International Journal of Epidemiology, 2019, 1695–1700
doi: 10.1093/ije/dyz044
Advance Access Publication Date: 16 March 2019
Original article

Miscellaneous

Are cannabis users less likely to gain weight? Results from a national 3-year prospective study

Omayma Alshaarawy [1]* and James C Anthony[2]

[1]Department of Family Medicine, Michigan State University, East Lansing, MI, USA and [2]Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, MI, USA

*Corresponding author. Department of Family Medicine, Michigan State University, East Lansing, MI 48824, USA. E-mail: alshaara@msu.edu

Editorial decision 21 February 2019; Accepted 1 March 2019

Abstract

Background: Pre-clinical studies indicate increased food intake and weight gain as cannabinoid effects. Cross-sectional epidemiological studies, however, indicate lower prevalence of obesity among cannabis users. Here, we aim to study the weight-gain research question in the prospectively conducted National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

Methods: NESARC was designed to produce nationally representative estimates for the US population. Participants (aged 18+) completed computer-assisted personal interviews on cannabis use, body weight and height at Waves 1 (W1, 2001–02) and 2 (W2, 2004–05). General linear modelling yields estimates for change in body mass index (BMI) regressed on cannabis-use status, with covariate adjustment based on a conceptual model for BMI determinants ($n = 33\,000$).

Results: At W2, 77% of the participants never used cannabis, 18% had discontinued use ('quit'), 3% were initiates and 2% were persistent users. Estimated W1-to-W2 BMI change shows an increase for all subgroups. Compared with never-users (reference), inverse slope estimates and attenuated change (%) in BMI between W1 and W2 are seen for cannabis-use subgroups: quitters [$\beta = -0.81$; 95% confidence interval (CI) = –1.01, –0.60], initiates ($\beta = -0.97$; 95% CI = –1.36, –0.57) and persistent users ($\beta = -1.26$; 95% CI = –1.81, –0.72).

Conclusion: This new prospective study builds from anecdotes, pre-clinical studies and cross-sectional evidence on inverse associations linking cannabis use and obesity and shows an inverse cannabis–BMI increase association. Confirmatory studies with rigorous cannabis and BMI assays will be needed.

Key words: Cannabis, BMI, NESARC

Key Messages

- Activation of the cannabinoid receptors in animal models is associated with increased food intake and weight gain.
- Cross-sectional epidemiological studies in humans indicate lower prevalence of obesity in cannabis users.
- In the prospectively conducted US National Epidemiologic Survey on Alcohol and Related Conditions, the mean change in body mass index in Wave 2 was 2.7%.
- Evidence shows attenuated body mass index gain for cannabis-use subgroups when compared with never-users.

Introduction

Exogenous cannabinoids are a group of related compounds derived from the cannabis plant commonly known as marijuana. User anecdotes suggest that cannabis use promotes appetite. In addition, increased caloric intake among cannabis users when compared with non-users has been documented in both cross-sectional[1] and prospectively gathered human epidemiological studies.[2]

Receptors of the cannabinoid system (CB1R and CB2R) have attracted scientific interest beyond cannabis use due to their versatile functions, including roles in modulating food intake and energy metabolism.[3] In pre-clinical studies, the administration of CB1R antagonists reduced food intake and body weight in rodent models.[4]

If cannabis use activates the cannabinoid receptors, the higher caloric intake and the lower physical activity levels among users[5] might lead one to expect a positive association between cannabis use and weight gain. Surprisingly, many human epidemiological studies show the opposite. For example, Le Strat and Le Foll analysed cross-sectional evidence from Wave 1 (W1) participants in the US National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and found a lower prevalence of obesity in cannabis users compared with non-users.[6] Other cross-sectional studies reported similar findings.[7,8]

The prospectively gathered evidence on this association is less consistent. An inverse cannabis–body mass index (BMI) association can be seen in estimates from the adolescent and young adult samples of the US National Longitudinal Survey of Adolescent Health and the Australian Mater-University of Queensland Study of Pregnancy.[9,10] Rodondi and colleagues, however, found no association linking lifetime cannabis use with BMI in the US Coronary Artery Risk Development in Young Adults Study.[2]

Prospective NESARC data have become available and so the aim of the current study is to investigate the association of cannabis-use status and change in BMI with two waves of NESARC data. Here, NESARC offers advantages including studying the adult population with relatively stable developmental growth, the relatively short follow-up and the large sample size.

