

## **A Randomised Controlled Trial of Cannabidiol (CBD) for the Treatment of Cannabis Use Disorder (CUD): a study protocol**

Nicholas Lintzeris<sup>1,2</sup>, Anjali Bhardwaj<sup>1,2</sup>, Dan Lubman<sup>3</sup>, Michael Doyle<sup>2</sup>, Adrian Dunlop<sup>4</sup>, Llew Mills<sup>1,2</sup>, Mary E Harrod<sup>5</sup>, Shalini Arugoniri<sup>3</sup>, Peter Malouf<sup>6</sup>, Paul Haber<sup>2,7</sup>, Tom P Freeman<sup>8</sup>, Mark Montebello<sup>2,9</sup>, Robert Graham<sup>10</sup>, Steven Childs<sup>11</sup>, Lauren Monds<sup>2,9</sup>, Meryem Jeffries<sup>10</sup>, Martin Nean<sup>4</sup> and Stephen Ella<sup>12</sup>

<sup>1</sup>Drug & Alcohol Services, South East Sydney Local Health District, Sydney, Australia,

<sup>2</sup>Faculty of Medicine, University of Sydney, Sydney, Australia, <sup>3</sup>Centre for Addiction and Mental Health, Turning Point, Victoria, Australia, <sup>4</sup>Drug & Alcohol Clinical Services, Hunter New England Local Health District, Newcastle, Australia, <sup>5</sup>NSW Users and AIDS Association, Sydney, Australia, <sup>6</sup>Townsville Aboriginal and Torres Strait Islander Corporation for Health Services, Queensland, Australia, <sup>7</sup>Drug Health Services, Sydney Local Health District, Sydney, Australia, <sup>8</sup>Addiction and Mental Health Group, University of Bath, UK, <sup>9</sup>Drug & Alcohol Services, North Sydney Local Health District, St Leonards, Australia, <sup>10</sup>Drug Health, Western Sydney Local Health District, Westmead, Australia, <sup>11</sup>Drug & Alcohol Services, Central Coast Local Health District, Australia, <sup>12</sup>Nunyarra Aboriginal Health, Central Coast Local Health District, Australia

Presenter's email: Anjali.bhardwaj@sydney.edu.au

**Background:** Cannabis use disorder (CUD) is increasingly common, affecting >150,000 Australians, and contributes to a range of health and social problems. Cannabis use is particularly prevalent among Aboriginal and Torres Strait Island people, with 24% aged ≥15 years reporting cannabis use in the past year, compared to 11.6% Australians. Results from a Phase IIa randomised clinical trial suggests that four-week treatment with cannabidiol (CBD), a cannabinoid with anticonvulsant, anxiolytic and antipsychotic effects, but without intoxicating or dependence-forming properties, reduces non-prescribed cannabis use in people with CUD. This study examines the efficacy, safety and quality of life of longer-term CBD treatment for patients with moderate-severe CUD.

**Method/ Design:** A phase III multi-site, randomised, double-blinded, placebo controlled parallel design, comparing a 12-week course of 400mg per day CBD (Epidyolex®) to placebo with both groups receiving 4-sessions of CBT-based counselling. Qualitative research interviews will be conducted with Aboriginal participants to explore their perspectives of treatment. 250 moderate-severe CUD adults (target 20% Aboriginal), with no significant medical, psychiatric or other substance use disorders, recruited from seven drug and alcohol clinics across NSW and VIC, Australia will be enrolled.

**Research Hypothesis:** It is expected that CBD compared to placebo will achieve significant reduction in non-prescribed cannabis use, measured by number of self-reported cannabis-free days and urinary THC-COOH levels.

**Discussion:** Current treatments for CUD have modest outcomes. Current psychosocial treatments for CUD indicate that over 80% of patients relapse within 1-6 months of treatment. Pharmacological treatments are highly effective with other substance use disorders making CBD a promising candidate as a treatment for CUD due to its excellent safety profile, and potential efficacy for this indication. Moreover, the anxiolytic, antipsychotic and neuroprotective effects of CBD may have added benefits by reversing many of the mental health and cognitive impairments seen with chronic cannabis use.

**Disclosure of Interest Statement:** This work was supported by a National Health and Medical Research Council (NHMRC) Project Grant (APP2014980).