectable, if present. However, it was not. In contrast, young adults *with* a chronic illness and *low* levels of psychological flexibility even reported better physical health during the pandemic. Perhaps our results reflect that the 'lockdown society', on average, better fits young adults with a chronic illness and low psychological flexibility than common modern (pre-pandemic) society; for instance, because lockdown society was less demanding than pre-pandemic society or offered people with a chronic illness better opportunities to adjust their lives to their disability and fluctuations of symptoms.

In relation frame theory it is assumed that psychological flexibility is beneficial for a person's health, and Acceptance and Commitment Therapy (ACT) is considered a means to promote it[37,38]. ACT has been indicated to enhance mental and physical health[39,40,41]. Results of our study suggest that it might be useful in future research in post-pandemic society, to compare the effects of interventions that enhance psychological flexibility, with interventions focused on creating less demanding and calmer circumstances. It should also be examined which of the two interventions is most effective for specific groups, such as people with a chronic illness and low psychological flexibility.

We might consider and test the effects of other possible interventions than ACT for those who are less able to deal with the acute or daily challenges in life, like those with low psychological flexibility. For instance, emotion awareness and expression therapy has been shown promising in fibromyalgia[42]. Also other theories

focus on affect regulation. Compassion-focused theory[43] and perspective articles about people with psychopathology[44] or psychosomatic chronic illnesses[45], emphasize the importance of cultivating safeness and affiliative and calming behavior in people with a chronic illness. Specifically for fibromyalgia it has been proposed that an imbalance in emotion regulation, reflected by an overactive 'threat' system and underactive 'soothing' system in conjunction with other mechanisms, contributes to fibromyalgia[45]. Threats are context or cues that are perceived as potentially dangerous or barriers to desired goals[43]. The opposite applies to soothing, experiencing safeness that favors engagement in resting, affiliative, or explorative behaviors. Acute or chronic stress, but also daily hassles and concerns, may fuel the hyperactive threat system in people with fibromyalgia[46,47]. It is possible that, in contrast to expectations, in people with fibromyalgia the pandemic was accompanied with less threats and more soothers, such as less pressure from work and more social connectedness, rest and balance or recognition for their symptoms, which are identified as beneficial for the imbalanced affect regulation in people with an IRD or CSS[48].

2.2. Core dimensions of psychological flexibility

Psychological flexibility includes six mutually interconnected processes. In clinical practice, each of the six processes can be linked to clinical targets in therapy[38]. However, they are rarely topic of empirical research. In the Netherlands, the 60-item Flexibility Index Test[49] (FIT-60) was constructed to measure all six dimensions. There were practical and statistical considerations to reduce the number of items and to expect that less than six dimensions reflect consistent individual differences in this questionnaire. The main aim of **chapter 6** was to clarify whether less than six processes are reflected by the assessments of the FIT-60 questionnaire, and as a consequence, whether the length of the questionnaire could be reduced. We examined how many factors, reflecting internally consistent individual differences, could be distinguished. A second aim was to get a first indication of the possible applicability of the resulting questionnaire in health research.

The six intended dimensions of the FIT-60 could not be derived from our factor analysis. Perhaps the interdependence of the processes as described by Hayes and coworkers[37], prevented us from finding all six processes. The Multidimensional Psychological Flexibility Inventory[50] (MPFI) appears a better instrument than the FIT-60 for a researcher or clinician who wants to validly assess all processes of psychological flexibility and inflexibility[51].

Our factor analysis of the sixty items of the FIT-60 generated a 2-factor solution. An 18-item questionnaire (FIT-18) was derived from the FIT-60, which included items representing the two predefined overarching dimensions of psychological flexibility: 'mindfulness and acceptance' and 'commitment and behavior change'. The 'mindfulness and acceptance' dimension was interpreted to reflect psychological *inflexibility* and the 'commitment and behavior change' dimension, psychological *flexibility*.

However, we should be hesitant with interpretation of these factors for at least three partly overlapping reasons. First, the two dimensions show a semantic difference. The first dimension includes exclusively negatively worded items and the second positively worded items, which could be the cause of getting a 2-factor solution[52]. Ideally, an equal number of positively and negatively worded items should be included in each dimension to prevent response tendencies such as acquiescence. However, this cannot be done with the FIT-60, because it contains too few positive worded items. Second, two-factor questionnaires often reflect the distinction between general approach (motivation) and (emotion) avoidance tendencies[53], which may also play a role in the 2-factor solution of FIT-18. Third, two-dimensional questionnaires might represent negative and positive affectivity[54], or the personality factors neuroticism and extraversion. While the ambition of questionnaires of psychological (in)flexibility is to assess processes and skills that may influence mood, it is an inherent problem of self-report measures that they reflect a substantial pervasive mood disposition[55]. Therefore, to get better insight into what the FIT-18 actually measures, future research of construct validity should include measures of approach and avoidance and positive and negative affectivity to test divergent validity, while taking account of response tendencies such as acquiescense.

