

Marijuana and Male Fertility: Who Knew?

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Disclosure

Consultant:

- Coloplast
- Biote

Advisory Board:

- Boston Scientific
- Progyny

Research/Educational Funding:

- National Institutes of Health (NIA); 1R01AG042934-01: “Adverse Events Associated with Testosterone Treatment in Hypogonadal Men”
- Boston Scientific
- Coloplast
- Endo

At the conclusion of this lecture, participants should be able to:



1. Describe the prevalence of and trends in marijuana use in the U.S.
2. Describe two sources of cannabinoids that impact male reproduction
3. Describe the effects of marijuana on semen quality

Life | SEX

Is Your Partner's Marijuana Habit Hurting Your Chances of Having a Baby?

BY RIGHT AS RAIN FEBRUARY 7, 2018



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Approximately what percent of Americans use marijuana?



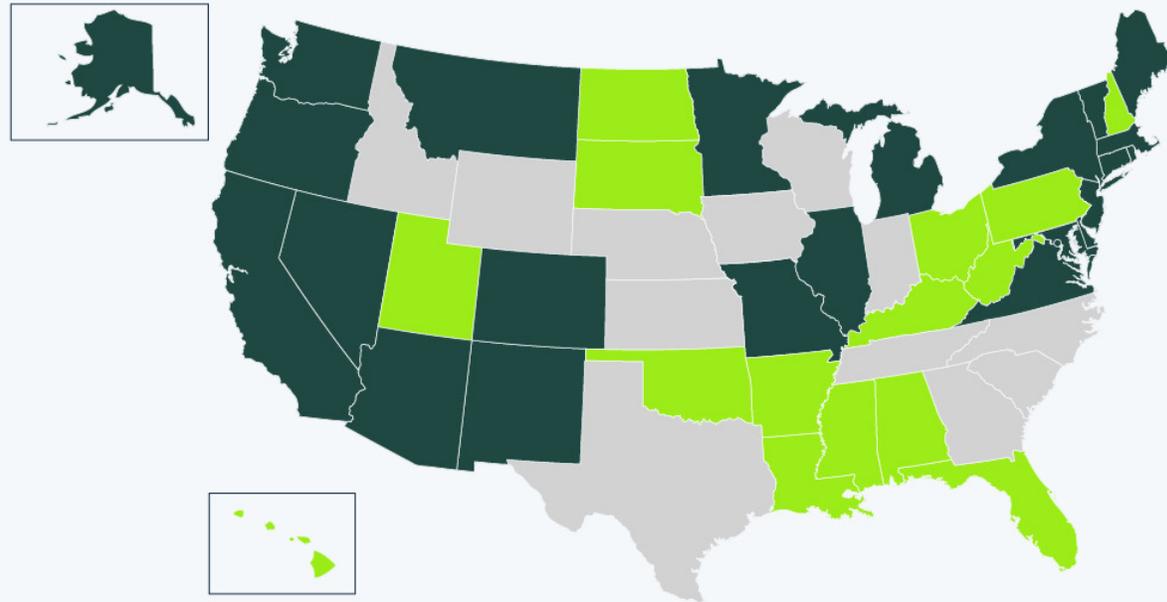
- A. 2%
- B. 5%
- C. 10%
- D. 18%

The State of Marijuana Legalization in the U.S.



