REVIEW

Annals of Internal Medicine

The Impact of the COVID-19 Pandemic and Associated Control Measures on the Mental Health of the General Population

A Systematic Review and Dose–Response Meta-analysis

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Background: To what extent the COVID-19 pandemic and its containment measures influenced mental health in the general population is still unclear.

Purpose: To assess the trajectory of mental health symptoms during the first year of the pandemic and examine dose–response relations with characteristics of the pandemic and its containment.

Data Sources: Relevant articles were identified from the living evidence database of the COVID-19 Open Access Project, which indexes COVID-19–related publications from MEDLINE via PubMed, Embase via Ovid, and PsycInfo. Preprint publications were not considered.

Study Selection: Longitudinal studies that reported data on the general population's mental health using validated scales and that were published before 31 March 2021 were eligible.

Data Extraction: An international crowd of 109 trained reviewers screened references and extracted study characteristics, participant characteristics, and symptom scores at each timepoint. Data were also included for the following country-specific variables: days since the first case of SARS-CoV-2 infection, the stringency of governmental containment measures, and the cumulative numbers of cases and deaths.

Data Synthesis: In a total of 43 studies (331 628 participants), changes in symptoms of psychological distress, sleep disturbances, and mental well-being varied substantially across studies. On average, depression and anxiety symptoms worsened in the first 2 months of the pandemic (standardized mean difference at 60 days, −0.39 [95% credible interval, −0.76 to −0.03]); thereafter, the trajectories were heterogeneous. There was a linear association of worsening depression and anxiety with increasing numbers of reported cases of SARS-CoV-2 infection and increasing stringency in governmental measures. Gender, age, country, deprivation, inequalities, risk of bias, and study design did not modify these associations.

Limitations: The certainty of the evidence was low because of the high risk of bias in included studies and the large amount of heterogeneity. Stringency measures and surges in cases were strongly correlated and changed over time. The observed associations should not be interpreted as causal relationships.

Conclusion: Although an initial increase in average symptoms of depression and anxiety and an association between higher numbers of reported cases and more stringent measures were found, changes in mental health symptoms varied substantially across studies after the first 2 months of the pandemic. This suggests that different populations responded differently to the psychological stress generated by the pandemic and its containment measures.

Primary Funding Source: Swiss National Science Foundation. (PROSPERO: CRD42020180049)

Ann Intern Med. 2022;175:1560-1571. doi:10.7326/M22-1507 **Annals.org**
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 18 October 2022.

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† For members of the MHCOVID Crowd Investigators, see the Appendix (available at Annals.org).

The World Health Organization and mental health experts have warned about a potential upsurge in mental ill health due to the COVID-19 pandemic and highlighted the need for research into the pandemic's effect (1–3). Quantifying an increase in mental health problems resulting from the pandemic is important for designing public health interventions. These interventions should maximize the benefits of measures to contain the spread of infection while minimizing their potential for harm in mental health problems and disruption of physical and mental health services.

With many studies on the effects of the pandemic on population mental health continually being published, systematic reviews of the literature are needed to make sense of the vast amounts of information. A World Health Organization scientific brief summarized systematic reviews of longitudinal studies estimating the changes in mental health symptoms or prevalence of mental disorders (4). It concluded that there was "a significant increase in mental health problems in the general population in the first year of the pandemic" (4). However, some systematic reviews and individual studies emphasized that the effect of the pandemic and its containment measures had not

See also:

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Supplement

been uniformly detrimental for mental health and that the effect of the pandemic on mental health overall had been limited (5–7).

The results from individual studies in the published systematic reviews varied widely, but the sources of the heterogeneity between studies were not elucidated. Possible reasons for the heterogeneous results include differences in time into the pandemic, the severity of the COVID-19 epidemic in study areas, and the severity of control measures implemented by the authorities.

To better understand the conflicting evidence about changes in mental health during the pandemic, we did a systematic review and Bayesian nonlinear dose–response meta-analysis. We aimed to describe how mental disorder symptoms changed in the general population during the first year of the pandemic and whether these changes were related to the severity of governmental containment measures or the total numbers of reported cases and deaths from COVID-19. Because this was an unprecedented global situation with several unknowns, we did not have specific hypotheses about the direction of the examined associations. We used "crowdsourcing," where trained researchers from 5 continents screened articles and extracted data online, to deal with the extensive literature that has accumulated on this topic over a short period (8).

METHODS

Data Sources and Searches

The protocol of this systematic review was registered with PROSPERO (CRD42020180049) (9). We searched MEDLINE (via PubMed), Embase (via Ovid), and PsycInfo without language restrictions using the living evidence database of the COVID-19 Open Access Project, which used broad search strategies to capture COVID-19–related literature from 1 January 2020 (Section 1.1 of **Supplement 1**, available at Annals.org) (10). The search terms used to populate this database and their bibliography deduplication method are described online (https://ispmbern.github.io/covid-19). We then applied our own search filter (11) to the records in this database. We restricted the search to reports published until 31 March 2021—the end of the first year of the pandemic—before widespread rollout of vaccination programs.

Study Selection

We included studies with participants from the general population that reported data on any mental health condition for at least 2 time points, with at least 1 time point during the pandemic, and used a validated rating scale. We included longitudinal studies (data from the same sample collected over time) and repeated cross-sectional studies (data from different samples drawn from the same population at multiple time points). Studies with participants enrolled on the basis of their gender (such as women) or age group (such as children) were eligible. We excluded studies of specific populations, such as people with a particular condition (for example, diabetes or anxiety disorder), occupation (for example, health care personnel or teachers), or setting (for example, nursing homes). We decided to exclude studies enrolling exclusively patients with COVID-19 as well, because at the time they represented only a small percentage of the population and because their burden in terms of containment measures often differed substantially from that of the rest of the population. We also excluded studies analyzing hospital records or databases of health care use and studies enrolling participants via social media (12). We list detailed inclusion and exclusion criteria and describe how we resolved disagreements in extracted data in Sections 1.3 and 1.4 of **Supplement 1**.

