



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

been more encouraging. The trial should therefore not be regarded as a definitive dismissal of the promise of these or related agents.³

Theoretically, depression in bipolar disorder is a more heterogeneous construct than mania, which is more monothematically biological in its causation. Depression is driven by a far wider array and admixture of biological factors, consequences of behaviours while manic, losses in domains such as educational and vocational horizons, relationships, personality, finances, guilt, stigma, and self-stigma, among others. Therefore, it is arguably ambitious at the outset to expect a singular biological therapy targeting one biological marker of the disorder to address all phenotypes of this heterogeneous clinical presentation. The complexity of bipolar depression might be an explanation more broadly for the relatively common failure of singular treatment approaches. These failures suggest that polyvalent and personalised therapies predicated on individualised profiles are needed to select from the diverse pharmacological, neurostimulatory, nutraceutical, lifestyle, and psychological approaches that are available.¹⁰ In sum, this might not be the last word on the potential role of anti-inflammatory drugs in the treatment of bipolar depression, but notwithstanding the methodological issues that accompany any clinical trial, the promise of targeting the inflammation pathway in the management of this challenging condition is today somewhat weaker.

MB is supported by a Senior Principal Research Fellowship (1059660 and 1156072) from the Australian National Health and Medical Research Council (NHMRC); reports grant or research support from the National Institutes of Health, Cooperative Research Centre, Simons Autism Foundation, Cancer Council of Victoria, Stanley Medical Research Foundation, Medical Benefits Fund, National Health and Medical Research Council, Medical Research Futures Fund, Beyond Blue, Rotary Health, A2 Milk Company, Meat and Livestock Board, Woolworths, Avant, and the Harry Windsor Foundation; reports having been a speaker for Astra Zeneca, Lundbeck, Merck, Pfizer; reports serving as a consultant

to Allergan, Astra Zeneca, Bioadvantex, Bionomics, Collaborative Medicinal Development, Lundbeck Merck, Pfizer, and Servier, outside the submitted work. EV has received grants and served as consultant, advisor, or speaker for Abbott, Allergan, Angelini, Dainippon Sumitomo Pharma, Janssen, Lundbeck, Novartis, Otsuka, Richter, Sage, Sanofi-Aventis, and Takeda, all outside the submitted work. OMD is a RD Wright NHMRC Biomedical Career Developmental Fellow (APP1145634), reports grants from the Brain and Behavior Foundation, Simons Autism Foundation, Stanley Medical Research Institute, Deakin University, Lilly, NHMRC, and Australasian Society for Bipolar and Depressive Disorders/Servier, and has received in kind support from BioMedica Nutraceuticals, NutritionCare, and Bioceuticals, all outside the submitted work.

*Michael Berk, Eduard Vieta, Olivia M Dean
michael.berk@deakin.edu.au

Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Deakin University, Barwon Health, Geelong, VIC 3220, Australia (MB, OMD); Orygen National Centre of Excellence in Youth Mental Health, Melbourne, VIC, Australia (MB); Centre for Youth Mental Health (MB), Department of Psychiatry (MB), and Florey Institute for Neuroscience and Mental Health (MB, OMD), University of Melbourne, Melbourne, VIC, Australia; Hospital Clinic, Institute of Neuroscience, University of Barcelona, Barcelona, Spain (EV); Institut d'Investigacions Biomèdiques August Pi i Sunyer, Department of Child and Adolescent Psychiatry and Psychology, Hospital Clinic, Barcelona, Spain (EV); and Centro de Investigación Biomédica en Red Salud Mental, Barcelona, Spain (EV)