Methods

Study population

The NESARC multi-stage stratified sampling design was devised to produce nationally representative estimates for the US civilian residents age 18 years and older in all 50 states and District of Columbia.[11] Individuals residing in households and military personnel living off base were included, as were residents of these non-institutional group quarters: boarding or rooming houses, non-transient hotels and motels, shelters, facilities for housing workers, college quarters and group homes. The Census Supplementary Survey formed the sampling frame for the household portion of the NESARC sample whereas the Census 2000 Group Quarters Inventory formed the sampling frame for the group quarters portion of the NESARC sample. Black and Hispanic housing units and adults aged 18–24 years were oversampled. Weights were constructed to adjust for probabilities of selection, non-response and oversampling, and to represent the US population. The study protocol was reviewed and approved by the cognizant institutional review board for protection of human subjects in research.[12]

At W1, in 2001–02, the participation level was 81.0% ($n = 43\,093$). At Wave 2 (W2, 2004–05), eligible W1 participants were reassessed, with a mean between-wave interval of 36.6 months ($n = 39\,959$). Excluded from W2 were W1 participants in institutions, on active duty in the armed forces throughout fieldwork intervals and seriously impaired persons, as well as the deceased or deported ($n = 3134$). Some eligible participants ($n = 5306$) were not re-interviewed due to refusals or failure to reach or locate them. The resulting W2 participation level was 86.7% ($n = 34\,653$). For the current study, we excluded participants with missing information on BMI or cannabis-use status. Those lost to follow-up or not included in the current study owing to missing variables were older and less likely to be White, drink alcohol or use cannabis (data are not shown in table/figure).

Outcome

Assessment involved computer-assisted personal interviews completed in participants' residences. The study's key

response variable is change in BMI, with body weight and height self-reported at both waves. BMI was calculated as weight in kilograms (kg) divided by height in metres squared. Absolute change in BMI was calculated as the difference between W2 and W1 BMI, whereas relative change in BMI was calculated as the difference between W2 and W1 BMI, divided by W1 BMI and expressed as a percentage.

Main exposure

At W1, participants were asked about ever using cannabis, recency and frequency of use. At W2, participants were asked whether they used cannabis since the W1 interview. Based on this information, we formed cannabis-use subgroups (Supplementary Table 1, available as Supplementary data at *IJE* online). Briefly, W2 cannabis-use status was categorized as never use (lifetime never use at both W1 and W2), discontinuation or quitting (ever use at W1 or between the waves but did not use cannabis in the 12 months prior to W2 interview), initiation (did not use in the 12 months prior to W1, but used cannabis in the 12 months prior to W2 interview) and persistent use (used cannabis in the 12 months prior to both W1 and W2 interviews).

Statistical analyses

After descriptive statistics, general linear modelling (GLM) was used to yield estimates for BMI change regressed on cannabis-use-status subgroup indicators. An initial model specified adjustment for age and age squared (to account for linear and quadratic relationships of age and BMI change). A term for sex was added. Both sex and age qualified as exogenous confounders, helped predict BMI change and are not subject to influence by cannabis or BMI change.[13,14] Motivated by prior studies,[15,16] a subsequent set of terms were added to the model including ethnic self-identification and covariates possibly influenced by cannabis use: education attainment, alcohol drinking and tobacco cigarette use. Alcohol-drinking and tobacco-smoking W2 status were categorized as never use, quitter, initiate and persistent use using the same definitions as applied to cannabis-use status explained above. W2 NESARC analysis weights were applied during estimation, with Taylor Series Linearization for variance estimation. Stata ('svy') software was used.

Results

At W2, 77% of the participants never used cannabis in their lifetime, 18% had discontinued use ('quit'), 3% were initiates and 2% were persistent users. Table 1 shows that cannabis use is associated with tobacco use, alcohol use, being male and being younger. In this sample, all initiates and persistent cannabis users were in young to middle adulthood (all <66 years old), whereas BMI decreased with age consistent with prior evidence (due to loss of muscle mass).[17]

Estimated W1-to-W2 BMI change shows an increase for all subgroups (Table 1). However, cannabis-associated inverse relationships can be seen once age is taken into account using the GLM covariate approach (Table 2) or with exclusion of participants >65 years of age (Supplementary Tables 2 and 3, available as Supplementary data at *IJE* online).