In examining the potential applicability of the FIT-18 in the general population, we observed that psychological flexibility was indicated to play a role in the association between symptom severity and mental, but not physical health. The 'mindfulness and acceptance' dimension was suggested to have a stronger role in preserving mental well-being in people with severe somatic symptoms, than in those with low symptom severity. The patterns of associations with health variables indicated that the two dimensions of psychological flexibility have a different meaning. Longitudinal and clinical experimental research is needed to get a more thorough understanding of the directionality of associations and the changeability of variables in different populations and under different circumstances.

In terms of applicability, the FIT-18 is a succinct questionnaire that can be quickly and easily applied in research and clinical practice. Our study was a very first exploration of its construct validity. Further research of construct validty and other psychometric properties is needed, including criterion validity and divergent and convergent validity, as well as sensitivity to change. If these properties have been confirmed, the FIT-18 might be useful to inform treatment by using it to screen whether only a mindfulness and acceptance-based or value-based therapeutic approach or both are indicated for a person, and to monitor and evaluate the outcome of therapy.

3. The pandemic and beyond

Our research enabled us to give an indication on how people with and without a chronic illness dealt with the challenges of pandemic life. In this final section the strengths and limitations of the thesis are considered and we aim to shed light on

what possible implications and directions for research could be, beyond the corona pandemic.

3.1 Methodological limitations

A strength of the current study is its time frame, including data collected before (2018) and during the acute (2020) and prolonged (2021) phases of the pandemic. This design enabled us to compare data on health and psychological flexibility assessed during and before the pandemic, which gave us an opportunity to get more insight into the differences in health of people, than most singular cross-sectional data collections during the pandemic. Our samples also included a high number of people with a chronic illness. This enabled us to compare data of those with and those without a chronic illness and get insight into whether and to what extent health differed between these groups during the pandemic.

A primary limitation is that the data were obtained from different samples across the three pandemic phases and that the samples were convenience rather than representative of the population. Our samples did not have similar numbers of participants in terms of gender, age, and education. Although all analyses were adjusted for these demographic covariates, the samples were approach in more or less the same way, and the samples at each phase were large enough to have small margins of error, it is still possible that differences in sampling influenced our results. For instance, the motivation to participate might have been different across the three samples. Some particpants who would not have participated before, may have participated during the pandemic, because they had time left or wanted to contribute to a study examining the significance of the pandemic. Others may or may not have participated, due to negative pandemic circumstances, such as stress or distress.

Nevertheless, it is reassuring that the results of our study were more or less similar to results from an extensive meta-analysis of longitudinal studies, comparing mental health during the acute phase, to pre-pandemic values[56]. Most symptom change estimates for general mental health, anxiety symptoms, and depression symptoms were close to zero and not statistically significant, and significant changes were of minimal to small magnitudes[56]. Such meta-analyses of the prolonged phase are not yet available. Ongoing and future research combining the assessments of large international datasets from longitudinal cohort studies may yield more reliable insight into the health and health changes of people during real-life stressors. The ideal research design would be to have ongoing data collection in fixed panels with baseline measurements before and after the pandemic. It would be valuable to include in these studies also enough people with a chronic illness, to gain better insight into the effects of, and coping with, the consequences of a real-life stressor on their mental and physical health.

Another limitation is that the data were collected through self-report questionnaires, which more likely reflect trait-like aspects, than processes that are intended by the psychological flexibility construct. Research could try to understand processes better, by using a day reconstruction method[57], analyses of unstructured text data[58], or experience sampling methods (e.g., intensive longitudinal data

collected with a smartphone) to examine dynamic processes[59]. Another possibility is to use a clinical experimental design, measuring psychological flexibility during a real-life stressor, while including an intervention such as ACT, cognitive restructuring therapy, emotion awareness and expression therapy, or a compassion-focused intervention and compare changes in psychological flexibility processes and health between these experimental conditions. This might give an indication of the development of strength of specific processes in individual persons.

Chronic illnesses were also self-reported and not confirmed by clinical assessment. There is a chance that some people were allocated to the wrong group, because they, for instance, reported less or more diseases than would actually have been observed by medical specialists. Our samples were convenience samples, with a purposive overrepresentation of people with a chronic illness. Also highly educated women were overrepresented, which was not intended. Although analyses were adjusted for differences in demographic variables, caution is needed in generalizing these results. One of our studies indicated that health was better for women with fibromyalgia during the pandemic, in line with results of other European studies[14,28,60], but not in line with results of studies in Mexican people with fibromyalgia[61]. This suggests that these findings are at best generalizable to women with fibromyalgia in Western European countries. Generalization beyond the report of self-perceived health in predominantly women and in the Dutch population during and before the pandemic is difficult. The pandemic is a unique situation and the prevalence of COVID-19 diseases and the nature of measures taken by governments differed between countries, which might yield different results per country.

A critical comment to our approach might be that we did not have perfect norm group data. For instance, **chapter 4** included only women with fibromyalgia, while the norm group included 35% men, which may have yielded somewhat different results in this study. Moreover, the norm groups are from over 25 years ago[62]. Given the observation that there has been a progressive increase in psychological distress from the middle of last century[63] to recent years[64], we should be cautious in making conclusions about finding detrimental health in our more recent samples. In our analyses in **chapter 5**, we used norm scores from 1996 as reference values and observed a larger decline in mental health from 2018 to 2021, than from 1996 to 2018. This gives an indication that the pandemic may have caused an additional decline of mental health, over and above the historical decline. Moreover, comparing scores to norm groups was not our primary goal in analyses; we used our own groups as a reference and performed comparisons between, for instance, people with and without a chronic illness.

