**Title: Mitigating the impacts of COVID: Where are the mental health trials?**

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**Opinion piece for The Lancet Psychiatry**

COVID-19 prompted the rapid mobilisation of health services and medical science in the face of unprecedented challenges. When COVID arrived in 2020, medical science delivered, and delivered very quickly. Using large-scale multi-centre trials, researchers in partnership with health services established the ability of cheap and scalable interventions (such as corticosteroids) to save lives, and very quickly demonstrated the futility of anecdotally-endorsed repurposed drugs (such as hydroxychloroquine). The effectiveness of vaccinations was very quickly established in phase II and III clinical trials, providing the confidence to roll out a successful vaccine programme.

Here we argue that trials have been fundamental to the global pandemic response, but we also reflect that mental health has not been part of this success story. In short, the mental health research community has been busy describing the nature of the impact of COVID, and less good at generating solutions and conducting clinical trials to establish ‘what works’ in mitigating this impact.

In the first instance it is instructive to look back at the first efforts of the mental health community in early 2020 in planning for the coming pandemic. In March 2020 an important rapid review was published in *The Lancet*.1 Brookes and colleagues explored the anticipated psychological impact of COVID (specifically the societal disruption that lockdown, infection and quarantine would bring), and what might be done to mitigate this. They predicted negative effects on mental health, and made broad suggestions for a public health response, including the identification of those at greatest risk (such as health workers or those with pre-existing psychiatric disorder). Some therapeutic suggestions were offered to reduce these effects, based on limited trial evidence, such as the offer of support groups for people who were quarantined at home. However, they noted a dearth of trial-based evidence to inform the mitigation of psychological impact and were unable to say with any confidence ‘what works’. Two position papers from early in the pandemic also highlighted research priorities in understanding the psychological impact of the pandemic;2,3 these formed a starting point from which to coordinate and deploy research effort and resources. There was general recognition of the need to assemble evidence of ‘what works’, but no specific encouragement to deliver an ambitious trials programme. The emphasis in both these documents was on mapping psychological impacts and underlying mechanisms.

Thereafter, others have observed an explosion of activity from the mental health research community,4,5 but this has been more about describing the problem rather than intervening. A thoughtful paper by Demokowicz and colleagues5 details a rapid but fragmented response, evidenced by the sheer volume of research studies with overlapping survey designs capturing quantitative data around depression, anxiety, and loneliness. Many of these studies have used suboptimal sampling methods,4 or analytic methods which do not account for biases or confounding. Demokowicz and colleagues make important suggestions for better cross-institutional collaboration, but make few comments on whether or how the research community has helped to mitigate the impact of COVID. Specifically, clinical trials are barely mentioned.

For physical health, the UK was at the forefront of the rapid evaluation of existing or repurposed treatments. The RECOVERY trial is the most notable example where the time from design to delivery of trials was reduced from years to weeks. Trialists drafted the RECOVERY protocol on 10 March 2020, and the results were announced for dexamethasone just 98 days later, after enrolling over 11 000 patients.6 Thereafter the treatment of COVID evolved rapidly and survival rates were transformed. In short, rapidly conducted trials saved lives.

How was this possible? The UK was able to make rapid advances following years of strategic investment in NHS research infrastructure (such as comprehensive research networks). At the start of the pandemic, researchers were told to halt all non-COVID-19 research and devote NHS research infrastructure to understanding and fighting the pandemic. A national prioritisation process was instituted (the Urgent Public Health (UPH) COVID-19 Programme [https://www.nihr.ac.uk/covid-studies/]). By May 2021, 98 UPH studies had been supported following an assessment process and scrutiny by a specially constituted committee. The UPH programme most notably supported the RECOVERY trial platform (<https://www.recoverytrial.net/>), described above, which has now recruited 40,000 participants to trials of physical treatments.6 Surprisingly, only two UPH studies relate to mental health. We know of the advantages of UPH since these were our own trials (BASIL ISRCTN940914797 and a follow-on trial BASIL+ ISRCTN63034289), designed to evaluate brief psychosocial interventions to prevent depression and loneliness in vulnerable populations (a research priority identified by Holmes and colleagues and O’Connor and colleagues).2,3 Two other ambitious randomised controlled trials are underway in the UK to specifically address mental health needs within the COVID context; SPARKLE which examines the use of an app for parents to mitigate the emotional and behavioural impacts of COVID on families,8 and CoCAT, which is evaluating an online intervention for children with anxiety problems during COVID restrictions (<https://osiresearch.org.uk/co-cat/>). These were not adopted by the UPH programme. The paucity of psychosocial evaluative research mirrors the global imbalance in trials, where research activity has focussed on pharmaceutical interventions rather than behavioural or public health solutions to the pandemic.9 However there are also examples where psychological insights and behavioural theory have been used to design and trial interventions designed to combat ‘vaccine hesitancy’.10