- 1 Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar Disord* 2018; **20**: 97–170.
- 2 Vieta E. Disruptive treatments in psychiatry. *Rev Psiquiatr Salud Ment* 2020; **13**: 1–4.
- 3 Dean OM, Kanchanatawan B, Ashton M, et al. Adjunctive minocycline treatment for major depressive disorder: a proof of concept trial. *Aust N Z J Psychiatry* 2017; **51**: 829–40.
- 4 Sethi R, Gómez-Coronado N, Walker AJ, et al. Neurobiology and therapeutic potential of cyclooxygenase-2 (COX-2) inhibitors for inflammation in neuropsychiatric disorders. *Front Psychiatry* 2019; **10**: 605.
- 5 Dean OM, Data-Franco J, Giorlando F, Berk M. Minocycline. *CNS drugs* 2012; **26**: 391–401.
- 6 Husain MI, Chaudhry IB, Khoso AB, et al. Minocycline and celecoxib as adjunctive treatments for bipolar depression: a multicentre, factorial design randomised controlled trial. *Lancet Psychiatry* 2020; **7**: 515–27.
- 7 McIntyre RS, Subramaniapillai M, Lee Y, et al. Efficacy of adjunctive infliximab vs placebo in the treatment of adults with bipolar I/II depression: a randomized clinical trial. *JAMA Psychiatry* 2019; **76**: 783–90.
- 8 Fernandes BS, Williams LM, Steiner J, et al. The new field of “precision psychiatry”. *BMC Med* 2017; **15**: 80.
- 9 Krol FJ, Hagin M, Vieta E, et al. Placebo—to be or not to be? Are there really alternatives to placebo-controlled trials? *Eur Neuropsychopharmacol* 2020; **32**: 1–11.
- 10 Vieta E, Berk M, Schulze TG, et al. Bipolar disorders. *Nat Rev Dis Primers* 2018; **8**: 18008.



Suicide risk and prevention during the COVID-19 pandemic

The mental health effects of the coronavirus disease 2019 (COVID-19) pandemic might be profound¹ and there are suggestions that suicide rates will rise, although this is not inevitable. Suicide is likely to become a more pressing concern as the pandemic spreads and has longer-term effects on the general population, the economy, and vulnerable groups. Preventing suicide therefore needs urgent consideration. The response

must capitalise on, but extend beyond, general mental health policies and practices.

There is some evidence that deaths by suicide increased in the USA during the 1918–19 influenza pandemic² and among older people in Hong Kong during the 2003 severe acute respiratory syndrome (SARS) epidemic.³ The current context is different and evolving. A wide-ranging interdisciplinary response that

Published Online
 April 21, 2020
[https://doi.org/10.1016/S2215-0366\(20\)30171-1](https://doi.org/10.1016/S2215-0366(20)30171-1)
 For the Royal College of Psychiatrists guidance see <https://www.rcpsych.ac.uk/about-us/responding-to-covid-19/responding-to-covid-19-guidance-for-clinicians>