In Table 2, a negative sign on regression slope estimates indicates an appreciably attenuated BMI gain for all cannabis-using subgroups, with the largest attenuation seen for the 'persistent use' subgroup [Δ BMI kg/m^2: $\beta = -0.45$; 95% confidence interval (CI) = –0.59, –0.30], then 'initiation' (Δ BMI kg/m^2: $\beta = -0.36$; 95% CI = –0.48, –0.24) and then 'quitting' (Δ BMI kg/m^2: $\beta = -0.24$; 95% CI = –0.30, –0.18). Table 2 discloses a congruent pattern of estimates when the outcome is respecified as relative BMI change. Covariate adjustment produced no appreciable departures from the age-adjusted estimates.

We conducted a post-estimation analysis with follow-up BMI at W2 set as a response variable and with baseline BMI at W1 set as a covariate. The result is a pattern of evidence that does not contradict the evidence from our preferred change score analysis (Supplementary Table 4, available as Supplementary data at *IJE* online). Additionally, when we used W1 lifetime cannabis-use status to define W2 categories (instead of W1 past 12-month use, Supplementary Tables 5 and 6, available as Supplementary data at *IJE* online), similar results are detected. A cannabis-associated attenuation of BMI gain also can be seen when tobacco history is respecified as a stratification variable (Table 3).

Discussion

This two-wave prospective study extends the evidence beyond initial NESARC cross-sectional inverse associations first reported by Le Strat and Le Foll. Its evidence shows an attenuated BMI gain for cannabis-use subgroups when compared with never-users and a possible gradient as we look across subgroups of quitting, initiation and persistent use.

Before detailed discussion of the study results, some study limitations deserve attention. Causal inferences are constrained, not only due to the observational nature of the study and the absence of experimental elements (e.g. randomization), but also because unobserved susceptibility

Table 1. Selected characteristics of the study participants by cannabis-use status as of Wave 2. Data for the US National Epidemiologic Survey on Alcohol and Related Conditions, Wave 2, 2004–05

W2 cannabis-use status[a]	Never-user $n = 26\,000$	Quitter $n = 5800$	Initiate $n = 800$	Persistent user $n = 650$	*P*-value
Weighted column % (SE) or weighted mean (SE)					
Age (years)	47.2 (0.07)	38.7 (0.09)	32.5 (0.21)	30.8 (0.24)	<0.001
Female	55 (0.2)	44 (0.4)	34 (0.7)	31 (1.0)	<0.001
Ethnic self-identification					
NH-White	71.0 (0.3)	79.3 (0.3)	74.8 (0.7)	75.2 (0.7)	<0.001
NH-Black	10.8 (0.2)	8.8 (0.2)	11.9 (0.4)	9.5 (0.6)	
Hispanic	11.4 (0.12)	6.9 (0.13)	7.6 (0.4)	7.9 (0.4)	
AI/AN	2.1 (0.12)	3.2 (0.17)	3.0 (0.5)	4.7 (0.3)	
Asian/Pacific Is.	4.6 (0.08)	1.9 (0.07)	2.7 (0.3)	2.7 (0.11)	
Education					
<High school	14.6 (0.17)	8.4 (0.3)	13.7 (0.6)	14.9 (0.9)	<0.001
High school	28.4 (0.22)	22.8 (0.4)	26.0 (0.8)	25.3 (0.9)	
>High school	57.0 (0.23)	68.8 (0.4)	60.4 (1.0)	59.8 (1.1)	
Tobacco-use status as of W2					
Never-user	57.1 (0.21)	30.1 (0.26)	28.3 (0.8)	18.6 (0.7)	<0.001
Quitter	23.5 (0.19)	32.5 (0.3)	15.7 (0.7)	15.0 (0.8)	
Initiate	1.8 (0.05)	1.1 (0.05)	9.6 (0.5)	2.8 (0.4)	
Persistent user	17.6 (0.22)	36.4 (0.4)	46.3 (0.9)	63.6 (0.9)	
Alcohol-use status as of W2					
Never-user	15.2 (0.18)	0.6 (0.08)	$n < 15$[a]	$n < 15$[a]	<0.001
Quitter	22.9 (0.21)	17.5 (0.3)	5.8 (0.5)	4.2 (0.25)	
Initiate	8.6 (0.12)	4.2 (0.17)	8.9 (0.3)	3.4 (0.5)	
Persistent user	53.3 (0.25)	77.7 (0.4)	84.8 (0.6)	92.2 (0.5)	
Δ BMI (kg/m^2)	0.61 (0.01)	0.60 (0.03)	0.64 (0.06)	0.59 (0.07)	0.94
% BMI change	2.73 (0.04)	2.68 (0.09)	3.03 (0.19)	2.81 (0.27)	0.47

[a]Sample counts are rounded using the differential privacy policy of the US Census Bureau to minimize potential disclosure risk.