Laws on recreational and medical marijuana use in the United States

■ Legal recreational & medical use ■ Medical use only

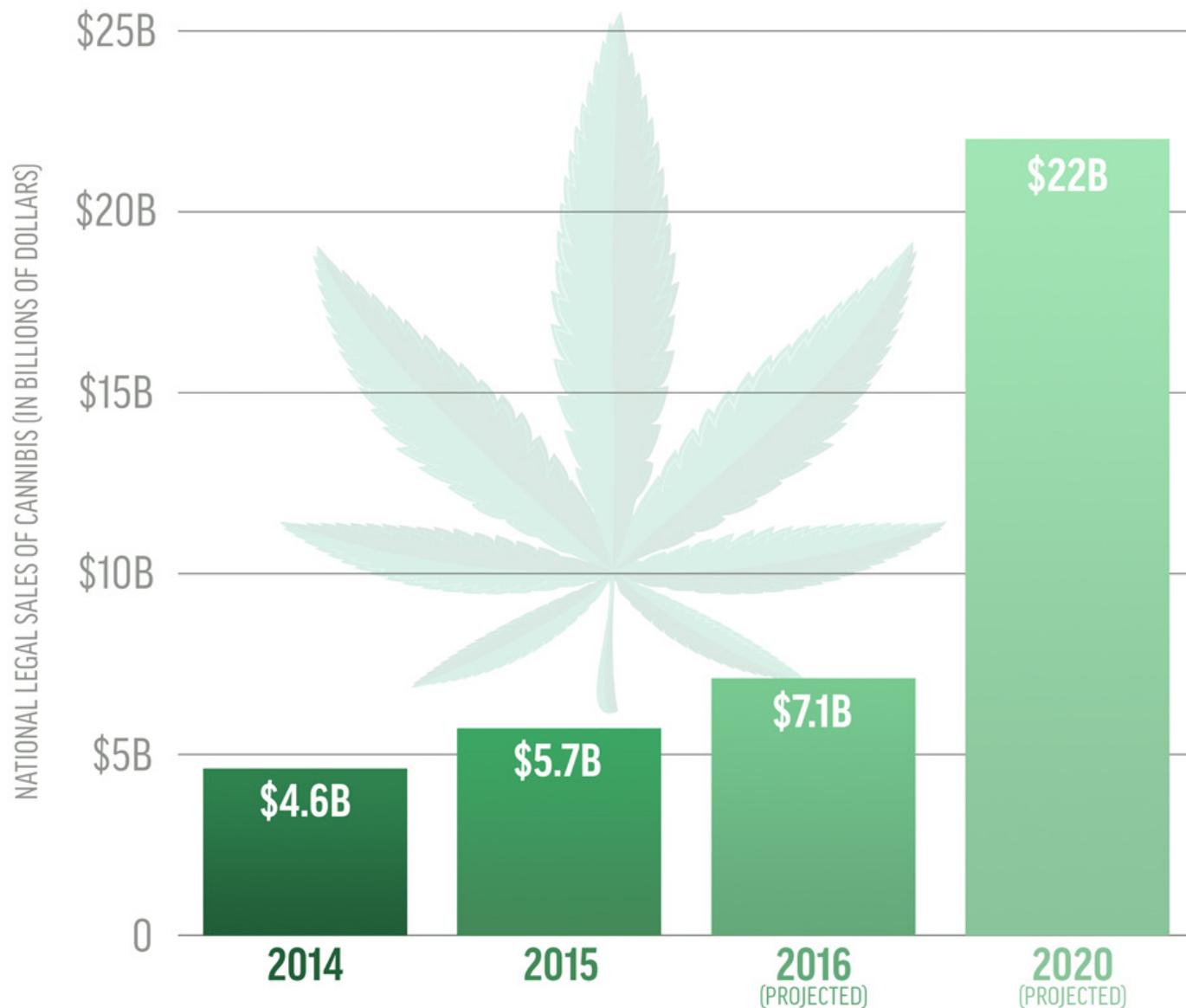


As of Aug. 30, 2023. Some states not highlighted allow limited medical marijuana access.

Sources: NORML



NATIONAL LEGAL SALES OF CANNIBIS ARE GETTING HIGHER



SOURCE: EXECUTIVE SUMMARY: THE STATE OF LEGAL MARIJUANA MARKETS, 4TH EDITION
(ARCHVIEW MARKET RESEARCH & NEW FRONTIER)

