Resources:

Cannabinoids For Medical Use: A Systematic review and meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc: et al

JAMA. 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358

Acute and Chronic Effects of Cannabinoids on Human Cognition – A systematic Review

Samantha J. Broyd, Hendrika H. van Hell, Camilla Beale, Murat Yucel. Nadia Solowij

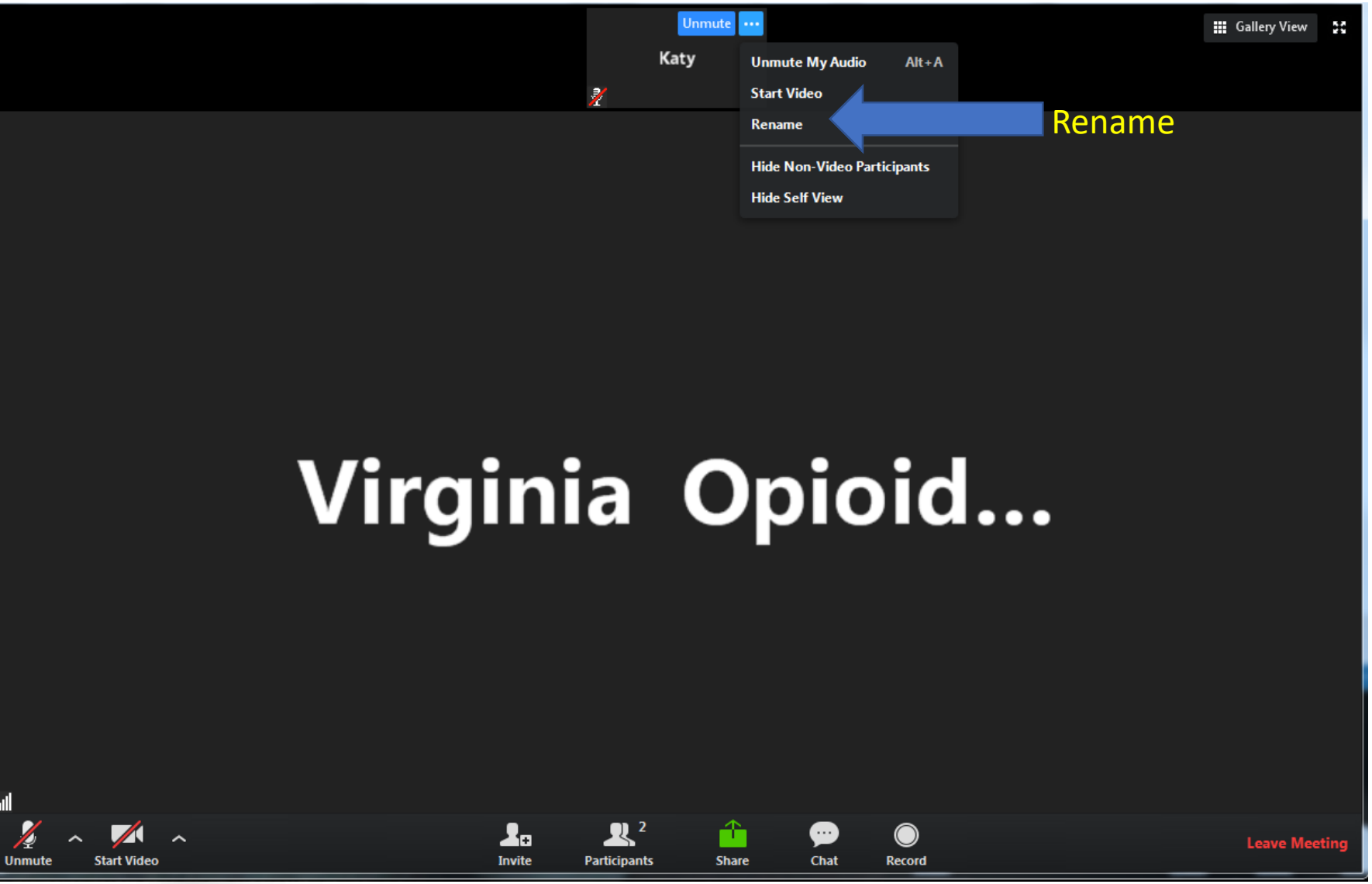
https://doi.org/10.1016/j.biopsych.2015.12.002

Virginia Opioid Addiction ECHO* Clinic

March 29, 2019

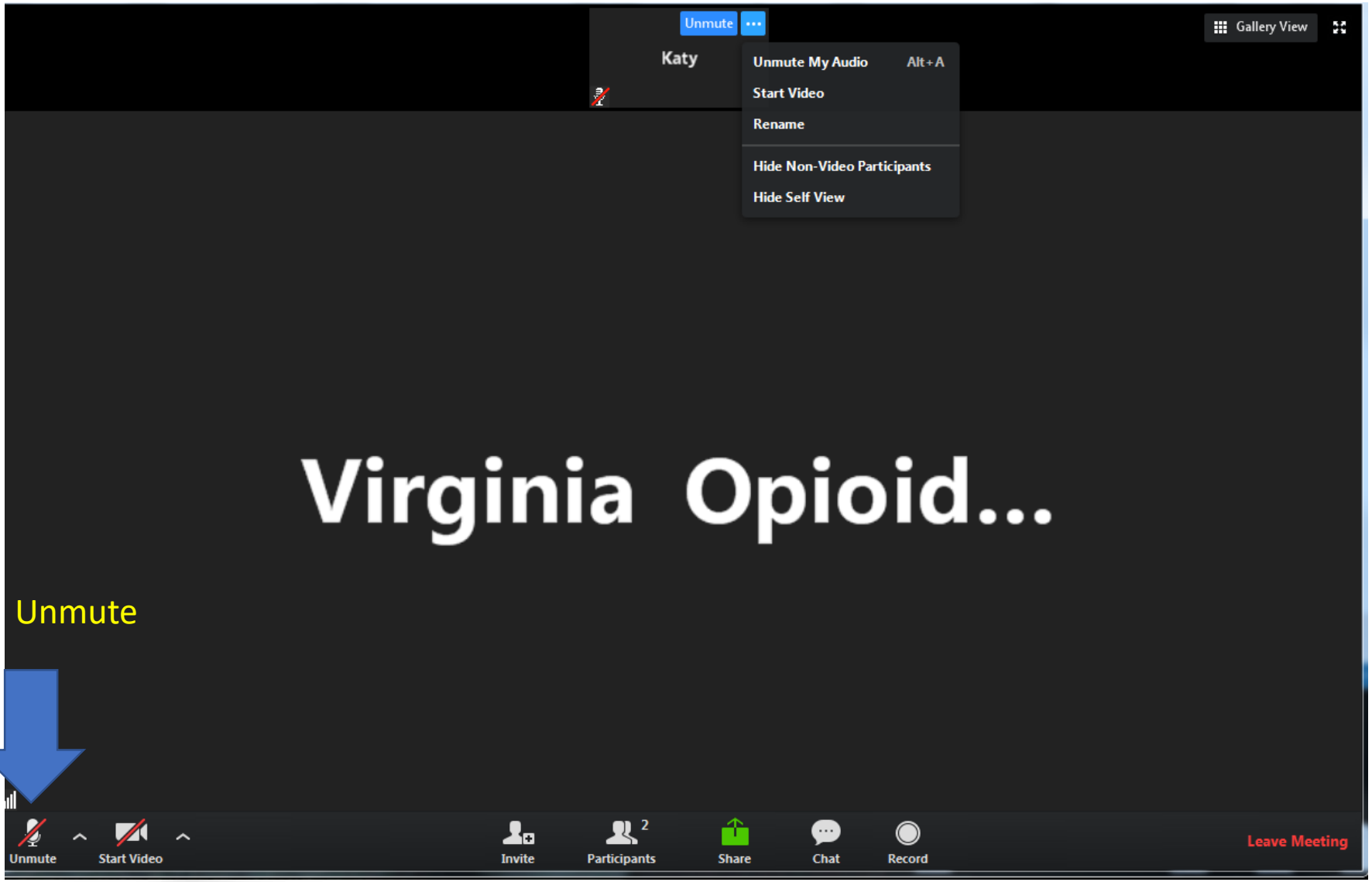
*ECHO: Extension of Community Healthcare Outcomes

Helpful Reminders



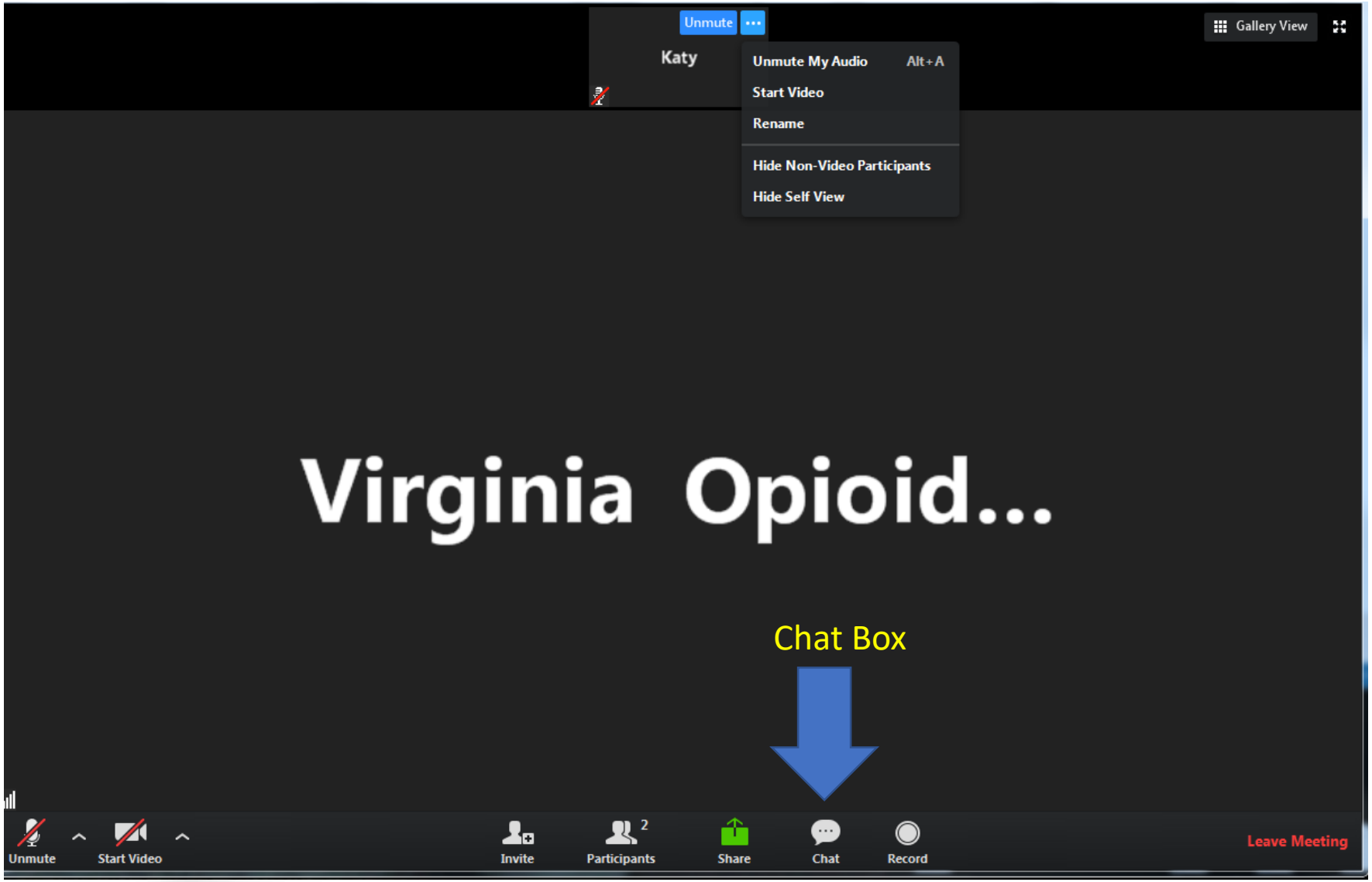
- Rename your Zoom screen, with your name and organization

Helpful Reminders



- You are all on mute please unmute to talk
- If joining by telephone audio only, *6 to mute and unmute

Helpful Reminders



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- Use the chat function to speak with IT or ask questions

VCU Opioid Addiction ECHO Clinics

VCU Health
VCU School of Medicine

VDH Virginia Department of Health | VDHLiveWell.com | Virginia Department of Behavioral Health & Developmental Services

- Bi-Weekly 1.5 hour tele-ECHO Clinics
- Every tele-ECHO clinic includes a 30 minute didactic presentation followed by case discussions
  - Didactic presentations are developed and delivered by inter-professional experts in substance use disorder
- Website Link: www.vcuhealth.org/echo

VCU

Hub Introductions

VCU Team	
Clinical Director	Mishka Terplan, MD, MPH, FACOG, FASAM
Administrative Medical Director ECHO Hub and Principal Investigator	Vimal Mishra, MD, MMCi
Clinical Expert	Lori Keyser-Marcus, PhD Courtney Holmes, PhD
Didactic Presentation	Lori Keyser-Marcus, PhD Courtney Holmes, PhD
Program Manager	Bhakti Dave, MPH
Practice Administrator	David Collins, MHA
IT Support	Vladimir Lavrentyev, MBA

Introductions:

- Name
- Organization

Reminder: Mute and Unmute to talk
*6 for phone audio
Use chat function for Introduction

What to Expect

I. Didactic Presentation
   I. **Medical and Non-Medical Cannabis: An Evidence Based Review**
   II. **Mishka Terplan, MD**

II. Case presentations
   I. Case 1
      I. Case summary
      II. Clarifying questions
      III. Recommendations
   II. Case 2
      I. Case summary
      II. Clarifying questions
      III. Recommendations

III. Closing and questions

Lets get started!

