

Letters

RESEARCH LETTER

Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products

As the use of cannabis (marijuana) for medical purposes has expanded, a variety of edible products for oral consumption has been developed. An estimated 16% to 26% of patients using medical cannabis consume edible products.^{1,2} Even though oral consumption lacks the harmful by-products of smoking, difficult dose titration can result in overdosing or underdosing, highlighting the importance of accurate product labeling.

Regulation and quality assurance for edible product cannabinoid content and labeling are generally lacking. We investigated the label accuracy of edible cannabis products.

Methods | An Internet directory of dispensaries, with a menu of products available at each, was used to determine purchase locations in San Francisco, California, Los Angeles, California, and Seattle, Washington. A list of dispensaries was generated, with individual businesses randomly selected until 3 were identified in each city that offered at least 1 edible cannabis product from each of 3 common categories (baked goods, beverages, candy or chocolate) with package labels that provided, at minimum, specific Δ^9 -tetrahydrocannabinol (THC) content.

Between August and October 2014, individuals with a physician's letter (in compliance with state laws) and no history of purchasing edible cannabis products were sent to the pre-selected dispensaries and instructed to buy as large a variety of products, in terms of type and labeled cannabinoid content, as possible within budget (\$400/city). Purchasers, but not dispensary staff, were aware that the products would be evaluated following purchase. None knew the details of the analyses or testing to be completed.

Cannabidiol (CBD) and THC are typically the most concentrated chemical components of cannabis and are believed to primarily drive therapeutic benefit.³ Studies suggest improved clinical benefit and fewer adverse effects with a THC:CBD ratio of 1:1.⁴ Even though other cannabinoids were analyzed, results focus on THC and CBD.

For testing, entire package contents were homogenized (crushed or mixed). Two 1.5-g (solid) or 25-g (liquid) samples of each product were tested via high-performance liquid chromatography, with results averaged and adjusted for total product weight.

When results of duplicate tests differed by more than 10% (cannabinoid heterogeneity), the entire product was analyzed (n = 37). Five randomly selected products in which duplicate testing was within 10% were subject to complete testing; results confirmed the accuracy of the duplicate test-

ing method. Products were considered accurately labeled if the measured THC and CBD content was within 10% of the labeled values, underlabeled if the content was more than 10% above the labeled values, and overlabeled if the content was more than 10% below the labeled values.

A χ^2 test was used (SPSS version 22; SPSS Inc) to evaluate effects of location on label accuracy. Significance was determined at $P < .05$ (2-sided).

Results | Of 75 products purchased (47 different brands), 17% were accurately labeled, 23% were underlabeled, and 60% were overlabeled with respect to THC content (Table 1). The greatest likelihood of obtaining overlabeled products was in Los Angeles and underlabeled products in Seattle ($\chi^2 = 12.94$, $P = .01$).

Non-THC content was generally low (Table 2). Forty-four products (59%) had detectable levels of CBD; only 13 had CBD content labeled. Four products were overlabeled and 9 were underlabeled for CBD. The median THC:CBD ratio of products with detectable CBD was 36:1, 7 had ratios of less than 10:1, and only 1 had a 1:1 ratio.

Discussion | Edible cannabis products from 3 major metropolitan areas, though unregulated, failed to meet basic label accuracy standards for pharmaceuticals. Greater than 50% of products evaluated had significantly less cannabinoid content than labeled, with some products containing negligible amounts of THC. Such products may not produce the desired medical benefit.

Other products contained significantly more THC than labeled, placing patients at risk of experiencing adverse effects.^{5,6} Because medical cannabis is recommended for specific health conditions, regulation and quality assurance are needed.

A limited number of cities, dispensaries, and products were included. Because no source lists all dispensaries, and many products are not labeled with cannabinoid content, a true random sample was not possible and the results may not be generalizable. However, this study illustrates the variability in label accuracy for edible cannabis products within 2 of the largest medical cannabis markets in the United States.

Ryan Vandrey, PhD
Jeffrey C. Raber, PhD
Mark E. Raber
Brad Douglass, PhD
Cameron Miller, MS
Marcel O. Bonn-Miller, PhD

Author Affiliations: Johns Hopkins University School of Medicine, Baltimore, Maryland (Vandrey); Werc Shop Laboratory, Pasadena, California (J. C. Raber, M. E. Raber); Werc Shop Laboratory, Bellevue, Washington (Douglass, Miller); University of Pennsylvania Perelman School of Medicine, Philadelphia (Bonn-Miller).

