Mass General Brigham

Recent Psychedelics Trials Overview

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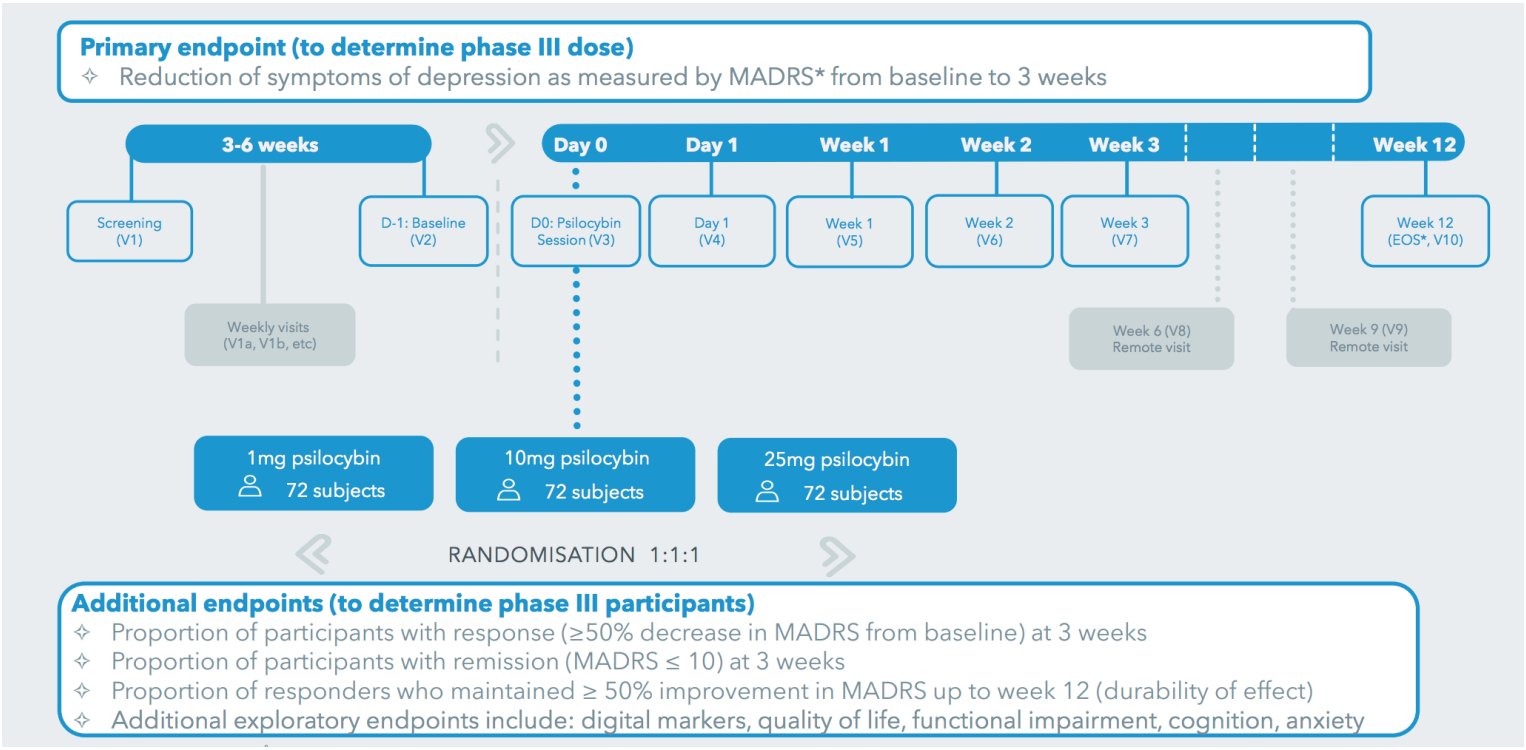
Psilocybin Assisted Psychotherapy for Depression

A randomised, controlled, double-blind trial, of a single dose of investigational psilocybin with psychological support in 233 patients with treatment resistant depression.



Goodwin, G. M., Aaronson, S. T., Alvarez, O., Arden, P. C., Baker, A., Bennett, J. C., ... & Malievskaia, E. (2022). Single-dose psilocybin for a treatment-resistant episode of major depression. *New England Journal of Medicine*, *387*(18), 1637-1648.