Data Extraction and Other Data Collected

We crowdsourced all screening tasks and the data extraction process by recruiting 109 health care or research professionals (the "crowd") from 28 countries on 5 continents. Crowd members received training and worked in pairs (based on their geographic proximity) using pretested online forms in REDCap (13). The protocol used to train the crowd is described on the project's website (https://mhcovid.ispm.unibe.ch/crowd.html).

We considered only studies that used validated rating scales, and we extracted data on anxiety, depression, alcohol and substance misuse, problematic social media and smartphone use, sleep disturbances, quality of life, life satisfaction, and mental (or psychological) well-being. Scales measuring more than 1 condition (such as anxiety and depression) or assessing general symptoms of mental ill health were considered under the category "psychological distress." We extracted the mean score, its SD, and the sample size for each time point separately for each scale. For every time point with data, we defined the following 4 exposure variables:

Time point in the pandemic: Days elapsed between the date of the first case of SARS-CoV-2 infection recorded in a country and the time point of data collection.

Stringency of the containment measures: Score on the Oxford COVID-19 Government Response Tracker index (0 to 100) representing the stringency of governmental containment and closure policies and a cumulative sum of stringency scores at each time point (14). We also examined the economic support index, the containment and health index, and separate components of these indices (school closing, workplace closing, stay-at-home requirements, and restrictions on internal movement and facial covering) in post hoc analyses (Section 3 of **Supplement 2**, available at Annals.org) (14).

Cumulative cases: The cumulative number per 100 000 people of confirmed reported cases of SARS-CoV-2 infection at the time point of data collection in the study country since the date of the first case recorded in that country.

Cumulative deaths: The cumulative number per 100 000 people of reported COVID-19–related deaths at the time point of data collection in the study country since the date of the first case of SARS-CoV-2 infection recorded in that country.

We extracted data on study characteristics (data collection method, country, and study design) and participant characteristics (age, gender, ethnicity, and percentage with preexisting conditions or COVID-19). We also recorded data on gross domestic product per capita and the Gini inequality index in 2019 for each of the included countries.

Table 1. Characteristics of the Included Studies

Characteristic	Systematic Review		Dose–Response Meta-analysis	
	Studies, *n* (%)	Time Points, *n* (%)	Studies, *n* (%)	Time Points, *n* (%)
Total	43 (100)	153 (100)	24 (100)	85 (100)
Population				
Adults	30 (69.8)	99 (64.7)	14 (58.3)	49 (57.6)
Elderly persons	6 (14.0)	20 (13.1)	5 (20.8)	16 (18.8)
Adolescents and adults	2 (4.7)	10 (6.5)	2 (8.3)	8 (9.4)
Adolescents	2 (4.7)	12 (7.8)	2 (8.3)	10 (11.8)
Children	3 (7.0)	12 (7.8)	1 (4.2)	2 (2.4)
Condition				
Depression	24 (55.8)	55 (35.9)	24 (100.0)	55 (64.7)
Anxiety	14 (32.6)	30 (19.6)	14 (58.3)	30 (35.3)
Psychological distress	12 (27.9)	32 (20.9)	–	–
Mental well-being	6 (14.0)	16 (10.5)	–	–
Sleep disturbance	4 (9.3)	8 (5.2)	–	–
Other conditions*	6 (14.0)	12 (7.8)	–	–
Design				
Cross-sectional	30 (68.9)	106 (69.3)	18 (75.0)	63 (74.1)
Longitudinal	13 (39.2)	47 (30.7)	6 (25.0)	22 (25.9)
Risk for unrepresentative sample				
Low	11 (25.6)	83 (54.2)	3 (12.5)	51 (60.0)
Unclear	10 (23.3)	44 (28.8)	7 (29.2)	17 (20.0)
High	22 (51.2)	26 (17.0)	14 (58.3)	17 (20.0)
Risk of information bias				
Low	38 (88.4)	19 (12.4)	20 (83.3)	11 (12.9)
Unclear	1 (2.3)	128 (83.7)	1 (4.2)	68 (80.0)
High	4 (9.3)	6 (3.9)	3 (12.5)	6 (7.1)
Risk of nonresponse bias				
Low	8 (18.6)	53 (34.6)	5 (20.8)	13 (15.3)
Unclear	15 (34.9)	29 (19.0)	12 (50.0)	18 (21.2)
High	20 (46.5)	71 (46.4)	7 (29.2)	54 (63.5)
Country				
United States	10 (23.3)	37 (24.2)	7 (29.2)	25 (29.4)
United Kingdom	8 (18.6)	30 (19.6)	4 (16.7)	18 (21.2)
China	5 (11.6)	20 (13.1)	2 (8.3)	6 (7.1)
Germany	5 (11.6)	21 (13.7)	3 (12.5)	14 (16.5)
Spain	4 (9.3)	12 (7.8)	3 (12.5)	6 (7.1)
Australia	2 (4.7)	10 (6.5)	2 (8.3)	8 (9.4)
Japan	2 (4.7)	4 (2.6)	1 (4.2)	2 (2.4)
Other†	7 (16.3)	19 (12.4)	2 (8.3)	6 (7.1)
Data collection				
Online questionnaire	31 (72.1)	110 (71.9)	17 (70.8)	60 (70.6)
Other data collection‡	12 (27.9)	43 (28.1)	7 (29.2)	25 (29.4)

* 1 study each, with 2 time points on internet gaming disorder, life satisfaction, post-traumatic stress disorder, problematic smartphone application use, problematic social media use, and somatoform disorder.
† 1 study each from Chile, the Czech Republic, Denmark, Austria/Switzerland/Germany, Israel, Italy, and the Netherlands.
‡ Interviews (online or telephone) and postal questionnaires alone or in combination with online questionnaires.

Section 2 of Supplement 2 provides details on variables and sources of information.

Risk of Bias Assessment

We developed a new tool to assess risk of bias in the included studies (Section 4.1 of Supplement 2). We examined items included in published instruments for prevalence studies and grouped them into categories according to the bias domain they address. We developed specific questions to evaluate how well the study sample represented the general population, the risk of nonresponse bias, and the risk of information bias. Each domain was judged to have low, high, or unclear risk of bias. Three investigators (N.P., G.S., and T.T.) piloted the instrument. We produced contour-enhanced funnel plots to explore possible publication bias (15).