Table 1. Accuracy of Product Labeling

	Accuracy of Labeled Tetrahydrocannabinol (THC) Content		
	Accurately Labeled ^a	Underlabeled ^b	Overlabeled ^c
Overall (3 Cities)			
Products tested, No. (%) (N = 75)	13 (17)	17 (23)	45 (60)
Type of product, No.			
Baked goods	2	7	13
Beverages	3	2	8
Candy or chocolate	8	8	24
Amount of THC, mg			
Label range	15 to 200	20 to 1000	2 to 325
Actual range	15 to 183	34 to 1236	<1 to 267
Deviation in THC content amount, % ^d			
Mean (SD)	-3 (4)	28 (13)	-47 (29)
Maximum	9	55	-99
San Francisco, California			
Products tested, No. (%) (n = 32) ^e	8 (25)	4 (13)	20 (62)
Type of product, No.			
Baked goods	2	4	5
Beverages	1	0	5
Candy or chocolate	5	0	10
Amount of THC, mg			
Label range	15 to 200	90 to 1000	2 to 325
Actual range	15 to 183	139 to 1236	1 to 267
Deviation in THC content amount, % ^d			
Mean (SD)	-4 (3)	28 (18)	-44 (27)
Maximum	9	55	-93
Los Angeles, California			
Products tested, No. (%) (n = 20) ^e	4 (20)	9 (45)	7 (35)
Type of product, No.			
Baked goods	0	3	2
Beverages	2	0	0
Candy or chocolate	2	6	5
Amount of THC, mg			
Label range	40 to 120	20 to 200	25 to 210
Actual range	42 to 122	66 to 301	2 to 141
Deviation in THC content amount, % ^d			
Mean (SD)	1 (4)	27 (14)	-55 (34)
Maximum	6	51	-99
Seattle, Washington			
Products tested, No. (%) (n = 23) ^e	1 (4)	4 (17)	18 (78)
Type of product, No.			
Baked goods	0	0	6
Beverages	0	2	3
Candy or chocolate	1	2	9
Amount of THC, mg			
Label range	180	34 to 180	20 to 250
Actual range	164	46 to 206	<1 to 136
Deviation in THC content amount, % ^d			
Mean (SD)	-9 (0)	29 (10)	-61 (29)
Maximum	-9	35	-99

^a The THC content was within 10% of the product label.

^b The THC content exceeded the label by more than 10%.

^c The THC content was more than 10% below the package label.

^d Actual vs labeled amount.

^e Reflects number of products able to be purchased for less than \$400.

Table 2. Observed Cannabinoid Content

Type of Cannabinoid	Cannabinoid Content, mg	
	Median (IQR) ^a	Range
Tetrahydrocannabinol	54 (99)	<1-1236
Tetrahydrocannabinolic acid	2 (15)	<1-173
Cannabidiol	2 (3)	<1-51
Cannabidiolic acid	1 (5)	<1-20
Cannabigerol	3 (3)	<1-43
Cannabinol	2 (2)	<1-20

^a Presented because observed values were not normally distributed.

Corresponding Author: Ryan Vandrey, PhD, Behavioral Pharmacology Research Unit, Johns Hopkins University School of Medicine, 5510 Nathan Shock Dr, Baltimore, MD 21224 (rvandrey@jhmi.edu).

Author Contributions: Dr Vandrey had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Vandrey, J. Raber, Douglass, Bonn-Miller.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Vandrey, J. Raber, M. Raber, Bonn-Miller.

Critical revision of the manuscript for important intellectual content: Vandrey, J. Raber, Douglass, Miller, Bonn-Miller.

Statistical analysis: Bonn-Miller.

Obtained funding: Vandrey.

Administrative, technical, or material support: All authors.

Study supervision: Vandrey, J. Raber, Douglass.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Bonn-Miller reported receiving personal fees and nonfinancial support from Tilray (Division of Privateer Holdings) and travel reimbursement from Americans for Safe Access. No other disclosures were reported.

Funding/Support: This project was funded by Johns Hopkins University School of Medicine except for the cost of analytical testing, which was covered by Werc Shop Laboratories.