Table 2. Association of cannabis use and change in BMI. Data for the US National Epidemiologic Survey on Alcohol and Related Conditions Wave 1 (2001–02) and Wave 2 (2004–05)

	Δ BMI (kg/m^2)					
W2 cannabis-use status	Age-adjusted β[a] (95% CI)	*P*-trend	Age- sex-adjusted β[b] (95% CI)	P-trend	Multivariable-adjusted β[c] (95% CI)	*P*-trend
Non-user	0 (Referent)	<0.001	0 (Referent)	<0.001	0 (Referent)	<0.001
Quitter	–0.24 (–0.30, –0.18)		–0.22 (–0.29, –0.16)		–0.21 (–0.28, –0.15)	
Recent initiate	–0.36 (–0.48, –0.24)		–0.32 (–0.44, –0.20)		–0.28 (–0.40, –0.16)	
Persistent users	–0.45 (–0.59, –0.30)		–0.40 (–0.55, –0.25)		–0.35 (–0.50, –0.20)	
	Δ BMI (%)					
	Age-adjusted β[a] (95% CI)	*P*-trend	Age- sex-adjusted β[b] (95% CI)	*P*-trend	Multivariable-adjusted β[c] (95% CI)	*P*-trend
Non-user	0 (Referent)	<0.001	0 (Referent)	<0.001	0 (Referent)	<0.001
Quitter	–1.00 (–1.19, –0.81)		–0.90 (–1.09, –0.70)		–0.81 (–1.01, –0.60)	
Recent initiate	–1.34 (–1.72, –0.96)		–1.14 (–1.52, –0.75)		–0.97 (–1.36, –0.57)	
Persistent users	–1.75 (–2.30, –1.20)		–1.51 (–2.06, –0.97)		–1.26 (–1.81, –0.72)	

[a]Estimates adjusted for age (years) and age squared.

[b]Estimates are additionally adjusted for sex (male is the referent).

[c]Estimates additionally adjusted for ethnic self-identification (NH-White is the referent), education (high school is the referent), W2 alcohol drinking (never use is the referent) and W2 tobacco use (never use is the referent).

Table 3. Association of cannabis use and change in BMI by tobacco-use status at W1. Data for the US National Epidemiologic Survey on Alcohol and Related Conditions Wave 1 (2001–02) and Wave 2 (2004–05)

	Δ BMI (kg/m^2)	
W2 cannabis-use status	Non-smoker ($n = 24\,500$[a]) β (95% CI)[b]	Smoker ($n = 8600$[a]) β (95% CI)[b]
Non-user	0 (Referent)	0 (Referent)
Quitter	–0.28 (–0.38, –0.19)	–0.10 (–0.23, 0.03)
Recent initiate	–0.32 (–0.49, –0.14)	–0.30 (–0.47, –0.13)
Persistent users	–0.43 (–0.69, –0.17)	–0.39 (–0.57, –0.21)
	Δ BMI (%)	
	β (95% CI)[b]	β (95% CI)[b]
Non-user	0 (Referent)	0 (Referent)
Quitter	–1.05 (–1.30, –0.81)	–0.43 (–0.84, –0.03)
Recent initiate	–1.04 (–1.53, –0.54)	–1.05 (–1.67, –0.43)
Persistent users	–1.50 (–2.31, –0.69)	–1.45 (–2.15, –0.75)

[a]Sample counts are rounded using the differential privacy policy of the US Census Bureau to minimize potential disclosure risk.