Data Synthesis and Analysis

We estimated the standardized mean differences (SMDs) in symptom scores between the earliest reported time point (for example, a prepandemic measurement) and all subsequent time points reported in a study (for

example, several measurements during the pandemic). A negative SMD meant that mental health worsened over time. We accounted for correlations between SMDs in studies reporting more than 2 time points and more than 1 condition using a multivariate normal likelihood. All models were fitted within a Bayesian framework as hierarchical random-effects models using JAGS in R, version 4.0.4 (16, 17). We present the posterior means, 95% credible intervals (CrIs), and 95% prediction intervals (PrIs) (18). Prediction intervals show the range of expected SMDs for any hypothetical study population similar to those in included studies. When interpreting the results, we distinguished between the average summary SMD from the meta-analysis and the expected SMDs shown in the range of the PrI. We estimated between-study heterogeneity by considering the SD of the random effects (τ) and the width of the PrI rather than the I^2 metric (18, 19). To enhance interpretation, we transformed summary SMDs into mean differences on the Patient Health Questionnaire-9 scale for depression and on the General Anxiety Disorder-7 scale for anxiety, using the observed pooled SDs of a large representative study (20).

We first used studies that report prepandemic scores to estimate a pre- versus during-pandemic summary SMD (henceforth "pre–during"). We used meta-regression to explore the relationship between SMDs and the following study and population characteristics: mean age, gender, risk of bias, sample size, timing of collection of prepandemic data, country (United States vs. China vs. other), gross domestic product per capita, and Gini index. We had planned to explore the role of preexisting physical and mental health conditions, but too few studies had relevant information.

We then used all studies (including those that provided data only during the pandemic) to model the trajectories in SMDs as nonlinear functions of each exposure variable. We synthesized study data in a Bayesian dose–response meta-analysis model with restricted cubic splines (21–23). Some exposure variables (such as cumulative cases) required log transformation. In sensitivity analyses, we used an alternative definition for days elapsed since the start of the pandemic: since 1 January 2020 in China and Hong Kong and 1 March 2020 for the rest of the world. We extended the model to include the linear effects of study and population characteristics. The statistical details of the analysis are presented in Section 5 of **Supplement 2**. We fitted all models with uninformative priors for summary SMDs and minimally informative priors for heterogeneity and regression coefficients (Section 5.9 of **Supplement 2**). To evaluate the convergence of the models, we monitored the mixing in trace plots with 3 different chains and the Gelman–Rubin statistic (24).

Certainty of the Evidence

For the pre–during meta-analysis, we used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to evaluate certainty in the evidence synthesis results, adapting the guidance for prognostic studies (25). There is no current guidance about how to evaluate certainty in a dose–response meta-analysis, so we adapted the GRADE guidance to our context (Section 4.2 of **Supplement 2**).

Role of the Funding Source

The Swiss National Science Foundation had no role in study design, data collection, data analysis, data interpretation, or writing and submission of the manuscript.

RESULTS

The flow of study selection is shown in the **Appendix Figure** (available at Annals.org). Overall, we included 43 studies with data from 331 628 participants and 153 combinations of conditions and time points (evidence profiles of the studies are in Section 10 of **Supplement 2**) (7, 20, 26–67). The 43 studies were done in 13 countries

Table 2. Characteristics of Study Participants, Countries, and the COVID-19 Epidemic

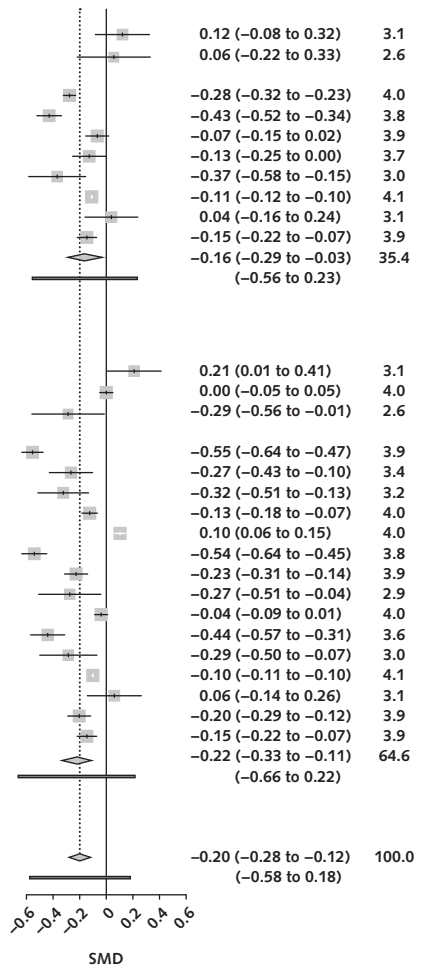
Characteristic	Systematic Review (43 Studies)		Dose–Response Meta-analysis (24 Studies)	
	Time Points With Data, *n*	Median (Range)	Time Points With Data, *n*	Median (Range)
Participant characteristics				
Participants, *n**	153	1035 (38–159 573)	85	721 (53–159 573)
Mean age, *y*	141	42 (5–75)	81	40 (7–75)
Female gender, %	151	55 (35–76)	85	62 (35–76)
Country characteristics†				
Gross domestic product per capita. *U.S. dollars*	151	46 406 (16 092–62 630)	85	49 455 (16 092–62 630)
Gini index	151	35 (25–44)	85	35 (25–44)
Days since first recorded COVID-19 case	151	87 (6–276)	85	89 (10–252)
COVID-19 epidemiology and response†				
Cumulative COVID-19 cases per 100 000 persons	104	186 (0–2701)	60	168 (0–2701)
Cumulative COVID-19 deaths per 100 000 persons	104	8 (0–75)	60	8 (0–75)
Stringency index	104	73 (0–94)	60	73 (11–85)
Economic support index	104	62 (0–100)	60	62 (0–100)
Containment and health index	104	63 (17–85)	60	62 (17–76)

* Average number of study participants over all time points and conditions.
† The description of the variables includes only time points during the pandemic; prepandemic values are all 0. One study combined data from Germany, Austria, and Switzerland (Schäfer et al, 2020 [44]) and was excluded from the summary of the variables.

