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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.

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Michael Berk, Eduard Vieta, Olivia M Dean

Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Deakin University, Barwon Health, Geelong, VIC 3220, Australia (MB, OMD); Oxygen 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, Barcelona, Spain (EV); and Centro de Investigación Biomédica en Red Salud Mental, Barcelona, Spain (EV)

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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.

**Figure:** Public health responses to mitigating suicide risk associated with the COVID-19 pandemic

COVID-19-coronavirus disease 2019.

| Selective and indicated interventions | Universal interventions |
|--------------------------------------|-------------------------|
| **Mental illness**                   | **Isolation, entrapment, loneliness, and bereavement** |
| **Experience of suicidal crisis**    | **Access to means**     |
| **Financial stressors**              | **Irresponsible media reporting** |
| **Domestic violence**                |                         |
| **Alcohol consumption**              |                         |
| **Mental health services and individual providers** | **Government** |
| Deliver care in different ways (eg, digital modalities); develop support for health-care staff affected by adverse exposures (eg, multiple traumatic deaths); ensure frontline staff are adequately supported; given breaks and protective equipment; and can access additional support. | Provide financial safety nets (eg, food, housing, and unemployment supports; emergency loans); ensure longer-term measures (eg, active labour market programmes) are put in place. |
| **Government** | **Government** |
| Adequate resourcing for interventions | Public health responses that ensure that those facing domestic violence have access to support and can leave home. |
| **Mental health services and individual providers** | **Communities** |
| Clear assessment and care pathways for people who are suicidal, including guidelines for remote assessment; digital resources to train expanded workforce; evidence-based online interventions and applications. | Provide support for those who are living alone. |
| **Crisis helplines** | **Friends and family** |
| Maintain or increase volunteer workforce and offer more flexible ways of working; digital resources to train expanded workforce; evidence-based online interventions and applications. | Check in regularly, if necessary via digital alternatives to face-to-face meetings. |
| **Government** | **Mental health services and individual providers** |
| Adequate resourcing for interventions | Ensure easily accessible help is available for bereaved individuals. |
| **Government** | **Government** |
| Adequate resourcing for interventions | Adequate resourcing for interventions. |

Researchers and data monitoring experts
Enhanced surveillance of risk factors related to COVID-19 (eg, via suicide and self-harm registers, population-based surveys, and real-time data from crisis helplines).

Comments

469
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.

Loss of employment and financial stressors are well-recognised risk factors for suicide. 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.

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 risk 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. Repeated exposure to stories about the crisis can increase fear and heighten suicide risk. Media professionals should ensure that reporting follows existing 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
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. Women are twice as likely to experience depression compared with men. This gender difference is the result of a sharp increase in the incidence of depression in girls during mid-adolescence.

There are many theories for the gender difference in depression, several of which are likely to be important. 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. We propose that gender should be classified as an exposure variable within this causal

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