Published in final edited form as:

J Dev Behav Pediatr. 2015 ; 36(9): 767–768. doi:10.1097/DBP.0000000000000219.

THE KNOWLEDGE GAPS FOR MEDICAL MARIJUANA IN PEDIATRIC CONDITIONS

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Keywords

adolescent; cannabis; marijuana abuse; attention deficit disorder with hyperactivity; child development disorders; pervasive

We thank Dr. Bou Khalil for his thoughtful comments. Shortly after the publication of our manuscript,¹ the American Academy of Pediatrics (AAP) reaffirmed its opposition to using marijuana for medicinal purposes not approved through the US Food and Drug Administration regulatory process, citing known adverse health effects and risks to the developing brain.² However, recognizing the dearth of high-quality, randomized controlled trials (RCTs) of cannabinoids for pediatric conditions, the AAP recommended moving marijuana from Drug Enforcement Agency Schedule 1 to Schedule 2 in order to pave the way for future clinical trials.

Anecdotal reports continue to emerge of children with intractable epilepsy^{3,4} and severe autism⁵ who show symptomatic improvement after being administered cannabinoids. The call from the public for research on cannabinoids is growing louder and many families are already using marijuana for childhood conditions^{6–9} – this despite very little evidence on efficacy and in the face of known long-term harms. The medical community has an urgent duty to respond. As we face a tide of rapidly changing attitudes and policies on marijuana in the US and elsewhere, it is urgent that we prioritize carefully conducted RCTs to close the current knowledge gap.

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Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Dr. Bou Khalil also raised the issue of the ‘gateway’ hypothesis. The gateway hypothesis, which emerged from work by Denise Kandel in 1975, suggests that youth using marijuana are more likely to transition to other, harder drugs.¹⁰ Whether the gateway hypothesis describes a true phenomenon continues to be hotly debated. Although large-scale epidemiologic studies unequivocally show an association between early marijuana use and subsequent harder drug use,¹¹ mechanisms underlying this association remain unclear. It is possible that using marijuana during adolescence leads to neurobiological changes that ‘prime’ the brain for addiction to other substances, a process that has been carefully described for nicotine, for example.¹² On the other hand, studies on the gateway hypothesis – like all observational studies of marijuana to date – are intrinsically limited by confounding. It is possible that individuals who use marijuana at a young age are the very individuals who are inherently more likely to eventually use other illicit drugs; for these youth, marijuana is simply the first drug that they happen to encounter in their escalation of drug use given its ready availability.¹³ An alternate explanation is that when youth buy marijuana on the black market, this offers a point of sale for other illicit drugs.¹⁴

Patients, families, and physicians are faced with a dearth of evidence on the safety, efficacy, and tolerability of cannabinoids in the face of abundant evidence on the long-term harms of marijuana use. Although high quality RCTs on cannabinoids are urgently needed, we agree with the AAP that “given that some children who may benefit from cannabinoids cannot wait for a meticulous and lengthy research process, [...] some exceptions should be made for compassionate use in children with debilitating or life-limiting diseases”.² However, we continue to recommend exercising caution, since some symptoms, such as aggressive behaviors in autism, may show improvement with marijuana simply because cannabinoids have a sedating effect. In using medical marijuana, families may be trading away their child’s future health and well-being for short-term symptom control.

Acknowledgments

Drs. Hadland and Harris are supported by the Division of Adolescent and Young Adult Medicine at Boston Children’s Hospital and the Leadership Education in Adolescent Health Training Program T71 MC00009 (MCH/HRSA). Dr. Hadland is also supported by a National Research Service Award 1T32 HD075727 (NIH/NICHD). Drs. Knight and Harris are supported by the National Institute on Alcohol Abuse and Alcoholism (1R01AA021904, 1R34AA023026, 1R01AA02243) and National Institute on Drug Abuse (3U10DA013720-15S3).

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