CIHR COVID-19 and Mental Health Knowledge Synthesis Operating Grant

Final Knowledge Synthesis

Mental Health during the COVID-19 Pandemic: A Living Systematic Review of Mental Health Burden, Factors Associated with Mental Health Outcomes, and Intervention Effectiveness in the General Population and Vulnerable Populations

Brett D. Thombs,[1-7] Olivia Bonardi,[1] Danielle B. Rice,[1,5] Jill T. Boruff,[8] Marleine Azar,[1] Chen He,[1] Sarah Markham,[9] Ying Sun,[1] Yin Wu,[1,2] Ankur Krishnan,[1] Yutong Wang,[10] Diana Jiang,[1] Kexin Li,[1] Anneke Yao,[5] Tiffany Dal Santo,[5] Amina Tasleem,[5] Ian Thombs-Vite,[1] Kevin Jutras,[1] Andrea Benedetti,[3,4,11]

[1]Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Quebec, Canada;

[2]Department of Psychiatry, McGill University, Montreal, Quebec, Canada;

[3]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Quebec, Canada;

[4]Department of Medicine, McGill University, Montreal, Quebec, Canada;

[5]Department of Psychology, McGill University, Montreal, Quebec, Canada;

[6]Department of Educational and Counselling Psychology, McGill University, Montreal, Quebec, Canada;

[7]Biomedical Ethics Unit, McGill University, Montreal, Quebec, Canada;

[8]Schulich Library of Physical Sciences, Life Sciences, and Engineering, McGill University, Montreal, Quebec, Canada;

[9]King's College, London, United Kingdom.

[10]Southeast University, China

[11]Respiratory Epidemiology and Clinical Research Unit, McGill University Health Centre,

Montreal, Quebec, Canada;

Introduction:

The coronavirus disease (COVID-19) pandemic has disrupted the lives of people across the world due to its rapid spread, high number of deaths, disruption of the social fabric, toll on health care systems, and devastating economic impact.[1] Fear of personal infection or infection of friends and family members is common in any infectious disease outbreak.[2] In COVID-19, there are also fears that health care systems may be overrun and adequate medical care will not be available; that isolation and movement restrictions will be long-lasting with a heavy toll on mental health, social functioning, and employment; and that individual and societal economic resources will be insufficient.[3-4] Serious mental health implications will extend beyond the acute outbreak period.[2,5,6]

Addressing mental health needs during the acute and extended phases of COVID-19 and preparing for possible future outbreaks requires evidence on mental health burden, factors associated with vulnerability, and effectiveness of feasibly delivered interventions that can be rapidly employed to prevent or address mental health challenges. High-quality evidence is needed for a range of populations, including vulnerable groups, such as medical staff involved in caring for patients with COVID-19; people infected with COVID-19 (hospitalized and not hospitalized); essential services personnel; people at risk of complications due to pre-existing medical conditions; individuals with pre-existing mental health conditions; individuals in correctional services, including incarcerated individuals; and others. Effective policy and intervention will require rapid synthesis and communication of the best available evidence in a format that is accessible to knowledge users and the public.

A "rapid review" from February 2020 examined the mental health impact of previous infectious disease outbreaks.[2] The review included evidence from 24 studies of people quarantined after being exposed to others who had been infected with severe acute respiratory syndrome in mainland China, Hong Kong, and Canada in 2003, equine influenza in Australia in 2007, H1N1

influenza in Australia in 2009, Ebola in West Africa in 2014, and Middle East Respiratory Syndrome in Korea in 2015. Socio-demographic characteristics found to be potentially associated with less favourable mental health outcomes among adults included history of mental illness, younger age, less education, female sex, and number of children. Factors related to social isolation that were potentially associated with worse outcomes included duration of isolation, access to supplies and information, financial resources, fear of infection and complications, degree of isolation, and boredom.[2] Results, however, were not consistent across studies, and there were important limitations in the evidence base that reduce ability to apply results to decision-making in COVID-19. In addition to the small number of available studies, small sample sizes, and sub-standard reporting, (1) few studies used validated mental health outcome measures; (2) no studies compared outcomes during quarantine to pre-outbreak mental health data, which reduces the ability to draw conclusions about changes in mental health and associated factors; (3) and no trials tested interventions to improve mental health symptoms during or following outbreaks. Furthermore, the scope of COVID-19 far exceeds that of other outbreaks, and the overall threat it poses is much greater.