Figure 1. Forest plot of SMDs of symptoms during the pandemic minus before the pandemic for anxiety and depression (*A*) and for other conditions, mental well-being, and life satisfaction (*B*).

A

Study, Year (Reference)	Country	Population	Sample Size, *n*	Proportion Female	Information Bias	Nonresponse Bias	Days in Pandemic, *n*	SMD (95% CrI)	Weight, %
Anxiety									
Lau et al, 2021 (31)	United Kingdom	Adolescents	97	0.64	Low risk	Unclear risk	30	0.12 (−0.08 to 0.32)	3.1
Schützwohl and Mergel, 2020 (61)	Germany	Adults	53	0.76	Low risk	Low risk	69	0.06 (−0.22 to 0.33)	2.6
Kwong et al, 2021 (48)	United Kingdom	Adults	1811	0.73	Low risk	High risk	87	−0.28 (−0.32 to −0.23)	4.0
Hawes et al, 2021 (45)	United States	Adolescents, adults	451	0.65	Low risk	High risk	89	−0.43 (−0.52 to −0.34)	3.8
Sharman et al, 2021 (42)	United Kingdom	Adults	1028	0.72	Low risk	Unclear risk	90	−0.07 (−0.15 to 0.02)	3.9
Magson et al, 2021 (55)	Australia	Adolescents	248	0.51	Low risk	Unclear risk	104	−0.13 (−0.25 to 0.00)	3.7
Krendl and Perry, 2021 (63)	United States	Elderly	87	0.53	Low risk	Low risk	105	−0.37 (−0.58 to −0.15)	3.0
Peters et al, 2020 (20)	Germany	Adults	113 928	0.52	Low risk	High risk	108	−0.11 (−0.12 to −0.10)	4.1
Lau et al, 2021 (31)	United Kingdom	Adolescents	99	0.64	Low risk	Unclear risk	121	0.04 (−0.16 to 0.24)	3.1
Herrera et al, 2021 (26)	Chile	Elderly	721	0.70	High risk	Unclear risk	252	−0.15 (−0.22 to −0.07)	3.9
Random-effects summary								−0.16 (−0.29 to −0.03)	35.4
Prediction interval								(−0.56 to 0.23)	
τ = 0.15 (CrI, 0.08 to 0.33)									
Depression									
Lau et al, 2021 (31)	United Kingdom	Adolescents	97	0.64	Low risk	Unclear risk	30	0.21 (0.01 to 0.41)	3.1
Sutin et al, 2021 (32)	United States	Adults	1590	0.46	High risk	Unclear risk	62	0.00 (−0.05 to 0.05)	4.0
Schützwohl and Mergel, 2020 (61)	Germany	Adults	53	0.76	Low risk	Low risk	69	−0.29 (−0.56 to −0.01)	2.6
Novotný et al, 2020 (56)	Czechia	Adults	715	0.53	High risk	High risk	72	−0.55 (−0.64 to −0.47)	3.9
Carvajal et al, 2022 (54)	Spain	Elderly	150	0.35	Low risk	High risk	74	−0.27 (−0.43 to −0.10)	3.4
Giménez–Dasí et al, 2020 (58)	Spain	Children	113	0.42	Low risk	Unclear risk	76	−0.32 (−0.51 to −0.13)	3.2
Wanberg et al, 2020 (62)	United States	Adults	1143	0.56	Low risk	Low risk	87	−0.13 (−0.18 to −0.07)	4.0
Kwong et al, 2021 (48)	United Kingdom	Adults	2219	0.73	Low risk	High risk	87	0.10 (0.06 to 0.15)	4.0
Hawes et al, 2021 (45)	United States	Adolescents, adults	451	0.65	Low risk	High risk	89	−0.54 (−0.64 to −0.45)	3.8
Sharman et al, 2021 (42)	United Kingdom	Adults	1028	0.72	Low risk	Unclear risk	90	−0.23 (−0.31 to −0.14)	3.9
Targa et al, 2021 (38)	Spain	Adults	71	0.75	Low risk	High risk	94	−0.27 (−0.51 to −0.04)	2.9
Sutin et al, 2021 (32)	United States	Adults	1590	0.46	High risk	Unclear risk	95	−0.04 (−0.09 to 0.01)	4.0
Magson et al, 2021 (55)	Australia	Adolescents	248	0.51	Low risk	Unclear risk	104	−0.44 (−0.57 to −0.31)	3.6
Krendl and Perry, 2021 (63)	United States	Elderly	87	0.53	Low risk	Low risk	105	−0.29 (−0.50 to −0.07)	3.0
Peters et al, 2020 (20)	Germany	Adults	113 928	0.52	Low risk	High risk	108	−0.10 (−0.11 to −0.10)	4.1
Lau et al, 2021 (31)	United Kingdom	Adolescents	99	0.64	Low risk	Unclear risk	121	0.06 (−0.14 to 0.26)	3.1
Fujita et al, 2021 (50)	Japan	Elderly	519	0.50	Low risk	Low risk	175	−0.20 (−0.29 to −0.12)	3.9
Herrera et al, 2021 (26)	Chile	Elderly	721	0.70	High risk	Unclear risk	252	−0.15 (−0.22 to −0.07)	3.9
Random-effects summary								−0.22 (−0.33 to −0.11)	64.6
Prediction interval								(−0.66 to 0.22)	
τ = 0.20 (CrI, 0.13 to 0.31)									
Random-effects model								−0.20 (−0.28 to −0.12)	100.0
Prediction interval								(−0.58 to 0.18)	
τ = 0.17 (CrI, 0.13 to 0.25)									
Test for subgroup differences: χ^2_4 = 0.38 (*P* = 0.54)									



(continued)

Studies are ordered by days since the first recorded infection. CrI = credible interval; SMD = standardized mean difference; τ = heterogeneity SD.