Forbes

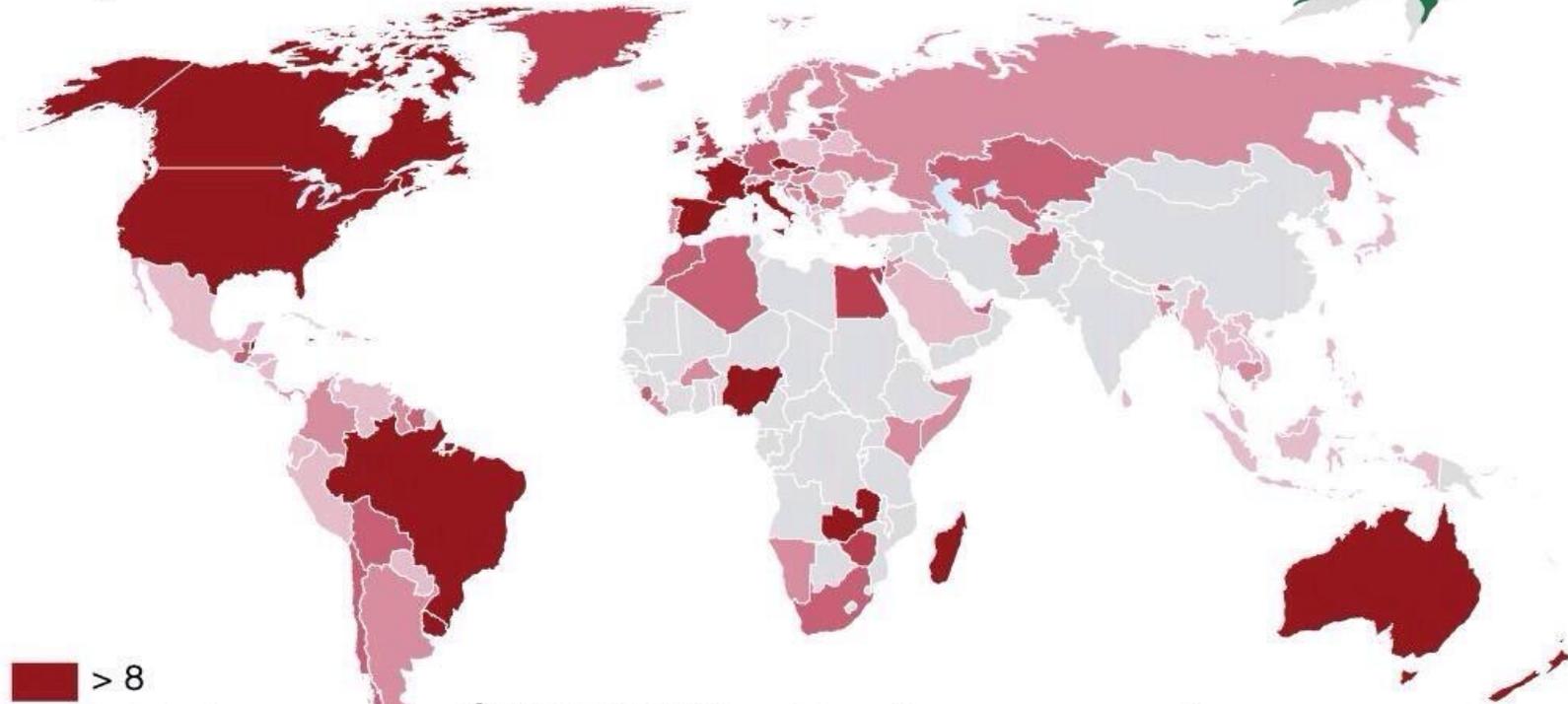
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Marijuana

With 180 million users worldwide, marijuana (cannabis) is the most common illegal drug



Percentage of population aged 15-64 using cannabis at least once a year



Global average consumption



Producer countries

- Afghanistan
- Colombia
- Mexico
- Netherlands
- Morocco
- Nigeria
- Paraguay
- South Africa

Source: UNODC (2010)