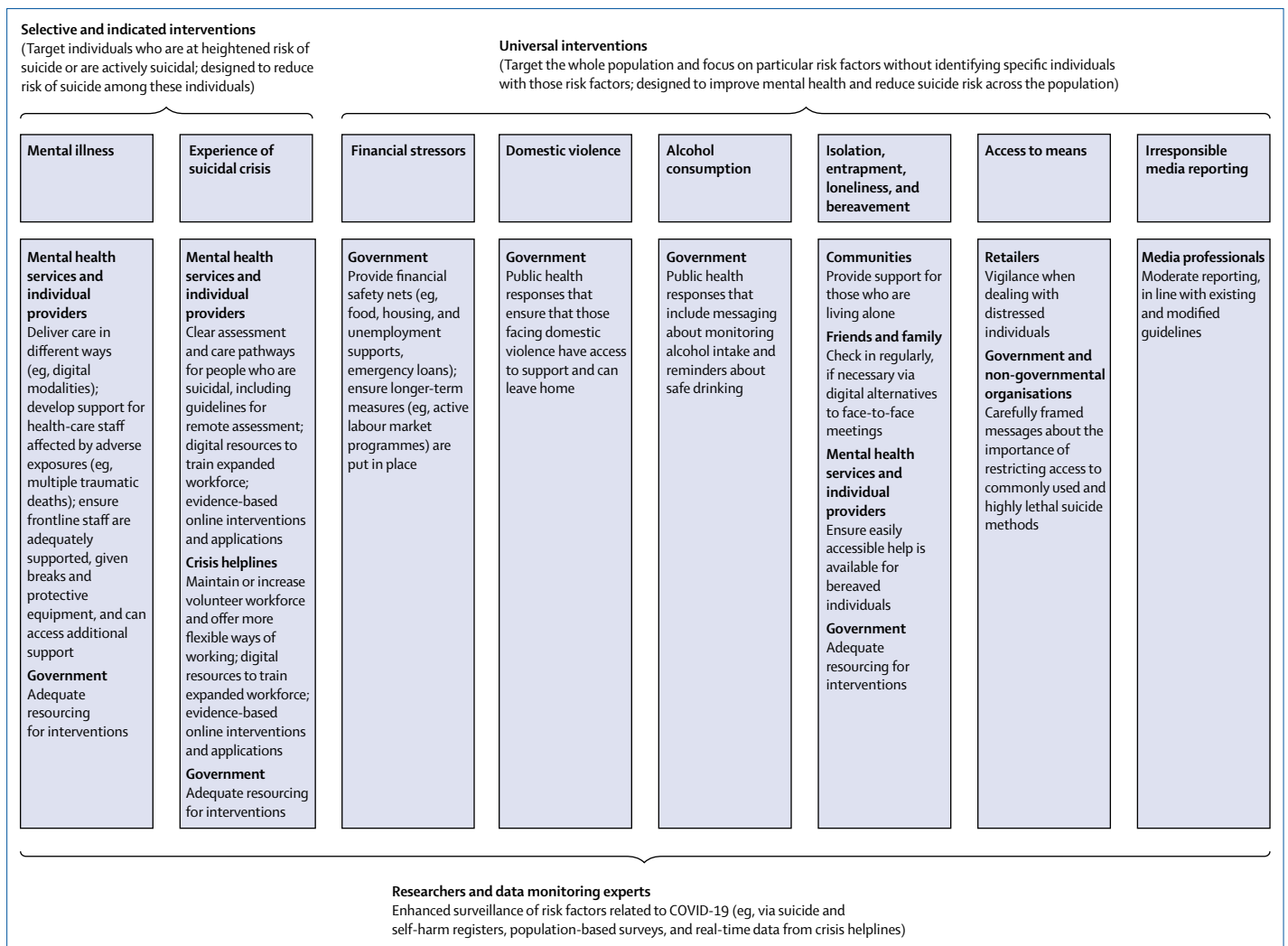


Figure: Public health responses to mitigating suicide risk associated with the COVID-19 pandemic
 COVID-19=coronavirus disease 2019.

recognises how the pandemic might heighten risk and applies knowledge about effective suicide prevention approaches is key. Selective, indicated, and universal interventions are required (figure).

The likely adverse effects of the pandemic on people with mental illness, and on population mental health in general, might be exacerbated by fear, self-isolation, and physical distancing.⁴ Suicide risk might be increased because of stigma towards individuals with COVID-19 and their families. Those with psychiatric disorders might experience worsening symptoms and others might develop new mental health problems, especially depression, anxiety, and post-traumatic stress (all associated with increased suicide risk). These mental health problems will be experienced by the general

population and those with high levels of exposure to illness caused by COVID-19, such as frontline health-care workers and those who develop the illness. The consequences for mental health services are already being felt (eg, increased workloads and the need to find new ways of working). Some services are developing expertise in conducting psychiatric assessments and delivering interventions remotely (eg, by telephone or digitally); these new working practices should be implemented more widely, but with consideration that not all patients will feel comfortable with such interactions and they may present implications for privacy. Making evidence-based online resources and interventions freely available at scale could benefit population mental health.

For COVID-19-specific guidelines on reporting on suicide see https://www.iasp.info/pdf/2020_briefing_statement_ABversion_reporting_on_suicide_during_covid19.pdf

People in suicidal crises require special attention. Some might not seek help, fearing that services are overwhelmed and that attending face-to-face appointments might put them at risk. Others may seek help from voluntary sector crisis helplines which might be stretched beyond capacity due to surges in calls and reductions in volunteers. Mental health services should develop clear remote assessment and care pathways for people who are suicidal, and staff training to support new ways of working. Helplines will require support to maintain or increase their volunteer workforce, and offer more flexible methods of working. Digital training resources would enable those who have not previously worked with people who are suicidal to take active roles in mental health services and helplines. Evidence-based online interventions and applications should be made available to support people who are suicidal.⁵

Loss of employment and financial stressors are well-recognised risk factors for suicide.⁶ Governments should provide financial safety nets (eg, food, housing, and unemployment supports). Consideration must be given not only to individuals' current situations but also their futures. For example, many young people have had their education interrupted and are anxious about their prospects. Educational institutions must seek alternative ways to deliver curricula and governments need to be prepared to offer them financial support if necessary. Active labour market programmes will also be crucial.⁶

The pandemic could adversely affect other known precipitants of suicide. For example, domestic violence and alcohol consumption might increase during lockdown. Public health responses must ensure that those facing interpersonal violence are supported and that safe drinking messages are communicated. Social isolation, entrapment, and loneliness contribute to suicide risk⁷ and are likely to increase during the pandemic, particularly for bereaved individuals. Providing community support for those living alone and encouraging families and friends to check in is helpful. Easily accessible help for bereaved individuals is crucial.