(with two thirds done in the United States, the United Kingdom, China, or Germany) (Table 1) and examined 11 conditions. Twenty-four studies (236 705 participants; 85 time points) contributed to the dose–response meta-analysis of depression and anxiety. The prepandemic data were collected as early as 2014, whereas the most recent data were from the end of November 2020.

The median sample size was 1035 participants. The median of the mean participant age was 42 years (range, 7 to 75 years), and more than half of the participants were women. The cumulative COVID-19 cases and deaths and the stringency, economic support, and containment and health indices varied widely across time points (Table 2). Of the 43 studies, 30 were repeated cross-sectional surveys. The risk for an unrepresentative sample and risk of nonresponse bias were high or unclear in most studies. In contrast, most studies showed a low risk of information bias (Table 1).

Meta-analysis of Pre- Versus During-Pandemic Mental Health Symptoms

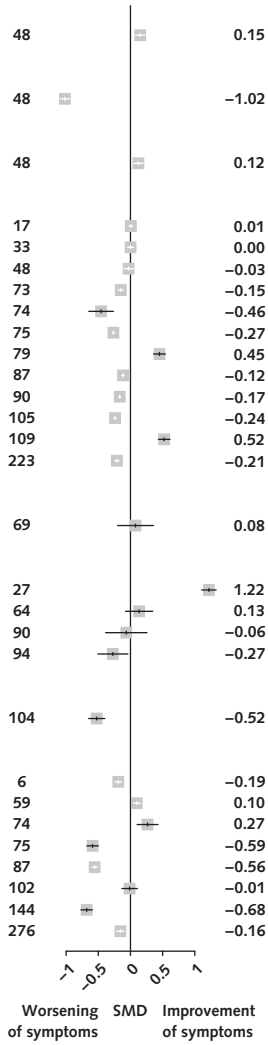
Of the 43 included studies, 31 provided measurements before and during the pandemic and contributed 54 SMDs to the pre-during meta-analysis. The summary SMD for anxiety was −0.16 (95% CrI, −0.29 to −0.03; 95% PrI, −0.56 to 0.23; 1.6 [CrI, 0.3 to 2.9] points of change on the General Anxiety Disorder-7 scale); results were similar for depression (SMD, −0.22 [CrI, −0.33 to −0.11; PrI, −0.66 to 0.22; 2.9 {CrI, 1.4 to 4.3} points of change on the Patient Health Questionnaire-9 scale]) (Figure 1, *A*). Synthesis of these 2 conditions indicates an average worsening of symptoms during the pandemic compared with prepandemic levels (SMD, −0.20), albeit with considerable heterogeneity in SMDs resulting in a large PrI (−0.58 to 0.18; common τ = 0.18). In meta-regression analyses, none of the study and population characteristics in Tables 1 and 2 explained the heterogeneity and

Figure 1–Continued.

B

Study, Year (Reference)	Country	Population	Sample Size, *n*	Proportion Female	Information Bias	Nonresponse Bias	Days in Pandemic, *n*	SMD (95% CrI)
Internet gaming disorder								
Chen et al, 2020 (46)	China	Children	2026	0.51	High risk	High risk	48	0.15 (0.08 to 0.23)
Problematic smartphone application use								
Chen et al, 2020 (46)	China	Children	2026	0.51	High risk	High risk	48	−1.02 (−1.10 to −0.94)
Problematic social media use								
Chen et al, 2020 (46)	China	Children	2026	0.51	High risk	High risk	48	0.12 (0.05 to 0.20)
Psychological distress								
van der Velden et al, 2020 (30)	Netherlands	Adults	3983	0.51	Low risk	Low risk	17	0.01 (−0.02 to 0.04)
Schäfer et al, 2020 (44)	Germany, Austria, Switzerland	Adults	1514	0.54	Low risk	Low risk	33	0.00 (−0.05 to 0.05)
Chen et al, 2020 (46)	China	Children	2026	0.51	High risk	High risk	48	−0.03 (−0.10 to 0.04)
Kikuchi et al, 2020 (36)	Japan	Adults	2078	0.51	Low risk	High risk	73	−0.15 (−0.19 to −0.11)
Meseguer de Pedro et al, 2021 (33)	Spain	Adults	198	0.55	Low risk	Low risk	74	−0.46 (−0.65 to −0.26)
Xue and McMunn, 2021 (43)	United Kingdom	Adults	15 426	0.58	Low risk	High risk	75	−0.27 (−0.28 to −0.25)
Ahrens et al, 2021 (39)	Germany	Adults	523	0.69	Low risk	High risk	79	0.45 (0.36 to 0.54)
Pierce et al, 2021 (7)	United Kingdom	Adults	17 452	0.42	Low risk	High risk	87	−0.12 (−0.14 to −0.09)
Proto and Quintana-Domeque, 2021 (37)	United Kingdom	Adults	14 523	–	Low risk	High risk	90	−0.17 (−0.18 to −0.15)
Xue and McMunn, 2021 (43)	United Kingdom	Adults	14 150	0.58	Low risk	High risk	105	−0.24 (−0.26 to −0.22)
Ahrens et al, 2021 (39)	Germany	Adults	523	0.69	Low risk	High risk	109	0.52 (0.43 to 0.61)
Wang et al, 2021 (35)	China	Older adults	2785	0.64	Low risk	Low risk	223	−0.21 (−0.25 to −0.17)
Somatoform disorder								
Schützwohl and Mergel, 2020 (61)	Germany	Adults	53	0.76	Low risk	Low risk	69	0.08 (−0.20 to 0.36)
Sleep disturbance								
Liu et al, 2020 (51)	China	Children	1619	0.50	Low risk	Low risk	27	1.22 (1.11 to 1.33)
Gao and Scullin, 2020 (59)	United States	Adults	86	0.45	Low risk	High risk	64	0.13 (−0.08 to 0.35)
Sella et al, 2021 (57)	Italy	Adults	38	0.53	Low risk	High risk	90	−0.06 (−0.39 to 0.26)
Targa et al, 2021 (38)	Spain	Adults	71	0.75	Low risk	High risk	94	−0.27 (−0.51 to −0.04)
Life satisfaction								
Magson et al, 2021 (55)	Australia	Adolescents	248	0.51	Low risk	Unclear risk	104	−0.52 (−0.65 to −0.40)
Mental well-being								
Sønderskov et al, 2021 (67)	Denmark	Adults	2458	0.53	Low risk	Unclear risk	6	−0.19 (−0.24 to −0.14)
Sønderskov et al, 2021 (67)	Denmark	Adults	2149	0.53	Low risk	Unclear risk	59	0.10 (0.05 to 0.15)
Carvajal et al, 2022 (54)	Spain	Older adults	150	0.35	Low risk	High risk	74	0.27 (0.10 to 0.43)
Kimhi et al, 2020 (28)	Israel	Adults	906	0.49	Low risk	Unclear risk	75	−0.59 (−0.68 to −0.50)
Kwong et al, 2021 (48)	United Kingdom	Adults	2231	0.73	Low risk	High risk	87	−0.56 (−0.60 to −0.52)
Kuehner et al, 2020 (52)	Germany	Adults	716	0.57	Low risk	High risk	102	−0.01 (−0.13 to 0.11)
Kimhi et al, 2020 (28)	Israel	Adults	906	0.49	Low risk	Unclear risk	144	−0.68 (−0.77 to −0.59)
Sønderskov et al, 2021 (67)	Denmark	Adults	1554	0.53	Low risk	Unclear risk	276	−0.16 (−0.22 to −0.10)