Didactic Presentation

Medical and Non-Medical Cannabis: An Evidence-Based Review

Mishka Terplan MD MPH FACOG DFASAM
VCU SOM
Project ECHO 4/5/19

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Cannabis and the History of Women's Health

- Since 2737 BCE Cannabis for treatment of female health issues: migraine, nausea and vomiting of pregnancy, heavy menses, painful menses, labor pain, labor augmentation, mastalgia …
- Mentioned in Chinese, Indian, Arabic, Greek, Egyptian, European… medical texts

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Commercial Use in U.S.

1611

Grown by Jamestown settlers for fiber

1629

Major crop in New England

1765

Grown by George Washington at Mount Vernon

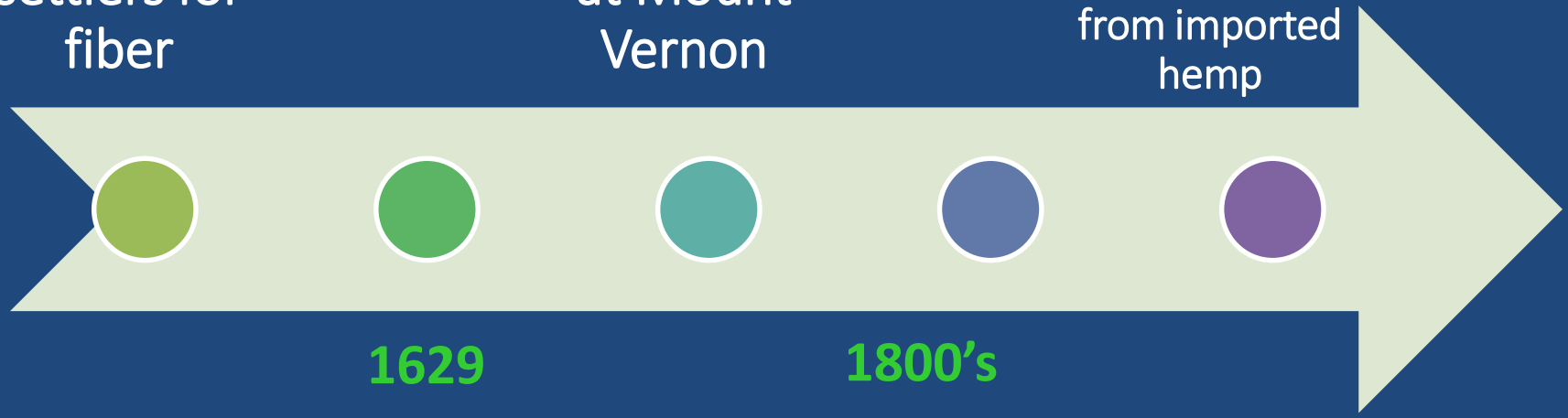
1800's

Grown throughout US, centered in Kentucky

- Cannabis slave plantations

Post Civil War

Declined due to invention of cotton gin and competition from imported hemp



Cannabis is …

- Probably the most satisfactory remedy for the treatment of migraine headaches
  - Dr William Osler, Textbook of Medicine 1892-1915
- A high potential for abuse and no accepted medical value
  - Controlled Substance Act 1970-2016

Terminology

- Cannabis Plant Names
  - Hemp
    - Refers to plant and its product
    - Oldest term
  - Marijuana
    - Refers to both plant and drug
    - New “slang” term
  - Cannabis
    - Refers to both plant and drug
    - DSM-5 “most appropriate scientific term”
- Categories of Cannabinoids
  - Phytocannabinoids
    - 104 cannabanoids
    - 545 total compounds
  - Endocannabinoids
    - 4+ cannabinoids
  - Synthetic cannabinoids
    - Multiple – pharmaceutical and recreational

Cannabis Ingredients:
Tetrahydrocannabinol (THC)

- Primary, but not only, psychoactive ingredient of plant
- Not isolated until 1964 due to technological problems
  - Compare to morphine (1804) and cocaine (1860)
- 1960's to present: THC content increased from 3% to 20%

Cannabinoids:
Cannabidiol (CBD)

- First isolated in 1940
- Medical benefits:
  - Anticonvulsant
  - Anti-anxiety
  - Counteracts psychoactive effect of THC
- Treated as Schedule 1 substance despite not being euphorogenic and is therefore illegal in US
  - Legal in many countries including Canada and UK

Cannabis Ingredients:
THC/CBD Ratio

- Inversely proportional
- Breeding drives developments of different strains based on goal of grower
  - "Charlotte's Web": 21% CBD, <0.1% THC (= hemp)

Changes in Cannabis Potency Over the Last 2 Decades (1995–2014): Analysis of Current Data in the United States

Mahmoud A. ElSohly, Zlatko Mehmedic, Susan Foster, Chandrani Gon, Suman Chandra, and James C. Church

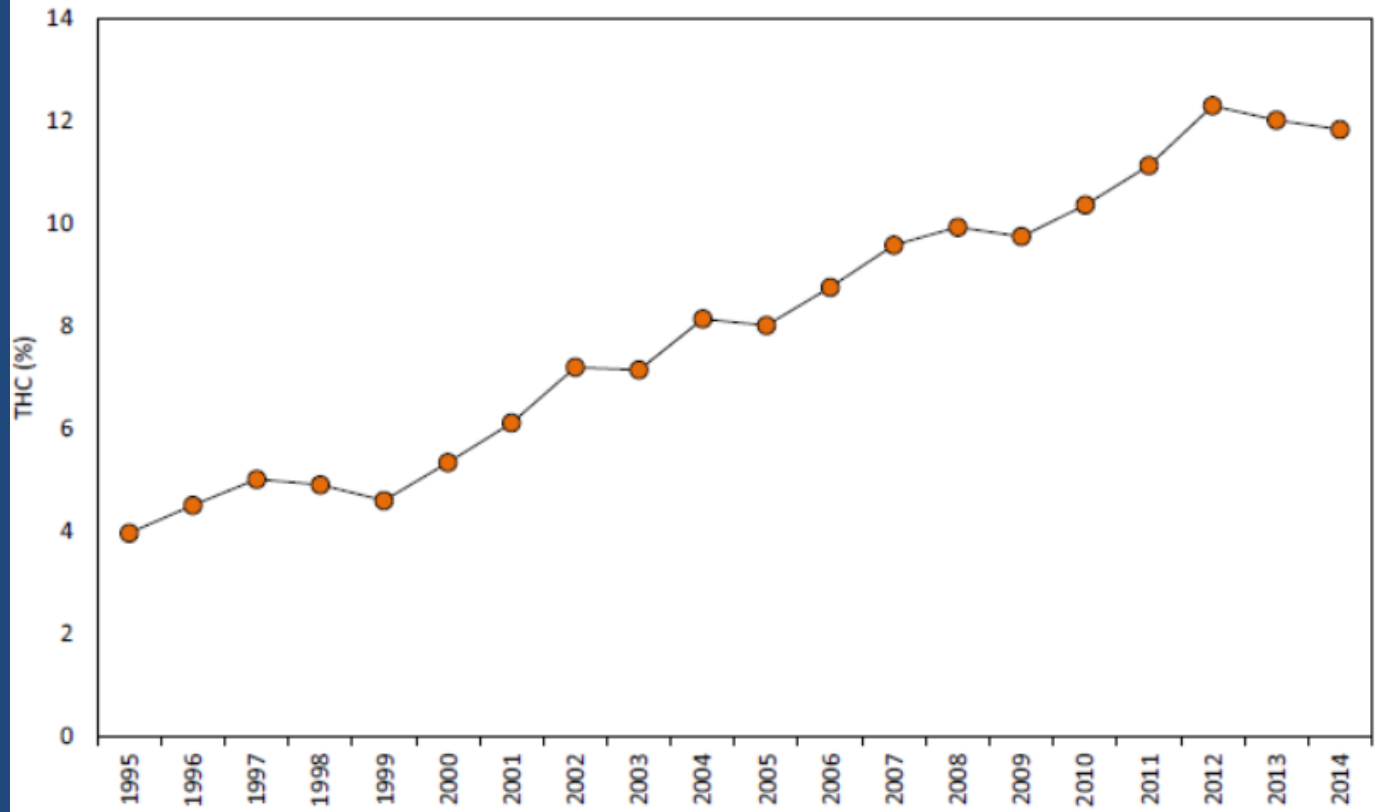


Figure 1. Average Δ^9-tetrahydrocannabinol (THC) concentration of Drug Enforcement Administration specimens by year, 1995–2014.

http://dx.doi.org/10.1016/j.biopsych.2016.01.004

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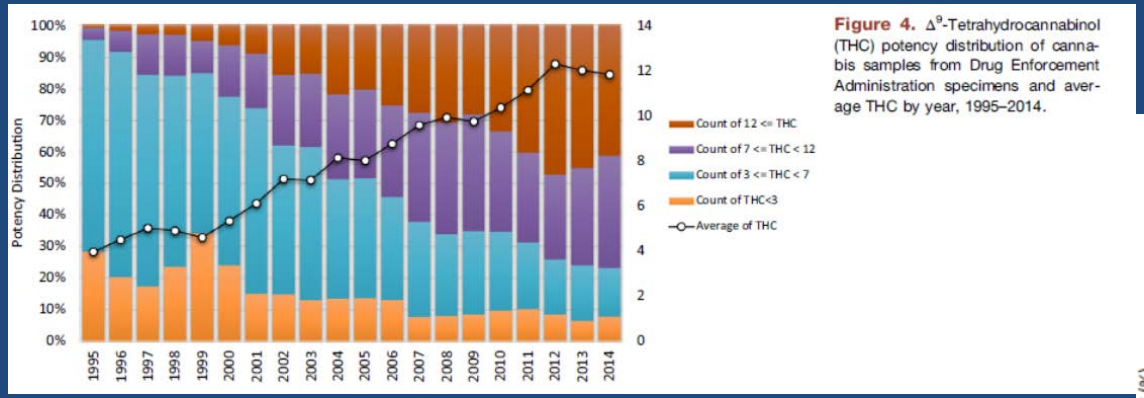


Figure 4. Δ^9-Tetrahydrocannabinol (THC) potency distribution of cannabis samples from Drug Enforcement Administration specimens and average THC by year, 1995–2014.