National Institutes of Health
Turning Discovery Into Health

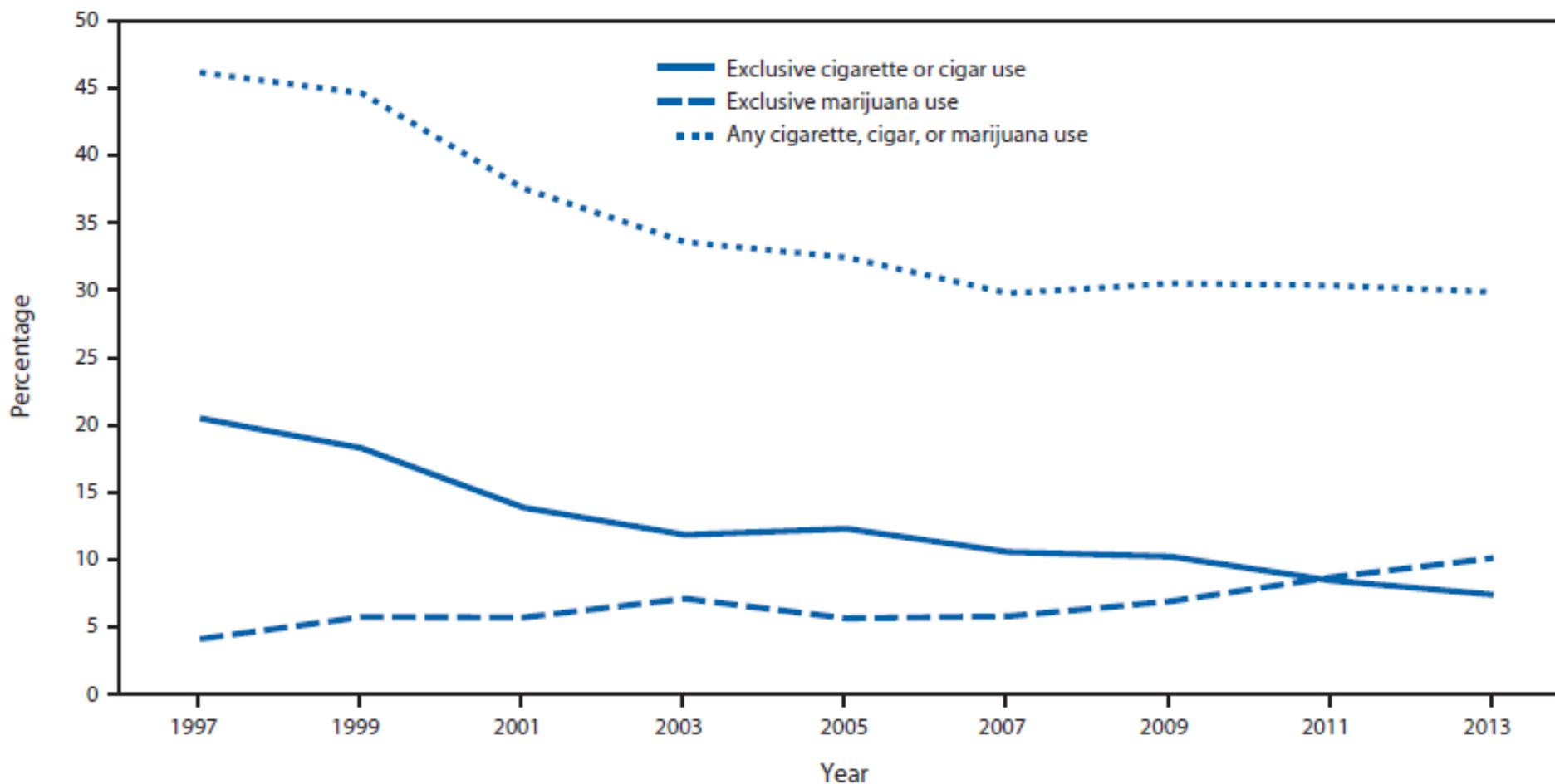
Wednesday, October 21, 2015

Prevalence of Marijuana Use Among U.S. Adults Doubles Over Past Decade

Surveys show 9.5 percent of Americans use marijuana; 30 percent of users meet criteria for a disorder.

48.2 million users in the United States in 2019, or ~18 %

Prevalence of exclusive cigarette or cigar use,^{*†} exclusive marijuana use,^{†§} and any cigarette, cigar, or marijuana use^{†¶**} among high school students^{††} during the 30 days preceding the surveys



CDC analyzed data from the 1997–2013 national Youth Risk Behavior Surveys

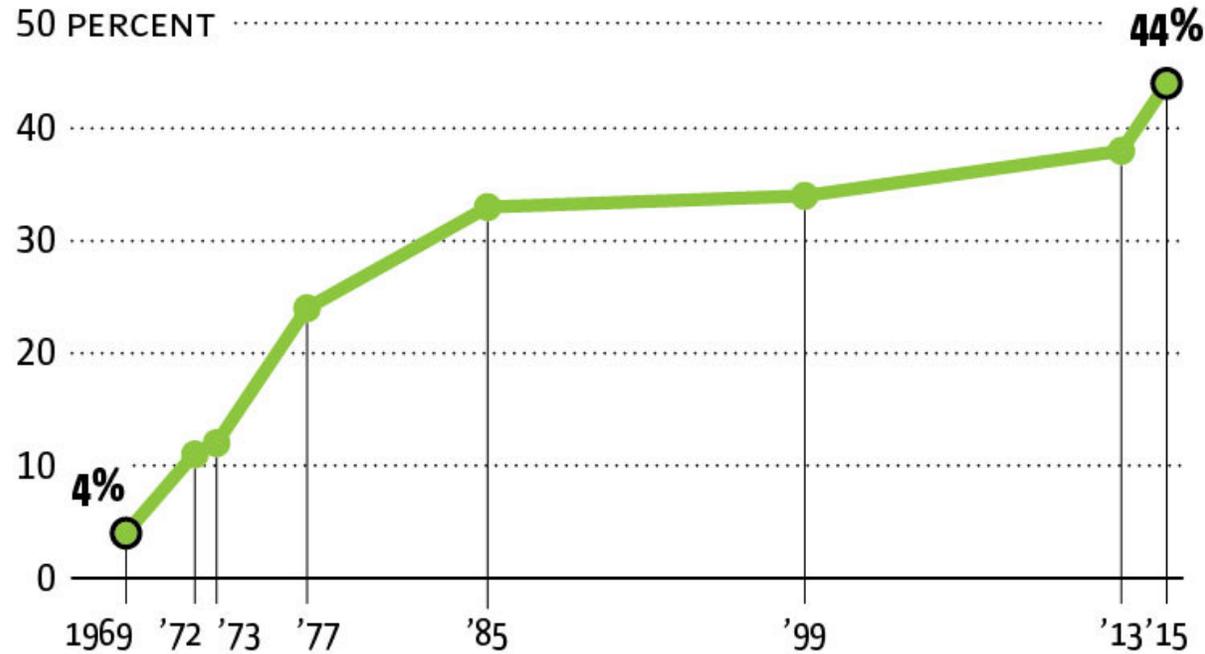
Support for the legalization of marijuana has:

- A. Plateaued since the 1960s
- B. Decreased since the 1960s
- C. Increased since the 1960s

Cannabis use over time

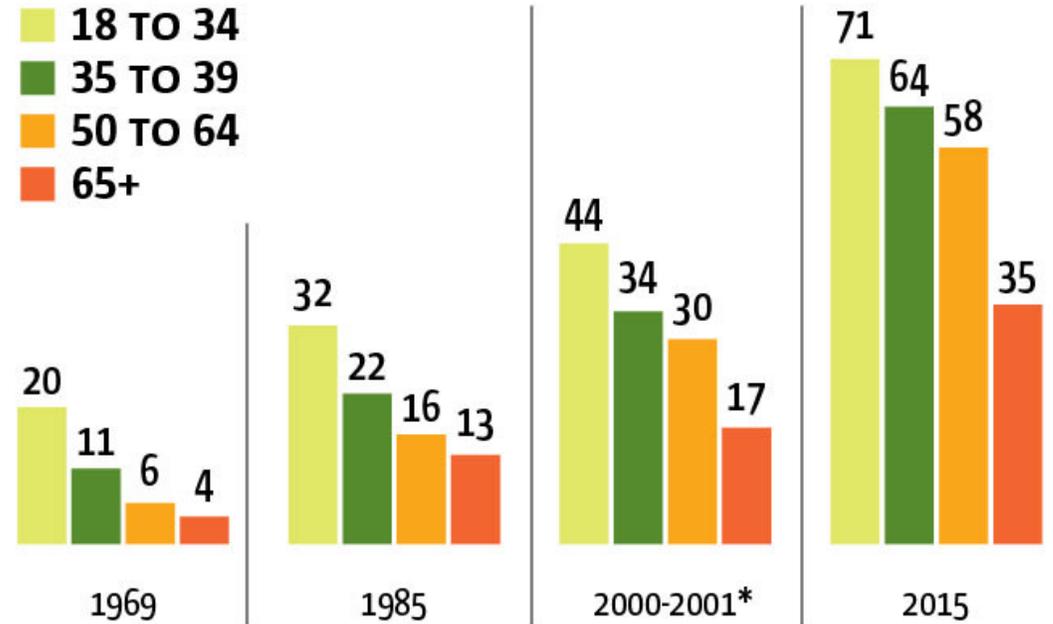
Marijuana support, use increases over years

Q: Have you ever tried marijuana? *Percent answered yes:*



Marijuana legalization support

Percent in favor, by age group



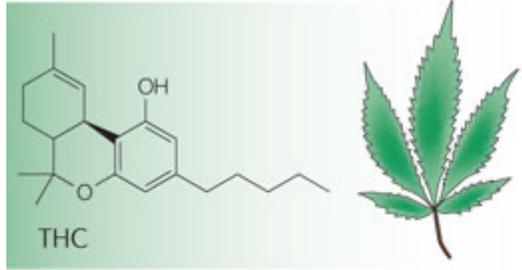
**Note: Years combined because the 2000 survey asked the question of a half-sample of respondents.*