In the current context of COVID-19, rather than a lack of evidence, a major barrier to effectively using mental health research evidence is the rapid publication of large numbers of studies of variable quality. An unprecedented amount of evidence is being produced and published, but much of it would not likely be published in normal times; a large proportion of studies is of limited usefulness or misleading. Successful uptake of evidence into practice in a way that will benefit the Canadian public requires that informative evidence be separated rapidly from evidence that is less useful or misleading due to poor methodology, inadequate reporting, or both. Rigorous curation is needed to clearly delineate the kind of evidence that will answer pressing questions and to identify well-conducted and reported studies to answer those questions. Living systematic reviews are systematic reviews that are continually updated and provide ongoing access to

results via online publication. They are logistically challenging, but provide value beyond conventional systematic reviews in situations where (1) important decisions that need to be made merit the resources involved; (2) certainty in existing evidence is low or very low, posing a barrier to decision-making; and (3) there is new evidence emerging to inform decisions.[7] It is hard to imagine a situation more fitting for a living systematic review than the COVID-19 outbreak.

We have initiated 3 living systematic reviews to provide daily evidence updates on key mental health questions during COVID-19. We have reviewed over 15,000 citations and have begun to post initial results on the project website (https://www.depressd.ca/covid-19-mental-health) along with narrative synthesis. We have also posted information on registrations of over 50 trials that are underway with descriptions of the most promising trials to inform the mental health response in Canada. Our first review will estimate the impact of COVID-19 on mental health overall and by key sub-populations by comparing changes in symptom levels or proportions of people with diagnoses or above symptom thresholds at different times across the pandemic (e.g., pre-COVID-19 versus COVID-19; initial announcement of pandemic versus peak; restrictive isolation versus post-isolation). The second review is synthesizing evidence to identify sociodemographic, medical, and pandemic-related factors associated with poor mental health outcomes. The third review evaluates evidence on effectiveness of interventions designed to prevent the onset of mental health problems or improve mental health outcomes.

Link to the project website:

https://www.depressd.ca/covid-19-mental-health

Narrative Syntheses

Changes in Mental Health Symptoms

Link to results tables:

https://www.depressd.ca/research-question-1-symptom-changes

Methods Notes:

Eligible studies must report changes in symptom levels, proportion of participants above a cut-off threshold, or proportion of participants who change by a pre-defined magnitude (e.g., minimal clinically important difference) across a delineated COVID-19 related event. This could include comparisons of pre-COVID-19 and COVID-19 symptoms, symptoms at the initiation of the outbreak to the peak, or symptoms during highly restrictive isolation periods to subsequent periods, for instance. Studies with < 100 participants are excluded.

We are not including cross-sectional studies that report percentages of participants with scores above cut-off thresholds on commonly used symptom questionnaires. Conclusions that can be drawn from that type of data about mental health effects from COVID-19 and clinical implications are limited, and, per our protocol, we have not included those studies. This is because percentages of people who score above a threshold on standardized questionnaires vary, sometimes dramatically, between populations, even in normal times. For example, the percentage of participants with scores of at least 10 on the Patient-Health Questionnaire-9[8], a commonly used measure of depressive symptoms, in large, randomly selected, regional or national general population samples, has been reported as 4% in Hong Kong (N = 6,028);[9] 6% in Germany (N = 5,018);[10] 7% in Shanghai, China (N = 1,045);[11] 8% in the United States (N = 10,257);[12] 8% in the province of Alberta, Canada (N = 3,304);[13] 11% in Sweden (N = 3,001);[14]

and 22% in Jiangsu Province, China (N = 8,400).[15] Even within populations from the same region, the percentage can vary dramatically depending on sample characteristics. In Jiangsu Province, for example, the percentage among rural residents (32%) is twice that of urban residents (16%); it is also several times higher for older adults (25% for 55-64 years; 87% for ≥ 65 years) than for young adults (8% for 18-34 years).[15] Further complicating interpretation when there is not a time-based or other relevant comparator, percentages from symptom measures such as the PHQ-9 tend to dramatically overestimate prevalence that would be obtained from validated methods for ascertaining prevalence of mental health disorders, and there is too much heterogeneity between samples in the difference to correct for this statistically.[16]

Summary of Results:

Nineteen studies have compared mental health symptoms prior to and during COVID-19; five of the studies were on undergraduate students (7890, 7899, 18242, 19533, 24660), eleven (17066, 21717, 9941, 22825, 24703, 27727, 27776, 30127, 41151, 27707, 75265) were from population-based surveys, two (24680, 52414) surveyed 435 and 131 people respectively, with pre-existing chronic medical conditions from a combination of countries including Canada, the United Kingdom, the United States, France, Denmark, Belgium, and Italy, and one (23486) surveyed 2288 sexual and gender minority people in the United States. The five studies of university students were from Switzerland, China, and the United States (N = 3); they included between 178 and 555 participants. The eleven population-based studies included samples from Brazil, Canada, China, the Czech Republic, Denmark, Ireland, New Zealand, the United Kingdom (N=5), and the United States (N=2); they included between 102 and 36,520 participants.

All studies of undergraduate students compared symptoms from pre-COVID-19 outbreak timepoints to symptoms at post-COVID-19 timepoints. In study 7890, which included 209

undergraduate students from Switzerland, symptoms of depression increased substantially by 0.53 (0.33 to 0.72) standard deviations, stress by 0.40 (0.20 to 0.59), loneliness, slightly, by 0.29 (0.10 to 0.49), and symptoms of anxiety, slightly, by 0.17 (-0.02 to 0.37). A second study (7899), of 178 undergraduate students from the United States reported that there were statistically significant changes in symptoms of both anxiety and depression, but it did not report data that allowed estimation of effect size; regression estimates of changes in depression symptoms, though, were substantially larger than those for anxiety. Another study (19533) from the United States, with 487 undergraduates, found that anxiety symptoms decreased significantly, though by a small amount, from the beginning of the semester and prior to COVID-19 to the end of the semester during COVID-19 (0.17 standard deviations, 95% CI 0.04 to 0.31). A third study (24660) from the United States, with 205 undergraduates, found large and moderate increases in both symptoms of depression (0.48 standard deviations, 95% CI 0.28 to 0.67), and symptoms of anxiety (0.35 standard deviations, 95% CI 0.15 to 0.54), respectively. In the study (18242) from China, there were small increases in combined anxiety and depressive symptoms and in negative affect.

Among population studies, almost all compared symptoms from pre-COVID-19 outbreak timepoints to symptoms at post-COVID-19 timepoints. In study 17066, which analyses 12,090 responses from a representative sample of British adults (UK Household Longitudinal Study, UKHLS), there was a small increase in general mental health symptoms of 0.31 standard deviations (95% CI 0.29 to 0.34; 1 point on GHQ – dichotomized items). Study 27707, analyses 9,748 responses to the same survey. It reports that there was an increase in the proportion of participants who scored above a mental health function threshold (GHQ-12 ≥ 4). The authors report an increase of 11% scoring above the threshold, from 19% at wave 9 of the UKHLS, to 30% in the COVID-19 wave, though there was not enough information provided to calculate a standardized mean difference. It was not possible to determine, though, the relative changes in

anxiety and depressive symptoms. Study 21717, which recruited a small international sample via an online platform (N=218), reports negligible changes in anxiety (-0.11 standard deviations, 95% CI -0.30 to 0.08), depression (0.08 standard deviations, 95% CI -0.11 to 0.27), rumination (-0.07 standard deviations, 95% CI -0.25 to 0.12), and distress (-0.09 standard deviations, 95% CI -0.28 to 0.10). Study 9941 compared mental health symptoms from the beginning of quarantine to symptoms 4 weeks later. Results indicated that among participants in Brazil (N=360), there were small increases in depression (0.20 standard deviations, 95% CI 0.05 to 0.34), anxiety (0.30 standard deviations, 95% CI 0.15 to 0.45), and stress (0.22 standard deviations, 95% CI 0.07 to 0.37). The study did not report how participants were recruited. Study 22825 recruited the 28 year old children of women residing in Avon, England who had been recruited during their pregnancies for the ALSPAC longitudinal study. Compared to participant responses completed at age 26, the COVID-19 data demonstrated negligible changes in continuous depression scores (N= 2219, -0.11 standard deviations, 95% CI -0.06 to -0.15). There were small increases in continuous anxiety scores (N= 1811, 0.26 standard deviations, 95% CI 0.21 to 0.30). Continuous well-being scores showed a large decrease (N=2231, -0.51 standard deviations, 95% CI -0.47 to -0.55). Study 24703, which recruited a moderate sized, nation-wide sample from the United States (N= 2088) via an online recruitment service, reports a negligible change in loneliness (0.02 standard deviations, 95% CI -0.04 to 0.08). Study 27727 recruited 102 Chinese participants from chat groups on social media platforms. Results indicate that from the peak of the COVID-19 outbreak in China, to the trough, there were negligible changes in stress (-0.02 standard deviations, 95% CI -0.30 to 0.25). Study 27776, which compares data following the Christchurch earthquake (2018) to data collected post-COVID-19 outbreak, also reports negligible changes in psychological distress (0.09 standard deviations, 95% CI 0.00 to 0.18). The 940 participants are part of a random, nationally diverse cohort which responds to the longitudinal New Zealand Attitudes and Values Study. Study 30127, commissioned the survey agency *Epinion* to conduct a two-wave COVID-19

