



21° Congresso Nazionale

Società Italiana di Tossicologia

www.sitox.org

BOLOGNA 20-22 Febbraio 2023

Pericolo, rischio e rapporto rischio-beneficio

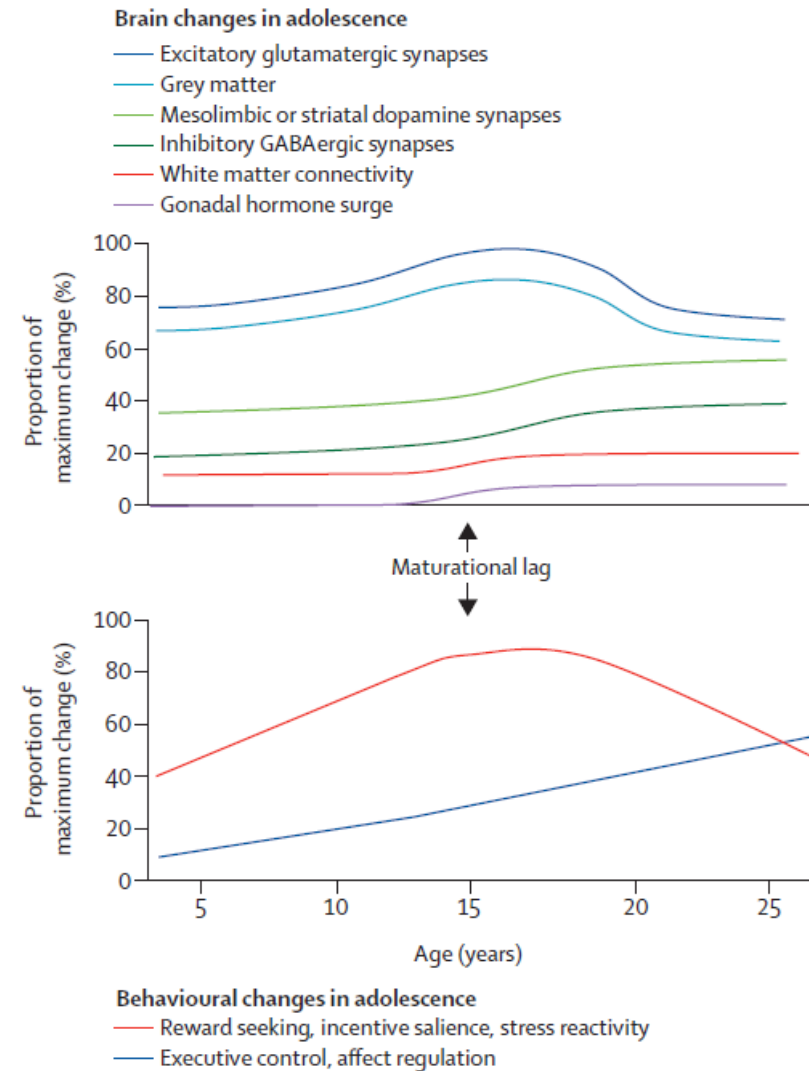
CONSUMO E DISTURBO DA USO DI CANNABIS IN ADOLESCENZA

Sarah Vecchio

ADOLESCENZA

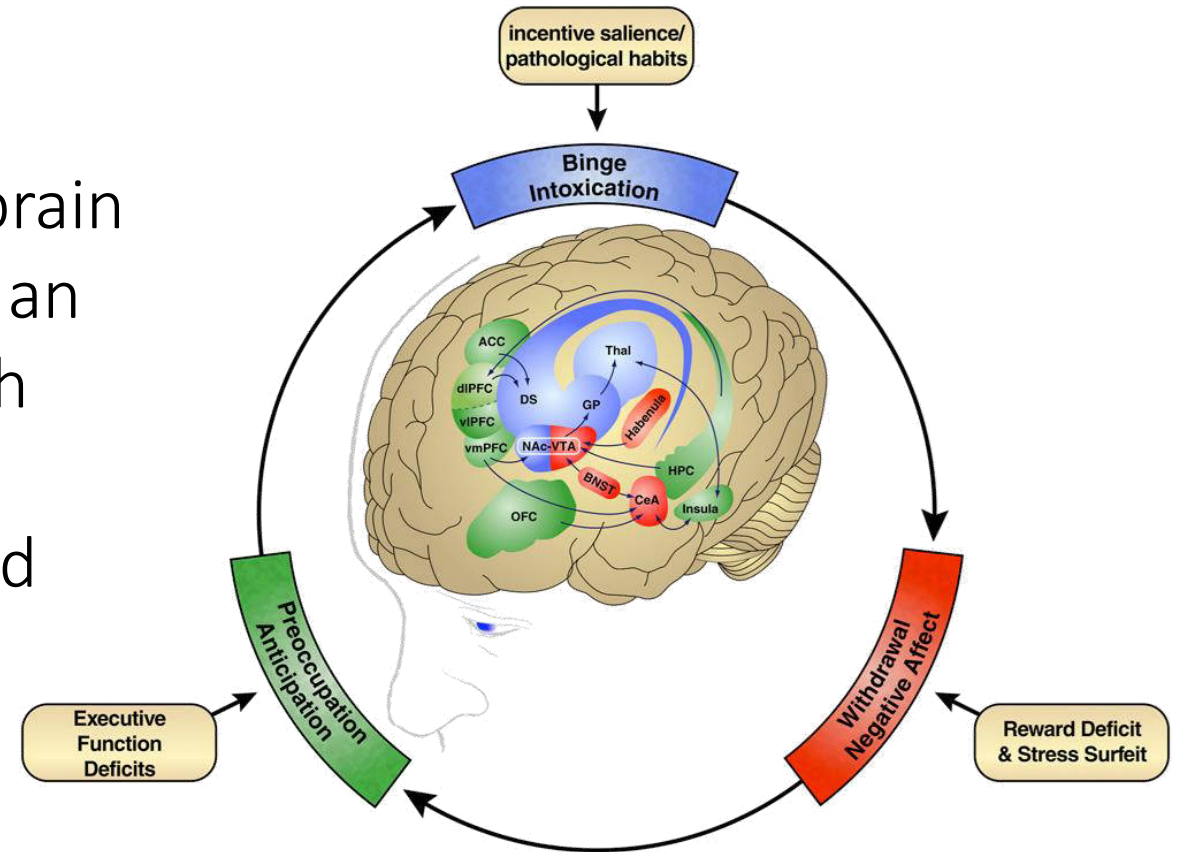
Adolescence is considered to be a dynamic period that begins with puberty and ends when one achieves an independent role in society (Dumontheil, 2016).

No agreed-upon age range constitutes 'adolescence', but definitions are usually 10-19 years or 10-24 years (Sawyer et al., 2018)

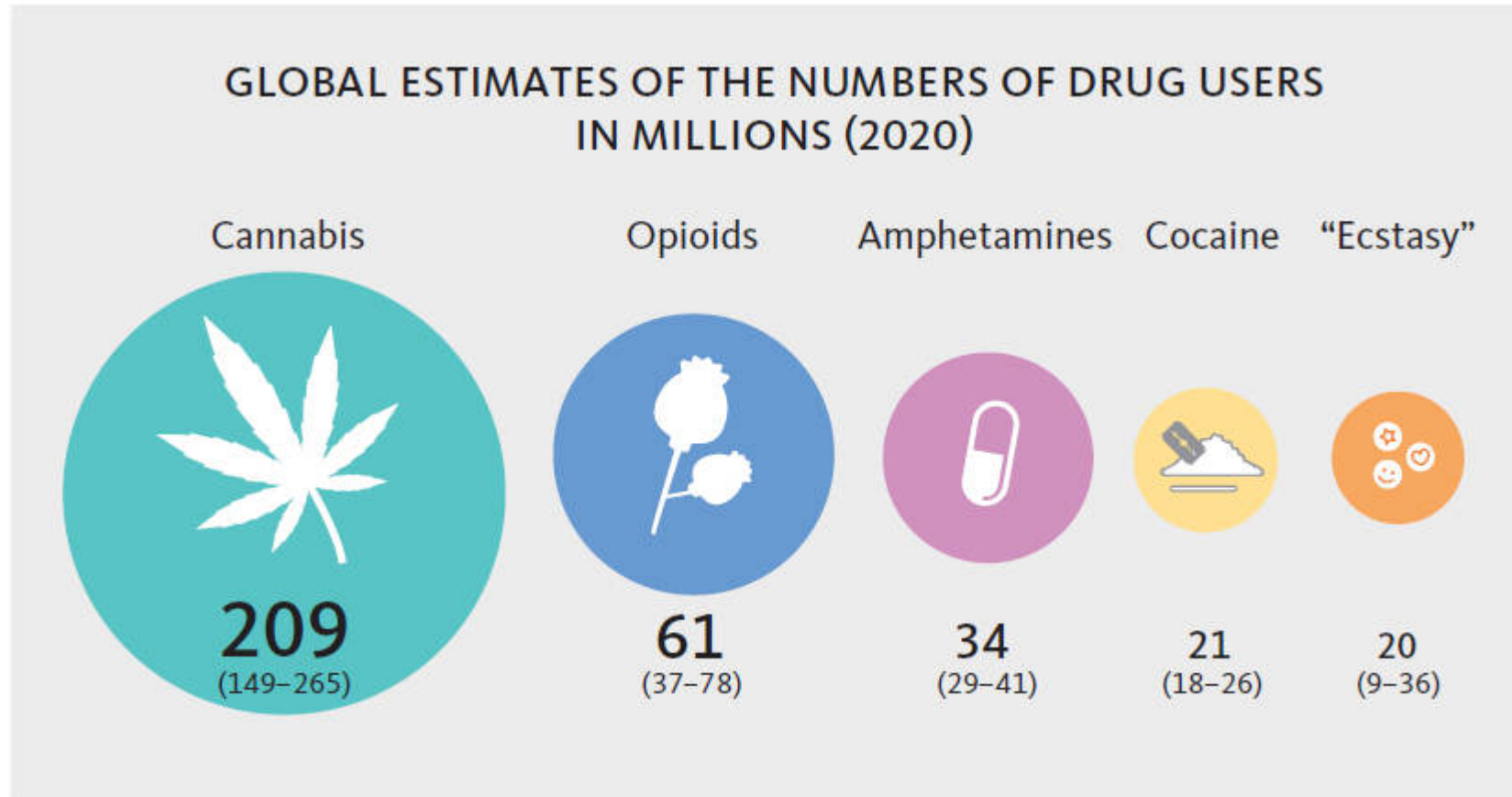


ADDICTION

A treatable, **chronic medical disease** involving complex interactions among brain circuits, genetics, the environment and an individual's life experiences. People with addiction use substances or engage in behaviours that become compulsive and often continue despite harmful consequences. (ASAM 2020)