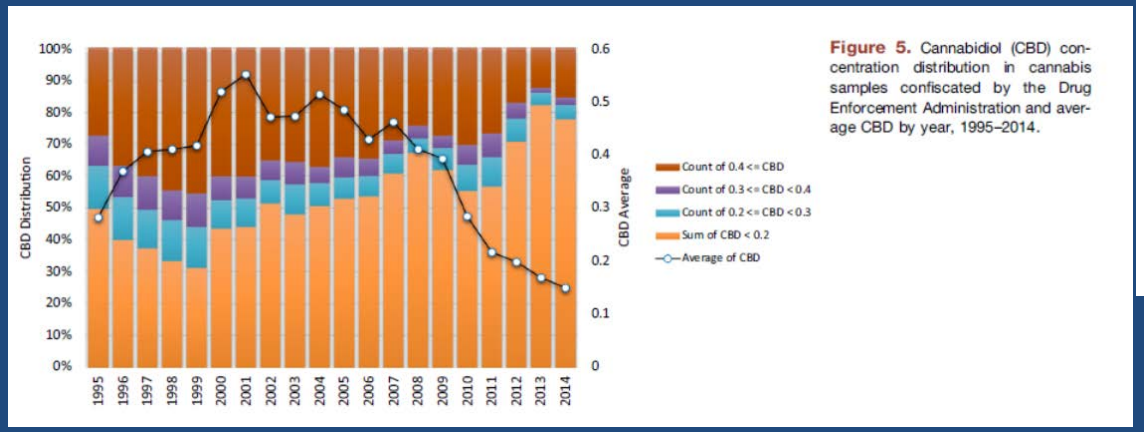
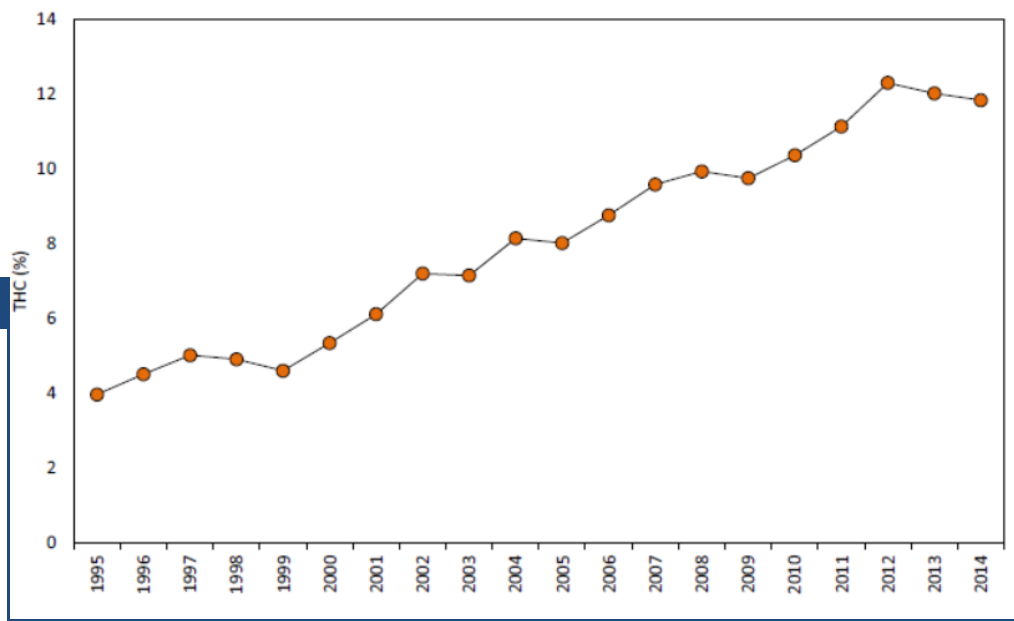


Figure 5. Cannabidiol (CBD) concentration distribution in cannabis samples confiscated by the Drug Enforcement Administration and average CBD by year, 1995–2014.



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Forensic Science International 272 (2017) 72–80

Contents lists available at ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forsciint

A study of cannabis potency in France over a 25 years period (1992–2016)

Laurence Dujourdy, Fabrice Besacier*

Institut National de Police Scientifique (INPS)–Laboratoire de Lyon (LPS69), 31 Avenue Franklin Roosevelt, 69134 Ecully Cedex, France

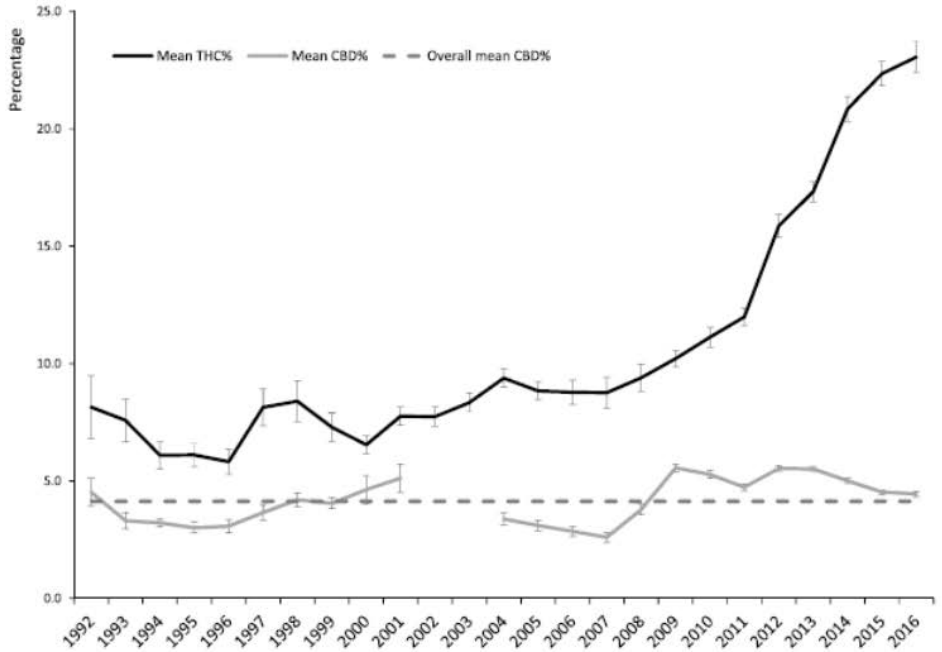

Fig. 5. Distribution frequency of THC and CBD (mean value) in cannabis resin by year, from 1992 to mid-2016. Error bars are based on standard error of the mean (standard deviation divided by the square root of the sample size) with 95% confidence interval—assuming that the means are distributed according to a normal distribution.

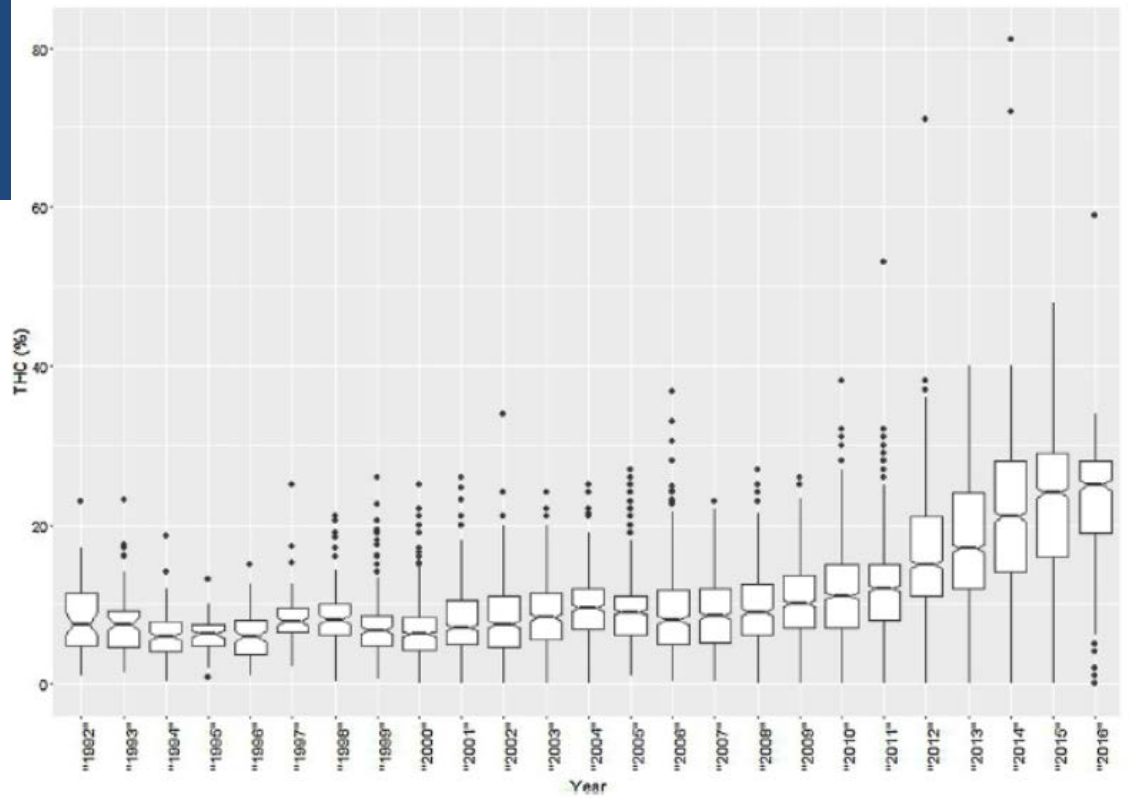

Fig. 2. Distribution (notched box plots) of THC concentration in cannabis resin from 1992 to mid-2016.

Marijuana use and use disorders in adults in the USA, 2002–14: analysis of annual cross-sectional surveys

Wilson M Compton, Beth Han, Christopher M Jones, Carlos Blanco, Arthur Hughes

Lancet Psychiatry 2016
Published Online
August 31, 2016
http://dx.doi.org/10.1016/S2215-0366(16)30208-5

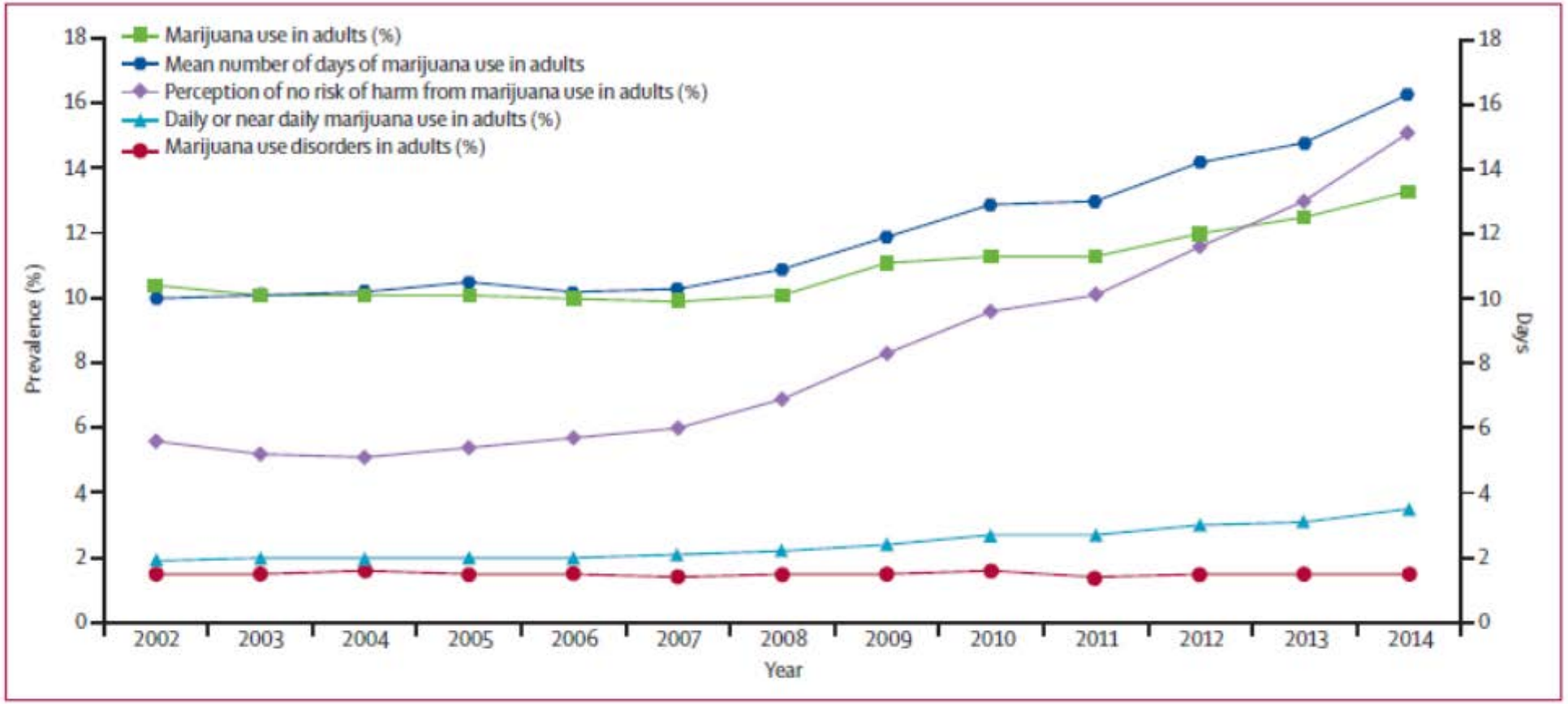

***Figure*: Trends in marijuana use patterns, marijuana use disorders, and perceived risk of harm**
Annual prevalence and trends in any marijuana use, daily or near daily marijuana use, marijuana use disorders, mean number of days of marijuana use, and perception of no risk of harm from marijuana use in adults in the USA. *Joinpoints indicate significant changes in non-linear trends.