Test for subgroup differences (fixed effect): $\chi^2_7 = 1119.10$ ($P < 0.01$)
Test for subgroup differences (random effects): $\chi^2_7 = 624.77$ ($P < 0.01$)

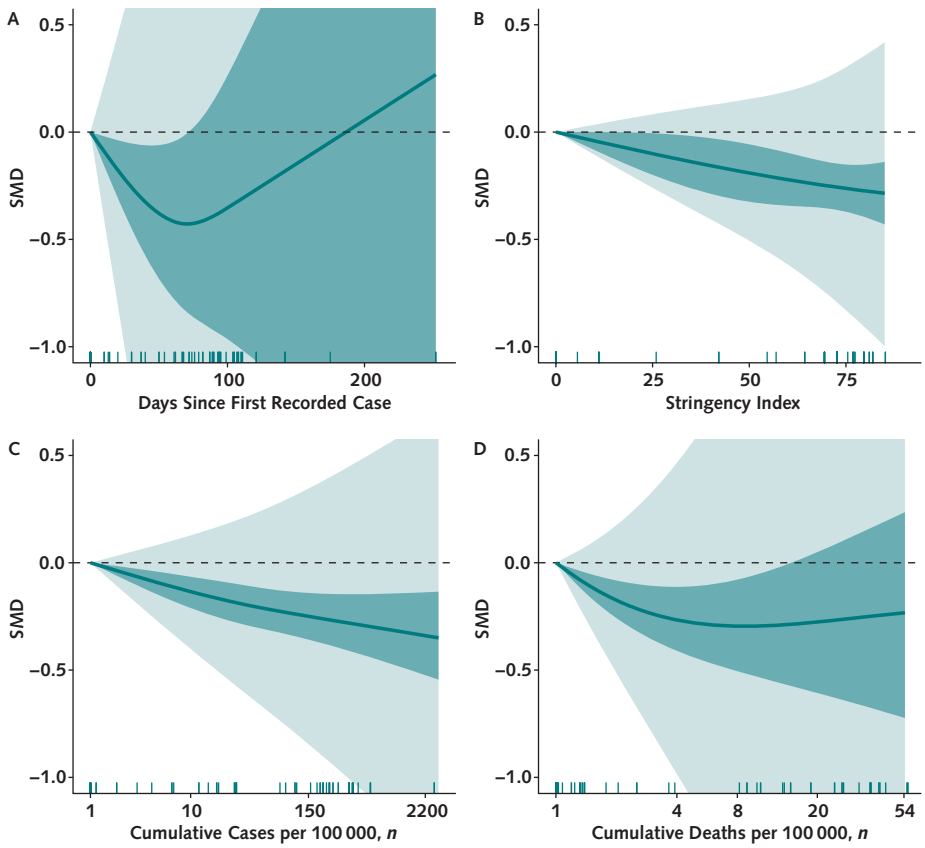


there was no evidence of an association between sample size and results (Section 2.1.2 of Supplement 1). The certainty of the evidence for the pre–during analysis for anxiety and depression was low, primarily because of the risk of bias in included studies and the high heterogeneity (see the summary of findings table in Section 2.1.6 of Supplement 1). The data for psychological distress were highly heterogeneous, with expected SMDs showing both important deterioration and alleviation of symptoms in study populations (PrI, −1.13 to 0.77) (Figure 1, *B*; Section 2.1.3 of Supplement 1). In meta-regressions, there was no evidence that any of the variables explained this heterogeneity. A potential reason is that scales for measuring personal distress are inherently more heterogenous than depression and anxiety scales. Whatever the reason, we decided to not synthesize the data. For the other conditions, the data were sparse, heterogeneous, or both, and we did not pursue any further synthesis. The only study on posttraumatic stress disorder did not provide prepandemic measurements.

Dose–Response Meta-analysis for the Longitudinal Trajectory of Symptoms of Anxiety and Depression

We performed dose-response meta-analysis only for the studies on anxiety and depression (24 studies; 85 condition-time points) (Table 1) because the estimated heterogeneity in the other conditions was too large. Figure 2 (panel A) shows the SMDs for anxiety and depression combined as a function of days since the first recorded case. The association had a U shape, with the lower point at about 60 days. The average symptoms worsened until up to 2 months, but with large uncertainty around the mean (SMD at 30 days, −0.24 [CrI, −0.45 to −0.04]; SMD at 60 days, −0.39 [CrI, −0.76 to −0.03]). After 2 months,

Figure 2. Dose–response meta-analysis plots of SMDs for symptoms of anxiety and depression as a function of days since the first case in the study country (*A*), the stringency index (*B*), cumulative number of cases (*C*), and cumulative number of deaths (*D*).