3.2. Implications beyond the pandemic

During the initial outbreak of the coronavirus, people with an IRD were considered to be at high risk of getting infected by the coronavirus[65]. After the peak period, the results regarding the impact of immunosuppressants on COVID-19 outcomes were mixed, with mostly little to no evidence that patients with an IRD, compared to those without, face more risk of contracting COVID-19, nor that they had a worse prognosis

when they were infected[66,67]. This may have taken away some of their stress and worry. However, in some (very) worried individuals, worry and distress may be or become excessive and turn into an anxiety disorder. To prevent excessive worry, people are advised to read and watch trustworthy, fact-based information in the media, instead of anxiety-provoking information[68] and in case of anxiety disorder, people should try to find appropriate professional help[9]. The results of **chapter 2** indicate that treatment as usual will do for most patients with an IRD. However, for individual patients who do experience poorer health due to the pandemic, a treatment strategy that includes personalized healthcare, as specified in most treatment recommendations[69,70], is probably most helpful in optimizing their level of adjustment problems, disease outcomes, and risk and resilience factors[71]. Future research could try to find which characteristics could be important, in referring patients to specific (individualized) therapeutic approaches.

This thesis tentatively indicated the importance of the need to fit interventions to the person. It was unexpected that during the pandemic physical health was better in women with fibromyalgia and in young adults with a chronic illness and low psychological flexibility. This raises the question whether a therapeutic approach aimed at increasing psychological flexibility might show different effects for those with low or high psychological flexibility, which could be investigated in existing interventions, because often psychological flexibility is monitored during these interventions. Perhaps our results make it worthwhile to also examine whether the group with low psychological flexibility could benefit more from an approach that creates an environment with less threats and more soothers[45], while in the group with higher psychological flexibility, an intervention that enhances this exisiting ability, could be more beneficial. Future research could make use of randomized control trials over a longer period, with different interventions, to get insight into what is most helpful for people with a chronic illness and low psychological flexibility. A design offering different treatment approaches to groups simultaniously or a cross-over design, would be methodologically stronger than the usual design comparing an intervention to a waiting-list treatment-as-usual group.

This thesis has implications for the research methods, that could be used by future studies in young adults. Even though results from our study are in line with meta-analyses and a handful longitudinal findings, that the pandemic is linked to poorer mental health in young adults[72,73,74,75,76], most studies lack a large-scale, repeated cross-sectional design, or a longitudinal cohort design with pre-pandemic assessments. In young adulthood, personal values, beliefs and life goals are in development, intimate relationships with other people are formed, and people develop in terms of education and work[77]. The governmental measures, with lockdowns and social isolations, seem to have had a detrimental effect on their mental health[72,75] and they could have, among others, disrupted young adults' common development, e.g., in terms of exploration of values, goals and relationships. Our results tentatively indicated that, on average, mental and physical health was poorer during, compared to before the pandemic. Research of large-scale longitudinal data from before, during and also after the pandemic, might give us a clearer insight

into the long-term or specific consequences of the pandemic for mental and physcial health of young adults. For instance, the Adolescent Brain and Cognitive Development (ABCD) longitudinal cohort study that started with baseline assessments before the COVID-19 pandemic could be used to get this insight[78].

Different governments took different safety measures to prevent the spread of the virus when vaccines were not yet available. Research that assessed the effectiveness of interventions to mitigate the spread the virus (other than vaccines), indicated that curfews, national lockdowns and the closing of educational institutions were effective in the initial acute phase of the pandemic[79,80]. However, it was suggested that these measures also had negative consequences on young adults' mental health[80], as indicated in our study in young adults, including the prolonged phase of the pandemic. Research comparing the effectiveness of interventions by different European governments in the prolonged phase of the pandemic, indicated that strictest limits on the size of public gatherings, remain effective tools for infection control in an ongoing pandemic. However, they indicated too that educational institutions, with appropriate safety measures, could have been made considerably safer, than they were in the acute phase[81]. It is suggested that closing of schools could have been avoided, if effective safety protocols were in place[81], which in turn might have been beneficial for young adults, as schools, among others, facilitate in the exploration of values and relationships. Not only the closing of schools, but also bars, sport- and night clubs and the limited possibilities of visiting family and friends might have had an effect on the life and perhaps the common development of young adults. The duration and implication of these safety measures differed among countries[81] and further research could compare the variety of measures that were initiated by governments. The aim could be to determine which measures were effective in preventing the spread of the virus, but at the same time had the least negative effects on mental and physical health.