Context of Classification as Schedule I

"Since there is still a considerable void in our knowledge of the plant and effects of the active drug contained in it, our recommendation is that marijuana be retained within Schedule I at least until the completion of certain studies now underway to resolve the issue."

Dr. Roger O. Egeberg
Assistant Secretary of Health
August 14, 1970

- High potential for abuse
- No currently accepted use for treatment in the United States
- Lack of accepted safety for use under medical supervision

Possible Medical Uses

- FDA approved for
  - Chemotherapy-induced nausea and vomiting
  - Appetite stimulation
- High quality evidence for
  - Chronic pain, neuropathic (especially HIV/AIDS)
    - Approved in Canada
  - Spasticity of multiple sclerosis, spinal cord injury
  - Anticonvulsant (CBD for Dravet Syndrome)
  - Glaucoma
- Poor quality evidence for
  - PTSD, anxiety, sleep

Cannabinoids and Pain

- Analgesic properties extensively documented and widely accepted in Western medical practice in 19th and early 20th Centuries
- Cannabinoids act centrally and peripherally
- CB1 receptors : 10 x more in CNS than mu-opioid receptors, especially in pain areas
  - Modulate neuronal excitability and inflammation
  - None present in brainstem
    - No overdose from respiratory depression

Original Investigation

Cannabinoids for Medical Use
A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

JAMA. 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358
Last corrected on November 5, 2015.

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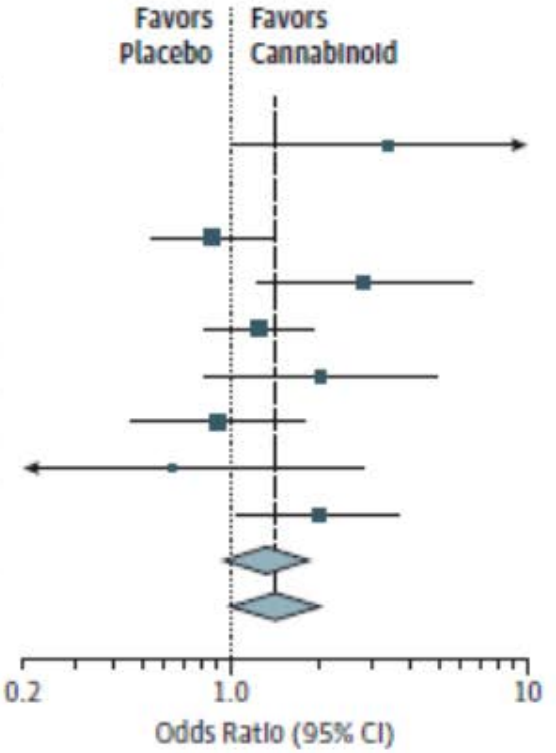
Figure 2. Improvement in Pain

Improvement in Pain With Cannabinoid vs Placebo by Study	Cannabinoid Events No.	Cannabinoid Events Total No.	Placebo Events No.	Placebo Events Total No.	Odds Ratio (95% CI)	Weight, %
Tetrahydrocannabinol (smoked)						
Abrams et al,[77] 2007	13	25	6	25	3.43 (1.03-11.48)	6.51
Nabiximols						
GW Pharmaceuticals,[22] 2005	54	149	59	148	0.86 (0.54-1.37)	19.02
Johnson et al,[69] 2010	23	53	12	56	2.81 (1.22-6.50)	10.87
Langford et al,[65] 2013	84	167	77	172	1.25 (0.81-1.91)	20.19
Nurmikko et al,[76] 2007	16	63	9	62	2.00 (0.81-4.96)	9.84
Portenoy et al,[67] 2012	22	90	24	91	0.90 (0.46-1.76)	14.04
Selvarajah et al,[70] 2010	8	15	9	14	0.63 (0.14-2.82)	4.63
Serpell et al,[88] 2014	34	123	19	117	1.97 (1.05-3.70)	14.91
Subtotal $I^2 = 44.5\%$, ($P = .0.94$)	241	660	209	660	1.32 (0.94-1.86)	93.49
Overall $I^2 = 47.6\%$, ($P = .0.64$)	254	685	215	685	1.41 (0.99-2.00)	100.00



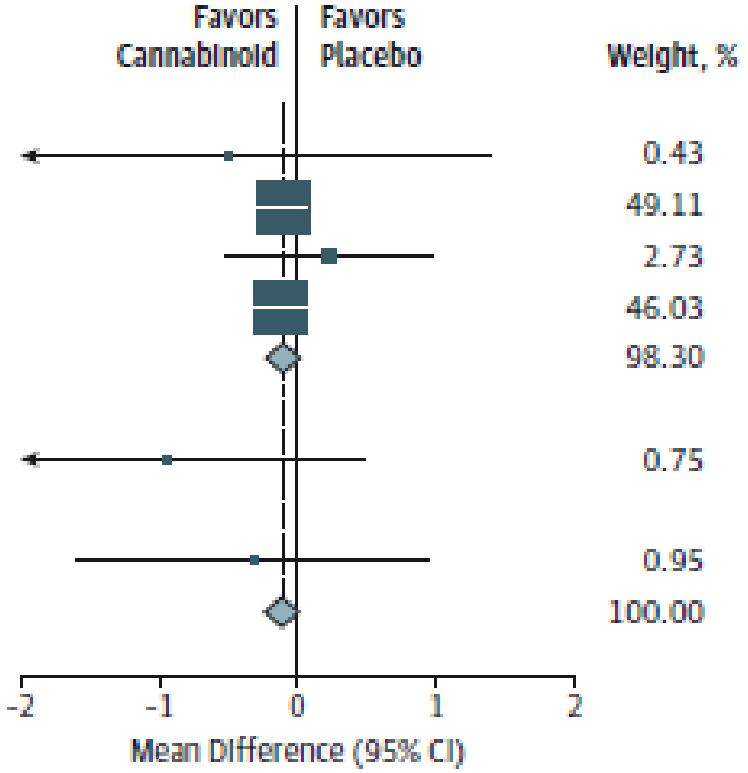
Cannabis and Pain

- Appears effective for different types of pain
  - Neuropathic, Fibromyalgia, rheumatoid arthritis
  - HIV neuropathy – no reduction in viral load or CD4 cell count
- Minimal tolerance
- No toxic overdoses or end organ failure
- Enhances analgesic effect of opioids

Spasticity

Figure 3. Change in Ashworth Score for Cannabinoid Compared With Placebo, Stratified According to Cannabinoid

Score Change With Cannabinoid vs Placebo by Study	Cannabinoid: No. of Patients	Cannabinoid: Mean (SD) Score Change	Placebo: No. of Patients	Placebo: Mean (SD) Score Change	Mean Difference (95% CI)	Weight, %
Nabiximols						
Collin,[125] 2010	156	-3.3 (9.25)	160	-2.8 (7.81)	-0.50 (-2.39 to 1.39)	0.43
Collin,[127] 2007	114	-.64 (.56)	63	-.53 (.58)	-0.11 (-0.29 to 0.07)	49.11
Wade,[129] 2004	73	-.37 (2.51)	70	-.59 (2.04)	0.22 (-0.53 to 0.97)	2.73
Berman,[87] 2007	40	-.13 (.43)	44	-.01 (.42)	-0.12 (-0.30 to 0.06)	46.03
Subtotal I^2=0.0%, (P=.0.82)	383		337		-0.11 (-0.23 to 0.02)	98.30
Dronabinol						
Zajicek,[131] 2003	197	-1.86 (7.95)	207	-.92 (6.56)	-0.94 (-2.37 to 0.49)	0.75
Tetrahydrocannabinol/cannabidiol						
Zajicek,[131] 2003	207	-1.24 (6.6)	207	-.92 (6.56)	-0.32 (-1.59 to 0.95)	0.95
Overall I^2=0.0%, (P=.80)	590		544		-0.12 (-0.24 to 0.01)	100.00



Original Investigation

Cannabinoids for Medical Use
A Systematic Review and Meta-analysis

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IMPORTANCE Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear.

OBJECTIVE To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids.

DATA SOURCES Twenty-eight databases from inception to April 2015.

STUDY SELECTION Randomized clinical trials of cannabinoids for the following indications: nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome.

DATA EXTRACTION AND SYNTHESIS Study quality was assessed using the Cochrane risk of bias tool. All review stages were conducted independently by 2 reviewers. Where possible, data were pooled using random-effects meta-analysis.

MAIN OUTCOMES AND MEASURES Patient-relevant/disease-specific outcomes, activities of daily living, quality of life, global impression of change, and AEs.

RESULTS A total of 79 trials (6462 participants) were included; 4 were judged at low risk of bias. Most trials showed improvement in symptoms associated with cannabinoids but these associations did not reach statistical significance in all trials. Compared with placebo, cannabinoids were associated with a greater average number of patients showing a complete nausea and vomiting response (47% vs 20%; odds ratio [OR], 3.82 [95% CI, 1.55-9.42]; 3 trials), reduction in pain (37% vs 31%; OR, 1.41 [95% CI, 0.99-2.00]; 8 trials), a greater average reduction in numerical rating scale pain assessment (on a 0-10-point scale; weighted mean difference [WMD], −0.46 [95% CI, −0.80 to −0.11]; 6 trials), and average reduction in the Ashworth spasticity scale (WMD, −0.12 [95% CI, −0.24 to 0.01]; 5 trials). There was an increased risk of short-term AEs with cannabinoids, including serious AEs. Common AEs included dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination.

CONCLUSIONS AND RELEVANCE There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term AEs.

Table 3. Summary Estimates From Meta-analyses for Each AE Assessed: Odds of Participants Experiencing AE With Cannabinoid vs Placebo or Active Comparison

	No. of Studies (No. of Patients)	Summary OR (95% CI)	I^2, %
General AE categories			
Any	29 (3714)	3.03 (2.42-3.80)	31
Serious	34 (3248)	1.41 (1.04-1.92)	0
Withdrawal due to AE	23 (2755)	2.94 (2.18-3.96)	2
MedDRA high-level grouping[164]			
Gastrointestinal disorders	10 (1960)	1.78 (1.43-2.22)	0
Infections and infestations	7 (1681)	1.13 (0.87-1.46)	0
Psychiatric disorders	8 (1672)	3.10 (1.81-5.29)	55
Nervous system disorders	10 (1521)	3.17 (2.20-4.58)	46
Musculoskeletal and connective tissues disorders	7 (1310)	1.32 (0.75-2.32)	34
General disorders and administration site conditions	6 (1208)	1.78 (1.34-2.36)	0
Death	5 (929)	1.01 (0.51-2.00)	0
Ear and labyrinth disorders	3 (922)	2.72 (1.55-4.75)	0
Respiratory, thoracic, and mediastinal disorders	5 (851)	0.80 (0.46-1.39)	0
Cardiac disorders	7 (833)	1.42 (0.58-3.48)	0
Blood disorders	3 (543)	1.42 (0.20-10.25)	18
Injury, poisoning and procedural complications	3 (543)	1.18 (0.48-2.93)	0
Renal and urinary disorders	3 (470)	2.45 (2.27-2.65)	0
Investigations	2 (427)	1.55 (0.36-6.71)	0
Metabolism and nutrition	2 (427)	2.37 (1.00-5.61)	0
Neoplasms, benign, malignant, and unspecified	2 (427)	0.99 (0.47-2.08)	0
Skin and subcutaneous	3 (405)	0.85 (0.34-2.13)	0
Eye disorders	1 (339)	1.42 (0.46-4.33)	NA
Reproductive system	1 (246)	1.55 (0.20-11.92)	NA
Hepatobiliary disorders	1 (181)	3.07 (0.12-76.29)	NA
Mental status change	3 (106)	2.49 (0.49-12.64)	0
Other body systems	1 (42)	2.59 (0.34-19.47)	NA
Injection site pain	1 (32)	2.49 (0.92-6.68)	NA
Individual AEs			
Dizziness	41 (4243)	5.09 (4.10-6.32)	18
Dry mouth	36 (4181)	3.50 (2.58-4.75)	28
Nausea	30 (3579)	2.08 (1.63-2.65)	0
Fatigue	20 (2717)	2.00 (1.54-2.62)	0
Somnolence	26 (3168)	2.83 (2.05-3.91)	27
Euphoria	27 (2420)	4.08 (2.18-7.64)	49
Depression	15 (2353)	1.32 (0.87-2.01)	0
Vomiting	17 (2191)	1.67 (1.13-2.47)	0
Diarrhea	17 (2077)	1.65 (1.04-2.62)	15
Disorientation	12 (1736)	5.41 (2.61-11.19)	0
Asthenia	15 (1717)	2.03 (1.35-3.06)	0
Drowsiness	18 (1272)	3.68 (2.24-6.01)	44
Anxiety	12 (1242)	1.98 (0.73-5.35)	54
Confusion	13 (1160)	4.03 (2.05-7.97)	0
Balance	6 (920)	2.62 (1.12-6.13)	0
Hallucination	10 (898)	2.19 (1.02-4.68)	0
Dyspnea	4 (375)	0.83 (0.26-2.63)	0
Paranoia	4 (492)	2.05 (0.42-10.10)	0
Psychosis	2 (37)	1.09 (0.07-16.35)	25
Seizures	2 (42)	0.91 (0.05-15.66)	0