population survey of 2,149 Danish adults. Results comparing symptoms before and after the phase 1 reopening in Denmark indicate a small increase in well-being (0.17 standard deviations, 95% CI 0.11 to 0.23). Study 41151 followed up with 715 participants from a randomly selected, 1% population-based sample of Brno, Czech Republic residents. After the national COVID-19 lockdown, results indicate a large increase in depression (0.44 standard deviations, 95% CI 0.34 to 0.55) and moderate increase in stress (0.29 standard deviations, 95% CI 0.19 to 0.40). Study 75265 compared responses of 36,520 adults in the UCL COVID-19 Social Study, a panel study weighted to population proportions. Data were collected for 20 weeks during the course of the pandemic and latent growth models were fitted, estimating an average of 0.11 weekly point decrease in depression symptoms and 0.10 weekly point decrease in anxiety symptoms over the 20 weeks. Not enough information was provided to calculate standardized mean differences.

Study 24680 surveyed a well-characterized, international cohort of people with the rare disease systemic sclerosis (N= 388-435). Between pre-COVID-19 and post-COVID-19 timepoints, there was a large increase in anxiety (0.51 standard deviations, 95% CI 0.37 to 0.64) and a negligible decrease in depression (-0.05 standard deviations, 95% CI -0.19 to 0.09). Study 52414 surveyed another international cohort of 131 people with progressive multiple sclerosis who were originally recruited for rehabilitation clinical trial. Results indicate that between pre-COVID-19 and post-COVID-19 timepoints, there were negligible changes in anxiety (0.02 standard deviations, 95% CI -0.22 to 0.27) and depression measured by BDI-II (0.09 standard deviations, 95% CI -0.15 to 0.34). The same study found a non-significant increase in depression using the HADS-D measure (0.21 standard deviations, 95% CI -0.03 to 0.46).

In a well-characterized cohort of sexual and gender minority people in the United States (N=2,288), study 23486 reported a small increase in depression (0.19 standard deviations, 95% CI 0.14 to 0.25) and a large increase in anxiety (0.54 standard deviations, 95% CI 0.48 to 0.60) following the COVID-19 outbreak.

Comment:

Among university students for whom social relationships are likely highly valued and for whom risk of complications from COVID-19 is generally lower than among other adults, symptoms of depression increased more than anxiety in three studies where that was reported; in one study, anxiety symptoms actually decreased among university students. The study on university students in Switzerland also reports moderate increases in stress and smaller increases in loneliness. The large population study in the UK (17066) reported general mental health symptoms and a small increase, but this did not allow interpretation of the types of symptoms experienced. The additional population studies generally show either small increases or negligible changes in anxiety, depression, and other mental health functions. A significant decrease in well-being measured in Avon, UK and significant increase in depression, measured in Brno, Czech Republic, were the largest changes reported for population studies. Emerging evidence on vulnerable populations suggests anxiety may be more important. The study in the rare disease cohort showed a large increase in anxiety while there were negligible changes in depression. The study on sexual and gender minority people indicated a similarly large increase in anxiety and a small increase in depression. It will be important to understand to what degree these finding are replicated in other university, vulnerable, and general populations.

Factors Associated with Levels or Changes in Symptoms

Link to results tables:

https://www.depressd.ca/research-question-2-factor

Methods Notes:

All eligible studies must conduct multivariable evaluations of factors associated with mental health symptoms, which may include, for instance, pre-COVID-19 participant or community characteristics, pre-existing health characteristics, and aspects of participants' experience during COVID-19 (e.g. infection, exposure to infected individuals, work status, lockdown status). Mental health outcomes must be based on validated diagnostic interviews, scales, or sets of items. Both cross-sectional and longitudinal designs are eligible, although cross-sectional designs will only be included if factors assessed were present prior to the outcome (e.g., sex, pre-existing medical condition) and not measured only concurrently. Thus, studies with multivariable analyses that include concurrent mental health or behavioural variables (e.g. information seeking, exercise) will be excluded, as these do not permit interpretation of directionality. Studies with < 100 participants will be excluded.