Box 2. Implications

This thesis yielded implications for researchers and practitioners:

- During a pandemic, treatment as usual will do for most patients with an inflammatory rheumatic disease or central sensitivity syndrome.
- The mental and physical health of young adults, either with or without a chronic illness, was low during the pandemic. This suggests that ongoing research of their health is important and that enhancement of their health should be a priority in health policy.
- More research should be devoted to discover what psychological flexibility, as measured with a questionnaire, exactly reflects. It is likely that it only partly reflects the processes or skills as intended by the original definition.
- Future research in post-pandemic society, could compare an intervention enhancing psychological flexibility to one focused on creating a less demanding and calmer life, to discover which is most effective in enhancing physical health of women with fibromyalgia and of young adults with a chronic illness and low psychological flexibility.
- The FIT-18 is a succinct questionnaire that can be easily and quickly applied in research and clinical practice. If good psychometric properties including divergent validity are confirmed, the questionnaire can be used to inform, monitor and evaluate therapy.

3.3. Concluding remarks

This thesis aimed to better understand the mental and physical health of people with and without chronic illnesses during the COVID-19 pandemic. In the early stages of the pandemic, many media and professional literature reported that the psychological impact of the pandemic was huge. We indeed observed that participants in our studies were worried about getting infected by the coronavirus. However, beyond this probably natural reaction to an actual threat, our results indicated that the psychological impact of the pandemic was modest for people with an IRD or CSS and that treatment as usual will do for most of them. For women with fibromyalgia physical health was even better during the pandemic, which tentatively indicates that in post-pandemic society they might benefit from management focused on creating a less demanding and calmer life. In young adults, especially mental health was lower during, than before the pandemic. Future research should monitor their development and mental health closely.

Overall, this thesis implies that, with exception of young adults, people were perhaps mentally and physically healthier than expected during the pandemic. The expected larger health-preserving role of psychological flexibility, in worse times of

the pandemic and in people with a chronic illness, was hardly confirmed. This suggests that more nuanced research is needed, regarding interventions that could support people with low flexibility in putting up with life after the pandemic.

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Appendices

Samenvatting (Dutch summary)

Rampen en crises bieden een unieke mogelijkheid om in het dagelijkse leven de effecten van stress op gezondheid te onderzoeken. In de afgelopen jaren beleefden we wereldwijd de coronacrisis. Zowel de kans op besmetting van jezelf of je naasten, als de maatregelen die door de regering werden genomen om verspreiding van het virus in te dammen, vormden een bedreiging voor de mentale en fysieke gezondheid. Onderzoek tijdens de pandemie geeft inzicht in de zorgen en stress van mensen en hoe ze omgaan met situaties die moeilijk te veranderen zijn.

Mensen verschillen in de manier waarop ze omgaan met uitdagende omstandigheden, zoals een pandemie. Een vaardigheid die je beter in staat stelt om te leren omgaan met tegenslagen, is psychologische flexibiliteit. Beschikken over psychologische flexibiliteit lijkt vooral nuttig als het tegenzit in het leven, bijvoorbeeld als je chronisch ziek bent of bijvoorbeeld tijdens een pandemie. Het komt tot uiting in het accepteren van onprettige gedachten of ervaringen en je inzetten om een leven te leiden dat voor jou persoonlijk waardevol is.

Dit proefschrift beschrijft onderzoek naar de mentale en fysieke gezondheid tijdens de COVID-19 pandemie bij mensen met en zonder een chronische ziekte. Daarnaast wordt onderzocht of psychologische flexibiliteit ertoe bijdraagt dat de mentale en fysieke gezondheid nog redelijk goed zijn in –wat verondersteld werd als– slechtere omstandigheden.

Voor dit onderzoek zijn op drie momenten gegevens verzameld in de algemene bevolking. Eerst vóór de pandemie, in 2018, en twee keer tijdens de pandemie: tijdens de eerste grote Nederlandse besmettingspiek (2020, de acute fase) en een jaar later, toen het aantal besmettingen opnieuw opliep en de maatregelen door de Nederlandse overheid weer werden aangescherpt (2021, de langdurige fase). Het onderzoek beschreven in hoofdstuk 2 en 3 maakt gebruik van de gegevens van voor de pandemie en uit de acute fase, terwijl voor het onderzoek beschreven in hoofdstuk 4 en 5 tevens gebruik wordt gemaakt van de gegevens die verzameld zijn in de langdurige fase.

Mentale en fysieke gezondheid tijdens een pandemie

In de beginfase van de pandemie werd gedacht dat mensen met een reumatische aandoening, anders dan artrose of fibromyalgie, meer risico zouden lopen op het krijgen van COVID-19. Zij gebruiken immers vaak medicatie die hun afweersysteem onderdrukt, waardoor zij bevattelijker zouden zijn voor infecties; ook de gevolgen van een besmetting zouden erger zijn voor hen. Daarnaast zouden de reumatische ziekte-activiteit en de symptomen kunnen toenemen, onder andere vanwege minder intensieve behandeling, doordat behandelcentra (deels) sloten. In hoofdstuk 2 hebben we onderzocht of mensen met een reumatische aandoening, in vergelijking tot mensen zonder een reumatische aandoening, zich meer zorgen maakten over het krijgen van COVID-19, meer gestresst waren en of dat hun mentaal welbevinden slechter zou zijn tijdens de acute fase van de pandemie. De resultaten lieten zien dat mensen met een reumatische aandoening inderdaad meer zorgen en stress ervoeren dan mensen zonder een reumatische aandoening, maar dat het mentaal welbevinden in beide groepen niet slechter was tijdens, dan voor de pandemie.