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Comparison of Orally Administered Cannabis Extract and Delta-9-Tetrahydrocannabinol in Treating Patients With Cancer-Related Anorexia-Cachexia Syndrome: A Multicenter, Phase III, Randomized, Double-Blind, Placebo-Controlled Clinical Trial From the Cannabis-In-Cachexia-Study-Group

Florian Strasser, Diana Luftner, Kurt Possinger, Gernot Ernst, Thomas Ruhstaller, Winfried Meissner, You-Dschun Ko, Martin Schnelle, Marcus Reif, and Thomas Cerny

A B S T R A C T

Purpose
To compare the effects of cannabis extract (CE), delta-9-tetrahydrocannabinol (THC), and placebo (PL) on appetite and quality of life (QOL) in patients with cancer-related anorexia-cachexia syndrome (CACS).

Patients and Methods
Adult patients with advanced cancer, CACS, weight loss (≥ 5% over 6 months), and Eastern Cooperative Oncology Group (ECOG) performance status (PS) ≤ 2 were randomly assigned (2:2:1) to receive CE (standardized for 2.5 mg THC and 1 mg cannabidiol) or THC (2.5 mg) or PL orally, twice daily for 6 weeks. Appetite, mood, and nausea were monitored daily with a visual analog scale (VAS); QOL was assessed with the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (composite score: questions 29 and 30). Cannabinoid-related toxicity was assessed every 2 weeks.

Results
Of 289 patients screened, 243 were randomly assigned and 164 (CE, 66 of 95 patients; THC, 65 of 100 patients; and PL, 33 of 48 patients) completed treatment. At baseline, groups were comparable for age (mean, 61 years), sex (54% men), weight loss (32% ≥ 10%), PS (13% ECOG = 2), antineoplastic treatment (50%), appetite (mean VAS score, 31/100 mm), and QOL (mean score, 30/100). Intent-to-treat analysis showed no significant differences between the three arms for appetite, QOL, or cannabinoid-related toxicity. Increased appetite was reported by 73%, 58%, and 69% of patients receiving CE, THC, or PL, respectively. An independent data review board recommended termination of recruitment because of insufficient differences between study arms.

Conclusion
CE at the oral dose administered was well tolerated by these patients with CACS. No differences in patients' appetite or QOL were found either between CE, THC, and PL or between CE and THC at the dosages investigated.

J Clin Oncol 24:3394-3400. © 2006 by American Society of Clinical Oncology

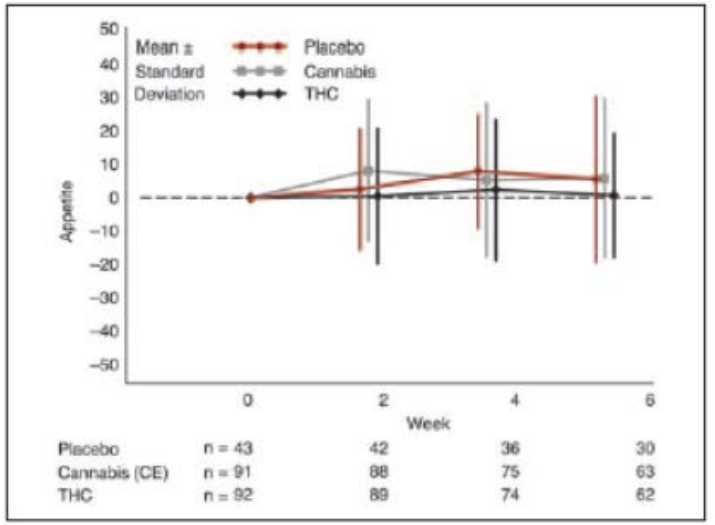

Fig 2. Changes in visual analog scale (VAS) scores from baseline for appetite in the intent-to-treat population. THC, delta-9-tetrahydrocannabinol. Appetite represents mean of daily appetite VAS scores for the 7 days of week 2 in each biweekly period of the 6-week study period.

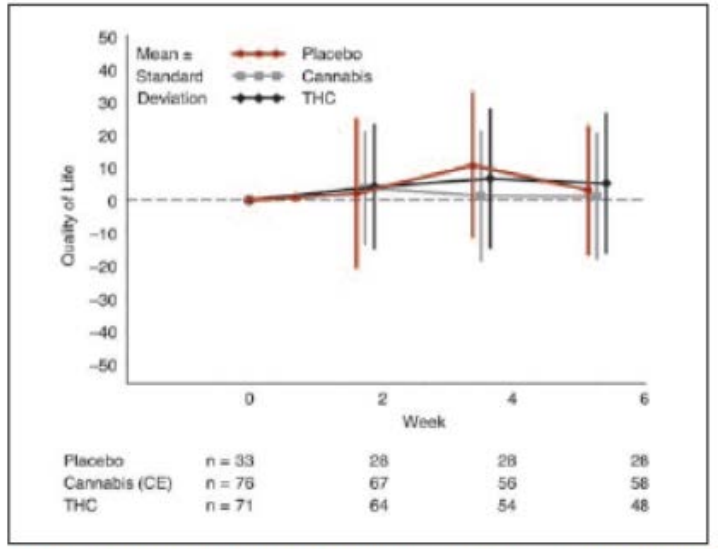

Fig 3. Changes in visual analog scale (VAS) scores from baseline for quality of life (QOL) in the intent-to-treat population. QOL values represent composite scores (mean) of questions 29 (Global Health Status) and 30 (QOL) on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 transformed into a single functional scale (range, 0 to 100). THC, delta-9-tetrahydrocannabinol.

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Placebo –
not anti-emetic controlled

PTSD, anxiety, sleep

- Studies mixed – at best
- Poor study design
- More likely that cannabis worsens rather than improves PTSD

Acute and Chronic Effects of Cannabinoids on Human Cognition—A Systematic Review

Samantha J. Broyd, Hendrika H. van Hell, Camilla Beale, Murat Yücel, and Nadia Solowij

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Table 1. Strength and Consistency of Evidence for Impairment Associated With Acute and Chronic Cannabis Use and for Recovery of Function With Abstinence From Research Published in the Past Decade[a]

Cognitive Domain	Acute[b]	Chronic[b]	Persistence With Abstinence[b]	Pertinent Cannabis Use Parameters	Number of Studies: Acute	Chronic	Abstinence
Memory							
Verbal learning and memory	+++	+++	+−	Frequency; lifetime use; duration; age of onset; sex	11 (36–44,77,87)	20 (44–58,60–62,66,142)	9 (55,57,60,63–67,95)
Working memory	+−	+−	+−	Frequency; lifetime use; recency; sex	20 (36–40,42,43,68–78,88,143)	16 (46,48,49,51–53,55,57, 79–84,115,119)	7 (55,57,64,65,67,79,85)
Other memory function	+	+−	−	Age of onset; frequency; recency	2 (42,144)	8 (45,49,78–80,119,144,145)	4 (63,65,79,95)
Attention							
Attention	+++	+++	+−	Dose; age of onset; length of abstinence; withdrawal effects	16 (36,37,39,42,43,68,70,71,76,77, 86–90,143)	14 (45,46,54,55,57,61,79–81,84, 91–94)	10 (55,57,63,64,67,79,91–93,95)
Attentional bias	+	+++	NA	Craving; dependence; frequency; CBD	1 (102)	7 (96–102)	None
Psychomotor Function	+++	+	+		18 (37,42,43,68,70,73,74,76,77,89,90, 103–107,143,146)	10 (46,48,51,54,57,66,78,80,91,108)	6 (57,63–65,67,91)
Executive Function							
Planning, reasoning, interference control, and problem solving	+−	+−	+−	Neurodevelopmental stage; age of onset; frequency	12 (37–41,77,86,89,103,104,106,109)	23 (46,48,52–54,57,60,61,66,78, 81–84,93,98,110–115,147)	9 (57,60,63–65,67,85,93,95)
Inhibition	++	+−	NA	Frequency; task complexity	5 (42,89,103,104,109)	9 (45,50,54,56,82,110,116–118)	None
Verbal fluency	−	+−	+−		3 (36,38,44)	6 (44,48,51,53,54,61)	4 (65,67,93,119)
Time estimation	+−	−	−		6 (73,74,77,86,148,149)	1 (55)	1 (55)
Decision Making	+−	+−	−	Age of onset; lifetime exposure; frequency; cannabis use disorder	7 (103,105,106,109,120–122)	17 (45,48,50,56,78,82,84,94,113,116, 117,123–126,128,150)	3 (85,127,128)

CBD, cannabidiol; NA, not available (not investigated).

[a]The prevalence of studies focused on acute vs. chronic effects is unequal, as is the focus on individual cognitive domains; strength metrics are based on qualitative interpretation of the literature, subjectively weighed on greater or lesser evidence for impairment across the published studies, considering the number of studies conducted and their quality (e.g., design, sample size), reached by consensus between the authors of this review.

[b]+++, strong and largely consistent evidence for impairment; ++, moderate evidence for impairment; +, weak evidence for impairment, being based on only a small number of studies; +−, mixed evidence; −, little or no evidence for impairment.

http://dx.doi.org/10.1016/j.biopsych.2015.12.002

Table 2. Key Findings for Cognitive Impairment in Cannabis Users

Acute Effects of Cannabis on Cognition
Impaired verbal learning and memory
Impaired working memory and other memory functions
Impaired attention, task and dose dependent
Impaired inhibition, less so for other executive functions
Impaired psychomotor function
Chronic Effects of Cannabis on Cognition
Impaired verbal learning and memory
Impaired attention and attentional bias
Possible impaired psychomotor function
Mixed evidence for executive function and decision making
Most associated with cannabis use parameters, particularly frequency of use and age of onset
Recovery of Function With Abstinence
Likely persistent effects on attention and psychomotor function
Possible persistent effects on verbal learning and memory
Evidence insufficient and mixed

Schizophrenia Bulletin vol. 42 no. 5 pp. 1262–1269, 2016
doi:10.1093/schbul/sbw003
Advance Access publication February 15, 2016

Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis

Arianna Marconi[1], Marta Di Forti[1], Cathryn M. Lewis[2], Robin M. Murray[1], and Evangelos Vassos[*,2]

[1]Department of Psychosis Studies, King's College London, Institute of Psychiatry Psychology & Neuroscience, London, UK; [2]King's College London, Institute of Psychiatry Psychology & Neuroscience, MRC SGDP Centre, London, UK

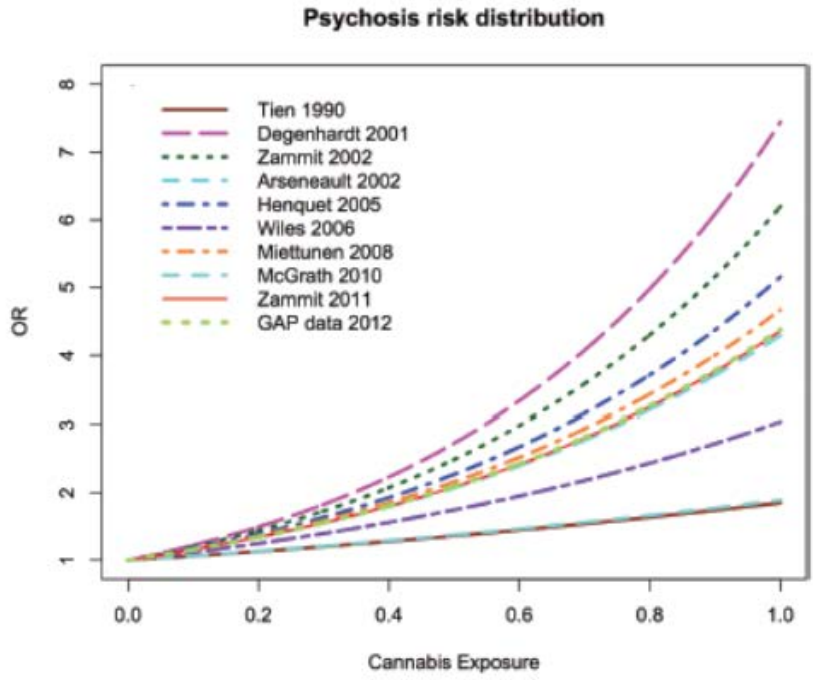

Fig. 2. Estimated risk ratio of psychosis by level of cannabis use in original studies.

