COVID-19 AND MENTAL HEALTH

INDIRECT AND POSSIBLY DIRECT CONSEQUENCES

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Coronavirus’s next victim? Our mental health

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One-third of US adults show signs of anxiety or depression amid coronavirus pandemic

Report: Direct correlation between COVID recession and increased rate of mental health issues

Flattening the Second (Hidden) Curve: Taking Care of Our Mental Health
Psychological Distress and Loneliness Reported by US Adults in 2018 and April 2020

Coronavirus disease 2019 (COVID-19) introduced stressors to mental health, including loneliness stemming from social isolation, fear of contracting the disease, economic strain, and uncertainty about the future. We fielded a national survey measuring symptoms of psychological distress and loneliness among US adults in April 2020 and compared results with national data from 2018.

Methods | We fielded the Johns Hopkins COVID-19 Civic Life and Public Health Survey from April 7 to April 13, 2020, using NORC’s AmeriSpeak Panel. AmeriSpeak is a probability-based panel designed to be representative of the US adult population. The panel is sourced from NORC’s area probability sample and from a US Postal Service address-based sample covering 97% of US households. The panel has a recruitment rate of 34% and includes approximately 35,000 members. The sample for the Johns Hopkins survey was drawn from this panel and the survey was administered online. NORC obtains informed consent prior to enrolling individuals in the panel. The Johns Hopkins Bloomberg School of Public Health institutional review board deemed this study not human participants research and waived informed consent.

We measured the prevalence of symptoms of serious psychological distress in the overall sample and among demographic subgroups using the Kessler 6 Psychological Distress Scale, with the validated measure of serious distress defined as a score of 13 or higher on the 0- to 24-point scale. We also measured the proportion of respondents who reported that they always or often feel lonely in response to the item “How often do you feel lonely?” with response options always, often, sometimes, rarely, and never.

We compared the prevalence of symptoms of serious psychological distress in April 2020 with an identical measure from the 2018 National Health Interview Survey (NHIS), which used the Kessler 6 scale among 5,417 adults aged 18
Over 20% of healthcare professionals report symptoms of depression and anxiety

Almost 40% of healthcare workers experience sleeping difficulties and/or insomnia

Rates of anxiety and depression were higher for female healthcare workers and nursing staff

Milder mood symptoms are common and screening should aim to identify mild and sub-threshold syndromes
POTENTIAL MENTAL HEALTH CONSEQUENCES OF COVID-19

• **Short-term**: Among people hospitalized with SARS or MERS - more than 25% experienced symptoms such as poor concentration, confusion and rapid fluctuations in mood – signs of possible *delirium*
  • Early data on COVID-19 indicate similar findings
• **Long-term**: Increases in depression, anxiety, self-harm, and suicide
  • *During SARS epidemic in 2003:*
    • 30% increase in suicide in those aged 65 years and older
    • ~50% of recovered patients remained anxious
    • 6 months after infection, 15% had significant depression, 15% had an anxiety disorder, 19% had chronic fatigue, 30% had PTSD
    • 29% of health-care workers experienced probable emotional distress
• Increases in domestic violence, child abuse (with less reporting of it), substance abuse, and gambling
• Loss of loved ones, grieving, PTSD
• Stress from social isolation, loss of financial resources, and repeated media consumption regarding pandemic
36.4% of all patients (and 45.5% of severely ill patients) had neurological manifestations, including:

- Loss of taste and smell
- Muscle weakness
- Seizures
- Hallucinations
- Stroke

Evidence from animal and human studies on other coronaviruses that brain infection can occur

Brainstem and thalamus may be particularly vulnerable

Effects on respiratory function better understood than effects on neurocognitive and emotional functioning

Some brain effects may be delayed

What About Direct Effects on CNS?
Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science

Emily A Holmes*, Rory C O’Connor*, V Hugh Perry, Irene Tracey, Simon Wessely, Louise Arseneault, Clive Ballard, Helen Christensen, Roxane Cohen Silver, Ian Everall, Tamsin Ford, Ann John, Thomas Kabir, Kate King, Ira Madan, Susan Michie, Andrew K Przybylski, Roz Shafran, Angela Sweeney, Carol M Worthman, Lucy Yardley, Katherine Cowan, Claire Cope, Matthew Hotopf†, Ed Bullmore†