Source: Gallup

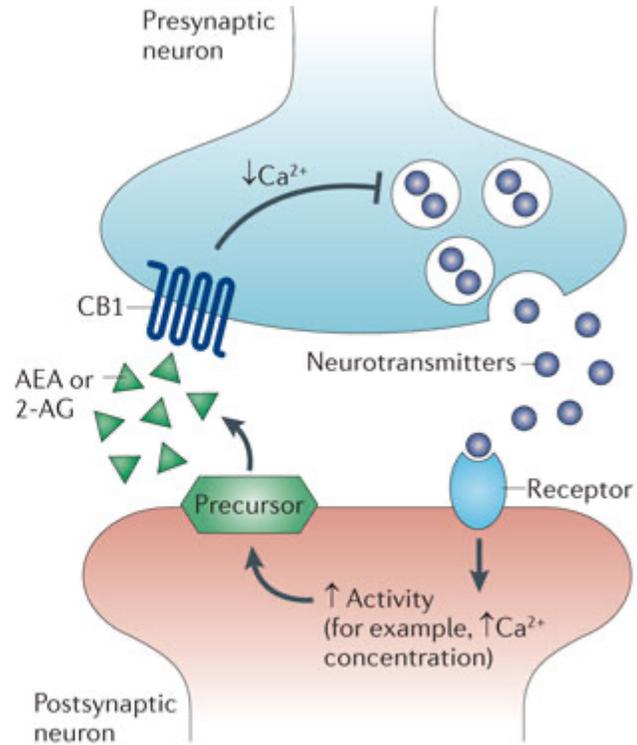
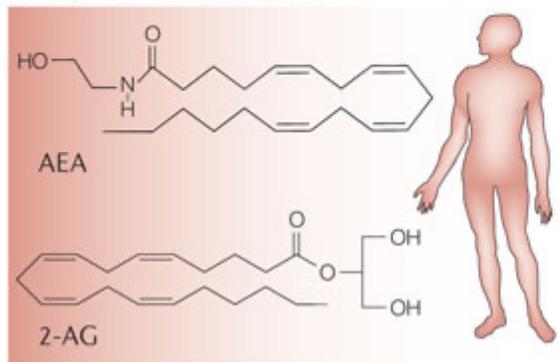
The Denver Post