CONSUMO DI CANNABIS: DIMENSIONI GLOBALI DEL FENOMENO



> 4% OF THE GLOBAL POPULATION AGED 15–64 HAD USED CANNABIS IN PAST YEAR
23% INCREASE BETWEEN 2010 AND 2020

CONSUMO DI CANNABIS: IMPATTO A BREVE E LUNGO TERMINE

Table 1 Common clinical adverse effects associated with cannabinoids use

Psychiatric conditions	An increased risk of psychotic disorders following acute and repeated consumption of cannabis in vulnerable individuals and naïve users. ^{27,28,41-44} Anxiety and panic attacks following intoxication especially in naive users. ³⁸ Chronic use is associated with mood disturbances, mania, and depression. ^{36,37,39,40} Cannabis addiction and dependency. ^{9,13}
Cognitive and CNS alterations	Impairment of a wide range of cognitive functions following cannabis intoxication in a dose-relation manner. ^{38-42,44,45} Impaired cognitive function following cannabis consumption was associated with an increased risk of having a road accident. ³¹⁻³⁵ Chronic use is associated with long-term brain functional and structural alterations. ^{31,32,45-50}
Effects on respiratory system	Acute cannabis consumption decreases airway resistance. ¹² Chronic cannabis use is associated with an increased risk for developing airway diseases and lung cancer. ⁵⁹⁻⁶⁶
Effect on cardiovascular system	An increase of cardiovascular activity, increase of heart rate, and decrease of blood pressure. ⁶⁴ Several reports have described a temporal relationship between cannabis use and acute myocardial infarction, cardiomyopathy, and sudden cardiac death. ⁶⁸⁻⁷²

CONSUMO DI CANNABIS NEL MONDO PER ETA' E GENERE

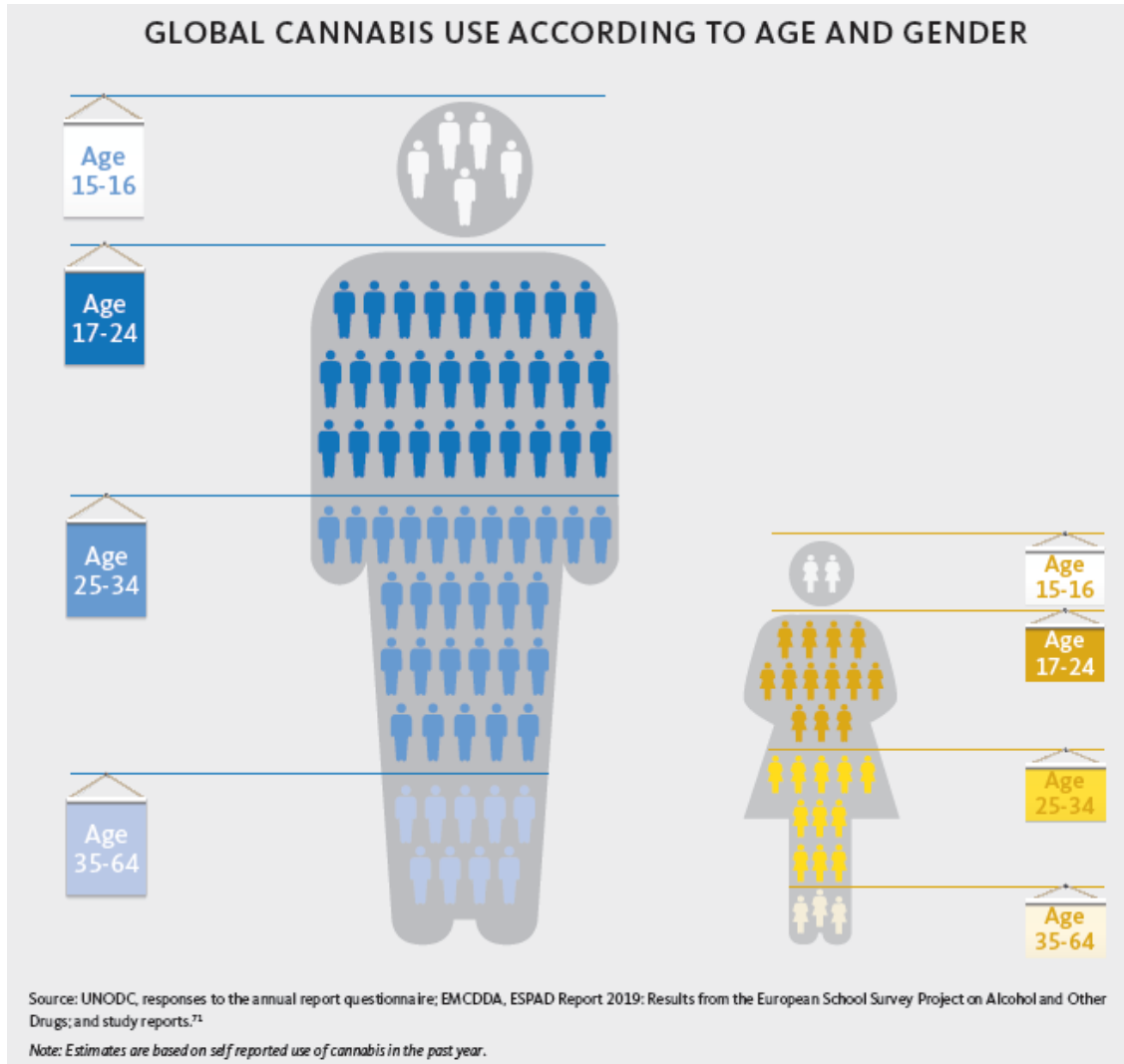
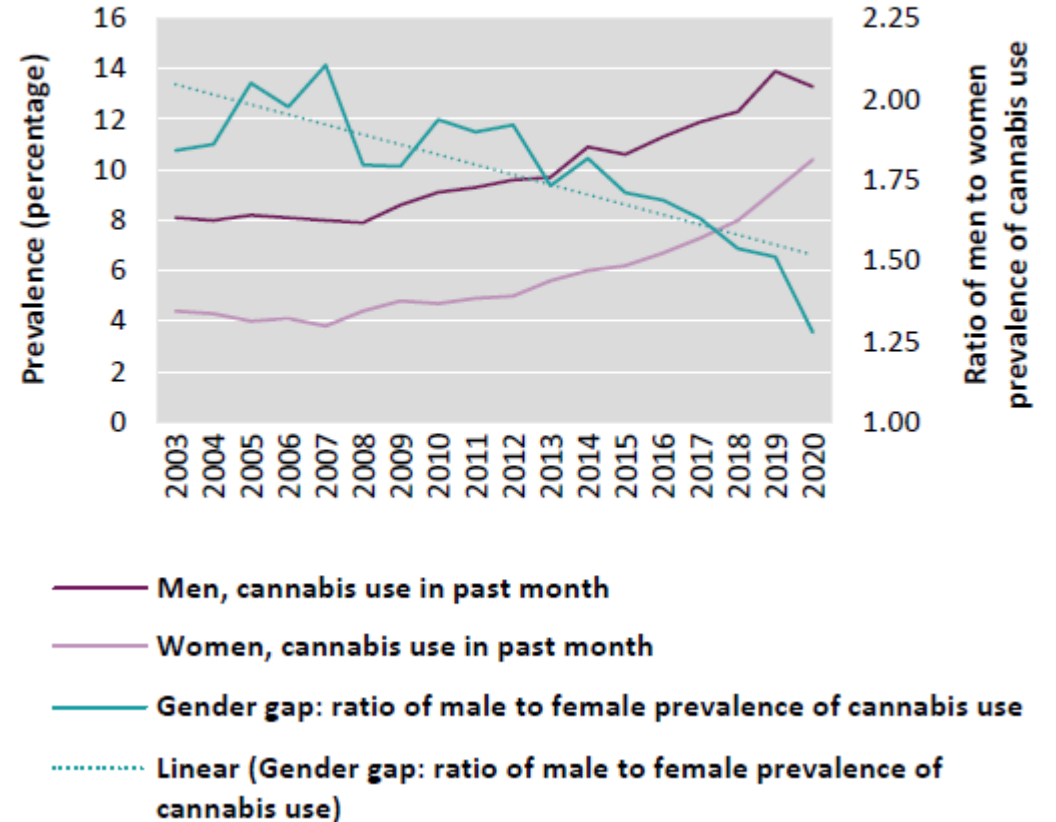


FIG. 8 Narrowing the gender gap in the past-month prevalence of cannabis use among the population aged 12 years and older in the United States, 2003–2020