Dark green shading indicates credible regions, and light green shading indicates prediction regions. SMD < 0 means that the symptoms worsen over time. SMD = standardized mean difference.

the slope became flatter, with even larger uncertainty, because of the small number of studies (SMD at 90 days, −0.38 [CrI, −0.90 to 0.15]). The PrIs calculated around these values were wide, suggesting that the expected trajectories in the study populations differed widely. A sensitivity analysis using a different definition of time elapsed since the beginning of the pandemic produced similar results (Section 6.2.1 of **Supplement 2**). We did 2 post hoc sensitivity analyses, including data only up to 120 days after the first case was recorded (because few data were available after this time point) and including only studies done in the Northern Hemisphere (where summer began approximately 3 months into the pandemic). Neither of these post hoc sensitivity analyses changed the interpretation of our results.

The association between the stringency index and depression and anxiety symptoms was approximately linear (**Figure 2**, *B*). Studies with a high stringency index (that is, >80; four studies from Spain, Chile, and China [26, 27, 38, 57]) showed on average a larger increase in symptoms than studies with a lower stringency index. We estimated median SMDs of stringency index values of 40 and 80 versus 0 to be −0.18 (CrI, −0.30 to −0.03; PrI, −0.42 to 0.11) and −0.27 (CrI, −0.39 to −0.15; PrI, −0.90 to 0.36), respectively.

Standardized mean differences decreased linearly with increasing values in the containment health index and similarly for the economic support index and the individual components, although these variables had small variability across studies and hence provide little information about the shape of association (Section 6.2.2 of **Supplement 2**). Restrictions in movement had the most precise and least heterogeneous detrimental association with anxiety and depression symptoms.

The association between log-cumulative cases and SMD was also almost linear (**Figure 2**, *C*), with the estimated SMDs ranging from −0.22 (CrI, −0.32 to −0.13; PrI, −0.74 to 0.29) for 100 cumulative cases per 100 000 people to −0.35 (CrI, −0.52 to −0.16; PrI, −1.28 to 0.59) for 2000 cumulative cases per 100 000 people. The SMD for 10 cumulative deaths per 100 000 people was −0.30 (CrI, −0.53 to −0.07; PrI, −1.59 to 0.99); for 30 deaths it was −0.25 (CrI, −0.63 to 0.12; PrI, −2.38 to 1.86). The association between cumulative deaths and depression and anxiety symptoms was uncertain, as shown by the increasing width of the CrIs and PrIs in **Figure 2** (panel D).

We performed meta-regression for all 4 dose–response meta-analyses, but we did not consistently identify any variable that could explain heterogeneity in the dose–response associations (Section 2.2.2 of **Supplement 1**). In a post hoc analysis, we fitted a multivariable dose–response model to estimate jointly the effect of the stringency index and the cumulative cases using only linear terms. The model indicated only an association with cumulative cases; the coefficient for the stringency index was close to 0 (Section 6.2.3 of **Supplement 2**). A multivariable model that also included days since the first case had poor convergence to allow any reliable conclusions.

The certainty of the evidence for the examined associations was very low for the pandemic's duration and the cumulative number of deaths (downgraded for within-study limitations, imprecision, and heterogeneity) and low for the stringency index or the cumulative number of cases (downgraded for within-study limitations and heterogeneity) (Section 2.2.3 of **Supplement 1**).

DISCUSSION

In this systematic review of 43 studies, the symptoms of mental health disorders in the general population worsened slightly, on average, during the first 2 months of the pandemic. The estimated and expected changes in symptoms varied in study populations from very detrimental to somewhat beneficial (expected SMDs ranged from −0.58 to 0.18 for anxiety and depression and from −1.13 to 0.77 for psychological distress). The heterogeneity could not be attributed to observed population or country characteristics. In dose–response meta-analyses, depression and anxiety symptoms increased during the first 2 months of the pandemic by up to a summary SMD of −0.39 and were positively associated with the stringency of governmental containment measures and with the cumulative numbers of reported cases and deaths. About half of the included studies had a sample that might not be representative of the general population or had unclear risk of information bias. Because of the heterogeneity and risk of bias in the studies, the certainty of these findings ranges from low to very low.

Strengths of this review include the methods used to quantify, present, and investigate the large amount of heterogeneity using PrIs and meta-regression. We took a conservative stance by refraining from synthesizing very heterogeneous data and by properly distinguishing between inferences about the average effect and expected effects in different study populations. The use of nonlinear dose–response meta-analysis is novel in systematic reviews of the pandemic's effect on mental health. We also developed a new risk of bias tool, tailored to our context, and we present the certainty in our conclusions following a prespecified methodology. The achievement of crowdsourcing the screening and data extraction process at such a large, global scale is another strength. Despite the dedication of more than 100 reviewers, a limitation of our study is the time taken to conduct the study and synthesize the findings up to 31 March 2021. The large number of records to be screened results from the volume of published literature about COVID-19 and the poor specificity of search terms to identify observational epidemiologic studies. We are currently updating our database, doing further analyses, and examining ways to improve the efficiency of the crowd's work to ensure sustainability.

Two previous systematic reviews of longitudinal studies focused on estimating the average effect of the pandemic on mental health, despite the very high heterogeneity between studies (5, 68). Considering only statistical significance or CIs of the average effect, these reviews concluded that the pandemic had a detrimental effect on people's mental health. A rapid systematic review concluded against a uniform effect of the lockdown on mental health (6). Most of the examined associations in these 3 reviews showed a heterogeneity index (I^2) greater than 90%, in which case many meta-analysts would refrain from drawing conclusions based on the summary mean and its statistical significance. In our data synthesis, we used nonlinear dose–response meta-analysis, which is more powerful than standard meta-regression because it can incorporate data from cohorts recruited exclusively during the pandemic; this may explain why Robinson and colleagues (5) did not find any evidence of association between changes in mean symptom score and various exposures.