Cannabinoid Sources

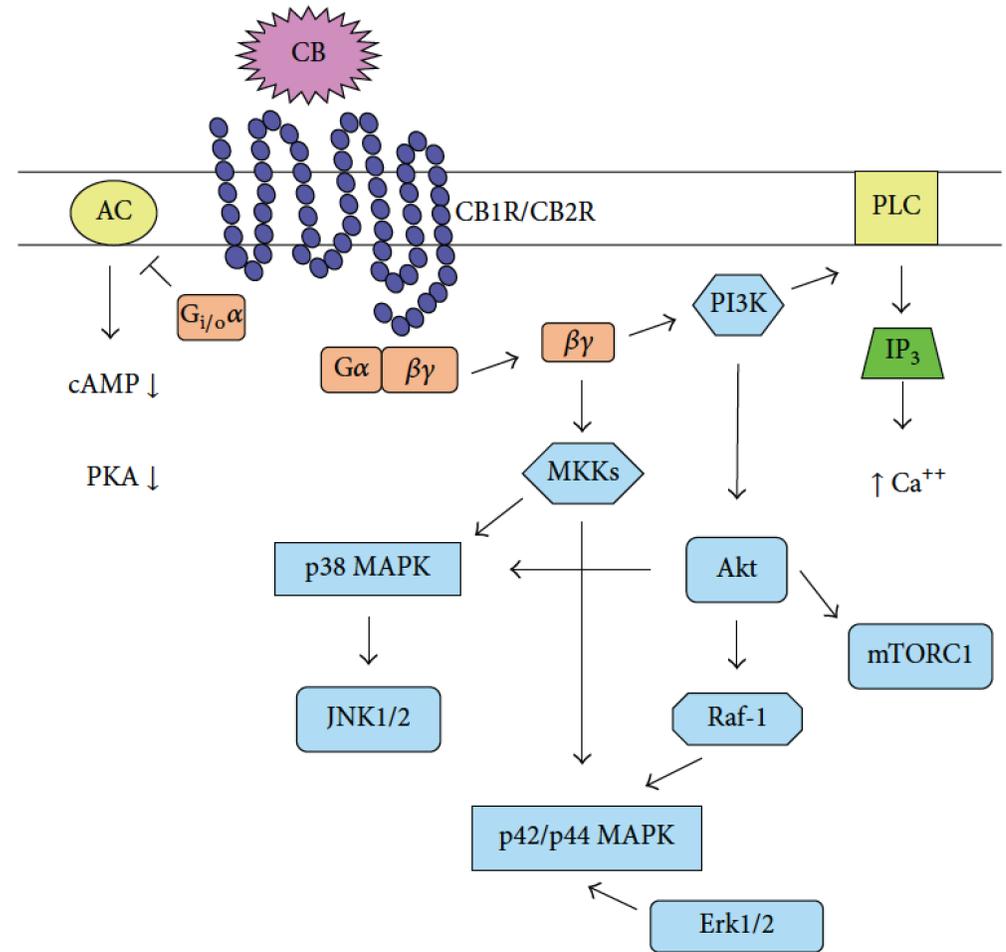
Plant-derived cannabinoid



Endogenous cannabinoids



Nature Reviews | Cancer



Velasco et al, 2012
McCoy et al, 2016

Evidence That Anandamide-Signaling Regulates Human Sperm Functions Required for Fertilization

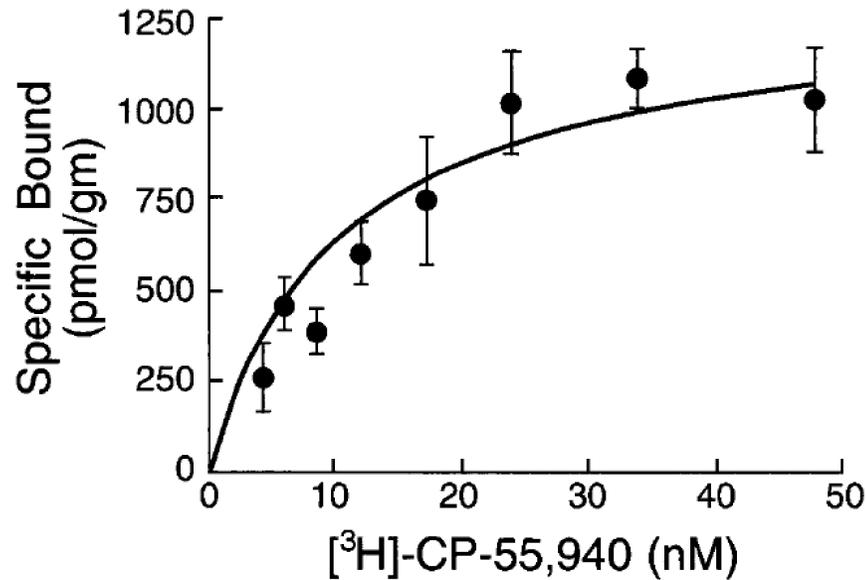


Fig. 1. Representative experiment performed in quadruplicate showing saturation of specific binding of [³H]CP55,940 to human sperm. Binding constants were estimated from seven independent experiments performed with sperm from three different donors: K_D 9.71 ± 1.04 nM; B_{max} 1.193 ± 0.15 pmoles/mg protein; Hill coefficient 1.32 ± 0.102 .

TABLE 1. Anandamide (nM) in Human Reproductive Fluids

Seminal plasma	Mid-cycle oviductal fluid	Follicular fluid
12.1 ± 2.1 (N = 15)	10.5 ± 2.4 (N = 14)	2.9 ± 0.9 (N = 9)

Samples of reproductive fluids were analyzed by high performance liquid chromatography/mass spectrometry.

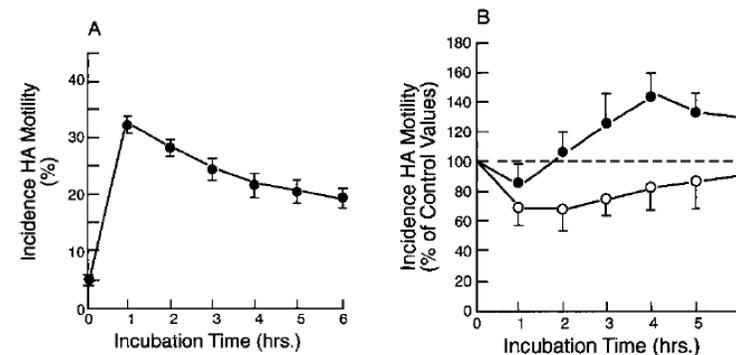


Fig. 2. Effects of AM-356 on hyperactivated motility (HA) in sperm during incubation for 6 hr. **(A)** Incidence of HA in sperm cultured in control medium. **(B)** Incidence of HA in sperm treated with AM-356 (0.25 nM) (closed circles) and (2.5 nM) (open circles). Data expressed as percent of control values. The effects of AM-356 on HA at (2.5 nM) were significantly different from those produced by AM-356 at (0.25 nM) ($P < 0.05$; ANOVA). N = 6 experiments using sperm from three different donors.