Aangezien in de acute fase in de media en vakliteratuur veelvuldig werd gewaarschuwd dat mensen met een reumatische aandoening meer risico zouden

lopen op COVID-19, lijken de grotere zorgen van mensen met een reumatische aandoening een vrij normale reactie op een levensechte bedreiging. Maar als realistische zorgen omslaan in angst, is het advies om de weerbaarheid te verhogen door positieve sociale contacten te blijven onderhouden, geloofwaardige nieuwsartikelen te lezen en professionele hulp te zoeken. Ons onderzoek beschreven in hoofdstuk 2 betreft de acute fase van de COVID-19 pandemie, in 2020. De resultaten laten zien dat het mentaal niet slechter ging met mensen met een reumatische aandoening. Dit duidt erop dat er voor de meeste mensen in zo'n situatie geen extra maatregelen nodig zijn voor behoud van hun mentale gezondheid.

Fibromyalgie, chronisch vermoeidheidsyndroom, en prikkelbaar darmsyndroom zijn aandoeningen die vallen onder de definitie van een centraal sensitiviteitssyndroom (CSS). Bij mensen met een CSS is het brein overgevoelig voor signalen, waardoor pijn en andere lichamelijke symptomen worden versterkt. Bij mensen met een overgevoelig brein zou stress een signaal kunnen zijn, die deze symptomen versterken. We onderzochten dit verband voor stress in reactie op de pandemie. Een hoofdbevinding beschreven in hoofdstuk 3 is dat mensen met een CSS niet méér lichamelijke symptomen hadden tijdens, dan voor de pandemie. Een mogelijke verklaring is dat voor een deel van de mensen de pandemie minder stressvol was dan verwacht; door (gedeeltelijke) lockdown minder werkdruk, meer gelegenheid om hun tijd flexibel in te delen; daarnaast meer erkenning van anderen voor hun ziekte en symptomen. Het onderzoek beschreven hoofdstuk 4 is gericht op vrouwen met fibromyalgie, in de eerste acute fase en in de langdurige fase van de pandemie een jaar later. Uit dit onderzoek komt naar voren dat de mentale en fysieke gezondheid van vrouwen met fibromyalgie niet slechter waren in de groepen tijdens beide fases van de pandemie, in vergelijking met een groep voor de pandemie. Hun lichamelijke gezondheid was tijdens de pandemie gemiddeld zelfs hoger, al was die nog steeds wel minder goed dan die van vrouwen zonder fibromyalgie. De omstandigheden tijdens de pandemie waren mogelijk gunstig voor sommige vrouwen met fibromyalgie. Minder sociale verplichtingen en de mogelijkheid om het leven aan te passen aan hun –in ernst wisselende– symptomen, kunnen onder andere hebben bijgedragen aan de betere fysieke gezondheid. Na de pandemie zou onderzocht kunnen worden of vrouwen met fibromyalgie baat hebben bij een kalmer, minder veeleisend leven.

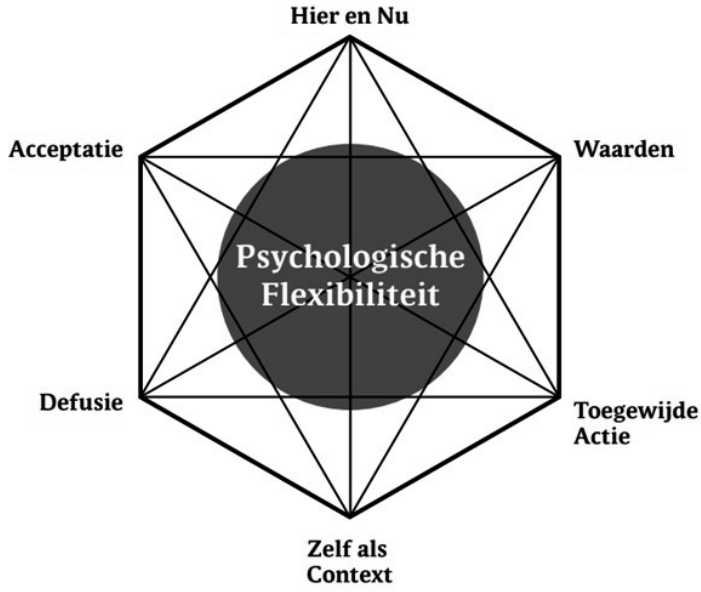
Een andere groep, waarvan het al snel na de uitbraak van het virus duidelijk werd dat die het mentaal moeilijk had, is de groep jongvolwassenen. Resultaten van onderzoek van andere onderzoekers naar hun welbevinden in de beginfase liepen echter sterk uiteen, waarbij een Brits onderzoek rapporteerde dat bijna tweederde van de jongvolwassenen voldeed aan de criteria van depressie of een angststoornis. Er werd in die allereerste onderzoeken echter nauwelijks een vergelijking gemaakt met gegevens van voor de pandemie. Daarnaast was er weinig bekend over hun fysieke gezondheid en al helemaal niet voor jongvolwassenen met een chronische aandoening. In hoofdstuk 5 hebben we de gerapporteerde mentale en fysieke gezondheid van jongvolwassenen met én zonder chronische aandoening beschreven, tijdens de acute én langdurige fase, en die vergeleken met gegevens van een overeenkomstige groep voor de pandemie. Het mentaal welbevinden was vooral minder goed in de groep tijdens de langdurige fase, in vergelijking met de groep voor de pandemie, bij jongvolwassen zowel met, als zonder chronische aandoening. Het fysieke welbevinden was alleen slechter bij jongvolwassen zonder chronische aandoening, terwijl dat zelfs beter was bij jongvolwassenen met een chronische aandoening. Misschien was de laatstgenoemde groep, door hun aandoening, al wat meer bedreven in het omgaan moeilijkheden en tegenslagen, al verklaart dit niet