Access to means is a major risk factor for suicide. In the current environment, certain lethal means (eg, firearms, pesticides, and analgesics) might be more readily available, stockpiled in homes. Retailers selling such products should be especially vigilant when dealing

with distressed individuals. Governments and non-governmental organisations should consider temporary sales restrictions and deliver carefully framed messages about reducing access to commonly used and highly lethal suicide means.

Irresponsible media reporting of suicide can lead to spikes in suicides.⁸ Repeated exposure to stories about the crisis can increase fear⁹ and heighten suicide risk. Media professionals should ensure that reporting follows existing¹⁰ and COVID-19-specific guidelines.

Comprehensive responses should be informed by enhanced surveillance of COVID-19-related risk factors contributing to suicidal behaviours. Some suicide and self-harm registers are now collecting data on COVID-19-related stressors contributing to the episode; summaries of these data will facilitate timely public health responses. Repeat representative cross-sectional and longitudinal surveys will help identify increases in population-level risk, as might anonymised real-time data on caller concerns from helplines. Monitoring demands and capacity of mental health-care providers over the coming months is also essential to ensure resources are directed to those parts of the system under greatest pressure. These efforts need to be appropriately resourced and coordinated.

The suicide-related consequences of the pandemic might vary depending on countries' public health control measures, sociocultural and demographic structures, availability of digital alternatives to face-to-face consultation, and existing supports. The effects might be worse in resource-poor settings where economic adversity is compounded by inadequate welfare supports. Other concerns in these settings include social effects of banning religious gatherings and funerals, interpersonal violence, and vulnerable migrant workers. COVID-19-related stigma and misinformation may be particularly acute in these settings; many of the solutions proposed above will be applicable globally, but additional efforts will be required in resource-poor settings.

These are unprecedented times. The pandemic will cause distress and leave many people vulnerable to mental health problems and suicidal behaviour. Mental health consequences are likely to be present for longer and peak later than the actual pandemic. However, research evidence and the experience of national strategies provide a strong basis for suicide

prevention. We should be prepared to take the actions highlighted here, backed by vigilance and international collaboration.

Affiliations of the International COVID-19 Suicide Prevention Research Collaboration are listed in the appendix. The views and recommendations in this Comment are endorsed by the International Association of Suicide Prevention, the American Foundation for Suicide Prevention, and the International Academy of Suicide Research. DG, KH, and NK are members of the Department of Health and Social Care (England) National Suicide Prevention Strategy Advisory Group; LA is the chair. DG has grants from the National Institute for Health Research (NIHR) outside the submitted work, and is a member of Samaritans Policy and Research Committee and Mover's Global Advisory Committee. LA and KH hold grants from the Department of Health and Social Care during the conduct of this work. AJ reports chairing the National Advisory Group on Suicide and Self-harm Prevention to Welsh Government and is national lead on suicide prevention for Public Health Wales. NK reports grants and personal fees from the Department of Health and Social Care, NIHR, National Institute of Health and Care Excellence (NICE), and Healthcare Quality and Improvement Partnership, outside the submitted work, and works with NHS England on national quality improvement. He has chaired NICE guideline committees for self-harm and depression and is currently the topic advisor for the new NICE guidelines for self-harm. RCO'C reports grants from NIHR, Medical Research Foundation, Scottish Government, NHS Health Scotland, and Public Health Scotland, outside the submitted work. He is also co-chair of the Academic Advisory Group to the Scottish Government's National Suicide Prevention Leadership Group, and a member of NICE's guideline development group for the new NICE guidelines for suicide and self-harm. All other authors declare no competing interests.

*David Gunnell, Louis Appleby, Ella Arensman, Keith Hawton, Ann John, Nav Kapur, Murad Khan, Rory C O'Connor, Jane Pirkis, and the COVID-19 Suicide Prevention Research Collaboration†
d.j.gunnell@bristol.ac.uk

†Study group members: Louis Appleby, Ella Arensman, Eric Caine, Lai-Fong Chan, Shu-Sen Chang, Ying-Yeh Chen, Helen Christensen, Rakhi Dandona, Michael Eddleston, Annette Erlangsen, David Gunnell, Jill Harkavy-Friedman, Keith Hawton, Ann John, Nav Kapur, Murad Khan, Olivia J Kirtley, Duleeka Knipe, Flemming Konradsen, Shiwei Liu, Sally McManus, Lars Mehlum, Matt Miller, Paul Moran, Jacqui Morrissey, Christine Moutier, Thomas Niederkrotenthaler, Merete Nordentoft, Rory O'Connor, Siobhan O'Neill, Andrew Page, Michael Phillips, Jane Pirkis, Steve Platt, Maurizio Pompili, Ping Qin, Mohsen Rezaeian, Morton M Silverman, Mark Sinyor, Steven Stack, Ellen Townsend, Gustavo Turecki, Lakshmi Vijayakumar, Paul Yip.