CONSUMO DI CANNABIS: STUDENTI ITALIANI

Figura 3.1.2 - Uso di sostanze psicoattive nella vita

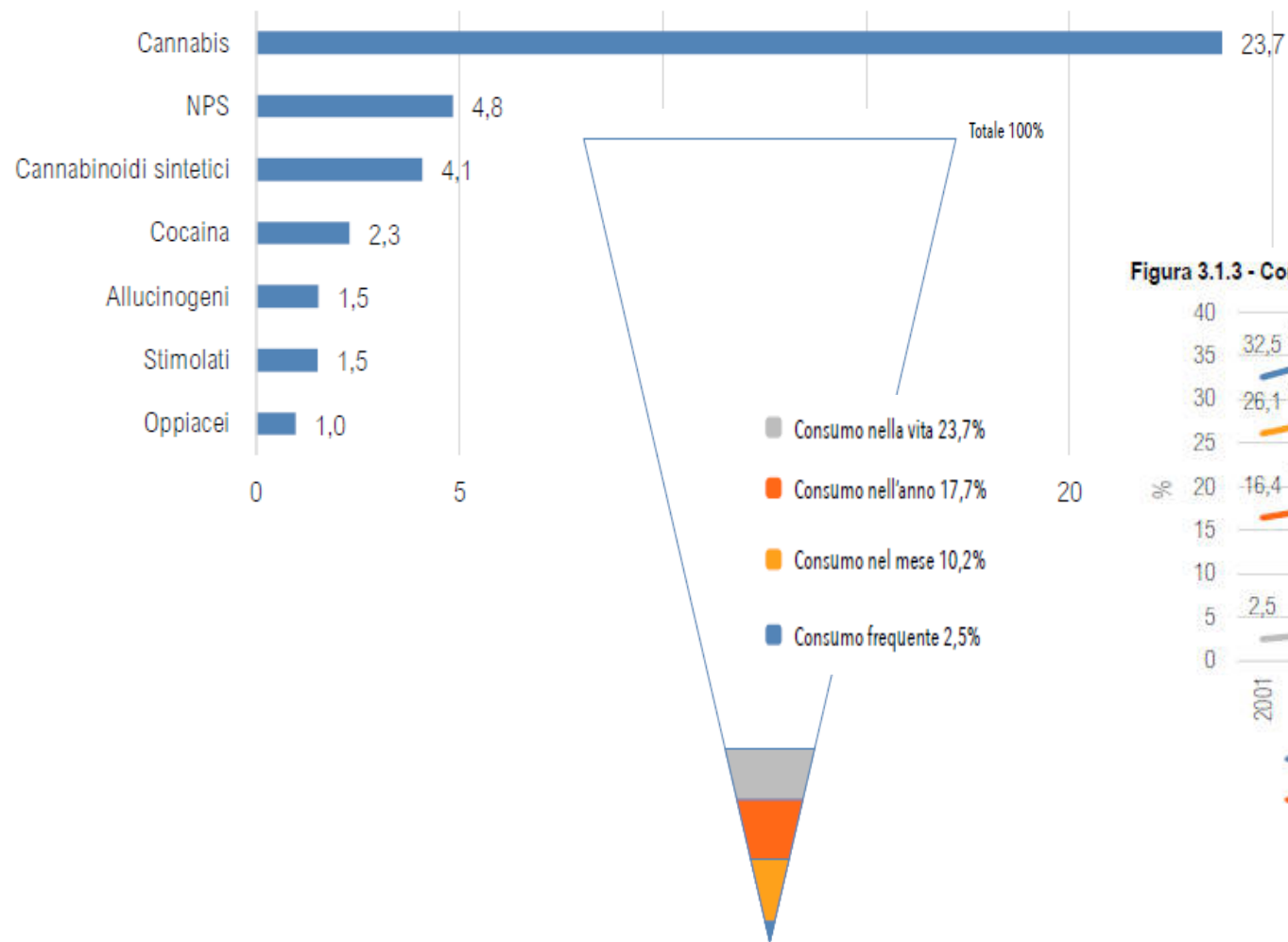
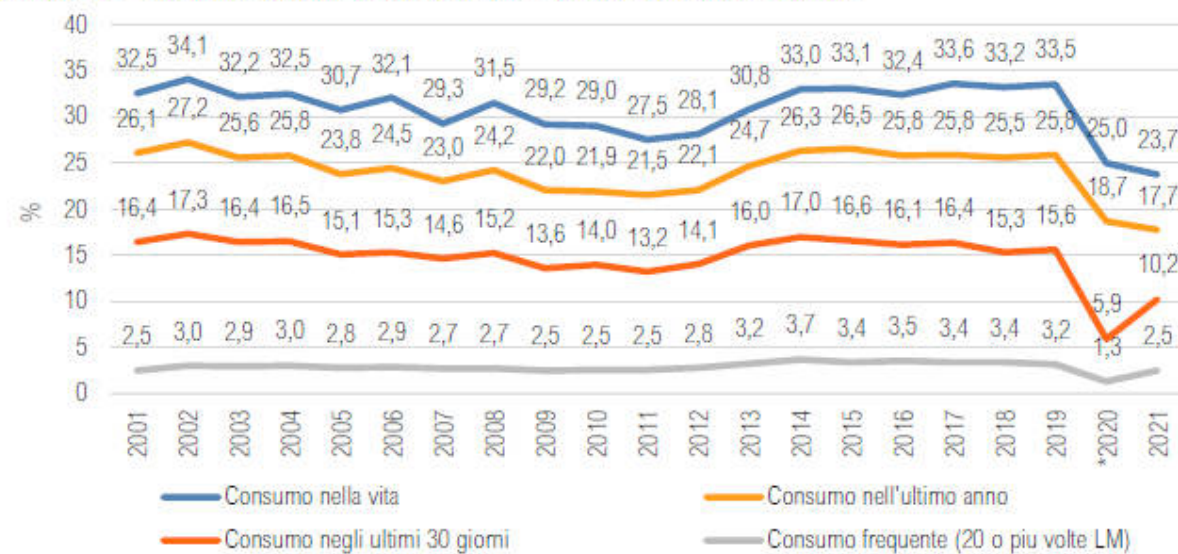
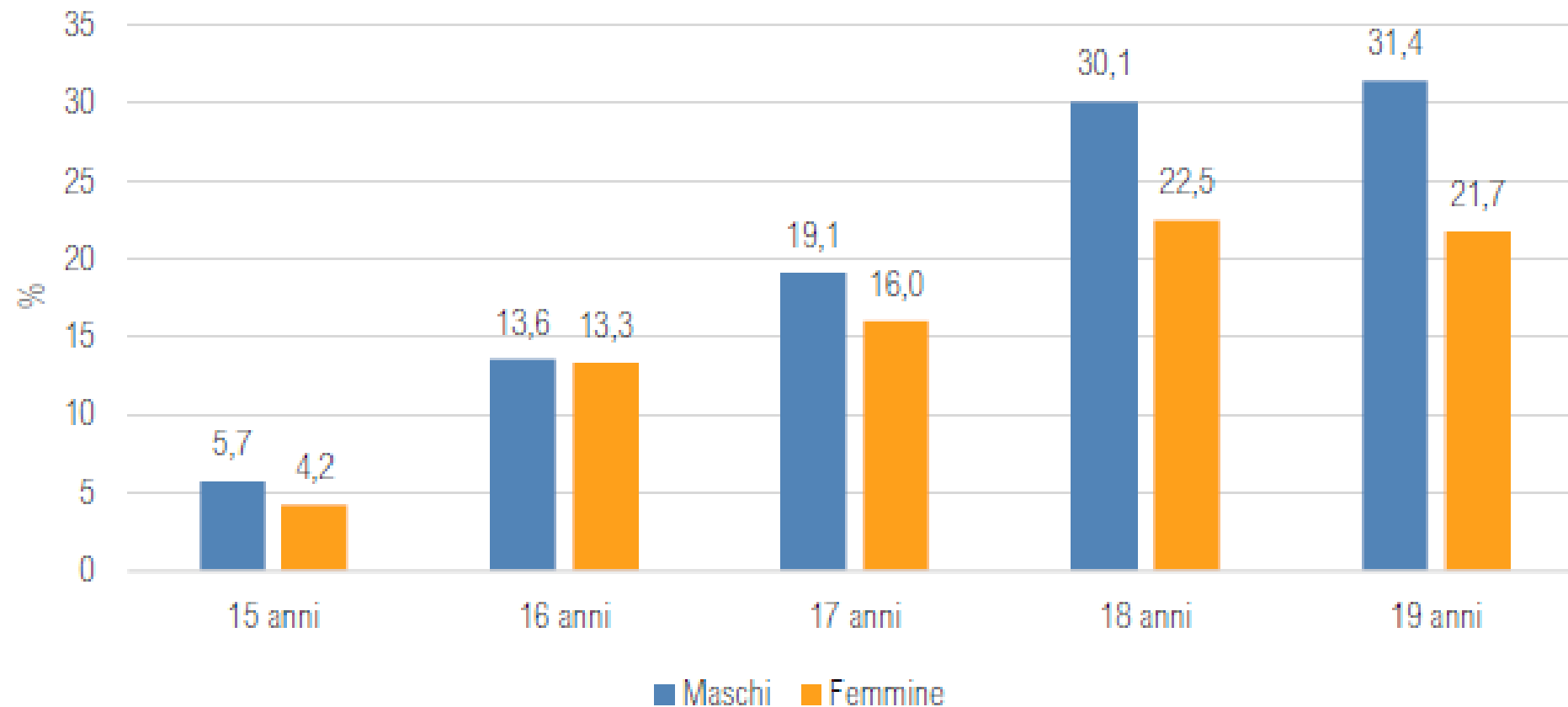


Figura 3.1.3 - Consumi di cannabis nella popolazione studentesca: trend percentuale