Psilocybin Assisted Psychotherapy for Depression

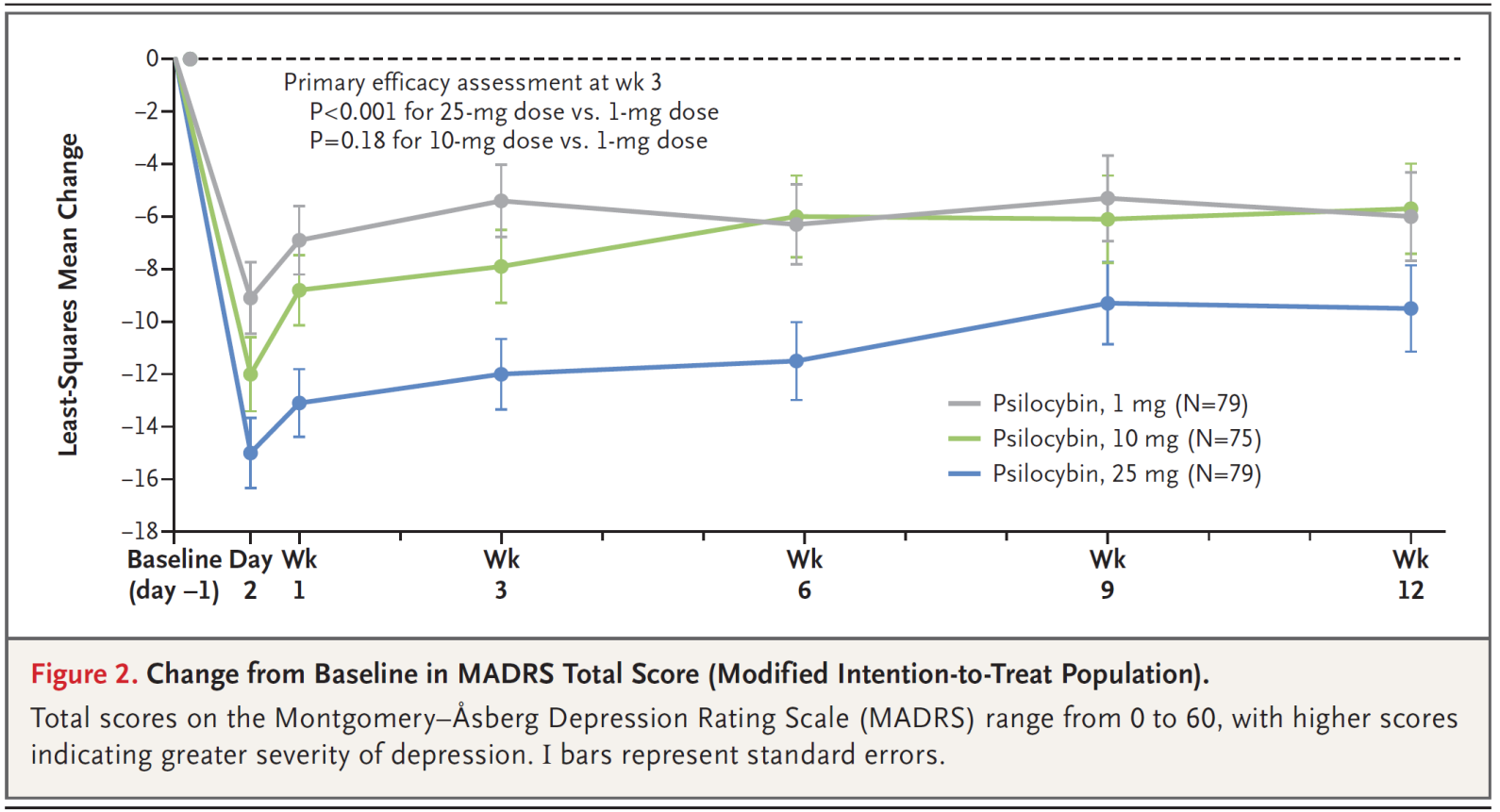


Figure 2. Change from Baseline in MADRS Total Score (Modified Intention-to-Treat Population).

Total scores on the Montgomery–Åsberg Depression Rating Scale (MADRS) range from 0 to 60, with higher scores indicating greater severity of depression. I bars represent standard errors.

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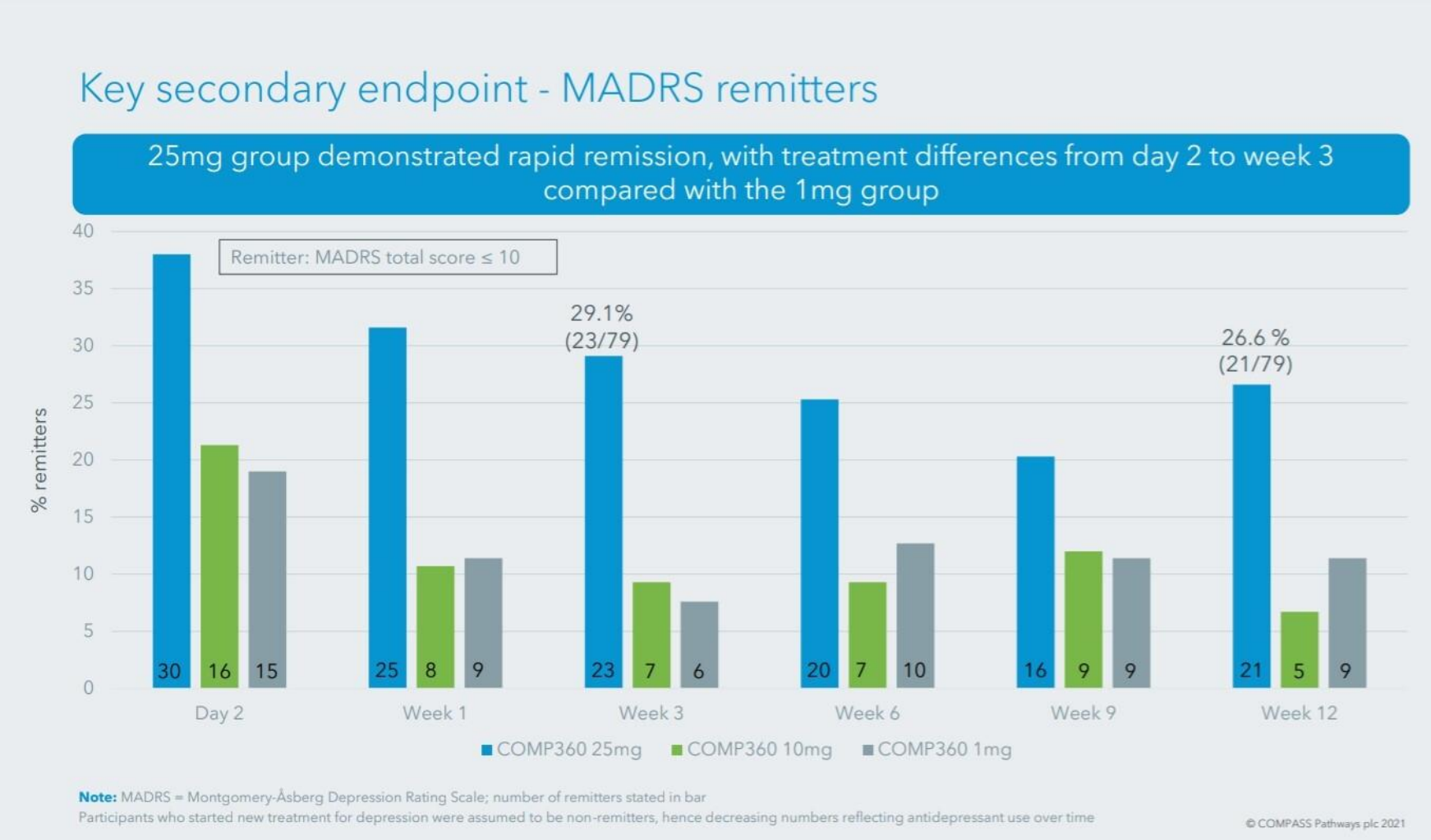