National Institute for Health Research Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol BS8 2PS, UK (DG); Centre for Mental Health and Safety, National Institute for Health Research Greater Manchester Patient Safety Translational Research Centre, Manchester Academic Health Sciences Centre, University of Manchester and Greater Manchester Mental Health NHS Foundation Trust, Manchester, UK (LA, NK); School of Public Health and National Suicide Research Foundation, College of Medicine and Health, University College Cork, Cork, Ireland (EA); Centre for Suicide Research, University Department of Psychiatry, Warneford Hospital, Oxford, UK (KH); Population Psychiatry, Suicide and Informatics, Medical School, Swansea University, Swansea, UK (AJ); Department of Psychiatry, Aga Khan University, Karachi, Pakistan (MK); Suicidal Behaviour Research Laboratory, Institute of Health & Wellbeing, University of Glasgow, Glasgow, UK (RCO'C); and Centre for Mental Health, Melbourne School of Population and Global Health, University of Melbourne, Melbourne, VIC, Australia (JP)

See Online for appendix

- Holmes EA, O'Connor RC, Perry VH, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry* 2020; published online April 15. [https://doi.org/10.1016/S2215-0366\(20\)30168-1](https://doi.org/10.1016/S2215-0366(20)30168-1).
- Wasserman IM. The impact of epidemic, war, prohibition and media on suicide: United States, 1910–1920. *Suicide Life Threat Behav* 1992; **22**: 240–54.
- Cheung YT, Chau PH, Yip PS. A revisit on older adults suicides and severe acute respiratory syndrome (SARS) epidemic in Hong Kong. *Int J Geriatr Psychiatry* 2008; **23**: 1231–38.
- Yao H, Chen JH, Xu YF. Patients with mental health disorders in the COVID-19 epidemic. *Lancet Psychiatry* 2020; **7**: e21.
- Torok M, Han J, Baker S, et al. Suicide prevention using self-guided digital interventions: a systematic review and meta-analysis of randomised controlled trials. *Lancet Digital Health* 2020; **2**: e25–36.
- Stuckler D, Basu S, Suhrcke M, Coutts A, McKee M. The public health effect of economic crises and alternative policy responses in Europe: an empirical analysis. *Lancet* 2009; **374**: 315–23.
- O'Connor RC, Kirtley OJ. The integrated motivational-volitional model of suicidal behaviour. *Philos Trans R Soc Lond B Biol Sci* 2018; **373**: 20170268.
- Niederkrotenthaler T, Braun M, Pirkis J, et al. Association between suicide reporting in the media and suicide: systematic review and meta-analysis. *BMJ* 2020; **368**: m575.
- Garfin DR, Silver RC, Holman EA. The novel coronavirus (COVID-2019) outbreak: amplification of public health consequences by media exposure. *Health Psychol* 2020; published online March 23. DOI:10.1037/hea0000875.
- World Health Organization. Preventing suicide: a resource for media professionals. Update 2017. https://www.who.int/mental_health/suicide-prevention/resource_booklet_2017/en (accessed March 4, 2020).

The role of gender inequalities in adolescent depression

The gender difference in the prevalence of depression is one of the most robust findings in psychiatric epidemiology and has been replicated across many cultures.¹ Women are twice as likely to experience depression compared with men.¹ This gender difference is the result of a sharp increase in the incidence of depression in girls during mid-adolescence.²

There are many theories for the gender difference in depression, several of which are likely to be important.³ Explanations can be divided into two broad categories, internal and external. Internal factors refer to biological or psychological characteristics, such as sex hormones or differences in cognitive vulnerability. External factors,

in contrast, are environmental or societal, such as child sexual abuse. However, the distinction between internal and external factors is an artificial one. The external environment in which people develop also influences their own vulnerability, thus becoming internalised. Gender inequalities occur from birth onwards, and could lead to increased vulnerabilities to depression in girls.

According to cognitive models of depression, an individual's early experiences can lead to negative self-concepts that influence how they perceive, interpret, and remember their environment, and can increase the risk of depression.⁴ We propose that gender should be classified as an exposure variable within this causal