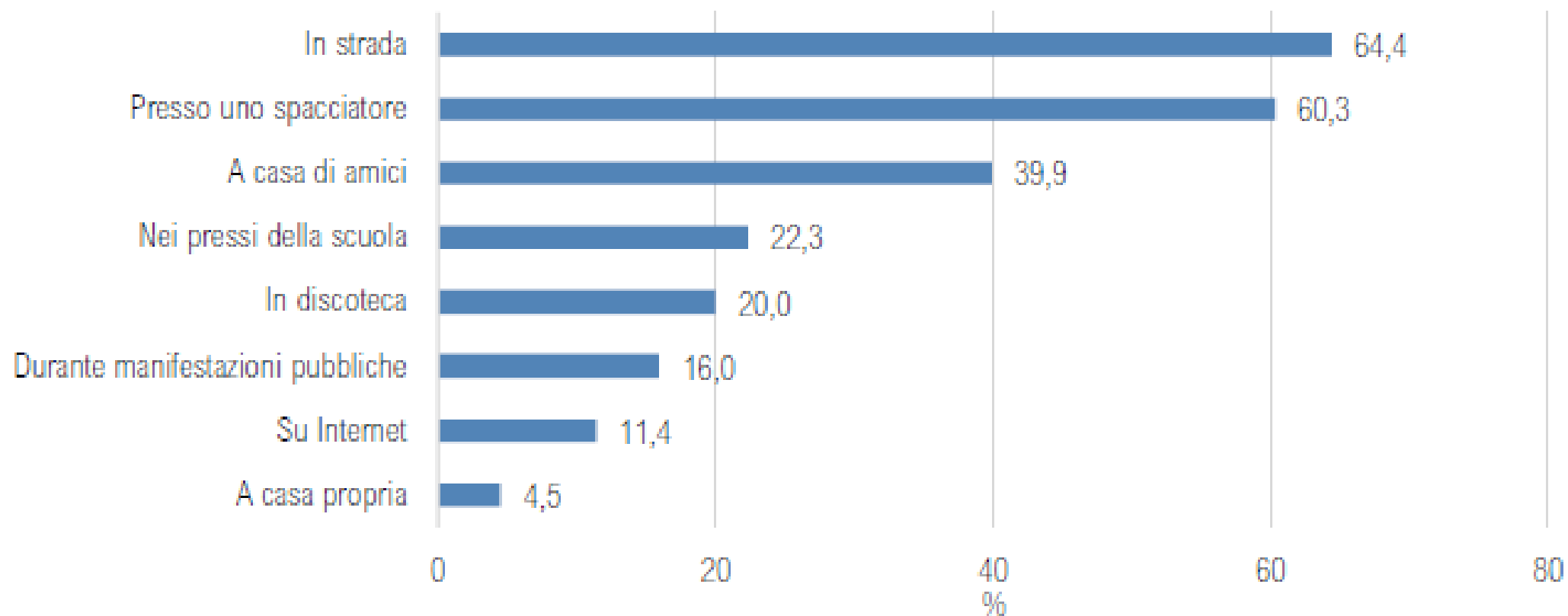
CONSUMO DI CANNABIS: STUDENTI ITALIANI

Figura 3.1.4 - Utilizzo di cannabis nell'ultimo anno per genere ed età



CONSUMO DI CANNABIS: STUDENTI ITALIANI

Figura 3.1.6 - Luoghi o contesti in cui ci si potrebbe procurare facilmente cannabis

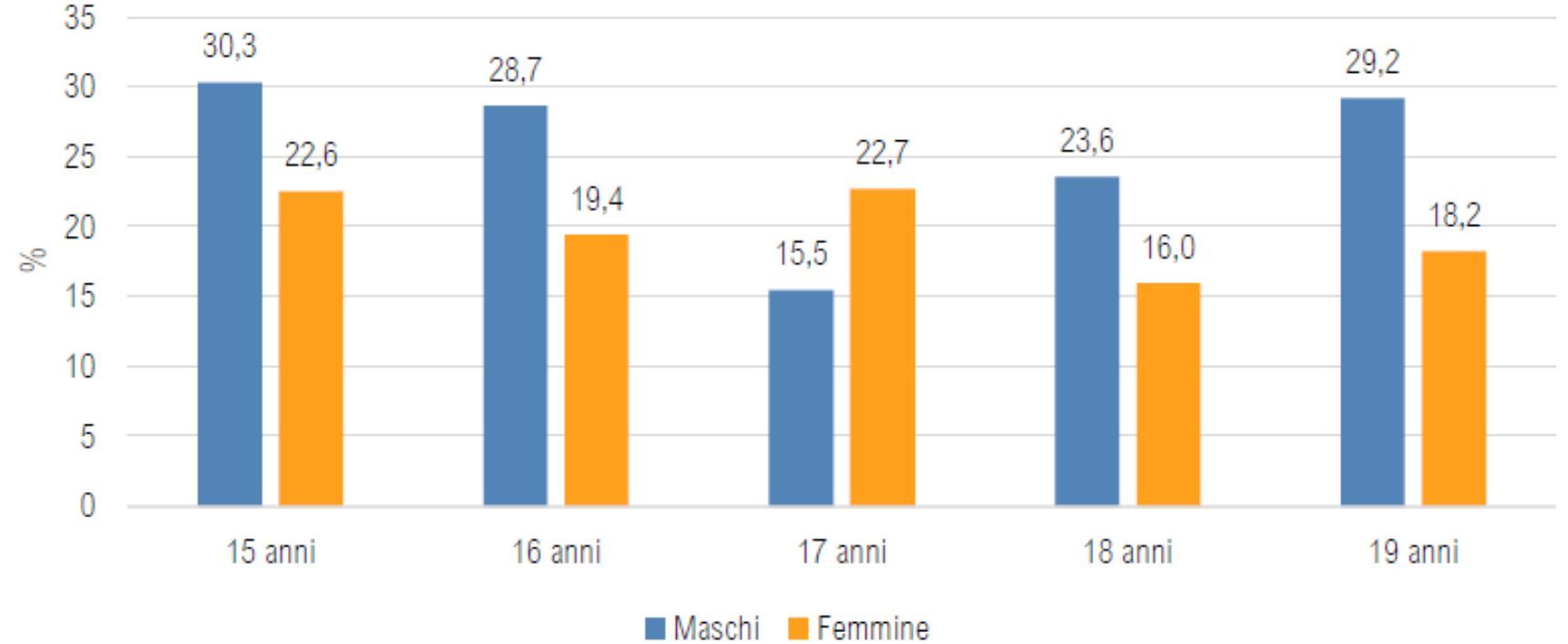


CANNABIS: CONSUMO A RISCHIO TRA GLI STUDENTI ITALIANI

Figura 3.1.31 - Test di screening CAST - Cannabis Abuse Screening Test

Ti sono capitate le seguenti situazioni negli ULTIMI 12 MESI?					
(Segna una sola casella per ogni riga)	Mai	Di rado	Di tanto in tanto	Piuttosto spesso	Molto spesso
a) Hai fumato cannabis prima di mezzogiorno?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Hai fumato cannabis da solo?					
c) Hai avuto problemi di memoria dopo aver fumato cannabis?					
d) Gli amici o i tuoi familiari ti hanno detto che dovresti ridurre il tuo uso di cannabis?					
e) Hai provato a ridurre o a smettere di consumare cannabis senza riuscirci?					
f) Hai avuto problemi a causa del tuo uso di cannabis (discussioni, risse, incidenti, brutti voti a scuola)?					

Figura 3.1.33 - Utilizzo "a rischio" di cannabis nell'ultimo anno per genere ed età



CANNABIS: CONSUMO A RISCHIO TRA GLI STUDENTI ITALIANI

Tabella 3.1.4 - Comportamenti potenzialmente dannosi tra gli utilizzatori di cannabis

	Consumatori "non a rischio" (%)	Consumatori "a rischio" (%)
Fare spesso giochi in cui si spendono soldi	6,4	17,2
Aver seriamente fatto male a qualcuno	6,1	13,1
Aver danneggiato beni pubblici/privati di proposito	8,2	20,2
Aver rubato qualcosa del valore di 10 euro o più	13,2	32,2
Aver venduto oggetti rubati	3,8	11,7
Aver avuto problemi con le Forze dell'Ordine/segnalazioni al Prefetto	16,2	35,1
Essere stati coinvolti in zuffe o risse	54,4	74,4
Aver avuto rapporti sessuali non protetti	32,9	55,2
Aver perso 3 o più giorni di scuola senza motivo nell'ultimo mese	16,1	30,9
Aver avuto problemi con gli insegnanti	44,6	67,6
Aver avuto gravi problemi con gli amici	45,5	57,7
Aver avuto gravi problemi con i genitori	47,1	64,6
Spendere solitamente più di 45 euro la settimana senza il controllo dei genitori	7,0	22,5
Essersi messi alla guida dopo aver assunto sostanze psicoattive	10,1	26,5
Essere saliti su un mezzo guidato da chi aveva assunto sostanze psicoattive	23,4	49,1
Aver scommesso denaro in giochi d'azzardo dopo aver assunto sostanze psicoattive	4,3	12,8
Aver danneggiato beni pubblici/privati dopo aver assunto sostanze psicoattive	7,7	26,1