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Phase 2, double-blind, randomized, controlled trial involving patients with long-standing, moderate-to-severe major depressive disorder, comparing psilocybin with escitalopram, a selective serotonin-reuptake inhibitor, over a 6-week period.

Patients were assigned in a 1:1 ratio to receive two separate doses of 25 mg of psilocybin 3 weeks apart plus 6 weeks of daily placebo (psilocybin group) or two separate doses of 1 mg of psilocybin 3 weeks apart plus 6 weeks of daily oral escitalopram (escitalopram group); all the patients received psychological support.

Carhart-Harris, R., Giribaldi, B., Watts, R., Baker-Jones, M., Murphy-Beiner, A., Murphy, R., ... & Nutt, D. J. (2021). Trial of psilocybin versus escitalopram for depression. New England Journal of Medicine, 384(15), 1402-1411.

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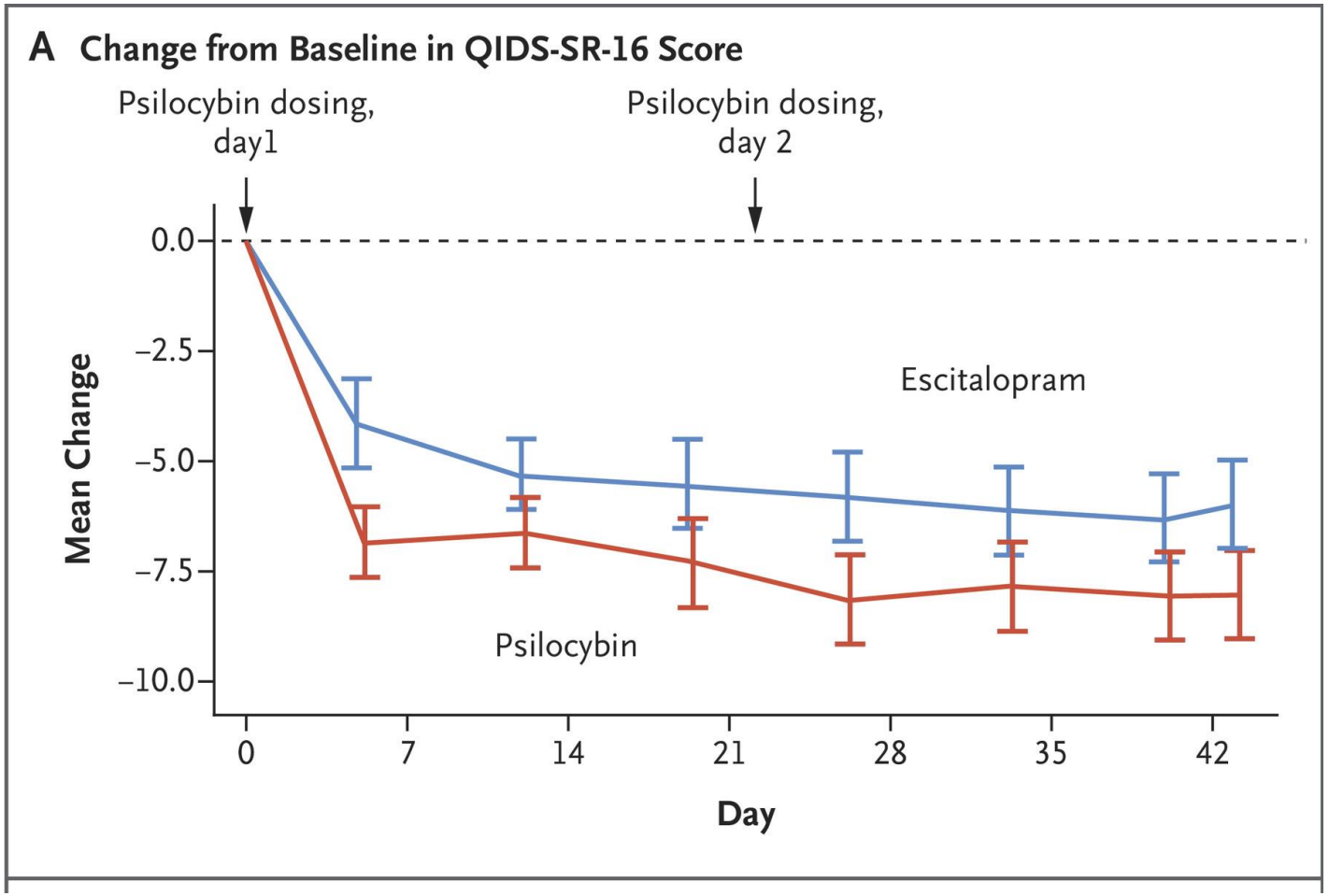