Summary of Results:

Results from the initial 42 studies have been posted.

*Comment***:**

Comments are forthcoming.

Effects of Interventions on Mental Health Symptoms

Link to results tables:

https://www.depressd.ca/research-question-3-intervention

Methods Notes:

Eligible intervention studies include randomized controlled trials and non-randomized controlled studies of interventions. Interventions must primarily target mental health and include a mental health primary outcomes.

Summary of Results:

We have identified and extracted data from two trials. In the first trial, the effect of progressive muscle relaxation (20-30 minutes for 5 consecutive days) on state anxiety was tested among patients in China hospitalized with COVID-19 compared to routine hospital care. The authors reported a standardized mean effect size of Hedges' g = 1.09 (95% CI 0.50 to 1.67) for 25 intervention patients compared to 26 patients in the routine care group. Trial reporting, however, was poor, and there was serious risk of bias concerns (see table). Furthermore, the effect size reported is approximately double what others have found for relaxation techniques on anxiety.[17,18] The second trial compared a very brief exercise in which paid online volunteers were asked to write psychologically affirming text, and their stress and well-being were compared immediately after to participants who wrote text about a colour.

We have identified 53 registrations for trials that appear to be eligible once completed. All but 5 of the interventions where delivery method is reported provide videoconference or teleconference interactive interventions or self-help interventions delivered via websites or videos. One intervention provides in-person peer-support for hospital staff. Two other

interventions provide in-person psychological counseling to COVID-19 patients. A similar intervention provides Basic Body Awareness training for medical staff and COVID-19 patients at a hospital. An intervention in Belgium provides face to face counseling from community health workers. Of the 53 trial registrations, 18 target the general population, 11 target medical staff, 9 target patients infected with COVID-19, 5 target people with pre-existing mental health conditions, 8 target people with pre-existing medical conditions, 1 targets university students, and 1 targets family members of COVID-19 patients. A trial in the Australian general population plans to enrol 9000 participants in online neighborhood engagement challenges. One trial, in Canadian medical staff, plans to enrol 1000 participants to test its peer-support model. One trial, in the German general population, plans to enrol 600 participants to test an online modular support program. One trial, in the Canadian general population plans to enrol 600 participants to test a virtual fitness intervention. One trial, in Spain, plans to enrol 560 medical staff to test a psychoeducation app. A trial in the German general population plans to enrol 544 participants to test a livestream exercise intervention. One trial, in the Canadian general population, plans to enrol 490 participants to test a workout app intervention. One trial, in the American general population, plans to enrol 400 participants to test an meditation app; 20 trials will attempt to enrol between 100 and 300 participants; the rest plan to enrol fewer than 100 participants. Registered trials are from Australia (N = 4), Brazil (N=1), Belgium (N=2), Canada (N = 5), China (N = 5), Denmark (N = 1), France (N = 1), Germany (N = 3), Honduras (N=1), Hungary (N=1), Israel (N=1), Iran (N = 7), Malaysia (N=1), Oman (N=1), Spain (N = 5), Sweden (N = 2), Turkey (N = 3), the United Kingdom (N=2), and the United States (N=7).

Most of the registered trials plan to recruit a small sample of participants and use standard interventions not adapted for COVID-19 (e.g., yoga, exercise). There are several feasibly implemented COVID-19 tailored interventions being tested that may be useful for rapid uptake, pending results. One trial, in Canadian medical staff, plans to enrol 1000 participants to test a

peer-support model in a stepped-wedge trial (NCT04373382, results expected February 2022). Another trial, which plans to enrol 600 participants, is testing an online modular support program to encourage coping with COVID-19 in the German general population (NCT04324190, results expected July 2020). Another trial of interest is enrolling 195 participants with the rare autoimmune disease scleroderma and at least mild symptoms of anxiety and testing the effect of a videoconference-delivered group intervention on anxiety (NCT04335279, results expected July 2020).

Comment:

Large trials with relevance to the general population and vulnerable groups are pending.

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