Fonte: CNR-IFC - Anno 2021

CANNABIS: CONSUMO A RISCHIO TRA GLI STUDENTI ITALIANI

Tabella 3.1.3 - Contiguità con altre sostanze tra gli utilizzatori di cannabis

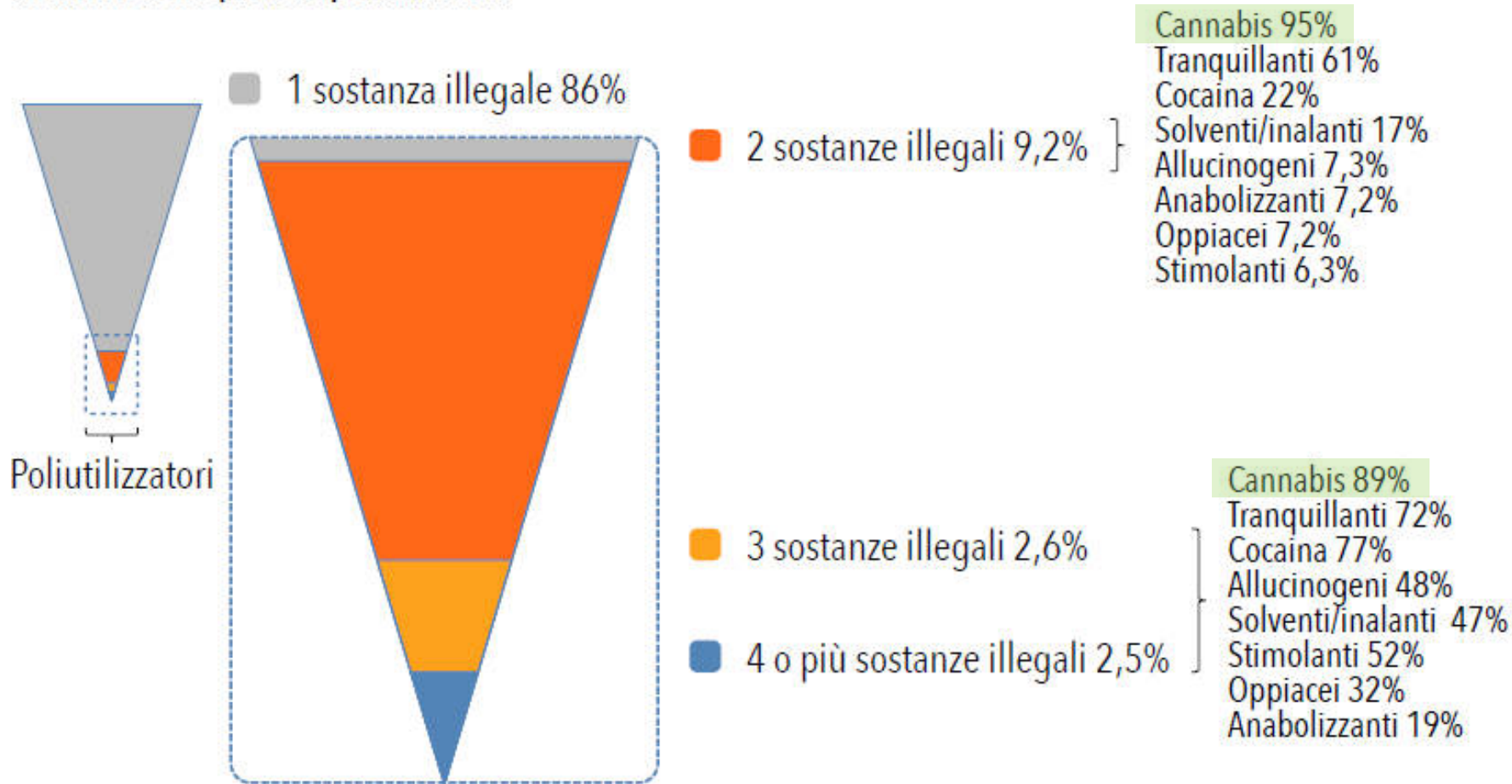
	Consumatori "non a rischio" (%)	Consumatori "a rischio" (%)
Bere alcolici tutti i giorni o quasi	7,9	21,1
Aver praticato <i>binge drinking</i> nell'ultimo mese	61,1	82,2
Essersi ubriacato nell'ultimo mese	54,9	72,9
Aver fumato più di 10 sigarette al giorno nell'ultimo anno	6,2	21,4
Aver assunto psicofarmaci senza prescrizione medica nell'ultimo mese	1,5	3,2

Fonte: CNR-IFC - Anno 2021

CANNABIS E POLICONSUMO: STUDENTI ITALIANI

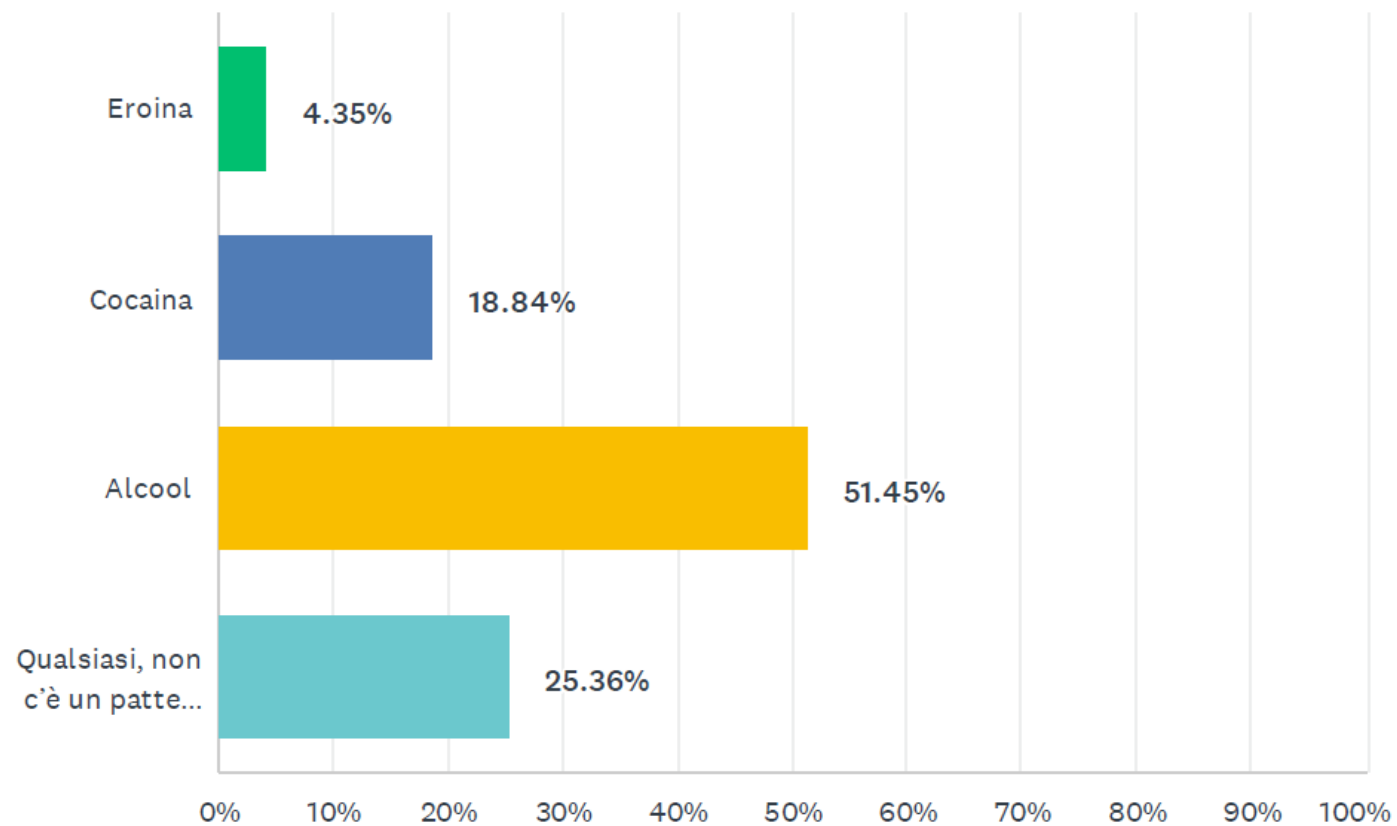


Figura 3.1.29 - Percentuale di utilizzatori nell'ultimo anno per numero di sostanze assunte e percentuale di sostanze all'interno della quota di "poliutilizzatori"



D3 Nella tua esperienza, qual è la sostanza che maggiormente viene consumata in regime di poliabuso insieme alla cannabis?

Risposte: 138 Saltate: 0



LA CANNABIS E IL CERVELLO DELL'ADOLESCENTE

Size of Effect	Heavy Alcohol Use/Binge Drinking	Heavy Cannabis Use	Alcohol and Cannabis Co-Use
Brain structure			
Small to moderate	<ul style="list-style-type: none"> • Disruptions observed in middle to late adolescence • Widespread decreases in gray matter volume and cortical thickness • Slowed white matter growth • Poor white matter integrity, partially explained by differences in sex hormones 	<ul style="list-style-type: none"> • Decreases in subcortical volume • Increases in frontoparietal cortical thickness • Neurodevelopmental disruptions may not recover over the short term 	
Small to large			<ul style="list-style-type: none"> • No added deleterious effect of co-use on white matter integrity vs. alcohol use only
Brain function			
Small			<ul style="list-style-type: none"> • Altered neural response in the insula during risk processing
Small to moderate	<ul style="list-style-type: none"> • Disrupted maturation of network efficiency • More significant effects among females 		
Small to large		<ul style="list-style-type: none"> • Altered rate of functional development in brain regions important for cognitive control • Some neural recovery possible after abstinence 	



LA CANNABIS E IL CERVELLO DELL'ADOLESCENTE



Size of Effect	Heavy Alcohol Use/Binge Drinking	Heavy Cannabis Use	Alcohol and Cannabis Co-Use
Neuropsychological function			
Small to large	<ul style="list-style-type: none">• Disruptions in development of:<ul style="list-style-type: none">▪ Impulse and attentional control▪ Learning and memory▪ Visual processing and functioning, particularly in females▪ Psychomotor speed	<ul style="list-style-type: none">• Disrupted executive functioning development, particularly in females• Decreased IQ with very heavy use• Improvements in working memory, planning, decision-making, and attention following reduced use	<ul style="list-style-type: none">• Attention deficits• Poor psychomotor speed• Progressive declines in learning, memory, and visuospatial functioning (driven by alcohol use)• Short-term abstinence not associated with improved visuospatial functioning



CANNABIS E POLICONSUMO



(a) Low-THC cannabis adulterated with MDMB-4en-PINACA seized by police, Cyprus, February 2021



(b) Low-THC cannabis with EDMB-PINACA and ADB-BUTINACA collected by drug checking service Checkit!, Austria, June 2021