[b]Estimates adjusted for age (years), age squared, sex (male is the referent), ethnic self-identification (NH-White is the referent), education (high school is the referent) and W2 alcohol drinking (never use is the referent).

traits might be operating. To illustrate unmeasured variables of potential importance, NESARC cannot fully account for variations in physical activity and food intake. However, prior evidence has suggested higher caloric intake and lower physical activity among cannabis users.[1,2,5]

When designing this study's analysis protocol, we were hesitant to apply propensity score matching (PSM) and inverse probability weighting (IPW) approaches due to some unresolved controversies about the application of PSM and IPW in observational studies with complex survey sampling designs, non-independence of observations and analysis weights that incorporate covariates often needed to improve model fit and balance in the separate PSM and IPW approaches.[18] In addition, the use of complete case analysis might lead to loss of precision due to the reduced sample size and might introduce bias if the data are not missing completely at random. We also note that, in NESARC, the assessments measured cannabis use and BMI via self-report only; standardized anthropometry and bioassays are needed to place limits on biases such as non-differential misclassification.

Despite limitations such as these, the study findings are of interest. Strengths include the large national sample size and participation levels, its prospective design with follow-up roughly 36 months after baseline and standardized computer-assisted interviews designed to promote accuracy and thoroughness of self-reports.

At present, with liberalized cannabis policies and with an increased prevalence of cannabis use among US adults,[14] cannabis history measurements may deserve greater attention in biomedical research on weight, obesity, related conditions and health-care costs attributed to these conditions.[19,20] In NESARC, persistent cannabis users and the initiates were under-represented in stably obese subgroups (i.e. BMI ≥ 30 kg/m^2 at both W1 and W2). In addition, these same actively cannabis-using subgroups were under-represented among newly incident cases of obesity observed at W2 (i.e. BMI <30 kg/m^2 at W1 but BMI ≥ 30 kg/m^2 at W2, results are not shown in table/figure).

Cannabis and cannabis-based medications have been used to promote appetite and prevent weight loss and wasting in HIV and cancer patients. Surprisingly, clinical trials demonstrated little to no impact of cannabis-active constituents on weight in patients with HIV or cancer,[21] suggesting the need for further investigations given the expected cannabis pro-obesity effects and the cannabinoid system emergence as a target for obesity pharmacotherapies. For example, rimonabant, a CB1R antagonist, was approved for the treatment of obesity in Europe after several trials showing weight-loss benefits.[22] Chronic cannabis use is associated with down-regulation of CB1R and this down-regulation might help to explain cannabis-associated lower BMI gain for persistent users due to the reduced density of CB1R expression in these users.[23] In this study, initiates might be at an intermediate level of down-regulation and quitters presumably are in a cannabinoid 'washout' phase.

Another speculation involves immunomodulatory roles of CB2R. The association of inflammation and obesity is widely established in pre-clinical and clinical studies.[24,25] The anti-inflammatory effects of CB2R might help explain lower weight gain of cannabis users. Schmitz *et al.* reported pro-inflammatory obesity in mice lacking

CB2R.[26] As noted above, inverse associations of our study can be also explained by other unmeasured behaviours in cannabis users rather than cannabis itself.

In summary, our findings suggest a cannabis-associated attenuation of BMI gain, with some evidence of a gradient from never-users to subgroups of past vs recently active cannabis users. Additional studies will help to increase our understanding of the functions of a complex cannabinoid system and its relationships with potentially beneficial cannabinoid effects on risk of obesity and cardiometabolic health.

Supplementary Data

Supplementary data are available at *IJE* online.

Acknowledgements

The authors wish to acknowledge the US Census Bureau and Dr Jahn K. Hakes for data analysis and support of the project. The authors also wish to acknowledge the project's funding sources (US National Institutes of Health/National Center for Complementary and Integrative Health AT009156 to O.A. and US National Institutes of Health/National Institute on Drug Abuse DA015799 for J.C.A.). The funding body had no role in the design of the study, collection and analysis of data or the decision to publish. The content is the sole responsibility of the authors and does not represent the official views of Michigan State University, the National Center for Complementary and Integrative Health, the National Institute on Drug Abuse or the National Institutes of Health.

Conflict of interest: None declared.