direct waarom hun fysiek welbevinden beter was tijdens dan voor de pandemie. We hebben onderzocht of psychologische flexibiliteit hierin een rol speelt.

Psychologische flexibiliteit als beschermende factor

Het is belangrijk om te weten hoe mensen ervoor kunnen zorgen dat hun mentale en fysieke gezondheid nog redelijk goed blijven, als de omstandigheden slechter zijn. Psychologische flexibiliteit lijkt nuttig als mensen te maken krijgen met min of meer oncontroleerbare situaties zoals een chronische aandoening of een pandemie. Psychologische flexibiliteit komt tot uiting in zes processen, die met elkaar samenhangen, zoals te zien in het hexaflex-model (figuur 1).

Figuur 1. *De zes processen van psychologische flexibiliteit*. Uit Hayes et al., 2006 (Vertaling: Batink & Delespaul, 2015)



Acceptatie: Ruimte maken voor vervelende emoties, gedachten en gewaarwordingen, in plaats van te proberen deze onder controle te brengen.

Defusie: Gedachten leren zien voor wat ze zijn, niet als waarheden waarnaar gehandeld moet worden (fusie), maar als producten van het verstand.

Zelf als Context: Iemand is meer dan alleen zijn gedachten, gevoelens en zelfbeeld; er is ook nog het observerende zelf dat deze waarneemt.

Hier en Nu: Aandacht hebben voor wat er op dit moment te ervaren is, in plaats van zich vooral richten op het verleden of de toekomst.

Waarden: Stilstaan bij de dingen die iemand echt belangrijk vindt.

Toegewijde Actie: Het eigen gedrag in de gewenste richting aanpassen: handelen naar eigen waarden.

Deze zes processen kunnen onderverdeeld worden in twee grotere groepen: '*acceptatie en mindfulness*' (eerste vier processen) en '*toegewijde actie en gedragsverandering*' (laatste vier processen. Het 'zelf als context' en 'hier en nu' behoren tot beide overkoepelende groepen). Psychologische flexibiliteit zou mensen met een chronische aandoening kunnen beschermen tegen de problemen die zij ervaren vanwege hun aandoening. Acceptance and Commitment Therapy (ACT) is een behandelvorm, die psychologische flexibiliteit beoogt te vergroten.

In Nederland is een vragenlijst ontwikkeld om de zes processen van psychologische flexibiliteit te meten: de FIT-60 (Flexibiliteits Index Test-60). Aangezien de zes processen met elkaar samenhangen, wordt in onderzoek vaak alleen de totaalscore van de FIT-60 gebruikt om psychologische flexibiliteit weer te geven. Dit hebben wij in onze onderzoeken ook gedaan, om te achterhalen of psychologische flexibiliteit een beschermende factor kan zijn voor mensen met een chronische aandoeningen of tijdens een pandemie. Mensen die de FIT-60 invullen, geven regelmatig aan de ze het een vrij lange vragenlijst vinden, die soms lastig te begrijpen is. In **hoofdstuk 6** hebben we daarom onderzoek beschreven of inderdaad alle zes processen met de FIT-60 gemeten kunnen worden en hoeveel vragen daarvoor nodig zijn. We hebben daarbij ook onderzocht of een kortere vragenlijst toepasbaar is, door te onderzoeken of de gerapporteerde gezondheid van mensen met lichamelijke symptomen met een kortere vragenlijst nog steeds beter is, als ze psychologisch flexibeler zijn. Ons onderzoek, gericht op hoe de 60 vragen samengevat konderen worden, liet twee groepen van vragen zien. De ene groep bestond uit 12 vragen die '*accepatie en mindfulness*' meten en de andere groep uit 6 vragen die '*toegewijde actie en gedragsverandering*' meten. Samen vormen deze 18 vragen de *FIT-18* vragenlijst. Mensen met lichamelijke symptomen die hoger scoorden op de 'acceptatie en mindfulness' vragen, hadden een beter mentaal welbevinden. Het lijkt er dus op dat psychologische flexibiliteit het mentale welbevinden beschermt als sprake is van ernstiger lichamelijke symptomen. In het proefschrift worden voorstellen gedaan voor verder onderzoek naar deze kortere FIT-18 vragenlijst.