The coronavirus disease 2019 (COVID-19) pandemic is having a profound effect on all aspects of society, including mental health and physical health. We explore the psychological, social, and neuroscientific effects of COVID-19 and set out the immediate priorities and longer-term strategies for mental health science research. These priorities were informed by surveys of the public and an expert panel convened by the UK Academy of Medical Sciences and the mental health research charity, MQ: Transforming Mental Health, in the first weeks of the pandemic in the UK in March, 2020. We urge UK research funding agencies to work with researchers, people with lived experience, and others to establish a high level coordination group to ensure that these research priorities are addressed, and to allow new ones to be identified over time. The need to maintain high-quality research standards is imperative. International collaboration and a global perspective will be beneficial. An immediate priority is collecting high-quality data on the mental health effects of the COVID-19 pandemic across the whole population and vulnerable groups, and on brain function, cognition, and mental health of patients with COVID-19. There is an urgent need for research to address how mental health consequences for vulnerable groups can be mitigated under pandemic conditions, and on the impact of repeated media consumption and health messaging around COVID-19. Discovery, evaluation, and refinement of mechanistically driven interventions to address the psychological, social, and neuroscientific aspects of the pandemic are required. Rising to this challenge will require integration across disciplines and sectors, and should be done together with people with lived experience. New funding will be required to meet these priorities, and it can be efficiently leveraged by the UK’s world-leading infrastructure. This Position Paper provides a strategy that may be both adapted for, and integrated with, research efforts in other countries.
RESEARCH PRIORITIES I – MH ASSESSMENT

- Monitoring increases in prevalence of mental health and neurological problems and disorders
- Identifying highest-risk populations, typically
  - Socially and economically disadvantaged groups
  - Older people and those with medical comorbidities
  - People with disabilities
  - Front-line health care workers
  - Children
  - People with pre-existing mental health conditions
  - People with neurodevelopmental disabilities
- Validity of data from digital assessment apps
- Identification of cohorts, and population studies are needed
RESEARCH PRIORITIES II - TREATMENT

- Effectiveness of remote mental health interventions led by a MH professional
- Effectiveness of digital mental health apps
- Effective ways to build and/or maintain resilience and wellness skills during social isolation
- Methods to maximize adherence to medical advice during pandemic while minimizing harm to the mental health of individuals
- In-person and remote methods to prevent depression and anxiety increases among health care workers
- Effectiveness of methods to prevent toxic and potentially fatal cleaning practices
RESEARCH PRIORITIES III – CNS EFFECTS OF COVID-19 ON MH

- Neuropsychiatric effects of COVID-19 still mostly unknown
  - Short-term (direct, and via neuroinflammation)
  - Long-term (e.g., Spanish flu pandemic leading to post-encephalitic Parkinsonism)
- BUT, closely related SARS and MERS coronaviruses are both neurotropic and neurotoxic, and caused mental health and neurological disorders
- Infrastructure is needed to study both short- and long-term effects of COVID-19 on brain and mental health
- Research needed on mechanisms of COVID-19 brain infection (neuronal, vascular?) and on its effects
  - Effects on the retina (a part of the CNS) have been observed, with reversible breakdown of the blood-retina barrier due to neuroinflammation, and so retina could serve as a model
- Biomarkers of these mechanisms and effects are needed!
- Databases of neuropsychological findings, psychiatric symptoms and diagnoses, and outcomes are needed
- A BIOPSYCHOSOCIAL APPROACH is critical for research on COVID-19, integrating
  - Brain and other systemic function, psychological factors, and environmental/demographic factors
- Other
Notice of Intent to Publish Funding Opportunity Announcements for the RADx-UP Initiatives

Notice Number: NOT-OD-20-112

Key Dates
Release Date: May 29, 2020
Estimated Publication Date of Funding Opportunity Announcement: June 8, 2020
First Estimated Application Due Date: July 2020
Earliest Estimated Award Date: September 2020
Earliest Estimated Start Date: August 2020

Related Announcements
None

Issued by
Office of The Director, National Institutes of Health (OD)

Purpose
NIH Institutes and Centers likely to participate include some or all of the following:
Office of the Director (OD)
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
National Cancer Institute (NCI)
National Center for Advancing Translational Sciences (NCATS)

Research Initiative Details

The goal of RADx-UP is to reduce COVID-19 associated morbidity and mortality disparities for those vulnerable and underserved populations that are disproportionately affected by, have the highest infection rates of, and/or are most at risk for adverse outcomes from contracting the virus. This Notice encourages researchers to leverage partnerships with key stakeholders to conduct community-engaged research to understand COVID-19 disparities and to increase access and effectiveness of diagnostic testing interventions among underserved COVID-19 medically and/or socially vulnerable populations.