Marijuana use has been implicated in the following semen changes

- A. Decrease in morphology
- B. Increase in concentration
- C. Decrease in motility
- D. Decrease in concentration
- E. A, C and D

Table III Multivariable analysis of risk factors for normal sperm morphology <4%.

Risk factor	Value	All		Age (years)					
		OR	95% CI ^a	18–30		31–40		>40	
				OR	95% CI ^a	OR	95% CI ^a	OR	95% CI ^a
Season	Spring	1.0	—	1	—	1	—	1	—
	Summer	1.99	1.43–2.72	2.21	1.22–4.00	1.73	1.13–2.67	2.74	0.88–8.54
	Autumn	1.01	0.71–1.44	1.09	0.57–2.07	0.92	0.58–1.44	1.35	0.39–4.73
	Winter	0.74	0.49–1.13	0.64	0.28–1.43	0.68	0.40–1.18	1.31	0.39–4.42
Cannabis use	No	1	—	1	—	1	—	1	—
	Yes	1.45	0.97–2.17	1.94	1.05–3.60	1.35	0.63–1.29	0.97	0.20–4.76
Abstinence	≤3 days	1	—	1	—	1	—	1	—
	4–5 days	1.01	0.77–1.34	1.24	0.75–2.05	0.90	0.63–1.29	1.11	0.47–2.64
	≥6 days	0.64	0.43–0.95	0.77	0.38–1.64	0.54	0.32–0.92	0.81	0.28–2.32

^aAdjusted for clustering within centre and other risk factors shown.

“...with the only practical advice to men attempting conception being to limit exposure to cannabis if they are regular users.”

Impact of marijuana use on semen quality

Pacey, 2014 (United Kingdom)

“cannabis use of nearly doubles the risk of abnormal morphology in men presenting for infertility care”

Hum Reprod. 2014 Aug;29(8):1629-36.

Gunderson, 2015 (Denmark)

“sperm concentration, motility, and morphology were all lower among men smoking marijuana more than once per week”

Am J Epidemiol. 2015 Sep 15;182(6):473-81

Verhaeghe, 2020 (France)

“Cannabis consumption exerts deleterious effects on sperm nuclear quality in infertile men”

Reprod Biomed Online. 2020 Feb;40(2):270-280)

What about men in my back yard?

- Prospective evaluation of semen quality among men seeking fertility evaluation
- Marijuana use legalized in Washington State on December 6, 2012
- Data collection occurred between July 2017 and April 2018
- All men completed a detailed questionnaire at the time of semen analysis
 - Exclusions: varicocele, infection, genetic abnormality, known gonadotoxins
- Marijuana use was characterized as:
 - Never used
 - Current use
 - 3 or more months since last use

Prospective analysis of marijuana use on semen quality

409 men completed the study

- 43% reported using marijuana
 - 41% were “past users”

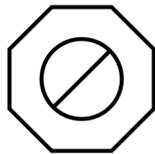
Odds of semen parameters below WHO reference values compared to never-users**

	Past users		Current users	
	Odds ratio	95% CI	Odd ratio	95% CI
Volume	1.1	0.5 – 2.8	2.8	1.2 – 6.4*
Concentration	2.0	0.9 – 4.1	1.3	0.7 – 2.7
Motility	0.7	0.4 – 1.2	0.5	0.3 – 0.9*
Morphology	2.3	1.4 – 3.7*	2.2	1.2 – 3.8*

*p<0.05; **Adjusted for age, smoking status, and BMI

Summary

- Evidence from multiple studies, across different populations of men suggests that Cannabis use may have negative repercussions for semen quality
- Reproductive health and fertility is likely modulated by many factors: age, baseline health, baseline fertility, genetics, co-exposures
- The verdict is out: how much exposure and when?
- The easy button:



Acknowledgements

- Charles Muller, PhD
- Marah Hehemann, MD
- Omer Raheem, MD
- Kevin Ostrowski, MD
- Saneal Rajanahally, MD
- Tony Chen, MD
- Judy Fustok, BS
- Kelly Song, BS
- Heather Rylander, PA-C
- Emma Chow, BS
- Sarah Holt, PhD

Design and Implementation of the Modern Men's Health Center

A Multidisciplinary Approach

Joseph P. Alukal
Steven Lamm
Thomas J. Walsh
Editors

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QUESTIONS?