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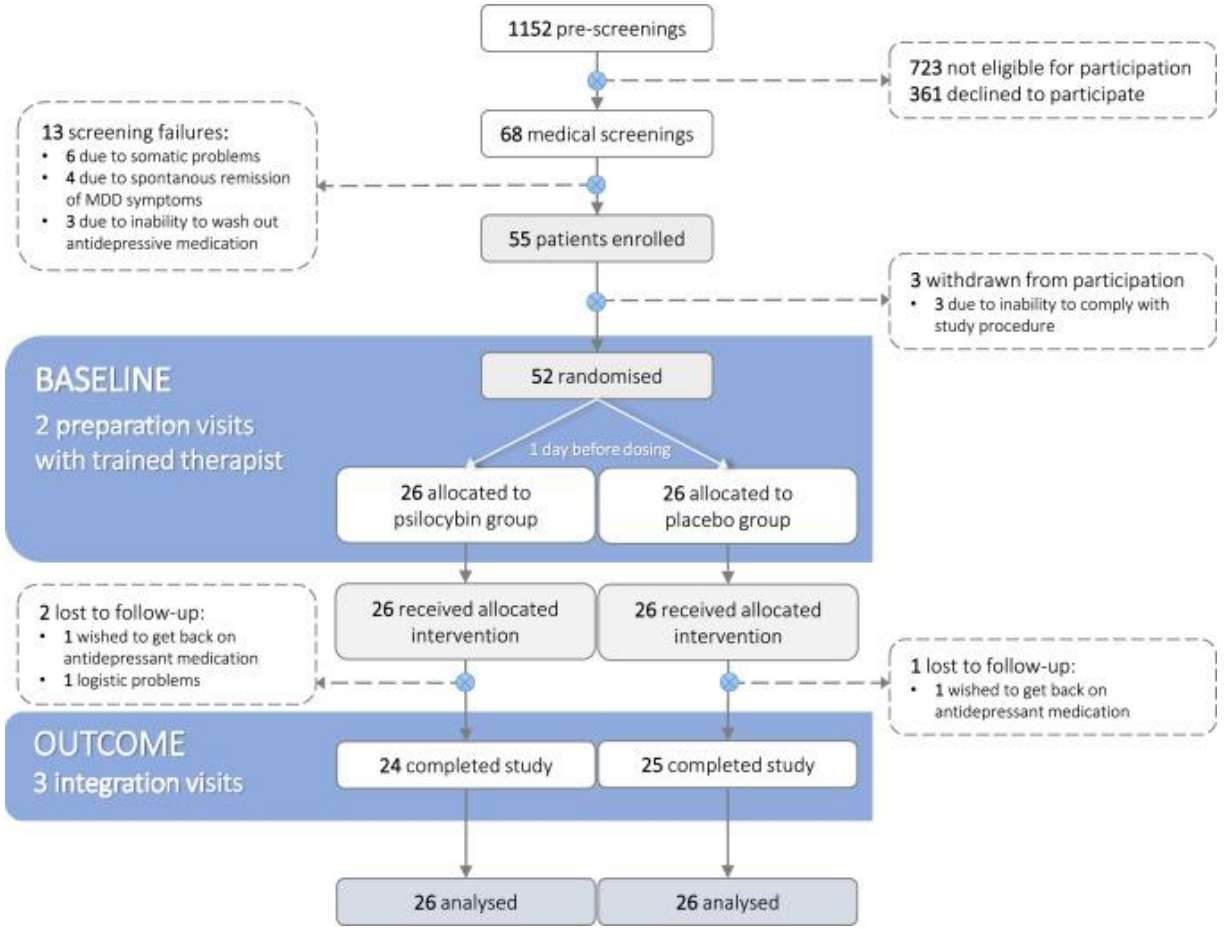

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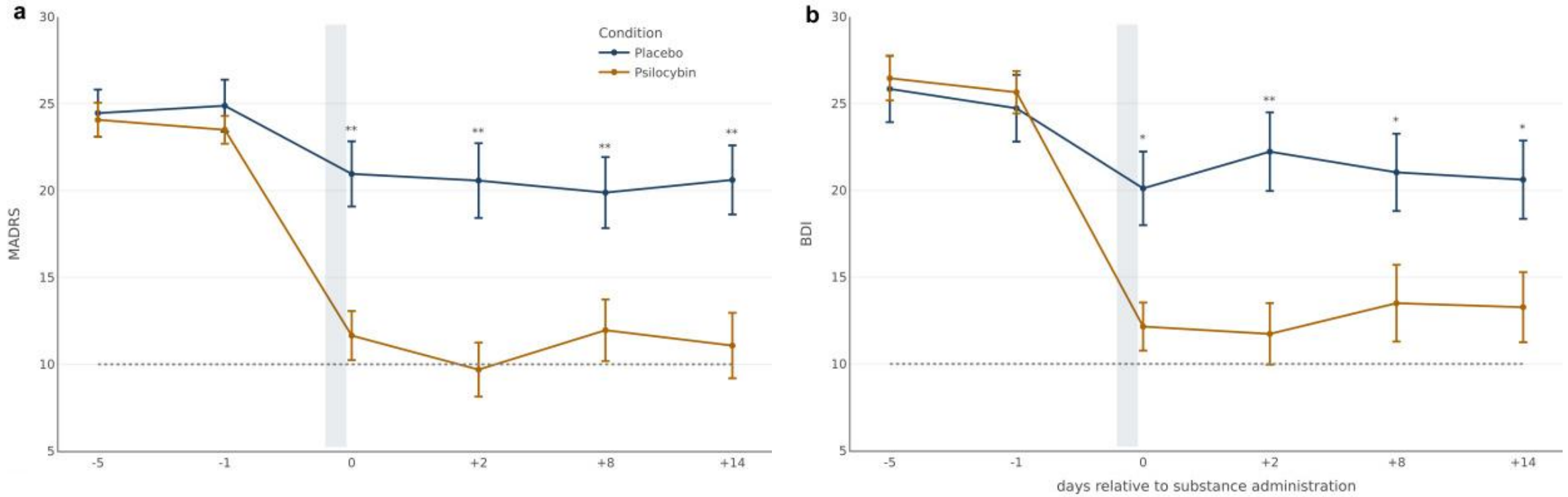