NIH plans to publish three NOsIs for competitive revision awards as follows:
1. To solicit emergency competitive revision applications to existing awards for large consortia, multi-site trials, centers and other current networks that have adequate capacity, infrastructure, and established community-engaged relationships to support large-scale testing interventions or have the capacity to ramp up quickly to reach underserved or vulnerable populations.
2. Similar to the above, but shifts eligibility to collaborative and individual research awards, generally focused on smaller underserved or vulnerable populations.
3. To solicit research to understand the social, ethical, and behavioral implications (SEBI) of COVID-19 testing in these populations.

The fourth funding opportunity using the U24 activity code will be announced for a Coordination and Data Collection Center (CDCC), a key component of the consortium. The CDCC will serve as a national resource, working with NIH scientific staff and consortium members to provide overarching support and guidance in the following four domains: (1) Administrative Operations and Logistics, (2) COVID-19 Testing Technology, (3) Community and Health System Engagement and (4) Data Collection, Integration and Sharing.

The NIH intends for the awardees of the three NOsIs to serve as one consortium of interlinked, community-engaged, intervention projects across the United States (coordinated by the CDCC) to deploy implementation strategies to improve the reach, acceptance, uptake, and sustainability of COVID-19 testing and ultimately understand COVID-19 health disparities.

Researchers planning to apply are strongly encouraged to read all four of these interrelated funding opportunities.
CDC Data for the USA – June 17th 2020

TOTAL CASES
2,132,321
27,975 New Cases*

TOTAL DEATHS
116,862
722 New Deaths*
A quick note on annoying nomenclature

<table>
<thead>
<tr>
<th>Disease</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronavirus Disease (COVID-19)</td>
<td>Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)</td>
</tr>
</tbody>
</table>
COVID-19 is not a binary outcome disease!

• There is a strong tendency to think of just two possible outcomes – mortality or survival.
• But as with most things in life, there is a large gray zone in between.
• Survival is of course great, but for many, it’s just the beginning of a long road and life may never look quite the same again.
• Asymptomatic disease is also good, but does asymptomatic really = no deleterious outcomes?
• About half of hospitalized coronavirus patients experience neurological symptoms including dizziness, difficulty concentrating, a loss of smell and taste, seizures, strokes, and weakness, according to a new review of research published in the Annals of Neurology.
University of Strasbourg (March 3rd to April 4th)

- 58 patients admitted to the hospital (Median Age of 63)
- 49 of 58 (84%) showed clinically meaningful neurological signs
- 11 individuals received an MRI scan - All showed perfusion anomalies
- 3 of these individuals showed MRI evidence of acute stroke

- Of 45 patients discharged, fifteen (33%) showed dysexecutive syndrome consisting of inattention, disorientation, or poorly organized movements in response to command.

Helms et al., 2020
Does the Corona Virus actually get into the brain?
Anosmia and COVID-19
A 25-year-old female radiographer with COVID-19. Signals indicate viral infection (arrow) in the right gyrus rectus, which helps process smell signals.

Politi et al., 2020
Hyperintensity in the olfactory bulbs
Brains in a dish - Spheroids

• 350 micrometers in diameter, they are about the size of the eye of a housefly and are just visible to the human eye
Brains in a dish (Spheroids)

Thomas Hartung, 
C. Korin Bullen, 
Helena Hogberg 
and colleagues 
at Johns Hopkins University

Important caveat – no Blood Brain Barrier
What about Vertical Transmission?

• Should we be worried about the effect of the virus on the unborn fetus?
• 15% of pregnant women with Covid-19 show severe disease (Lloken et al., 2020) – compare that to a rate of about 2% in women in this age bracket (18-49)

• 2nd Trimester infections from the initial surge will be coming to term between July and September
• We won’t see the first offspring “infected” during the first trimester until October through December
Things we Neuroscientists are worried about

• We have yet to see whether there are implications for babies born to mothers who contracted COVID-19 in their first and second trimesters – these children haven’t been born yet.

• But we do have very recent evidence that it can be transmitted vertically. Vivanti and colleagues (Paris Saclay University Hospital) have presented a case study showing infection in a newborn, with evidence for neurological findings.
Protecting our most vulnerable.

People With Intellectual Disabilities And Autism Die Of COVID-19 At A Higher Rate

In New York and Pennsylvania, COVID-19 case-fatality rates for people with intellectual and developmental disabilities are higher than the states' overall rates. (Case-fatality rates are deaths as a percentage of total confirmed cases within the population.)

- People with intellectual or developmental disabilities
- State overall

New York:
- 8% of people with intellectual or developmental disabilities died of COVID-19
- 10% of the state's overall population died of COVID-19

Pennsylvania:
- 3% of people with intellectual or developmental disabilities died of COVID-19
- 14% of the state's overall population died of COVID-19

Notes:
- Data as of June 3. Numbers for people with intellectual disabilities reflect those who get services from the state.