Role of the Funder/Sponsor: Neither Johns Hopkins University nor Werc Shop Laboratories played a role in the design or conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Correction: This article was corrected on June 23, 2015, to fix labels in the text and in Table 1.

- Grella CE, Rodriguez L, Kim T. Patterns of medical marijuana use among individuals sampled from medical marijuana dispensaries in Los Angeles. *J Psychoactive Drugs*. 2014;46(4):263-272.
- Walsh Z, Callaway R, Belle-Isle L, et al. Cannabis for therapeutic purposes: patient characteristics, access, and reasons for use. *Int J Drug Policy*. 2013;24(6):511-516.
- Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*. 2011;163(7):1344-1364.
- Vermersch P. Sativex[®] (tetrahydrocannabinol + cannabidiol), an endocannabinoid system modulator: basic features and main clinical data. *Expert Rev Neurother*. 2011;11(4)(suppl):15-19.
- Favrat B, Ménétrey A, Augsburg M, et al. Two cases of "cannabis acute psychosis" following the administration of oral cannabis. *BMC Psychiatry*. 2005; 5:17.
- Monte AA, Zane RD, Heard KJ. The implications of marijuana legalization in Colorado. *JAMA*. 2015;313(3):241-242.

COMMENT & RESPONSE

Housing for Homeless Adults With Mental Illness

To the Editor In a randomized trial of scattered-site housing with intensive case management for homeless adults with

mental illness compared with usual access to services, Dr Stergiopoulos and colleagues¹ found that the intervention resulted in increased housing stability during 24 months without improving generic quality of life. The modest effects are promising, but the particular distribution of psychiatric diagnoses within the study population suggests the effects may not be able to be extrapolated to the entire homeless population.

First, no information was given on whether the research interviewers were clinically trained. Fazel et al² have shown that the use of trained interviewers leads to lower prevalence rates of depressive disorder. Not using trained interviewers might therefore be an explanation for the high proportion of homeless adults with depressive episodes (59%) and panic disorder (23%) in the sample, but only 20% with psychotic disorders.

Second, because a major problem of homeless people is alcohol and drug dependence³ and psychiatric comorbidity is common in this population,⁴ the authors should conduct analyses to identify subgroups with better and worse responses.

Third, the influence of housing stability on adherence to drug treatment among homeless people with mental illness is relevant because higher adherence might lead to at least symptomatic relief in this population. Such effects might not be detected with a quality-of-life questionnaire, and measuring functional outcome is a challenging task in patients who are mentally ill.⁵

Michael Dettling, MD
Ion Anghelescu, MD

Author Affiliations: Psychiatry and Psychotherapy, Charité-University Medicine Berlin, Germany (Dettling); Department of Psychiatry, Clinic Dr Fontheim, Liebenburg, Germany (Anghelescu).

Corresponding Author: Michael Dettling, MD, Charité-University Medicine Berlin, Psychiatry and Psychotherapy, Hindenburgdamm 30, Berlin 12203, Germany (michael.dettling@charite.de).

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

- Stergiopoulos V, Hwang SW, Gozdzik A, et al; At Home/Chez Soi Investigators. Effect of scattered-site housing using rent supplements and intensive case management on housing stability among homeless adults with mental illness: a randomized trial. *JAMA*. 2015;313(9):905-915.
- Fazel S, Geddes JR, Kushel M. The health of homeless people in high-income countries: descriptive epidemiology, health consequences, and clinical and policy recommendations. *Lancet*. 2014;384(9953):1529-1540.
- Längle G, Egerter B, Albrecht F, Petrasch M, Buchkremer G. Prevalence of mental illness among homeless men in the community—approach to a full census in a southern German university town. *Soc Psychiatry Psychiatr Epidemiol*. 2005;40(5):382-390.
- Torchalla I, Strehlau V, Li K, Krausz M. Substance use and predictors of substance dependence in homeless women. *Drug Alcohol Depend*. 2011;118(2-3):173-179.
- Awad AG, Voruganti LN. Measuring quality of life in patients with schizophrenia: an update. *Pharmacoeconomics*. 2012;30(3):183-195.

In Reply The At Home/Chez Soi study recruited adults experiencing homelessness and mental illness and stratified them into high- and moderate-needs groups. The preva-