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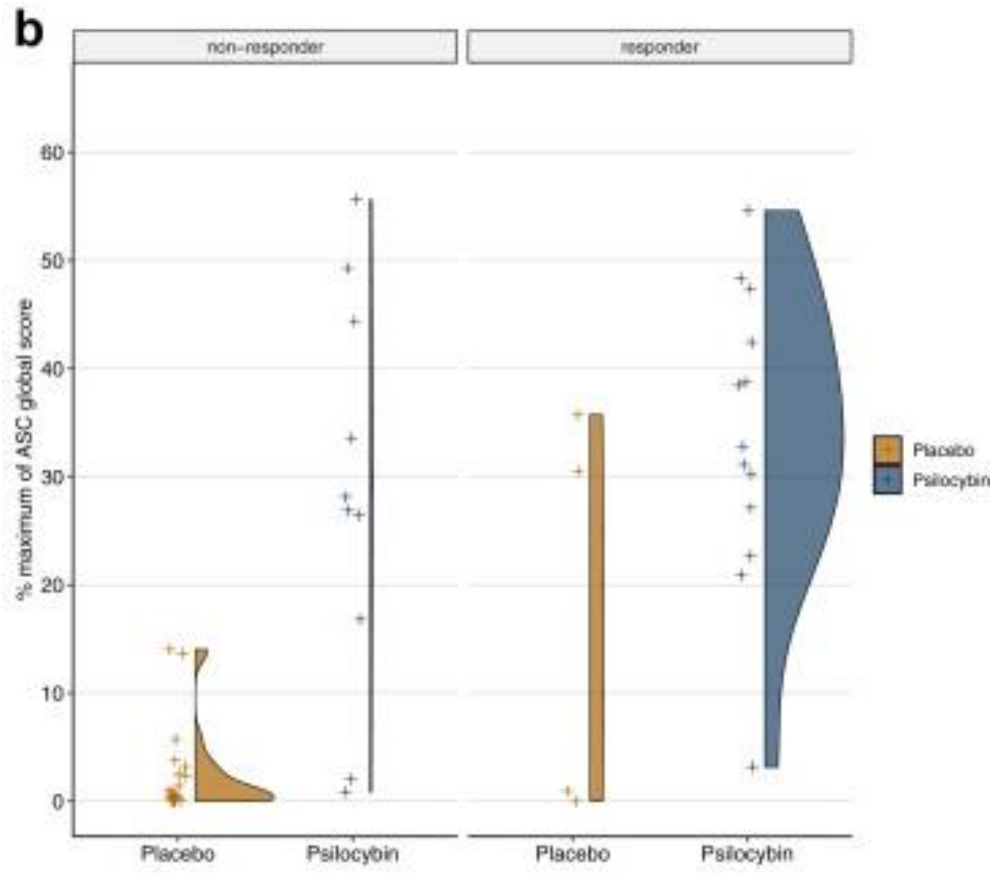

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Ayahuasca for Depression

Double-blind, placebo-controlled study of ayahuasca in 29 patients with TRD.

After a medication washout, patients had one administration, where they either received a liquid dose of ayahuasca or placebo, supported by two therapists next door, with the session lasting 8hrs.

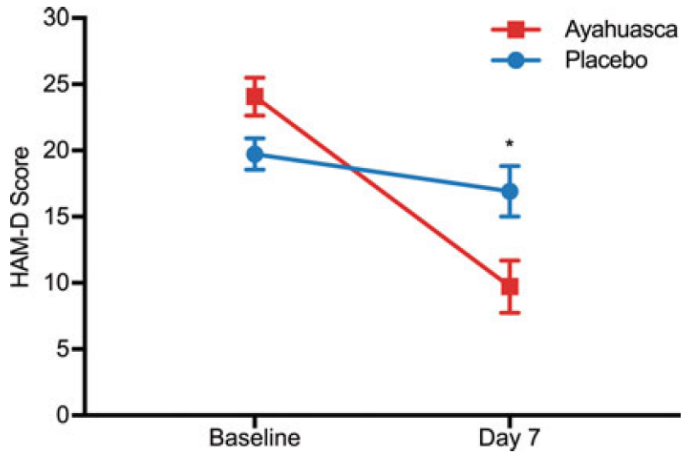


Fig. 2. HAM-D scores at baseline and seven days after dosing. Statistical analysis shows a significant difference between ayahuasca (squares) and placebo (circles) seven days after dosing ($p = 0.019$). Between-group effect size is high (Cohen's $d = 0.98$). Values are (mean ± S.E.M.). HAM-D scores: mild depression (8–16), moderate (17–23), severe (⩾24).