References

1. Smit E, Crespo CJ. Dietary intake and nutritional status of US adult marijuana users: results from the Third National Health and Nutrition Examination Survey. *PHN* 2001;**4**:781–86.
2. Rodondi N, Pletcher MJ, Liu K, Hulley SB, Sidney S. Marijuana use, diet, body mass index, and cardiovascular risk factors (from the CARDIA Study). *Am J Cardiol* 2006;**98**:478–84.
3. Di Marzo V, Matias I. Endocannabinoid control of food intake and energy balance. *Nat Neurosci* 2005;**8**:585.
4. Verty AN, Lockie SH, Stefanidis A, Oldfield BJ. Anti-obesity effects of the combined administration of CB1 receptor antagonist rimonabant and melanin-concentrating hormone antagonist SNAP-94847 in diet-induced obese mice. *Int J Obes* 2013;**37**:279–87.
5. Vidot DC, Bispo JB, Hlaing WM, Prado G, Messiah SE. Moderate and vigorous physical activity patterns among marijuana users: results from the 2007–2014 National Health and Nutrition Examination Surveys. *Drug Alcohol Depend* 2017;**178**:43–48.
6. Le Strat Y, Le Foll B. Obesity and cannabis use: results from 2 representative national surveys. *Am J Epidemiol* 2011;**174**:929–33.
7. Penner EA, Buettner H, Mittleman MA. The impact of marijuana use on glucose, insulin, and insulin resistance among US adults. *Am J Med* 2013;**126**:583–89.
8. Rajavashisth TB, Shaheen M, Norris KC *et al*. Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III. *BMJ Open* 2012;**2**:e000494.
9. Hayatbakhsh MR, O'Callaghan MJ, Mamun AA, Williams GM, Clavarino A, Najman JM. Cannabis use and obesity and young adults. *Am J Drug Alcohol Abuse* 2010;**36**:350–56.
10. Beulaygue IC, French MT. Got munchies? Estimating the relationship between marijuana use and body mass index. *J Ment Health Policy Econ* 2016;**19**:123–40.
11. Hasin DS, Grant BF. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2: review and summary of findings. *Soc Psychiatry Psychiatr Epidemiol* 2015;**50**:1609–40.
12. Grant BF, Moore TC, Kaplan K, *Source and Accuracy Statement: Wave 1 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)*. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism, 2003, p. 52.
13. Slagter SN, van Waateringe RP, van Beek AP, van der Klauw MM, Wolffenbuttel BHR, van Vliet-Ostaptchouk JV. Sex, BMI and age differences in metabolic syndrome: the Dutch Lifelines Cohort Study. *Endocr Connections* 2017;**6**:278–88.
14. Anthony JC, Lopez-Quintero C, Alshaarawy O. Cannabis epidemiology: a selective review. *Curr Pharm Des* 2017;**22**:6340–52.
15. Hasin DS, Saha TD, Kerridge BT *et al*. Prevalence of marijuana use disorders in the United States between 2001–2002 and 2012–2013. *JAMA Psychiatry* 2015;**72**:1235–42.
16. Truong KD, Sturm R. Weight gain trends across sociodemographic groups in the United States. *Am J Public Health* 2005;**95**:1602–06.
17. Abramowitz MK, Hall CB, Amodu A, Sharma D, Androga L, Hawkins M. Muscle mass, BMI, and mortality among adults in the United States: a population-based cohort study. *PLoS One* 2018;**13**:e0194697.
18. Lenis D, Ackerman B, Stuart EA. Measuring model misspecification: application to propensity score methods with complex survey data. *Comput Stat Data Anal* 2018;**128**:48–57.
19. Finucane MM, Stevens GA, Cowan MJ *et al*. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet (London, England)* 2011;**377**:557–67.
20. Drøyvold WB, Midthjell K, Nilsen TIL, Holmen J. Change in body mass index and its impact on blood pressure: a prospective population study. *Int J Obes* 2005;**29**:650.
21. National Academies of Sciences EaM. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press, 2017.
22. Sam AH, Salem V, Ghatei MA. Rimonabant: from RIO to ban. *J Obes* 2011;**2011**:432607.
23. Hirvonen J, Goodwin R, Li CT *et al*. Reversible and regionally selective downregulation of brain cannabinoid CB1 receptors in chronic daily cannabis smokers. *Mol Psychiatry* 2012;**17**:642–49.
24. Fain JN. Release of interleukins and other inflammatory cytokines by human adipose tissue is enhanced in obesity and primarily due to the nonfat cells. *Vitam Horm* 2006;**74**:443–77.
25. Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. *Diabetes Res Clin Pract* 2014;**105**:141–50.
26. Schmitz K, Mangels N, Häussler A, Ferreirós N, Fleming I, Tegeder I. Pro-inflammatory obesity in aged cannabinoid-2 receptor-deficient mice. *Int J Obes (Lond)* 2016;**40**:366.