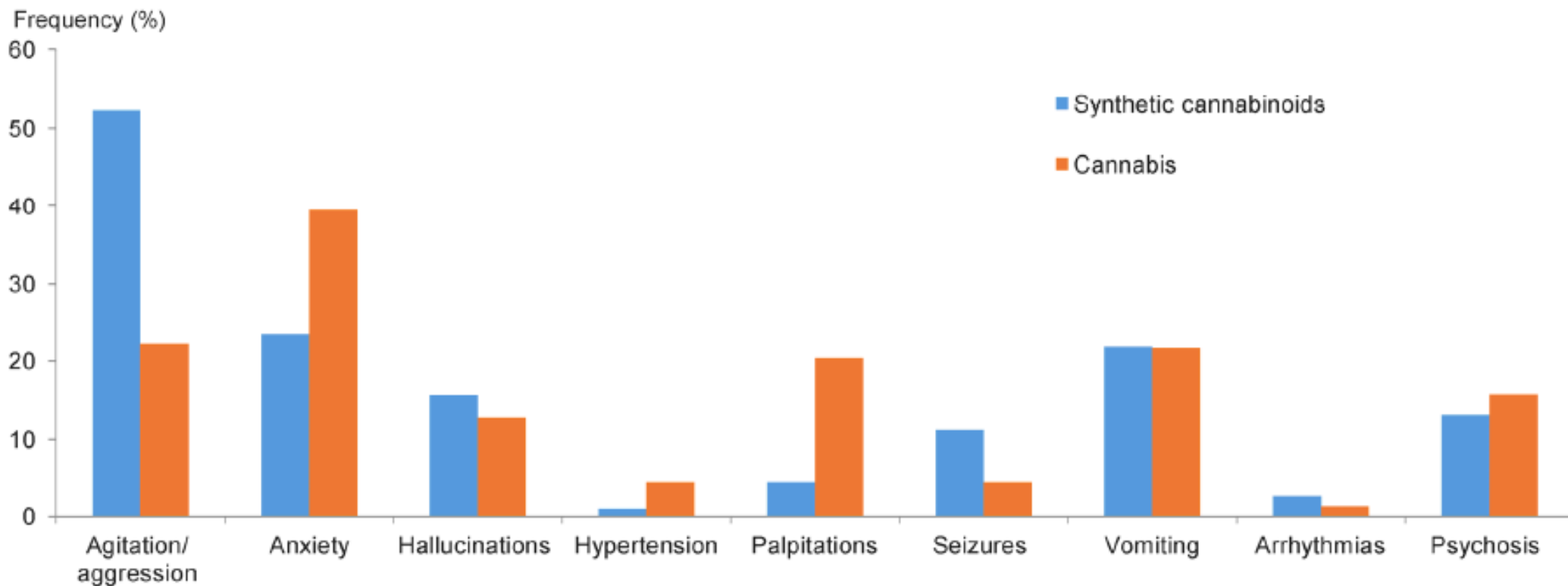
FIGURE 13

Equipment including a compressor/sprayer from a production site used for spraying low-THC cannabis with synthetic cannabinoids seized by Swiss police, autumn 2021

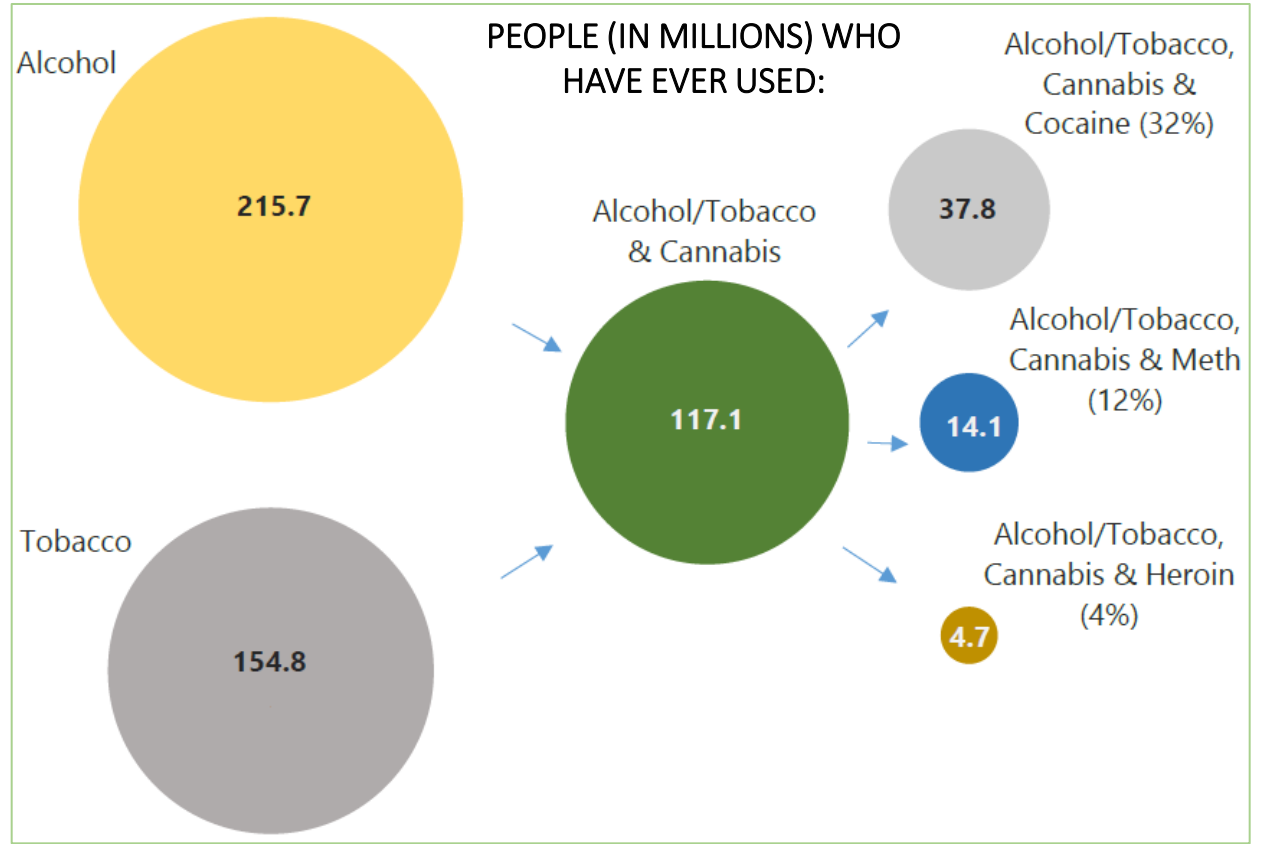
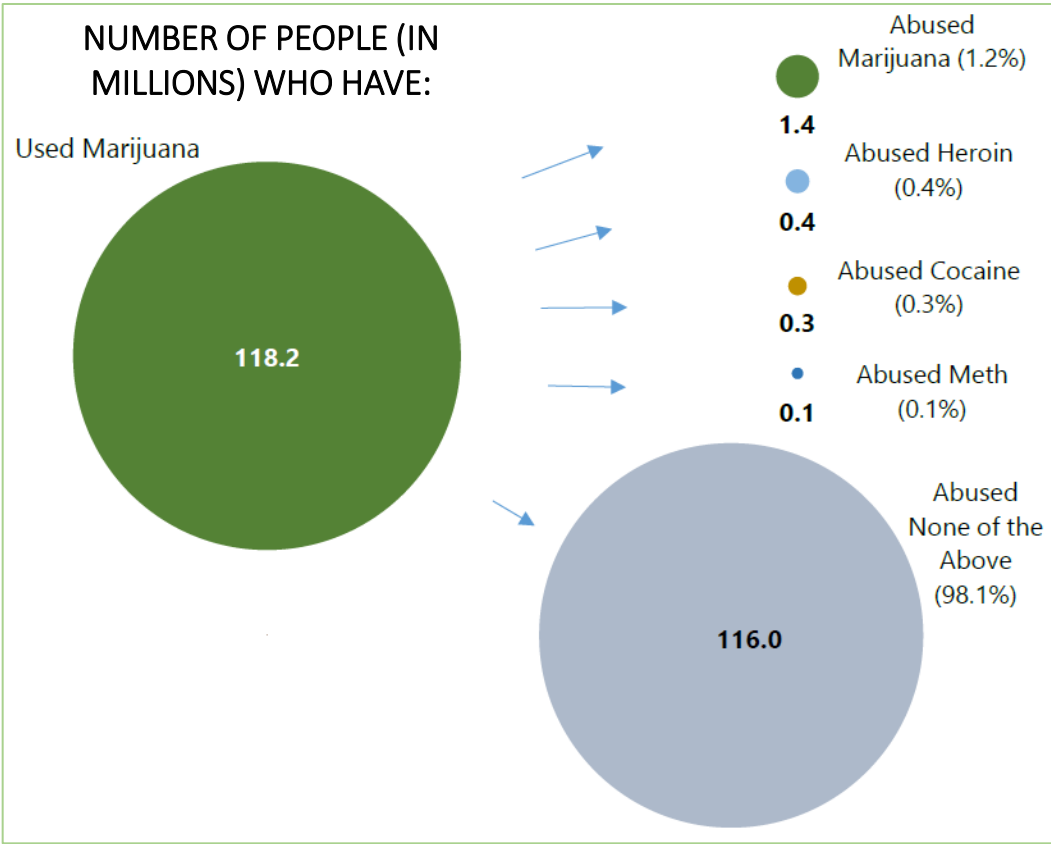


CANNABIS vs CANNABINOIDI SINTETICI

Most frequently observed clinical features among Euro-DEN Plus presentations involving only synthetic cannabinoids and Euro-DEN Plus presentations involving only cannabis, 2014-17



IS CANNABIS A GATEWAY DRUG?



INCREMENTO DELLA DIFFUSIONE DI CANNABIS

ELEVATA ACCETTABILITÀ SOCIALE

- Cannabis ad uso ricreazionale
- Cannabis ad uso terapeutico
- Industria della canapa (alimentare, tessile etc)
- Cannabis light

NUOVE MODALITÀ DI CONSUMO

DEPENALIZZAZIONE/LEGALIZZAZIONE

RIDUZIONE DEI PREZZI

PRODOTTI A BASSO CONTENUTO DI THC

Los Angeles Times

Want to get high (but not too high) this holiday season? Here are 7 low-dose options



PRODOTTI A BASSO CONTENUTO DI THC

These strains have been bred to contain a higher percentage of cannabidiol (CBD) than tetrahydrocannabinol (THC).