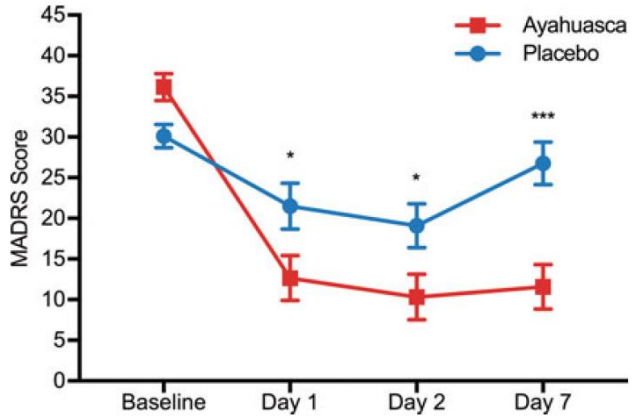
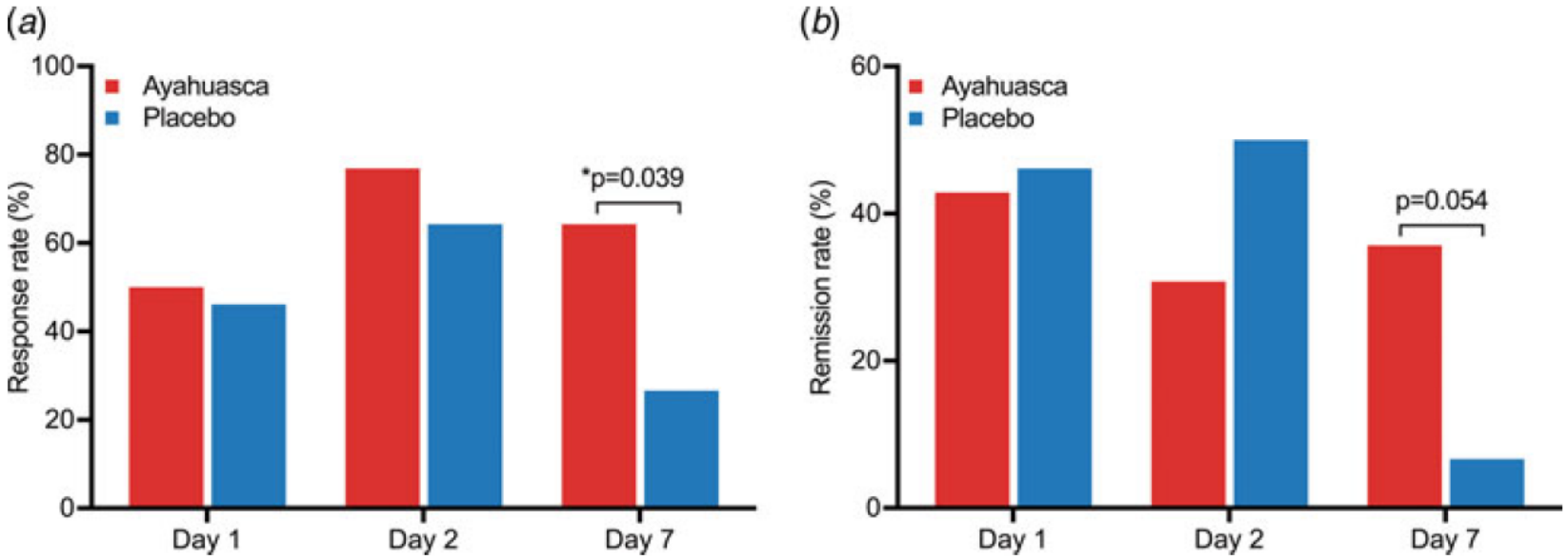


Fig. 3. MADRS scores as a function of time. Significant differences are observed between ayahuasca (squares) and placebo (circles) at D1 ($p = 0.04$), D2 ($p = 0.04$) and D7 ($p < 0.0001$). Between groups effect sizes are high at all time points after dosing: D1 (Cohen's $d = 0.84$), D2 (Cohen's $d = 0.84$), and D7 (Cohen's $d = 1.49$). Values are (mean ± S.E.M.). MADRS scores: mild depression (11–19), moderate (20–34), severe (⩾35). $^{*}p < 0.05$; $^{***}p < 0.0001$.

Palhano-Fontes, F., Barreto, D., Onias, H., Andrade, K. C., Novaes, M. M., Pessoa, J. A., ... & Araújo, D. B. (2019). Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial. *Psychological medicine*, *49*(4), 655-663.

Ayahuasca for Depression



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5 Me-O-DMT for Depression

Phase 2 Clinical Trial: Patients with TRD followed a proprietary individualized dosing regimen (IDR) with up to three increasing doses of 5 Me-O-DMT (6 mg, 12 mg and 18 mg) on a single day (short psychedelic experience on the order of minutes).

The primary endpoint was remission on the Montgomery–Asberg Depression Rating Scale (MADRS ⩽10) at day 7 after dosing.

7 of 8 patients (87.5%) in remission($p<0.0001$) with final dose to reach peak effect.

DMT for Depression

Phase IIa Clinical Trial: Intravenous DMT (20-30 min psychedelic experience) with supportive therapy in 34 patients with moderate/severeMDD

