

**Response to Commentaries:**

**The Grassy Knoll... and an Elephant.**

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*“... as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns -- the ones we don't know we don't know.”*

Secretary of Defense Donald H. Rumsfeld, February 12, 2002[1]

Copeland [2] suggests that there are currently enough known knowns about cannabis use and its consequences for us to develop suitable evidence-based and targeted cannabis-related policies, treatment guidelines, and prevention and intervention strategies. As is apparent from the other commentaries [3-6], this is not a universally held opinion. For example, there known unknowns that are essential for evidence-based and targeted clinical practice and public health strategies which are discussed by Hammersley [3] (e.g., lack of a theory of dependence that fits cannabis using behaviour), Patton [4] (e.g., lack of knowledge of the predictive value of different indicators of use for health and developmental outcomes), and Andreasson [5] (e.g., lack of knowledge about the hidden population of cannabis users). All of the commentaries support the known known status of methodological limitations in the cannabis use literature [2-6].

Copeland, citing longitudinal studies, implies the association between cannabis use and psychosis is a known known [2]. However, as pointed out by Hammersley [3], the lack of any theory explaining how cannabis use might cause psychosis suggests that the nature of this relationship is a known unknown. Additionally, while longitudinal studies contribute to the determination of causality, this is only possible if confounding is adequately controlled, the cannabis data collected is appropriately detailed, and the assumptions on which the studies

are based are accurate [7]. Meta-analytic studies are only as accurate as the studies on which they are based [3].

Similarly, the inference that the relationship between high frequency of use and adverse outcomes is a known known [2] does not stand up once the methodological issues associated with frequency of use variables [4-7] are considered. The association between early onset of use and adverse outcomes also requires closer scrutiny because early onset of cannabis use is itself an outcome variable (or symptom) of adverse childhood experiences (e.g., neglect, abuse) [8]. Thus, another known unknown relates to what we actually assess when onset of use is employed as an independent variable to investigate adverse outcomes of use.

Although cannabis usage rates appear to be declining or stabilising in Western countries [2,9], this does not mean that use is not relatively normalised among young people in these societies [10]. Cannabis use is typically initiated in the late teens or early twenties [11], thus, if we want to get a feel for how normalised cannabis use is we need to not only consider the recent usage statistics for 14-19 year olds (12.9% in 2007) cited by Copeland [2] but also those for 20-29 year olds (20.8% in 2007)[12]. Similarly, it is important to consider lifetime prevalence rates, which were 20.0% and 49.5%, respectively [12].

Earleywine's 'elephant in the room' (adverse outcomes for users associated with the illegality of cannabis) [6] also deserves attention. We would contend that, although seldom acknowledged, this is already known. If we are serious about reducing the harms of cannabis use, for individual users and society at large, we cannot ignore those harms associated with the illegality of use [6]. Correspondingly, it is concerning that the legal status of cannabis hinders our ability to understand the effects of cannabis use by limiting research

options [5,6]. The prohibition debate should also include consideration of the harms to society that relate to our restricted ability to investigate the medicinal properties of cannabis, and the harms to those unable to use cannabis legally to alleviate suffering from diseases such as MS [13] and HIV [14].

As for the unknown unknowns, further research is always needed [3-5]. We hope other researchers, clinicians, policymakers, legislators, and users will join us in our quest to increase what is known about cannabis use and to develop sensible, evidence-based public health policies and legislation [3-6]. Transparency in this process, through open debate of what is known and unknown about cannabis use and its consequences [7], is essential if we are to move beyond the grass ceiling [4].

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