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Cannabis and the Development of Psychosis

10+ longitudinal studies – all show an association between cannabis use and psychosis

Risk in context:

- Individual: Increase from 1-2%
- Population: Additional 3,000,000 events

Psychological Medicine (2014), **44**, 797–810. © Cambridge University Press 2013
doi:10.1017/S0033291713001438

ORIGINAL ARTIC

The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies

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[8] *Schizophrenia Program, Centre for Addiction and Mental Health, Toronto, Ontario, Canada*
[9] *Division of Brain and Therapeutics, Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada*
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[11] *Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada*

Background. Longitudinal studies reporting the association between cannabis use and developing depression provide mixed results. The objective of this study was to establish the extent to which different patterns of use of cannabis are associated with the development of depression using meta-analysis of longitudinal studies.

Method. Peer-reviewed publications reporting the risk of developing depression in cannabis users were located using searches of EMBASE, Medline, PsychINFO and ISI Web of Science. Only longitudinal studies that controlled for depression at baseline were included. Data on several study characteristics, including measures of cannabis use, measures of depression and control variables, were extracted. Odds ratios (ORs) were extracted by age and length of follow-up.

Results. After screening for 4764 articles, 57 articles were selected for full-text review, of which 14 were included in the quantitative analysis (total number of subjects=76058). The OR for cannabis users developing depression compared with controls was 1.17 [95% confidence interval (CI) 1.05–1.30]. The OR for heavy cannabis users developing depression was 1.62 (95% CI 1.21–2.16), compared with non-users or light users. Meta-regression revealed no significant differences in effect based on age of subjects and marginal difference in effect based on length of follow-up in the individual studies. There was large heterogeneity in the number and type of control variables in the different studies.

Conclusions. Cannabis use, and particularly heavy cannabis use, may be associated with an increased risk for developing depressive disorders. There is need for further longitudinal exploration of the association between cannabis use and developing depression, particularly taking into account cumulative exposure to cannabis and potentially significant confounding factors.

Received 20 January 2013; Revised 4 May 2013; Accepted 11 May 2013; First published online 24 June 2013

Key words: Cannabis, depression, epidemiology, meta-analysis, psychiatry.

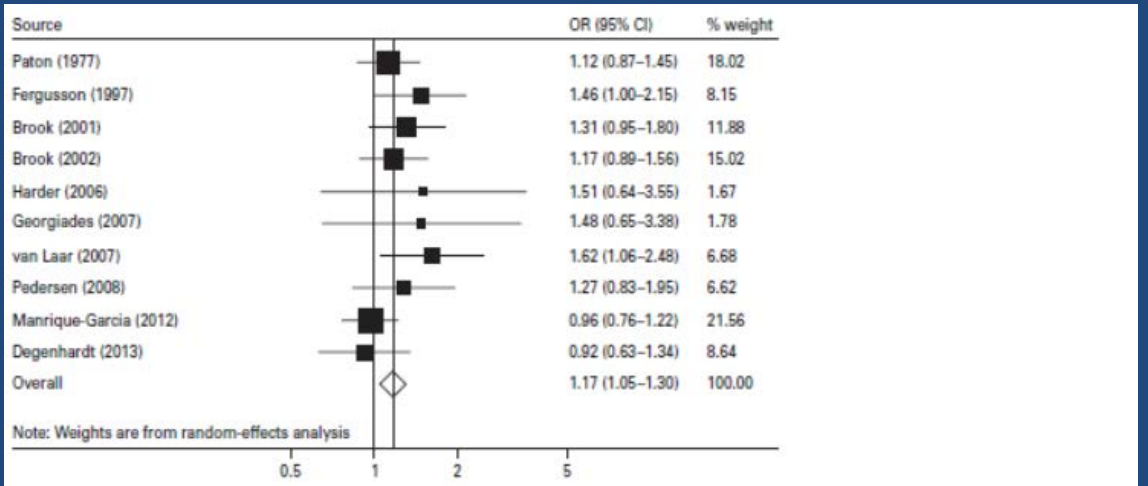

Fig. 2. Forest plot showing adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for any depressive outcome according to cannabis use in individual studies (random effects).

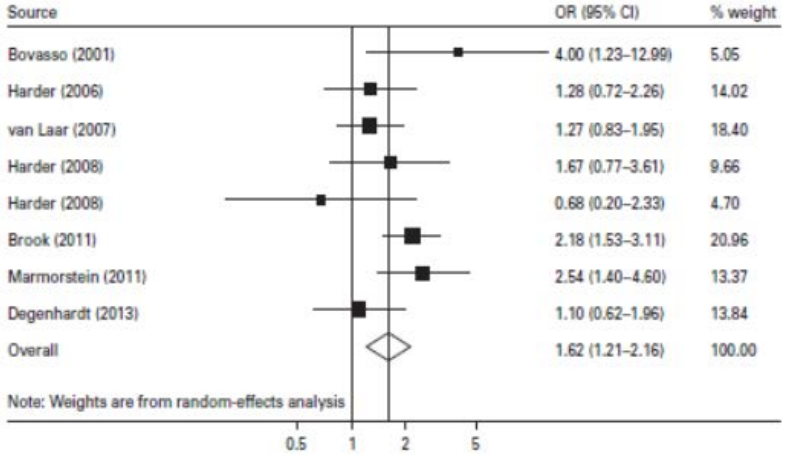

Fig. 3. Forest plot showing adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for any depressive outcome according to heavy cannabis use (defined as a cannabis use disorder or at-least weekly use) in individual studies (random effects).

Cannabis Withdrawal Syndrome

- New diagnostic category in DSM-5
- Symptoms usually mild
  - Irritability, anxiety, insomnia, disturbing dreams, decreased appetite, restlessness, depressed mood
- Cravings can be clinically significant
- Time course
  - Onset 24 to 72 hours, peak within first week, duration 1 to 2 weeks
    - Sleep difficulties may last more than 30 days
- Usually manageable with mild medication
  - Research: positive response to dronabinol

Drunk and Drugged Driving

- Alcohol effects have greater impact on complex tasks that require conscious control
- Cannabis effects have greater impact on automatic driving functions
- Cannabis users are more aware of being impaired and tend to use various behavioral strategies to compensate for impairments
  - ➢ Adding alcohol eliminates the ability to use these strategies effectively
  - ❖ Result: impairments at doses that would be insignificant if either substances were used alone

Quasi Medical Cannabis in VA

- VA GA 2018 session: debate centered on patients suffering from intractable epilepsy
- HB 1251: doctors can recommend CBD or THC-A cannabis oil for any condition
- While the law is being implemented, patients can possess the oil if it meets the state's requirement of at least 15% CBD or THC-A and no more than 5% THC, and they have in their possession doctor’s recommendation form (called a “written certification”)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 25, 2017 VOL. 376 NO. 21

Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome

Orrin Devinsky, M.D., J. Helen Cross, Ph.D., F.R.C.P.C.H., Linda Laux, M.D., Eric Marsh, M.D., Ian Miller, M.D., Rima Nabbout, M.D., Ingrid E. Scheffer, M.B., B.S., Ph.D., Elizabeth A. Thiele, M.D., Ph.D., and Stephen Wright, M.D., for the Cannabidiol in Dravet Syndrome Study Group*

Table 2. Primary Efficacy End Point of Percentage Change in Convulsive-Seizure Frequency in Each Trial Group.*

Variable	Cannabidiol	Placebo	Adjusted Median Difference (95% CI)	P Value†
			percentage points	
No. of convulsive seizures per mo — median (range)				
Baseline	12.4 (3.9 to 1717)	14.9 (3.7 to 718)		
Treatment period	5.9 (0.0 to 2159)	14.1 (0.9 to 709)		
Percentage change in seizure frequency — median (range)	−38.9 (−100 to 337)	−13.3 (−91.5 to 230)	−22.8 (−41.1 to −5.4)	0.01

* CI denotes confidence interval.
† The P value was calculated with the use of a Wilcoxon rank-sum test with the Hodges–Lehmann approach.

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Dravet Syndrome: complex childhood epilepsy associated with drug-resistant seizures and high mortality

Double blind placebo controlled – 14 weeks trial compared w 4 week base line

Patients with at least 50% reduction in convulsive-seizure activity – 43% in CBD vs 27% in placebo (OR 2.00, [0.93-4.30])

5% became seizure free w CBD 0% w placebo

More side effects and withdrawals from CBD group (D, V, fatigue, pyrexia somnolence and abnormal LFTs

Questions

Synthetic Cannabinoids: History

- 1970s-80s. Synthesized for scientific research
  - Trying to identify the molecular structure that activates the endocannabinoid receptors
- Results became publicly available as research papers and patents
- Information appropriated by drug dealers
- 2004. Appeared in Europe as “Spice,” “K2”
- Subsequent chemical alterations to evade illegality and detection
  - Broad array of non-cannabinoid molecules

Synthetic Cannabinoids: Clinical

- Motivation to use: initially promoted as a safer and legal alternative to cannabis
- Routes of administration
  - Smoked after being sprayed on herbal material or as vaporized liquid
  - Drunk as a tea
- Full agonists: 100 times more potent than THC (a partial agonist)
- Acute effects
  - Tachycardia, increased BP, nausea and vomiting
  - Anxiety, agitation, paranoia, hallucinations, violence

Synthetic Cannabinoids: Treatment

- No specific treatment for toxicity or withdrawal
- Management problem in acute care settings

Synthetic Cannabinoids: Good News

- 2012. Synthetic Drug Abuse Prevention Act
- 2013-15. Increased enforcement of laws
- 2013-15. Significant decrease in use by 8th, 10th, 12th graders. See "Monitoring the Future" (www.monitoringthefuture.org)
  - Appears to be due to both increased perception of risk and decreased availability

Cannabis Use Disorder

Use of cannabis for at least a one year period, with the presence of **at least two** of the following symptoms, accompanied by significant impairment of functioning and distress:

- Difficulty containing use of cannabis- the drug is used in larger amounts and over a longer period than intended.
- Repeated failed efforts to discontinue or reduce the amount of cannabis that is used
- An inordinate amount of time is occupied acquiring, using, or recovering from the effects of cannabis.
- Cravings or desires to use cannabis. This can include intrusive thoughts and images, and dreams about cannabis, or olfactory perceptions of the smell of cannabis, due to preoccupation with cannabis.
- Continued use of cannabis despite adverse consequences from its use, such as criminal charges, ultimatums of abandonment from spouse/partner/friends, and poor productivity.

Cannabis Use Disorder (Continued)

- Other important activities in life, such as work, school, hygiene, and responsibility to family and friends are superseded by the desire to use cannabis.
- Cannabis is used in contexts that are potentially dangerous, such as operating a motor vehicle.
- Use of cannabis continues despite awareness of physical or psychological problems attributed to use- e.g., anergia, amotivation, chronic cough.
- Tolerance to Cannabis, as defined by progressively larger amounts of cannabis are needed to obtain the psychoactive effect experienced when use first commenced, or, noticeably reduced effect of use of the same amount of cannabis
- Withdrawal, defined as the typical withdrawal syndrome associate with cannabis, or cannabis or a similar substance is used to prevent withdrawal symptoms.