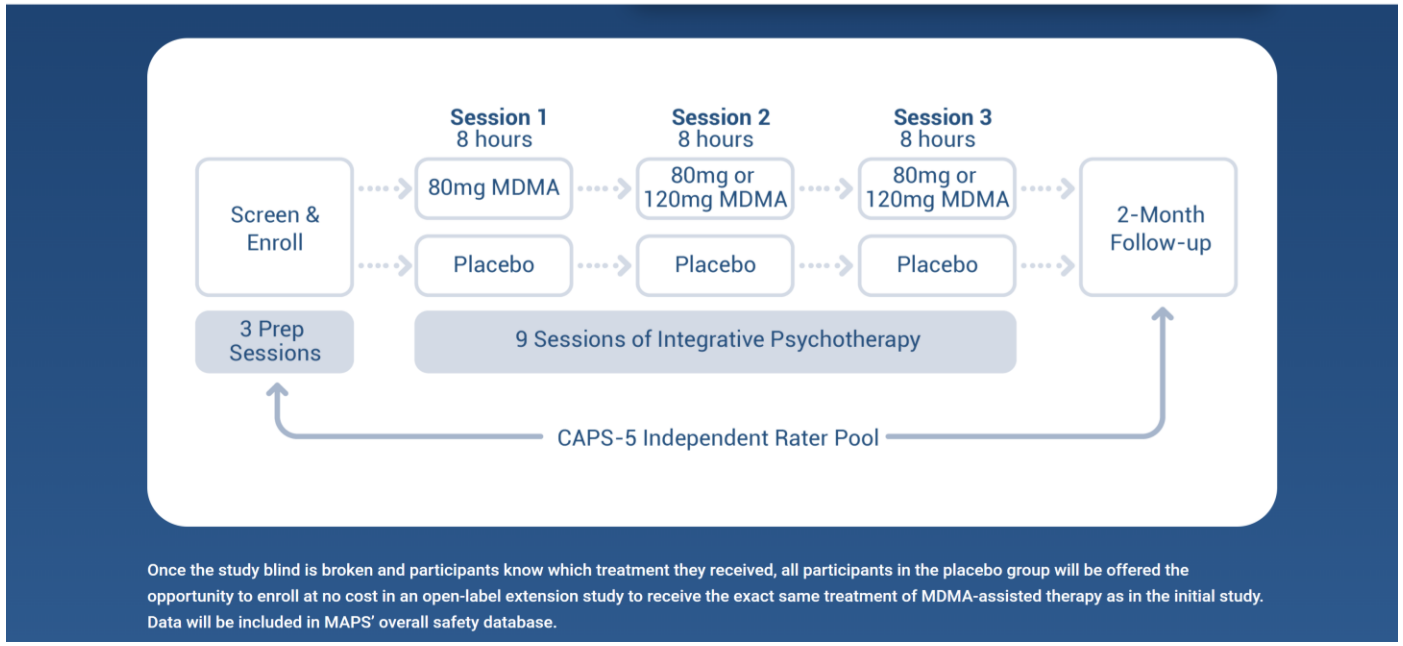
The primary endpoint was the Montgomery–Asberg Depression Rating Scale (MADRS). They found a statistically significant difference in MADRS scores between DMT (21.5mg) and placebo at two-weeks post-dose as measured by MADRS change from baseline (-7.4;p=0.02)

Rapid onset at one-week post-dose with a statistically significant difference in MADRS of -10.8 versus placebo (p=0.002).

57% remission rate (MADRS <10) at 12-weeks following a single dose.

MDMA Assisted Psychotherapy for PTSD

A randomized, double-blind, placebo-controlled, multi-site phase 3 clinical trial to test the efficacy and safety of 3,4-methylenedioxymethamphetamine (MDMA)-assisted therapy for the treatment of 90 patients with severe PTSD, including those with common comorbidities.



Therapists Marcela Ot'alora and Bruce Poulter are trained to conduct MDMA-assisted psychotherapy. In this reenactment, they demonstrate how they help guide and watch over a patient who is revisiting traumatic memories while under the influence of MDMA.

Courtesy of the Multidisciplinary Association for Psychedelic Studies

Mitchell, J. M., Bogenschutz, M., Lilienstein, A., Harrison, C., Kleiman, S., Parker-Guilbert, K., ... & Doblin, R. (2021). MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. Nature Medicine, 27(6), 1025-1033.

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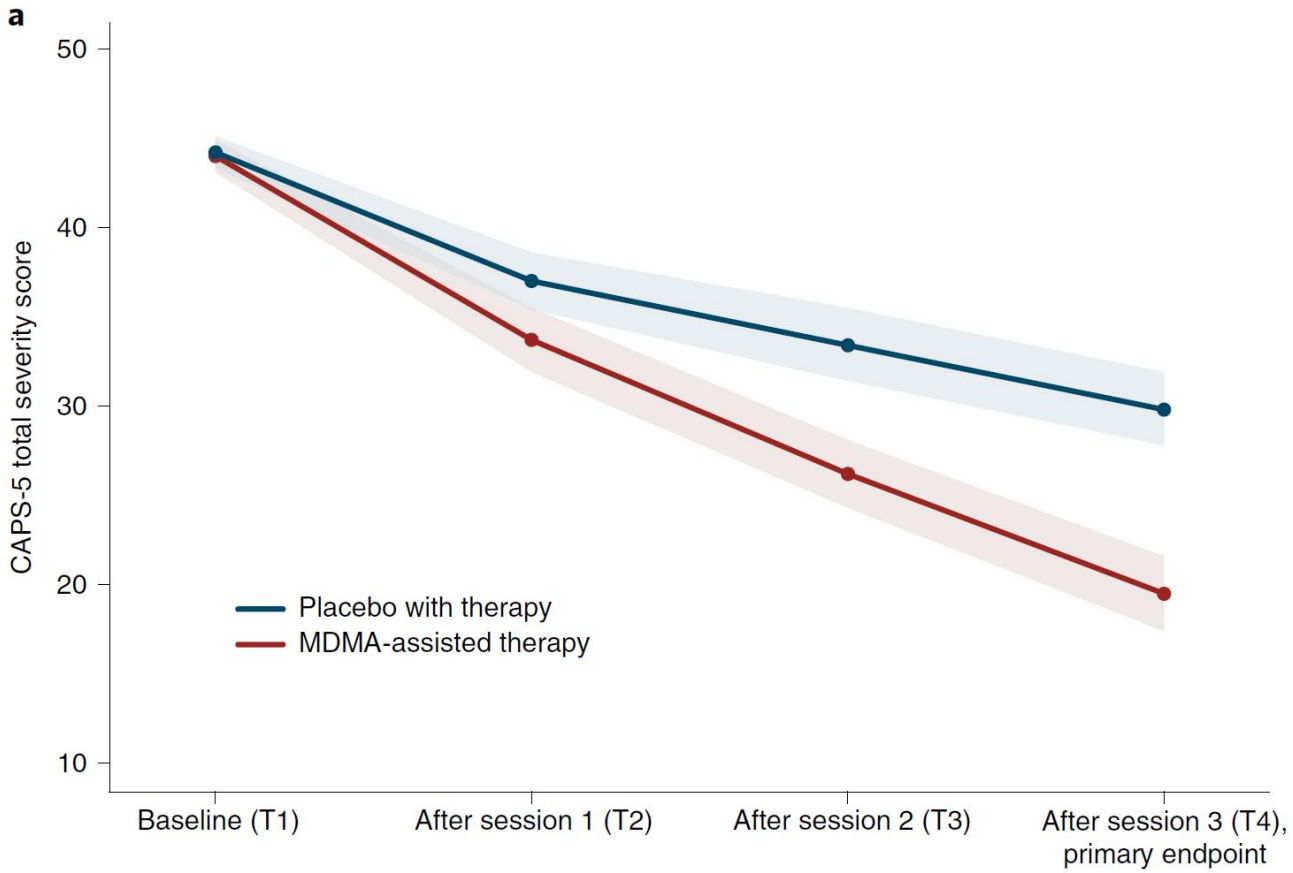