Although our data showed an overall increase in mental health symptoms from before to during the pandemic, there were a few studies in which symptoms decreased from their prepandemic values. A small study of 99 mainly young people identified by snowball sampling suggested improvement in depression symptoms during the pandemic, and decreased academic stress during the initial phase of the pandemic is a possible explanation (31). A study by Kwong and colleagues (48) was based on a birth cohort with relatively high prevalence of depressive symptoms (25%) before the pandemic. Why this prevalence decreased to 18% during the pandemic remains unclear, and the authors do not provide any explanation.

The observed associations between the exposure variables and changes in mental health symptoms should not be interpreted as causal relationships. The numbers of cases and the stringency of the measures are strongly correlated over time, and it is very difficult to disentangle their effects on mental health. Surges in cases can have a direct detrimental effect on mental health (for example, because of concerns about personal risk or infections of family members and friends) and in most countries prompted an increase in the stringency of containment measures. Strict containment measures may flatten the curve of cases, yielding a potentially positive effect on mental health, while also increasing isolation, intensifying caretaker duties, and creating concerns about the economic consequences of closures, yielding a potentially negative effect on mental health. In addition, fear of the unknown in the face of an unprecedented global crisis and concerns about authoritarian state control may have independently affected public mental health or mediated the effect of the number of cases and the stringency of containment measures.

Estimating the effect of participant-level variables, such as age, gender, and economic situation, without the

risk of aggregation-level bias requires access to individual participant data from the included studies. Because we had access only to aggregated country-level data (for both the outcome and the stringency index), we could not account for individual differences in work and living conditions or for regional variations in policies within countries. For example, persons with young children would be more affected by schools closing, and regions relying economically on tourism would be affected mostly by travel restrictions and restaurant closures. Our findings apply to the general population at the beginning of the pandemic and do not include important developments, such as the Delta variant wave in India. Effective vaccines and treatments became available in 2021, but new SARS-CoV-2 variants of concern have also emerged. These developments, as well as prolonged economic difficulties, may introduce additional sources of heterogeneity in future studies, which will need to be investigated in updates of this systematic review. An individual participant data meta-analysis could potentially identify participant-level characteristics (such as changes in employment, financial situation, or living arrangement) associated with higher resilience or vulnerability in times of a global pandemic. Finally, the number of included longitudinal studies was small; implementing standardized longitudinal assessments of mental health in existing large cohorts would help address future major world events in a more uniform and efficient way.

The implications of our findings should be seen through the lens of our study's limitations discussed earlier. At the start of the pandemic, we found a worsening on average of symptoms of anxiety and depression, which increased with stringency in governmental measures; however, the degree and extent of this worsening and how much may be due to other factors, such as increased cumulative cases, are uncertain. Policymakers can balance the information from this study against evidence that containment measures efficiently controlled the spread of the virus, relieved pressure on health systems, and prevented deaths from COVID-19 (69, 70). Also, we found that some study populations clearly had a substantial worsening of anxiety and depression symptoms, particularly at the beginning of the pandemic and with increasing numbers of reported cases. Even if the degree of worsening of symptoms is relatively small, if many people are affected the overall effect can be large. This means that, while this pandemic continues and to prepare for future pandemics, governments need to ensure that adequate mental health service provision and appropriate interventions exist for those who need them (71). Further research is needed, particularly in low- and middle-income countries and for such conditions as alcohol and substance misuse. Overall, our analysis indicates that during a global pandemic we should never lose sight of the negative consequences on mental health for the average population or the community, but also that some populations have completely different trajectories in mental health. On the basis of these data, it is also reasonable to expect a wide range of reactions in future pandemics.

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Note: Dr. Salanti, Dr. Peter, Ms. Tonia, and Mr. Holloway had direct access to and verified the underlying data reported in the article. All authors agreed with the results and conclusions of this article, had access to all of the data, take responsibility for the accuracy of the analysis, had authority over manuscript preparation and the decision to submit the manuscript for publication, and approved this manuscript.

Disclaimer: The views expressed are those of the authors and not necessarily those of the Swiss National Science Foundation, the U.K. National Health Service, the National Institute for Health and Care Research (NIHR), or the U.K. Department of Health. This work reflects only the authors' view. The European Commission is not responsible for any use that may be made of the information it contains.

Acknowledgment: The authors thank the 35 investigators who screened the abstracts of all studies identified by the search. Their names and affiliations are listed in **Supplement 1** (available at Annals.org). Dr. Low thanks Dr. Leonie Heron and Ms. Hira Imeri.

Financial Support: By grant 198418 from the National Research Programme 78 COVID-19 of the Swiss National Science Foundation. Dr. Cipriani is supported by the NIHR Oxford Cognitive Health Clinical Research Facility, by an NIHR Research Professorship (grant

RP-2017-08-ST2-006), by the NIHR Oxford and Thames Valley Applied Research Collaboration, and by the NIHR Oxford Health Biomedical Research Centre (grant BRC-1215-20005). Dr. Haas is supported by an Ambizione fellowship from the Swiss National Science Foundation (193381). Dr. Egger was supported by special project funding (grant 189498) from the Swiss National Science Foundation. Dr. Low received funding for the COVID-19 Open Access Project from the Swiss National Science Foundation (grant 176233) and the European Union's Horizon 2020 research and innovation program, project EpiPose (grant 101003688). From the MHCOVID Crowd Investigators, Dr. Lasserre has received grant funding from the Swiss National Science Foundation Early Postdoc Mobility fellowship (P2LAP3_191273).

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M22-1507.

Reproducible Research Statement: *Study protocol:* Available in PROSPERO (CRD42020180049). *Statistical code:* The analysis scripts are available in https://github.com/esm-ispm-unibe-ch-REPRODUCIBLE/MHCOVID2022-The-impact-of-the-COVID-19-pandemic-and-associated-control-measures-on-MH. *Data set:* The full data set is available online in BORIS (Bern Open Repository and Information System, https://doi.org/10.48620/75). The data are also available in https://github.com/esm-ispm-unibe-ch-REPRODUCIBLE/MHCOVID2022-The-impact-of-the-COVID-19-pandemic-and-associated-control-measures-on-MH.

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Appendix Figure. Study flow diagram.