Mild – Two or Three Symptoms
Moderate- Four or five symptoms
Severe- Six or more symptoms

Questions?

Case Presentation
Tierra Ruffin, LPC

- 12:35-12:55 [20 min]
  - 5 min: Presentation
  - 2 min: Clarifying questions- Spokes
  - 2 min: Clarifying questions – Hub
  - 2 min: Recommendations – Spokes
  - 2 min: Recommendations – Hub
  - 5 min: Summary - Hub

Reminder: Mute and Unmute to talk
*6 for phone audio
Use chat function for questions

Case Presentation
Tierra Ruffin, LPC

Please state your main question(s) or what feedback/suggestions you would like from the group today?

I have a client who is currently a member within our OBOT clinic who is prescribed suboxone. Within our OBOT program we require individuals to participate in 1:1 Therapy, as well as groups at a minimum 1x a week. I'm having a difficult time getting this individual to commit to the therapeutic portion. He only desires the medication piece.

Case History

Attention: Please DO NOT provide any patient specific information nor include any Protected Health Information!

Demographic Information (e.g. age, sex, race, education level, employment, living situation, social support, etc.)

Age: 40 - Male - Caucasian male. Education: High School, Employment: Landscaper, and in construction work over the course of the past several years., No transportation and currently residing in a small town on the outskirts of Hampton. Currently residing with his parents, and in the process of a divorce. He has custody of his 11 year old son, and appears ashamed to participate in treatment.

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Case Presentation
Tierra Ruffin, LPC

Physical, Behavioral, and Mental health background information (e.g. medical diagnosis, reason for receiving opioids, lab results, current medications, current or past counseling or therapy treatment, barriers to patient care, etc.)

Current Diagnosis: F14.20 Cocaine Dependence, F12.20 Cannabis Dependence, F11.20 Opioid Dependence, PTSD
Currently receiving opioids due to "Popping pills, and found that heroin was cheaper." He reported that he had been using heroin for over 2 years and was "popping pills" for longer than that.

He reported that he had quite a few surgeries in the past (back and knees).

He was provided counseling in 2009 during an inpatient stay to assist him in stopping the abuse of pills. He was provided a follow-up therapy appointment upon discharge. He attended 1 session, and never returned.

he also saw a therapist at the age of 14 due to behavioral concerns at school. He does not remember his experience in therapy.

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Case Presentation
Tierra Ruffin, LPC

What interventions have you tried up to this point ?
Additional case history (e.g. treatments, medications, referrals, etc.)

Brand new client, I saw him for the first time for his diagnostic on 3/22. However, we are a team within PIR and OBOT and have found that he continues to lack motivation. He is assigned to an evening group, and attended the initial group on 4/2. He entered the group with the attitude: "How long do I have to come here?!"
Up to this point we have communicated the guidelines of the programs and he has expressed to all of us that he does not want to be in therapy.

What is your plan for future treatment? What are the patient's goals for treatment?

To follow the guidelines of the program which are individual therapy, group therapy and the medication. His initial statement when creating his tx plan was "I'd like to make enough money to get my divorce finalized." He does not have a desire to stop the Suboxone medication. He is limited in the scope of his goal setting.

REMINDER: Please ensure that NO patient specific identifiable information (PHI) is included in this submission. Please read, sign, and click SUBMIT when completed.

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Case Presentation Follow-Up
Faisal Mohsin, MD

- 12:35-12:55 [20 min]
  - 5 min: Presentation
  - 2 min: Clarifying questions- Spokes
  - 2 min: Clarifying questions – Hub
  - 2 min: Recommendations – Spokes
  - 2 min: Recommendations – Hub
  - 5 min: Summary - Hub

Reminder: Mute and Unmute to talk
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Case Presentation Follow-Up
Faisal Mohsin, MD

QUESTION: How do we re-engage the client back into treatment? Client cancelled his upcoming appointment for medication management and Suboxone.

Background: 33 y.o. Caucasian Male, lives with girlfriend, and 5 children in their own house. He is not very close to his immediate family members. Given events pertaining to his past substance use. Patient had recently reported during one of his group meetings that his girlfriend was on the verge of leaving him. He owns his own landscaping business, but because of seasonal variations, business had slowed down which led him to seek a part time job and he is now working as a welder. He is the main provider for his family.

Labs:
Buprenorphine >1000ng/ml (cutoff 0.5ng/ml LC/MS)
Norbuprenorphine 56ng/ml (cut off 0.5ng/ml LC/MS)

Creatinine 68 mg/dl

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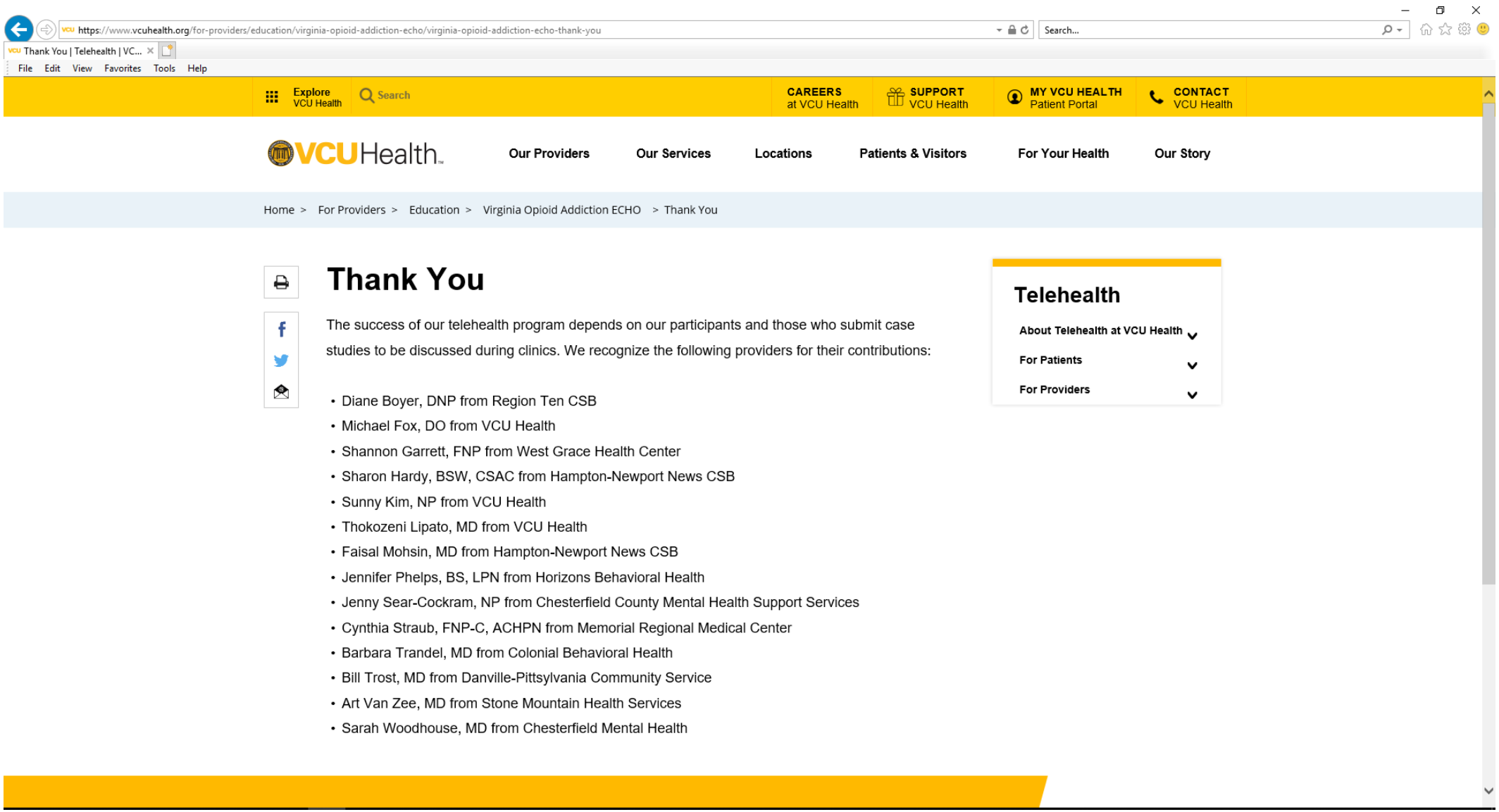
Case Studies

- Case studies
  - Submit: www.vcuhealth.org/echo
  - Receive feedback from participants and content experts



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Opportunity to formally submit feedback

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- Overall feedback related to session content and flow?
- Ideas for guest speakers?

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- www.vcuhealth.org/echo

- To claim CME credit for today's session
- Feedback
  - Overall feedback related to session content and flow?
  - Ideas for guest speakers?

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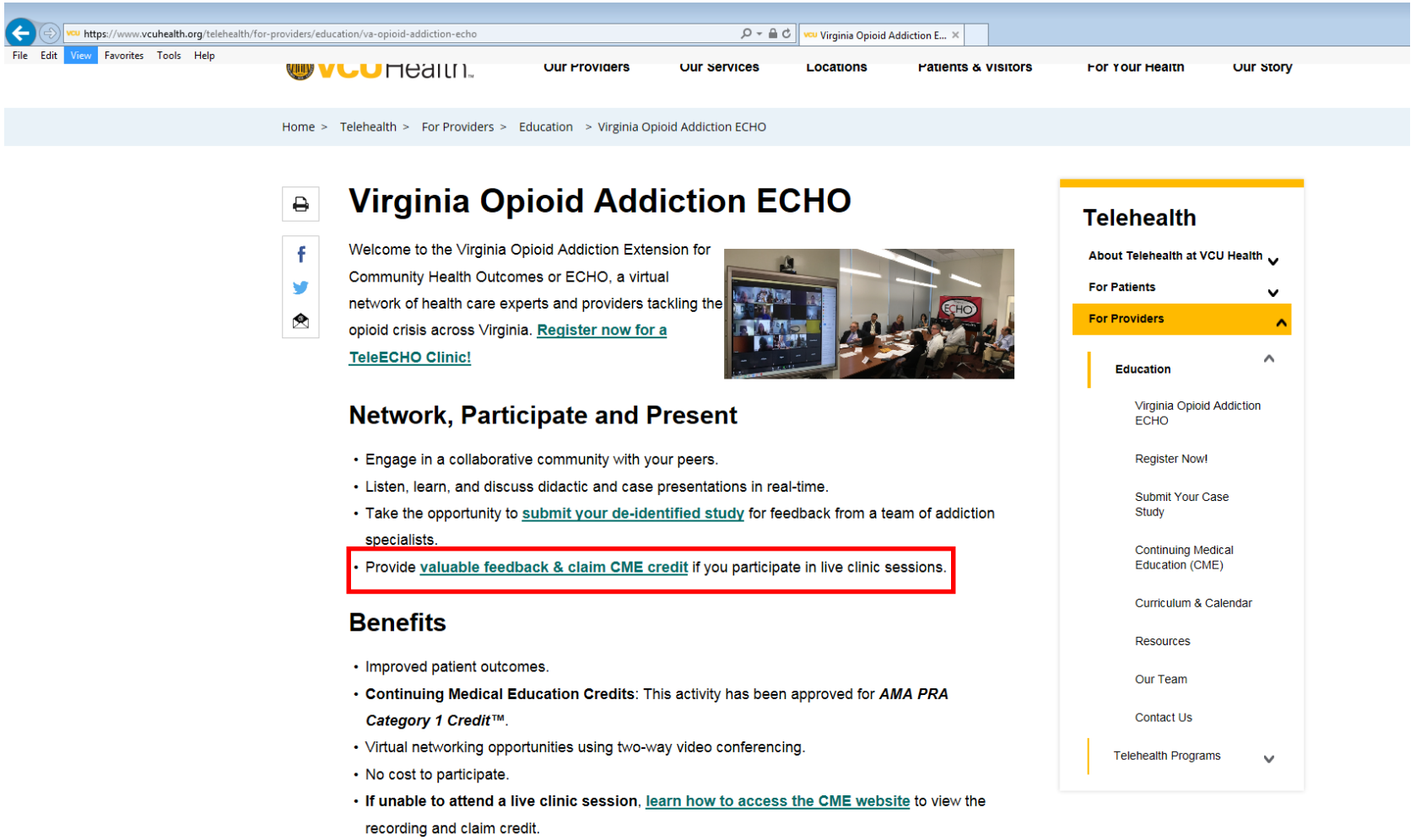