1. Harle-Tsu
2. Suzy Q
3. Charlotte's Web
4. Ringo's Gift
5. Remedy
6. Cherry Wine
7. ACDC
8. Elektra
9. Sour Space Candy
10. Lifter
11. Harlequin
12. Sour Tsunami
13. CBD Critical Mass
14. Pennywise
15. Cannatonic

Anxious? Achy? Existential? These 15 High-CBD, Low-THC Cannabis Strains May Bring Relief



CHERRY
Wine

Cherry Wine was created and bred by Tree of Life Seeds. "The Wife" used in this high grade hemp hybrid was bred by our good friends at 303 seeds. The pheno of "The Wife" we isolated for this project practically drips resin and was the first phenotype we saw that had no detectable THC with a whopping 25% CBD! Paired with our CBD rich Charlotte's Cherries male, which tested for non detectable THC via leaf analysis, this hybrid brings farmers and medical growers alike a true connoisseur CBD hemp cultivar. @tree_of_life_seeds

CANNABIS: MODALITÀ DI CONSUMO

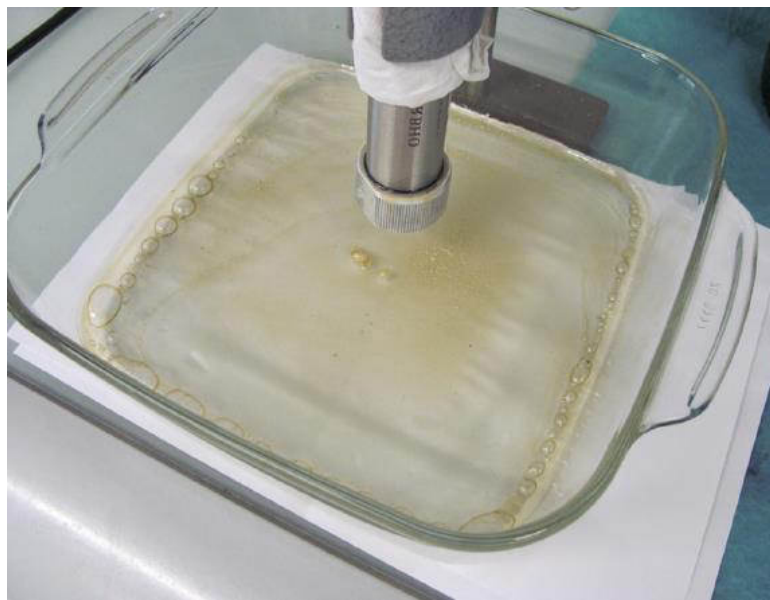
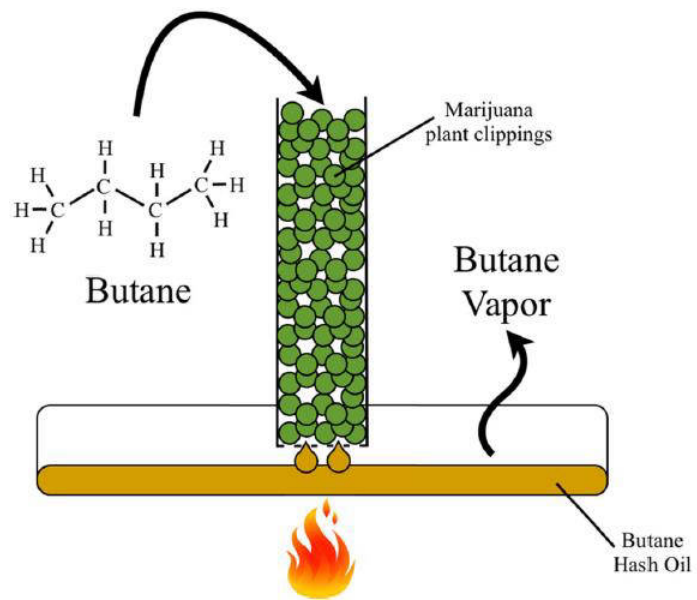


Table 2 Heterogeneity in methods of administration of cannabis products.

<i>Method</i>	<i>Route</i>	<i>Combined with nicotine or tobacco</i>
Joint	Inhaled, combusted	Yes/no
Pipe	Inhaled, combusted	Yes/no
Blunt	Inhaled, combusted	Yes
Bong	Inhaled, combusted	Yes/no
Dabbing	Inhaled, combusted	Yes/no
Vaporizer	Inhaled, vaporized	Yes/no
Vape pen	Inhaled, vaporized	Yes/no
Edible	Oral	No
Liquid	Oral	No

<i>Country, year</i>	<i>Reference</i>	<i>Outdoor-grown herbal</i>	<i>Indoor-grown herbal</i>	<i>Resin</i>	<i>Concentrates</i>
USA, 2017	[22]	9% THC, < 1% CBD	18% THC, < 1% CBD	46% THC, < 1% CBD	56% THC, < 1% CBD
Australia, 2010–12	[23]	15% THC, < 1% CBD	19% THC, < 1% CBD	–	–
UK, 2015–16	[24]	3% THC, < 1% CBD	14% THC, < 1% CBD	6% THC, 2% CBD	78% THC, < 1% CBD
Netherlands, 2015	[25]	5% THC, < 1% CBD	15% THC, < 1% CBD	18% THC, 8% CBD	–
France, 2016	[26]	–	–	23% THC, 4% CBD	–
Denmark, 2017	[27]	–	–	23% THC, 6% CBD	–

