Cannabidiol for the treatment of Cannabis Use Disorder: Findings from a Phase-III, multicentre, randomised, double-blind, placebo-controlled clinical trial.

Llew Mills[1,2], Anjali K. Bhardwaj[1,2*], Michael Doyle[1], Arshman Sahid[1,2], Mark Montebello[1,3], Lauren Monds[1,3], Shalini Arunogiri[4], Paul Haber[1,5], Valentina Lorenzetti[6], Dan I. Lubman[4], Peter Malouf[7], Mary E. Harrod[8], Adrian Dunlop[9], Tom Freeman[10] and Nicholas Lintzeris[1,2]

[1] Faculty of Medicine, University of Sydney, Camperdown, NSW, Australia.
[2] Drug and Alcohol Services, South East Sydney Local Health District, Sydney, NSW, Australia.
[3] Drug and Alcohol Services, North Sydney Local Health District, St Leonards, NSW, Australia.
[4] Centre for Addiction and Mental Health, Turning Point, Victoria, Australia.
[5] Drug Health Services, Sydney Local Health District, Sydney, Australia.
[6] Faculty of Health Science, Australian Catholic University, Victoria, Australia.
[7] Medicine and Health, University of New South Wales, Sydney, NSW, Australia.
[8] NSW Users and AIDS Association, Sydney, NSW, Australia.
[9] Drug and Alcohol Clinical Services, Hunter New England Local Health District, Newcastle, NSW, Australia.
[10] Addiction and Mental Health Group, University of Bath, Bath, UK.

Presenter's email: *llew.mills@sydney.edu.au*

Introduction: Cannabidiol (CBD) − a non-psychoactive compound contained in cannabis − could realistically be called the modern-day snake oil, being promoted as a treatment for everything from acne to anxiety. Preclinical and observational case studies have suggested that CBD may be effective for treating cannabis use disorder among those who wish to reduce their use. Several trials have tested the efficacy of medication containing both THC and CBD, but ours is the first randomised controlled trial to test the efficacy of a 100% CBD medication.

Methods: We conducted a 24-week, Phase-III, multisite, double-blinded, randomised clinical trial aiming to test whether 400 mg of daily CBD associated with greater reductions in self-reported cannabis use and urinary concentrations of cannabis than placebo. Secondary endpoints were craving and withdrawal severity, treatment retention, safety, patient satisfaction and motivation to quit. Participants received standard case management alongside cognitive behavioural therapy. Patient outcomes were measured at baseline, 3, 6, 9 and 12 weeks and again at a 24-week follow-up, 12 weeks after discontinuing medication

Results: We recruited 253 participants, 127 placebo and 126 CBD. While participants reduced their cannabis use overall, there was no significant between-group difference in days used over the 84-day trial (estimated mean difference = -1.3 [95%CI: -6.2, 3.3]), at any of the on-study measurement points, nor at the 24-week follow-up. No group differences were observed in any of the secondary endpoints nor in treatment retention. CBD was well-tolerated and not associated with any serious side-effects even at our relatively high doses.

Conclusions: The fact that CBD is a non-psychoactive and non-addictive molecule makes it an attractive first-line medication for cannabis use disorder. However, our findings suggest that CBD has no noticeable benefits over placebo. Clinicians reluctant to prescribe a THC-based medication for cannabis use disorder should not consider standalone CBD to be a viable alternative.

Disclosure of Interest Statement:
The authors declare no competing interests.