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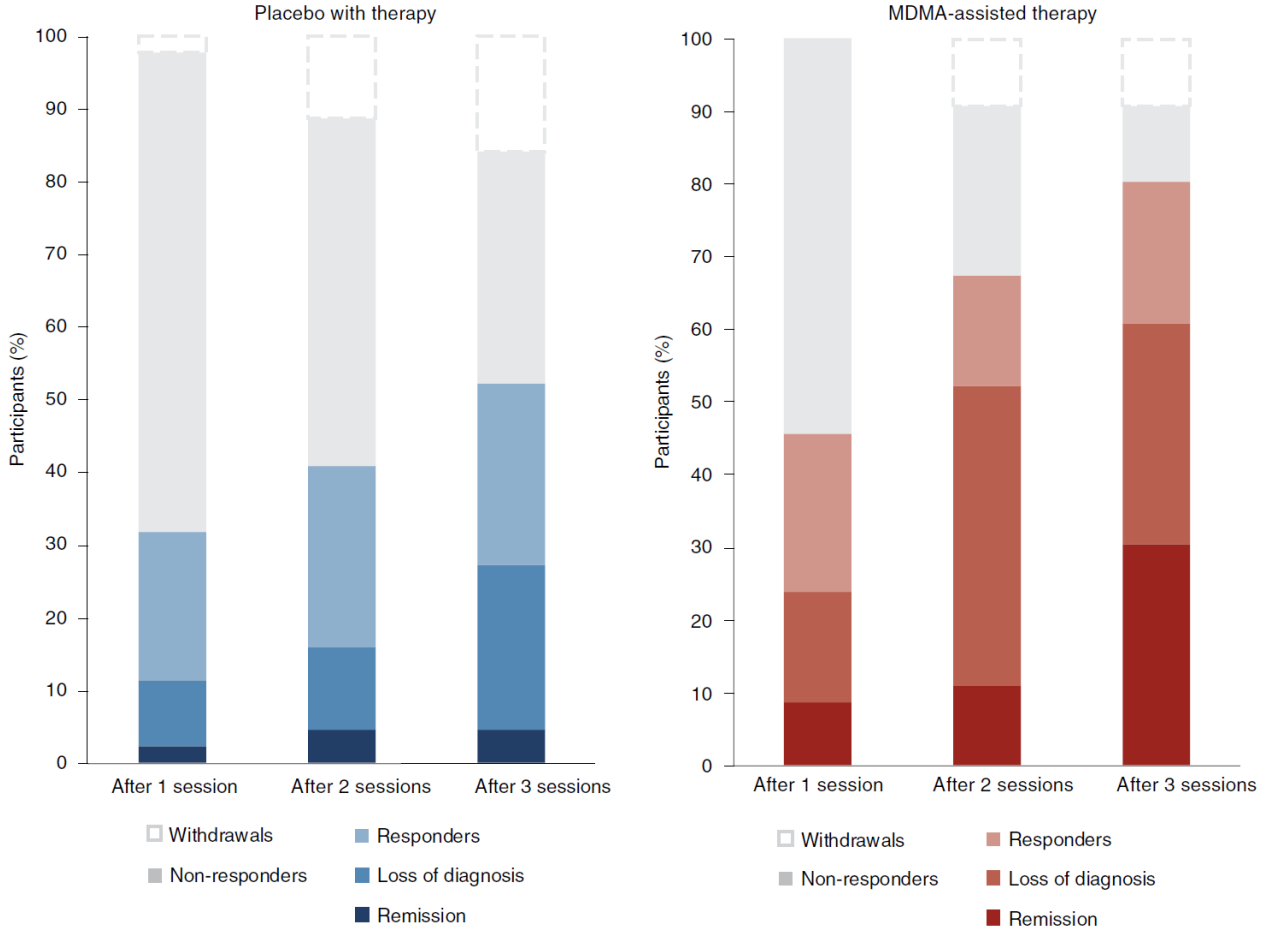

Fig. 3 | Treatment response and remission for MDMA and placebo groups as a percentage of total participants randomized to each arm (MDMA, *n* = 46; placebo, *n* = 44). Responders (clinically significant improvement, defined as a >10-point decrease on CAPS-5), loss of diagnosis (specific

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