Authors' reply

Carsten Hjorthøj and colleagues question the extent to which the effects of cannabidiol as a pharmacological treatment for cannabis use disorder might be clinically meaningful. As they pointed out, and as discussed in our Article,[1] the phase 2a trial was not designed to estimate the magnitude of efficacy. However, phase 2a trials can be valuable when testing a novel indication with no previous evidence on what doses might be efficacious or safe. We found that cannabidiol 400 mg and cannabidiol 800 mg were more efficacious than placebo according to both primary endpoints (reduced urinary 11-nor-9-carboxy-δ-9-tetrahydrocannabinol:creatinine ratio and increased days with abstinence from cannabis during treatment) based on a priori Bayesian criteria. We did not make inferences about clinical relevance in our Article and it would be premature to do so because our phase 2a trial was not intended to address this question. Larger phase 2b or phase 3 trials are needed to determine how efficacious and clinically meaningful the effects of cannabidiol are at the doses we identified in our trial.

We used a 4-week treatment design, similar to the first randomised clinical trial of cannabidiol for the treatment of psychosis. More research is needed to test different dosing durations and formulations. Three randomised clinical trials have investigated nabiximols (low dose cannabidiol and tetrahydrocannabinol).[2–4] Only one trial found a reduction in cannabis use compared with placebo,[4] and none of the trials reported increases in sustained abstinence compared with placebo.

Hjorthøj and colleagues believe that a change in paradigm is needed in the treatment of cannabis use disorder, away from a focus on reduction in use and towards complete abstinence. Their views contrast with expert consensus on clinical outcomes for cannabis use disorder trials, published in 2020:[5] the primary recommendation is that sustained abstinence from cannabis should not be considered the primary outcome for all cannabis use disorder clinical trials because it has multiple limitations. Furthermore, given the absence of any recommended pharmacotherapies at present, a treatment that consistently reduces cannabis use would represent a major achievement towards decreasing the global burden of cannabis use disorders.

We declare no competing interests.

*Tom P Freeman, Chandni Hindocha, Gianluca Baio, H Valerie Curran
t.p.freeman@bath.ac.uk

Addiction and Mental Health Group, Department of Psychology, University of Bath, Bath BA2 7AY, UK (TPF); Clinical Psychopharmacology Unit (TPF, CH, HVC), Translational Psychiatry Research Group, Research Department of Mental Health Neuroscience, Division of Psychiatry (TPF, CH), Department of Statistical Science (GB), University College London, London, UK; National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK (TPF); and National Institute for Health Research, University College London Hospitals Biomedical Research Centre, London, UK (CH, HVC)

1 Freeman TP, Hindocha C, Baio G, et al. Cannabidiol for the treatment of cannabis use disorder: a phase 2a, double-blind, placebo-controlled, randomised, adaptive Bayesian trial. *Lancet Psychiatry* 2020; published online July 28. https://doi.org/10.1016/S2215-0366(20)30290-X.

2 Trigo JM, Soliman A, Quilty LC, et al. Nabiximols combined with motivational enhancement/cognitive behavioral therapy for the treatment of cannabis dependence: a pilot randomized clinical trial. *PLoS One* 2018; **13:** e0190768.

3 Allsop DJ, Copeland J, Lintzeris N, et al. Nabiximols as an agonist replacement therapy during cannabis withdrawal: a randomized clinical trial. *JAMA Psychiatry* 2014; **71:** 281–91.

4 Lintzeris N, Bhardwaj A, Mills L, et al. Nabiximols for the treatment of cannabis dependence: a randomized clinical trial. *JAMA Internal Medicine* 2019; **179:** 1242–53.

5 Loflin MJ, Kiluk BD, Huestis MA, et al. The state of clinical outcome assessments for cannabis use disorder clinical trials: a review and research agenda. *Drug Alcohol Depend* 2020; **212:** 107993.

Panel sampling in health research

In *The Lancet Psychiatry*, Matthias Pierce and colleagues[1,2] identify the importance of sampling in studying mental health effects of COVID-19. We found that a mental health survey[3] using a commercial panel (of approximately 20 000 people) overrepresented mentally unhealthy respondents by approximately 2·5 times. This overrepresentation occurred despite multiple measures to ensure representativeness: prespecified demographic and geographical sampling quotas; post-collection checks on the distribution of socioeconomic parameters; and adjustments for mismatches between clinical psychological scores and use of health-care services. Further random subsampling, before analysis, was required to correct for this sampling bias.

It seems that self-selected commercial survey panels in general might be biased towards mentally unhealthy or unhappy individuals. Commercial survey organisations operate through networks of subcontractors who hold customer contact lists. Individuals self-select to take part, for a small financial incentive. This might create bias towards people who are in difficult financial circumstances, and hence are under mental stress. The turnover in these self-selected panels is high.

It is now easy to target precise population segments using social media, but difficult to obtain random representative population samples. Political[4] and personality[5] representativeness have been tested. Surveys measuring mental health specifically can correct for bias during analysis.[3] However, commercial surveys are also widely adopted in physical and social health research, and these might risk invalid results if they omit mental health measures.

We declare no competing interests.

*Alienor Chauvenet, *Ralf Buckley, Leah Hague, Chris Fleming, Paula Brough
r.buckley@griffith.edu.au

School of Environment and Science (AC, RB), School of Applied Psychology (LH, PB), and School of Business (CF), Griffith University, Gold Coast Campus, QLD 4222, Australia