symptoms (OR 1·70 [1·07–2·70], p=0·0251). When examining trauma subtypes up to age 11 years (exposure up to age 6 years was not examined due to low frequencies), interpersonal trauma was consistently associated with increased odds of DMDD, even when adjusting for confounders and previous mental health problems (OR 1·83 [1·03–3·24], p=0·0394). By contrast, non-interpersonal trauma was associated with increased odds of DMDD in unadjusted analysis (OR 1·89 [1·10–3·25], p=0·0205), but not in adjusted analyses. Finally, to establish temporality, when examining trauma exposure up to age 6 years, childhood trauma was not associated with DMDD at age 11 years. However, just 14 children diagnosed with DMDD were exposed to trauma up to age 6 years; thus, these analyses had limited power.

In sum, the association between childhood trauma and DMDD is of a similar magnitude to the previously reported associations for other common mental disorders in the 2004 Pelotas Birth Cohort,[2] with preliminary evidence to indicate that interpersonal trauma might be a particularly important exposure in relation to this disorder. However, temporal evidence that can inform causal direction of effects is needed.

We declare no competing interests.

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Psychotherapy and psychedelic drugs

In *The Lancet Psychiatry*, Ioana A Cristea and colleagues[1] propose that new treatments for mental disorders should be routinely compared with psychotherapy. The authors used psychedelic therapy for post-traumatic stress disorder (PTSD) with 3,4-methylenedioxy-methamphetamine (MDMA) as a recent example. I share the authors' opinion that psychotherapy is a primary treatment option in psychiatry that should always be considered, and that the psychotherapy component of psychedelic-assisted therapy should be regulated. Nevertheless, I oppose the notion that new psychedelic treatments for trauma-related mental disorders should be directly compared with psychotherapy in clinical trials.

One should bear in mind how difficult it can be for many patients to tolerate exposure therapy and the high drop-out rate exposure therapy has. In patients with PTSD, the most common reason for non-response is insufficient stabilisation, so that patients are overwhelmed by exposure-based therapies and also often reject this therapy, which is consistent with studies showing that fewer than 10% of military veterans with PTSD choose trauma exposure as a treatment.[2] As a result, when establishing the rules and regulations for testing and providing access to psychedelic therapies, we should consider that many patients who could benefit from treatment will be unwilling to take part in standard psychotherapy (or therapy studies) yet will be open to trying psychedelic-assisted psychotherapy.

The psychotherapies used in drug-assisted trials are based on cumulative and converging therapeutic experiences over decades: the effectiveness and safety of the psychological aspect of psychedelic-assisted psychotherapy cannot be meaningfully tested independently. The psychotherapies used in the psychedelic drug trials have been standardised and treatment manuals have been prepared by the Multidisciplinary Association for Psychedelic Studies[3] and Compass Pathways.[4] The non-directive, integrative approach of the psychotherapies used in the psychedelic drug trials has the important advantage that they are less likely to cause long-lasting side-effects, such as overwhelming anxiety and retraumatisation, than other widely used therapeutic approaches. For example, a study of mindfulness-based psychotherapy in the USA enrolling adults seeking mindfulness meditation training for the alleviation of mild stress-related and trauma-related disorders reported high rates of meditation-related side-effects: 11 (14%) of 78 participants who completed treatment and provided data reported "lasting bad effects".[5]

The requirement to directly test all psychedelic therapies against psychotherapy would reduce the generalisability of the findings because it would exclude patients who reject standard psychotherapy and who might benefit particularly strongly from psychedelic therapy. In addition, including a failed course of psychotherapy in the definition of treatment-resistance would exclude many individuals with severe mental illness from a novel and promising treatment approach. Finally, psychedelic therapies have long traditional roots in many cultures, whereas standardised psychotherapy, particularly cognitive behavioural therapy, is a novel, western approach to mental illness. Although clinical trials for regulatory purposes are necessary for all new interventions, the need to directly compare

psychedelic-assisted therapies with a specific standard psychotherapy would unnecessarily prioritise the western approach over traditional and indigenous inspired ones, which is questionable from a political and cultural standpoint.

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Authors' reply

Regarding our proposal[1] that existent evidence-based psychological treatments should routinely be used as control conditions, Gregor Hasler argues that an exception should be made for psychedelic-assisted psychotherapies. The rationale would be the alleged impossibility of independently testing the efficacy and safety of the psychotherapy component in psychedelic-assisted psychotherapy. Yet it is exactly this untestable component combined with placebo that is administered to trial participants in the control group. Treating patients in a randomised trial with an intervention of unclear safety, let alone efficacy, violates foundational principles, such as the guarantee of access to the best available standard of care (hence not standing to lose by participating in a trial) and equipoise (ie, uncertainty about the relative benefits and harms of the treatments compared). Moreover, we cannot envision why a manualised psychological intervention, such as the psychotherapy component in psychedelic-assisted psychotherapy, could not be independently tested. Furthermore, Hasler's arguments about existent psychological interventions, particularly exposure for post-traumatic stress disorder (PTSD), are unsubstantiated. First, there is an array of efficacious psychological therapies for PTSD, both trauma-focused and non-trauma-focused,[2] with the latter not centred on exposure. Second, the notion that patients frequently reject exposure treatment is unsupported,[3] with the study[4] cited by Hasler concluding that "the current treatment preference literature shows that exposure treatment is a well accepted and preferred treatment for trauma-related difficulties". Finally, Hasler expresses concern that our proposal discriminates against non-Western and indigenous approaches, omitting that PTSD and trauma are themselves Western ways of understanding human experience and that there are current evidence-based psychotherapies, such as mindfulness-based approaches, that originated from non-Western cultures. Conversely, we believe even more attention should be directed to the psychological treatment component of psychedelic-assisted psychotherapies, by posing questions regarding the competences, training, supervision, and certification of providers, delivery settings, and more.

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