What have we learned from delivering mental health trials in the time of COVID?

First, trials can be more efficient. When supported by UPH and with a facilitative approval process we were able to design the BASIL trial and recruit the first participant within 11 weeks. 12 Trusts signed up to deliver the BASIL trial. For CoCAT the time from study start date to first recruit was 14 weeks, with 19 NHS Trusts participating, and this was mostly attributable to an efficient approvals process. This is an important lesson for the efficient delivery of trials in mental health and we should not discard this model as we move beyond the pandemic.

Second, trials require large collaborative networks in their design and delivery. The fragmentation and duplication of effort by the mental health research community under COVID is now clearly described5 and we believe describing the nature of the problem via repeated surveys has acted against the collective delivery of trials. Patients and the public should expect collaboration, coproduction and research prioritisation to deliver fully powered trials. Again, the RECOVERY trial demonstrates the art of the possible, where 176 hospitals were up and recruiting within weeks and a series of treatment uncertainties were resolved very quickly.6 As one treatment uncertainty was resolved, further questions were prioritised by an independent expert group. We suggest funders will expect this level of collaboration, responsiveness and efficiency in the future. We also reflect on the positive experience reported by collaborating centres from CoCAT and BASIL. As with RECOVERY, for many clinicians it was their first experience of trials collaboration. By contributing to collaborative interventional research, they told us they gained personally and professionally.

COVID will have continuing and long-term impacts on mental health, and there remain many unknowns. For some problems, the scaling up of existing treats is a sufficient response. However, many problems will be new and will exacerbate pre-existing health inequalities.5 They will require new evidence-informed solutions. Some of the impacts of COVID are in sections of the population where innovative (and unevaluated) methods of delivery (such as eHealth) are needed in non-mental health settings, such as schools. Other impacts are on the NHS workforce, where the problems of workplace stress and moral injury require scalable interventions and decisions about when, how and whether to intervene. Some new problems, such as ‘long COVID’ will require greater levels of integration of psychosocial models of care with physical health services. Where evidence is not available to inform mental health practice and policy, then trials should be rapidly designed and delivered at scale to establish what works and to discard that which is ineffective. Mental health should always be on the same page as physical health, and this has become even more urgent during COVID. Our speciality has not yet delivered the equivalent of the RECOVERY trial and we should reflect on why this is. Surveys are a necessary, but not a sufficient response. We would suggest that it is time to rebalance research activity away from describing the nature of the problem to intervening and evaluating ‘what works’.

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Prof Ekers reports that he is a member of the committee which adopts and monitors studies for the Urgent Public Health COVID-19 Studies programme

Prof McMillan reports that he is an independent member of the Trial Steering Committee for the Co-CAT trial, which is funded by the DHSC/UKRI mental health programme.

Prof. Wright reports that he is Director of the Bradford Institute for Health Research, and is Director of the NIHR Yorkshire and Humberside Applied Research Collaboration (YHARC). He was charged with the delivery of UPH studies (including the RECOVERY trial) in a large NHS hospital trust.

Prof. Creswell is PI for the CoCAT trial (funded by the DHSC/UKRI mental health programme) and Co-I for the SPARKLE trial and Co-SPACE study (both funded by the UKRI COVID-19 responsive mode).

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