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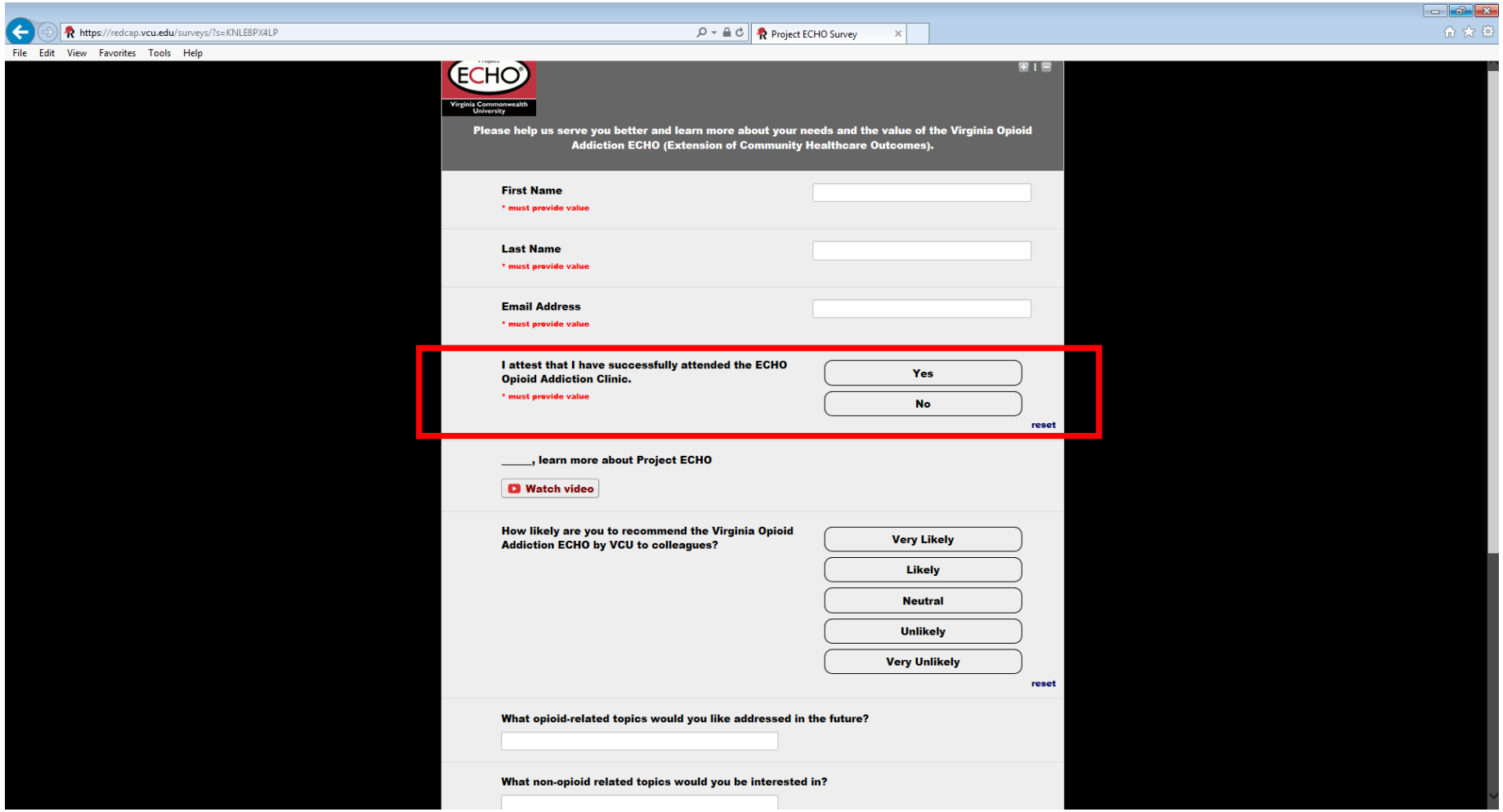

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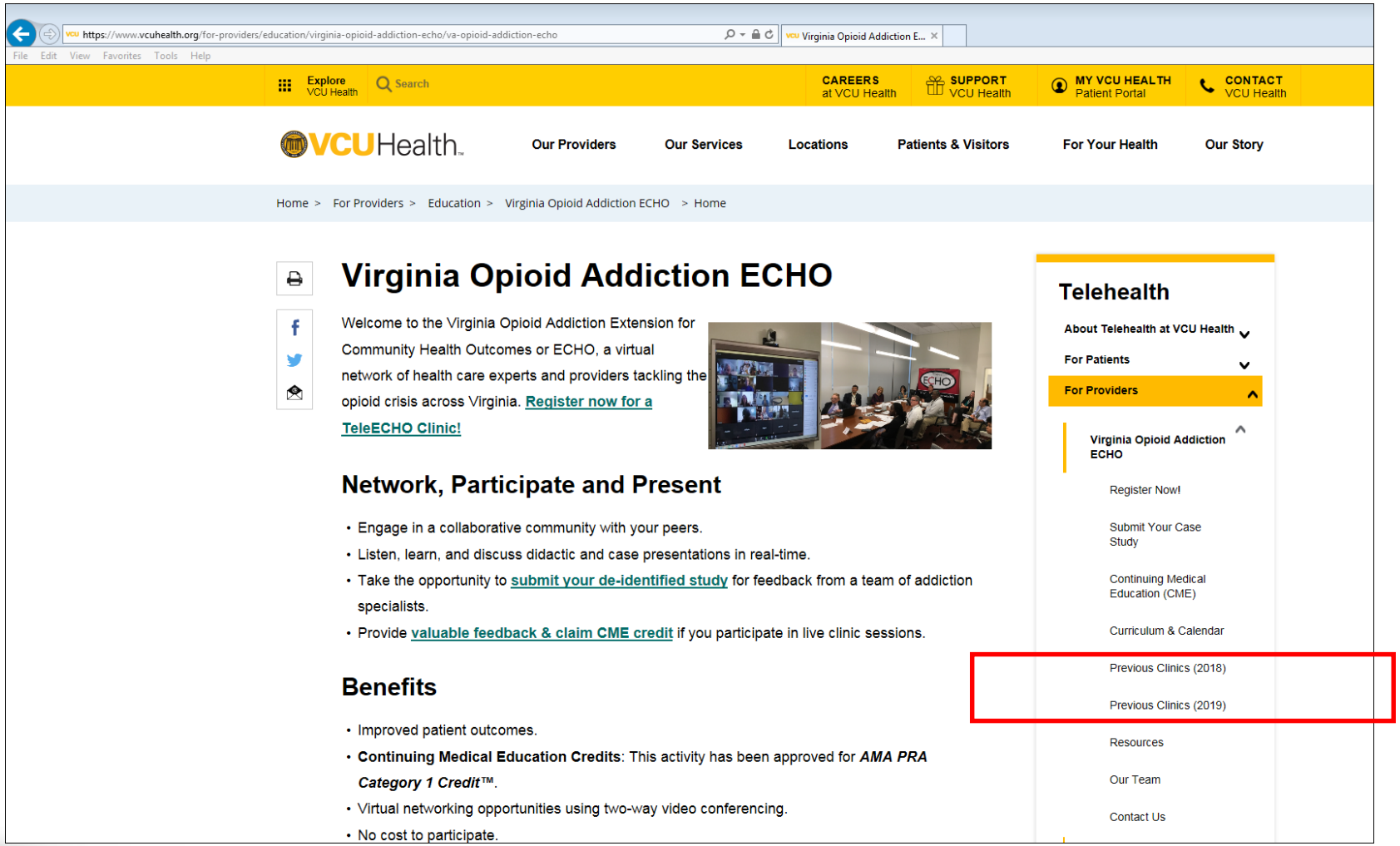

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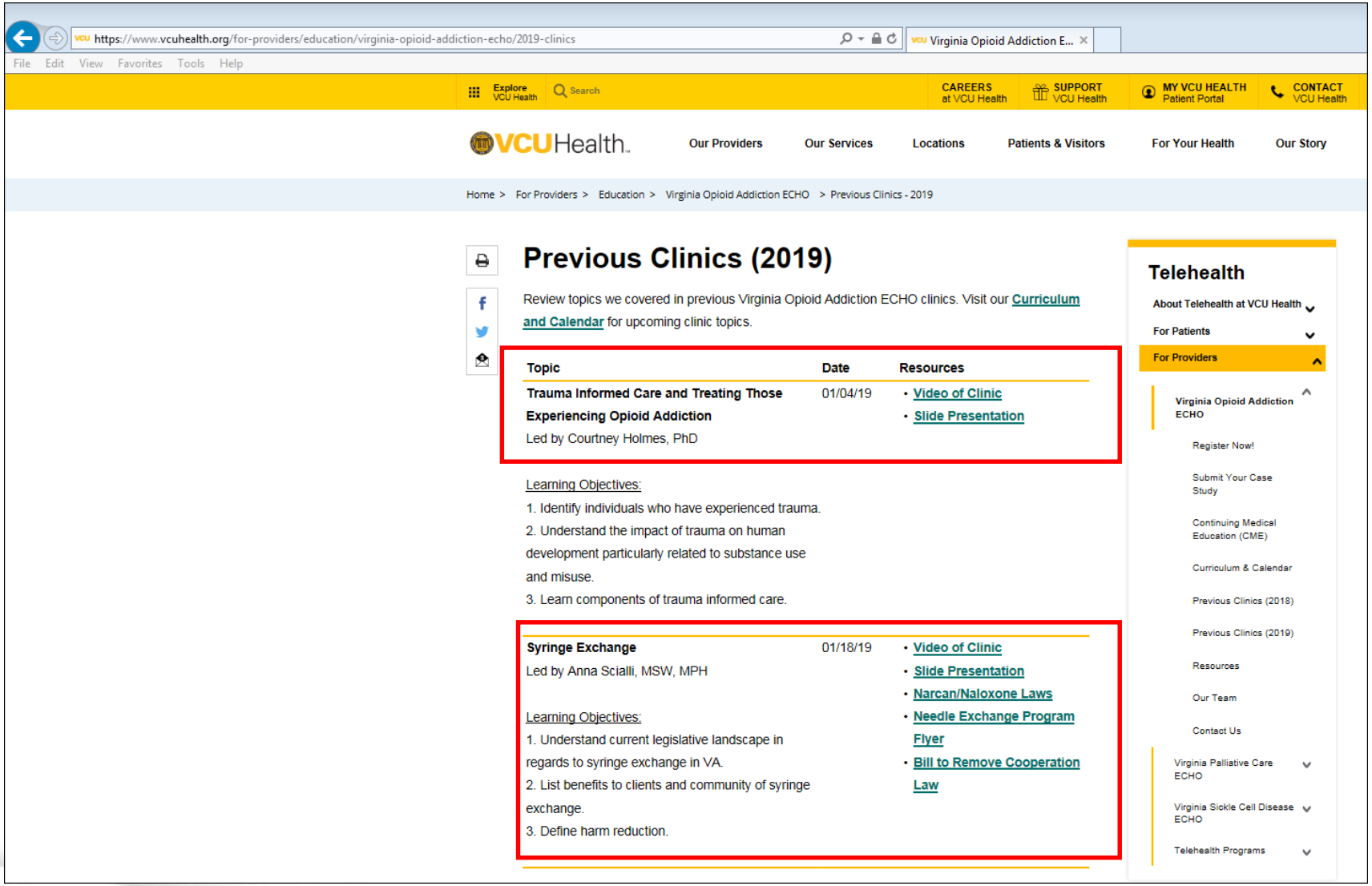

VCU Virginia Opioid Addiction TeleECHO Clinics

Bi-Weekly Fridays - 12-1:30 pm

Mark Your Calendar --- Upcoming Sessions

April 19:	Addressing Vocational Needs of People with SUD	Rebecca Farthing, MS, CRC Elizabeth Phillips, MS, CRC
May 3:	Peer Recovery from OUDs	Tom Bannard, MBA
May 17:	Chronic Pain Self Management	Joyce Nussbaum

Please refer and register at vcuhealth.org/echo

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THANK YOU!

VCU

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