Dat psychologische flexibiliteit mogelijk een beschermende rol kan spelen tegen de afname van gezondheid is dus wél af te leiden uit de resultaten van hoofdstuk 6, maar niet uit resultaten beschreven in de andere hoofdstukken. Onze verwachting was dat psychologische flexibiliteit vooral een beschermende rol zou kunnen spelen onder *ongunstige* omstandigheden en bij mensen *met* een chronische aandoening. We stelden echter vast dat er een samenhang was van meer psychologische flexibiliteit met betere gezondheid in de groep *voor* de pandemie (hoofdstuk 2), en bij mensen *zonder* chronische aandoening (hoofdstuk 3); dus juist onder omstandigheden die *gunstiger* lijken te zijn voor de gezondheid. Jongvolwassenen *met* een chronische aandoening en *lage* psychologische flexibiliteit, rapporteerden zelfs betere fysieke gezondheid *tijdens* de pandemie (hoofdstuk 5).

Het is mogelijk dat er in de acute fase (hoofdstuk 2 & 3) geen beschermende rol van psychologische flexibiliteit gevonden kon worden, doordat het mentale welbevinden in die fase niet slechter was; er viel als het ware weinig te beschermen. Voor het onderzoek beschreven in hoofdstuk 4 en 5 maakten we gebruik van gegevens uit de langdurige fase. Toen waren het mentaal en fysiek welbevinden van jongvolwassenen inderdaad minder goed dan voor pandemie. Toch vonden we daarbij geen aanwijzingen voor een beschermende rol van psychologische flexibiliteit en in hoofdstuk 5 zelfs eerder het tegenovergestelde bij jongvolwassenen met een chronische aandoening. Onderzoek om deze onverwachte uitkomsten te verklaren hebben we niet kunnen doen, maar een mogelijke verklaring kan liggen in de

gevolgen van maatregelen, zoals lockdowns. Het leven tijdens de pandemie was misschien minder veeleisend; jongvolwassenen met een chronische aandoening zouden hun werk flexibeler kunnen indelen en hadden minder sociale verplichtingen, waardoor ze mogelijk meer rust konden nemen als hun aandoening opspeelde. Het 'normale' leven lijkt veeleisend te zijn voor de huidige generatie jongvolwassenen, vooral voor degenen met een chronische aandoening. Als je dan minder 'mindful' bent en vervelende emoties moeilijk kunt accepteren, dan kan het leven soms overweldigend zijn. Verder onderzoek zou zich kunnen richten op de vraag of deze groep jongvolwassenen, na de pandemie, meer baat zou kunnen hebben bij het aanleren van meer psychologische flexibiliteit of bij een behandelvorm die zich richt op het creëren van een kalmer, minder veeleisend, leven.

Over de methoden

Doordat in dit onderzoek op drie momenten de gegevens zijn verzameld, waren wij in staat om het welbevinden en psychologische flexibiliteit op twee momenten tijdens de pandemie met voor de pandemie te vergelijken. Veel andere onderzoeken konden dit niet doen, doordat ze alleen gegevens verzamelden tijdens de pandemie. Daarnaast hebben veel mensen met een chronische aandoening meegedaan aan ons onderzoek, wat ons tevens in staat heeft gesteld om de gezondheid van mensen met en zonder een chronische aandoening te vergelijken. Toch zit er ook een zwakte in dit onderzoek. De verzamelde gegevens zijn van verschillende groepen mensen en niet van dezelfde personen op drie tijdstippen. We weten niet in hoeverre de resultaten van het onderzoek te maken hebben met het uitvoeren van metingen in verschillende groepen mensen. Onderzoek, waarbij een groot aantal mensen over langere tijd gevolgd worden, kan beter inzicht bieden in de verandering van gezondheid van mensen en hoe zij omgaan met een pandemie of andere rampen en crises. Echter, het is geruststellend om te zien dat onze resultaten in lijn zijn met bevindingen uit recente onderzoeken, die wel dezelfde mensen over langere tijd volgden.

Gevolgtrekkingen

- Tijdens een pandemie lijken er geen aanvullende maatregelen nodig om de mentale en fysieke gezondheid van mensen met een reumatische aandoening of centraal sensitiviteitssyndroom te waarborgen.
- De mentale en fysieke gezondheid van jongvolwassenen zijn laag tijdens de pandemie. Dit geldt zowel voor jongvolwassenen met als zonder chronische ziekte, met één uitzondering: jongvolwassenen met een chronische aandoening en lage psychologische flexibiliteit hadden een beter fysiek welbevinden tijdens de pandemie. Meer en langlopend onderzoek naar de gezondheid van jongvolwassenen is belangrijk en beleid moet gericht zijn op behoud van hun gezondheid tijdens een pandemie.
- Meer onderzoek zou gedaan kunnen worden naar wat de uitkomsten van een vragenlijst die psychologische flexibiliteit meet precies weergeven. Het is mogelijk dat niet alle processen –zoals ze zijn weergegeven in de originele definitie– kunnen worden gemeten.
- Om te zien wat het meest effectief is voor mensen met fibromyalgie en voor jongvolwassenen met een chronische aandoening die weinig psychologische flexibel zijn, zou onderzoek na de pandemie twee behandelvormen kunnen vergelijken: therapie die psychologische flexibiliteit vergroot en een behandelvorm die zich richt op het creëren van een kalmer, minder veeleisend, leven.
- De FIT-18 is een beknopte vragenlijst die gemakkelijk toegepast kan worden, zowel in onderzoek als de klinische praktijk. Verder onderzoek naar wat de vragenlijst precies meet is nodig.

Slotopmerking

Dit proefschrift had als doel om de mentale en fysieke gezondheid van mensen met en zonder chronische ziekten in kaart te brengen tijdens de COVID-19 pandemie. In het begin van de pandemie meldden media en vakliteratuur herhaald dat de gevolgen van de pandemie voor de mentale gezondheid zeer nadelig waren. We zagen in ons onderzoek wel dat de deelnemers aan onze onderzoeken wat meer gestresst waren en zich zorgen maakten om besmet te raken met het coronavirus. Maar, afgezien van deze waarschijnlijk vrij natuurlijke reactie op een levensechte dreiging, gaven onze resultaten aan dat de gevolgen van de pandemie voor de gezondheid bescheiden waren; ook voor mensen met een chronische aandoening. Het lijkt er daarom op dat voor het merendeel van deze patiënten geen aanvullende maatregelen nodig zijn om de mentale en psychische gezondheid te waarborgen. Voor vrouwen met fibromyalgie was de gerapporteerde fysieke gezondheid nog steeds laag in de groep tijdens de pandemie, maar wel beter dan in de groep voor de pandemie. Buiten de pandemie zou onderzocht kunnen worden of een therapievorm die zich richt op een kalmer en minder veeleisend leven, zoals zij het mogelijk ervoeren tijdens de pandemie, gunstig zou kunnen zijn voor deze groep. Bij jongvolwassenen was met name de mentale gezondheid minder goed tijdens, dan vóór de pandemie. Onderzoek zou hun ontwikkeling en mentale gezondheid nauwlettend moeten volgen en beleid in de gezondheidszorg moet erop gericht zijn hun welbevinden te behouden tijdens crises, zoals de pandemie.

Samenvattend kunnen we uit resultaten van dit proefschrift concluderen dat tijdens de pandemie, met uitzondering van jongvolwassenen, mensen –en specifiek diegene met een chronische aandoening– wat betreft mentale en fysiek gezondheid er

minder slecht aan toe waren dan we vooraf verwacht hadden. Dat psychologische flexibiliteit een beschermde rol zou kunnen spelen in tijden van een pandemie en bij mensen met een chronische ziekte, kon ons onderzoek niet bevestigen of uitsluiten. Er is verfijnder onderzoek nodig naar hoe psychologische flexibiliteit het beste gemeten kan worden. Dat zou kunnen via (de verbetering van) bestaande vragenlijsten, maar er kan ook gedacht worden aan andere meetmethoden die mogelijk de dynamische processen van psychologische flexibiliteit beter meten. Daarnaast kan onderzocht worden of –en welke– behandelvormen afgeleid kunnen worden uit de observatie dat mensen met lage psychologische flexibiliteit het relatief goed deden tijdens de pandemie.

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Bedankt!

Tim

Curriculum Vitae

Tim Koppert was born on the 12th of June 1990 in Gouda, The Netherlands. He enjoyed growing up in the city of cheese, while attending a Waldorf school nearby. After graduating high school in The Hague, he decided to study Philosophy and Psychology at Utrecht University. There, his interest in teaching was sparked. Just after achieving his Master's degree in Clinical and Health Psychology in 2016, he started working as a full-time teacher and tutor at Utrecht University. It was in 2018, that he decided to further develop his academic skills. He wanted to research why people stay healthy, even when they are facing challenging circumstances. However, there was no ready to roll project that matched his wishes and he approached professor Rinie Geenen for a position as an external PhD candidate, because at the same time he had started working as a teacher at Leiden University. This meant he had perform his research in his leisure time. While the first steps were taken towards a research proposal, the world was startled by the outbreak of the COVID-19 pandemic. On the evening that the then Dutch Prime Minister addressed the nation on television, he knew where his project was heading and from there on, his PhD research project began to take shape. He wanted to know how people were dealing with this public health crisis and aimed to better understand the mental and physical health of people with and without chronic illnesses during the COVID-19 pandemic. The results of this journey are described in this dissertation. Currently, he lives in Leiden with his wife Anne-Fleur and their two amazing children Philip and Juliëtte. They are expecting a third child next spring.

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Tim Koppert was born on the 12th of June 1990 in Gouda, The Netherlands. After achieving his Master's degree in Clinical and Health Psychology in 2016, he started working as a full-time psychology teacher, first in Utrecht and currently at Leiden University. His PhD research aimed to better understand the mental and physical health of people with and without chronic illnesses during the COVID-19 pandemic.