BUTAN HASH OIL e DABBING



VAPING

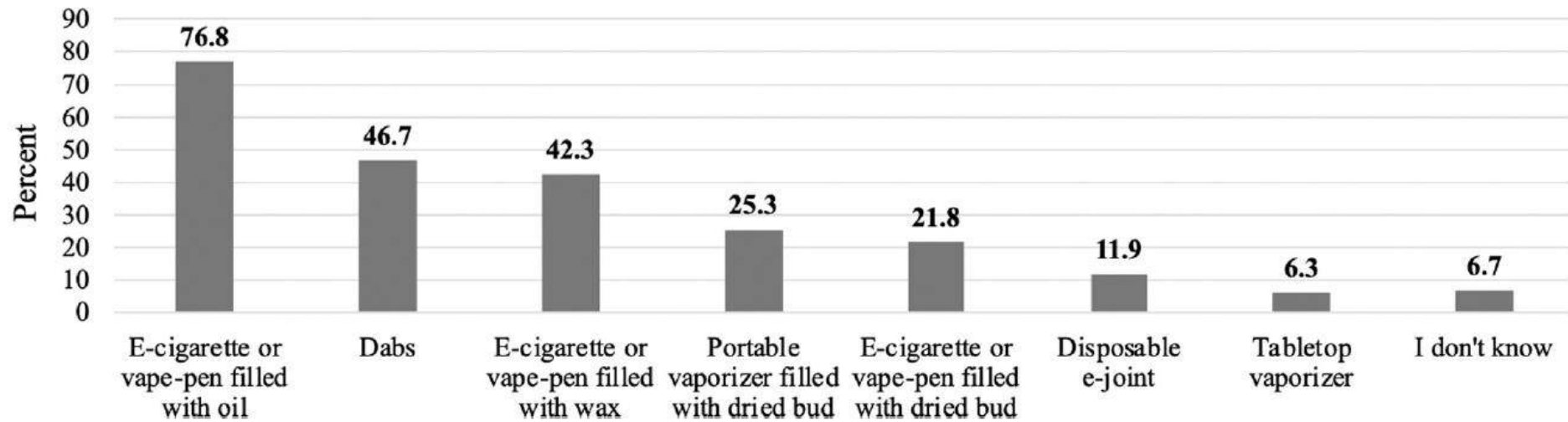
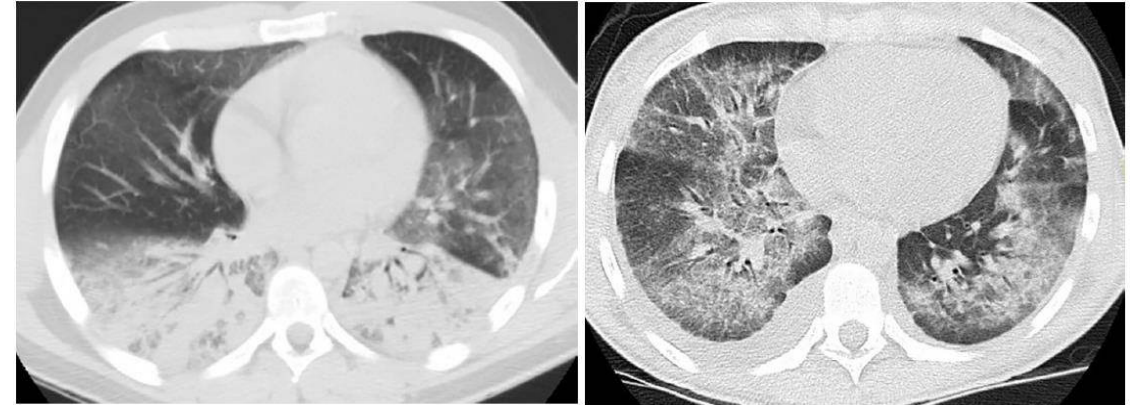
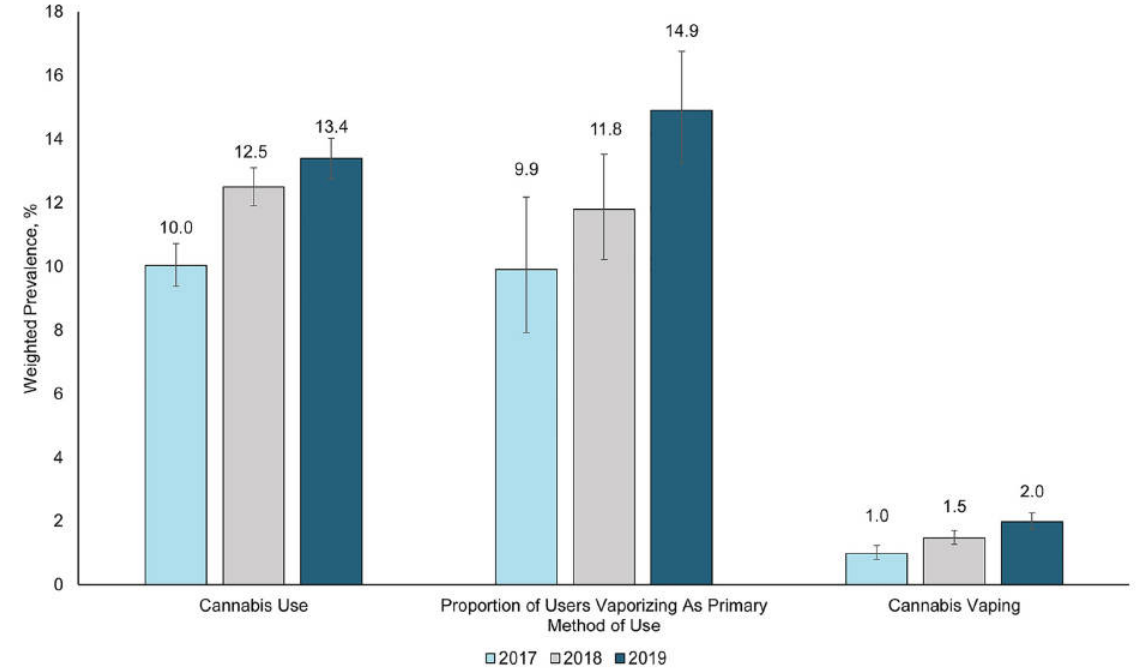
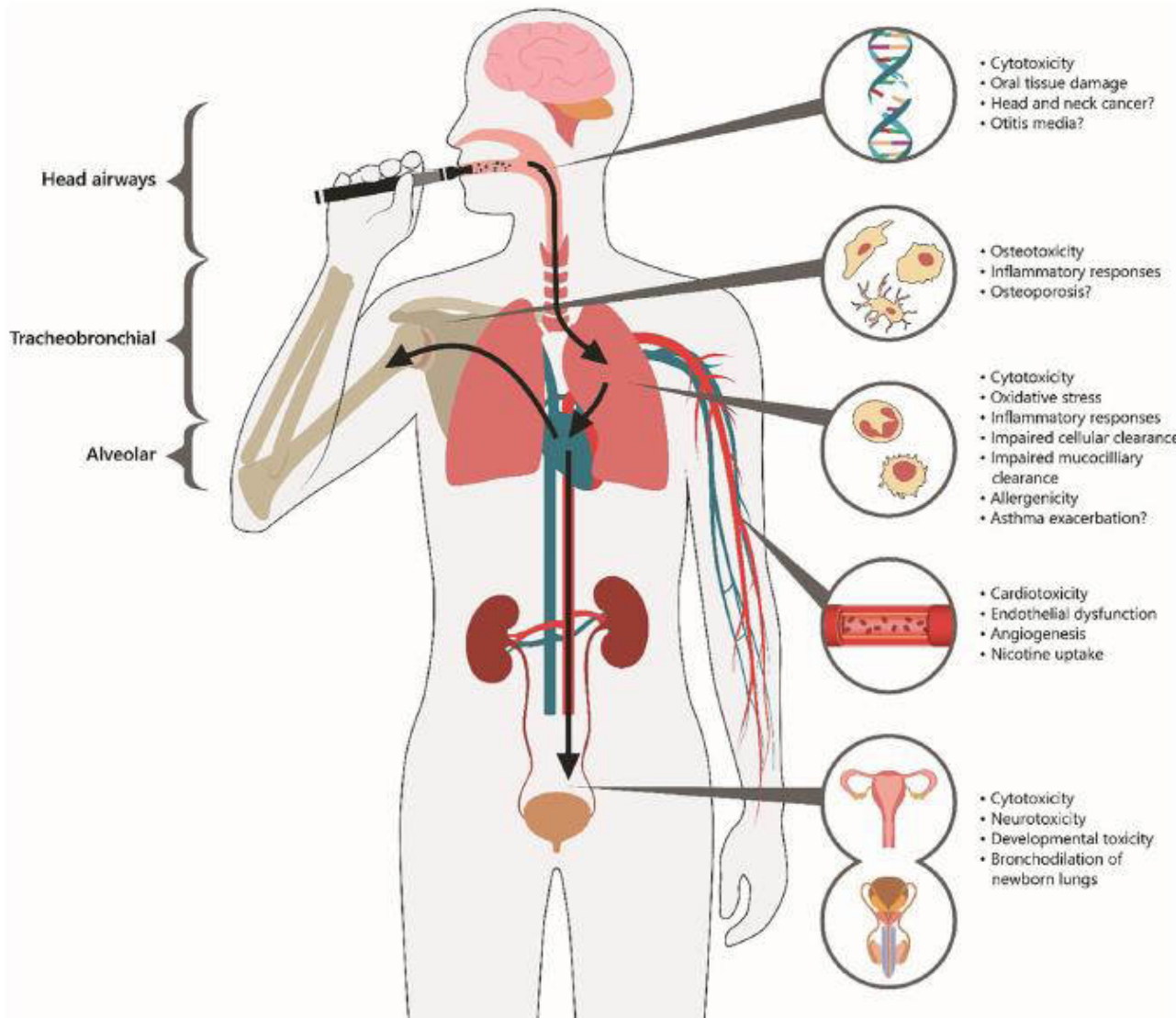


Fig. 2. Endorsement of lifetime modalities of vaporizing cannabis among past-month cannabis vapers (n = 524).

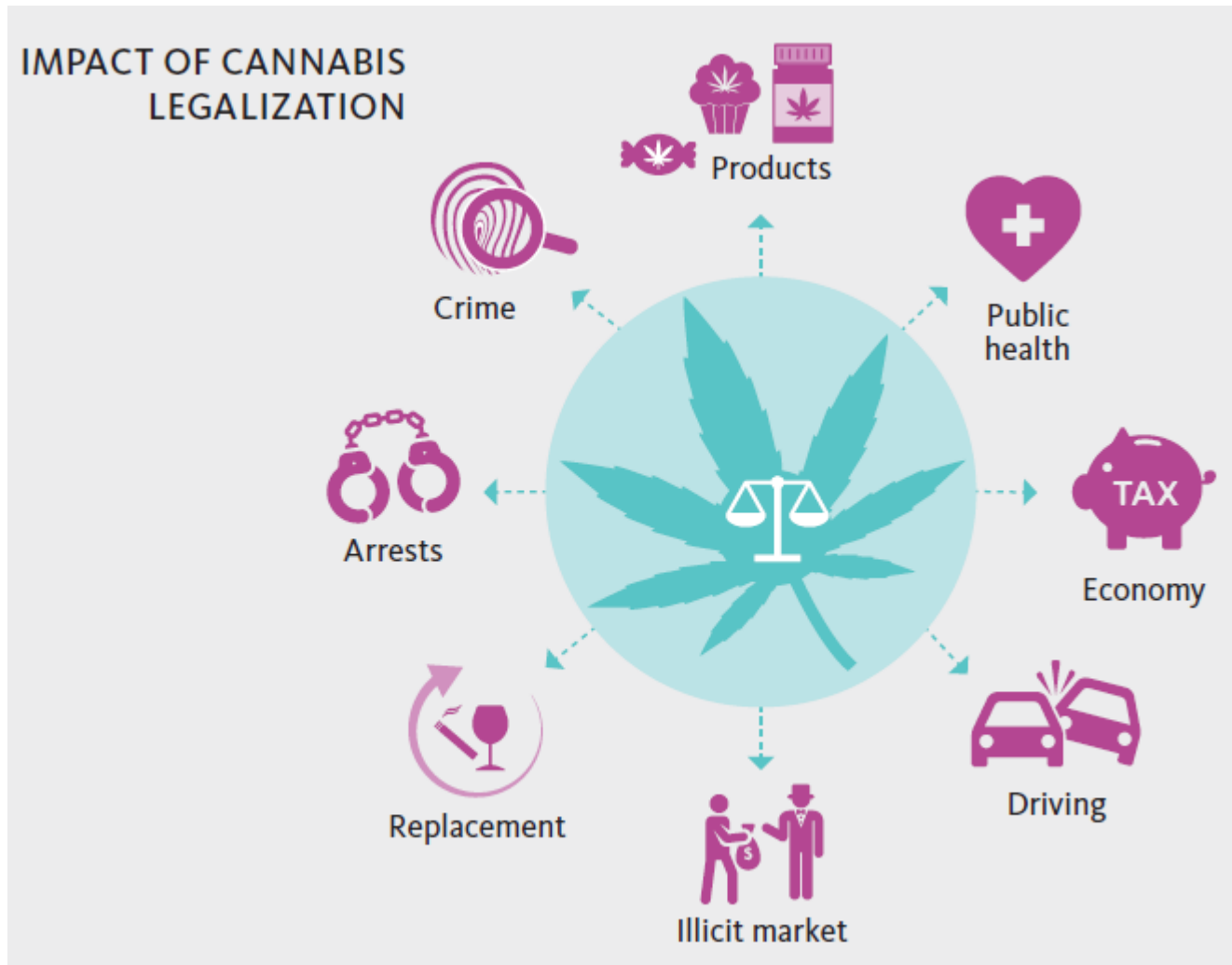


VAPING



Stefaniak AB, LeBouf RF, Ranpara AC, Leonard SS. Toxicology of flavoring- and cannabis-containing e-liquids used in electronic delivery systems. *Pharmacol Ther.* 2021 Aug;224:107838. Adapa S et al. Cannabis Vaping-Induced Acute Pulmonary Toxicity: Case Series and Review of Literature. *J Investig Med High Impact Case Rep.* 2020 Boakye E et al. Cannabis vaping among adults in the US: Prevalence, trends, and association with high-risk behaviors and adverse respiratory conditions. *Prev Med.* 2021

POLITICHE DI LEGALIZZAZIONE



DEPENALISATION: something remains a criminal offence, but is no longer punished, e.g. now the case may be closed.

DECRIMINALISATION: an offence is reclassified from criminal to non-criminal. It remains an offence and may be punished by the police or other agencies, rather than a court.

LEGALISATION: there is a move from a prohibited behaviour (criminal or not) to a permitted behaviour. This is usually used to describe supply, rather than possession, of drugs.



SEQUESTRI E REATI CONNESSI ALLA CANNABIS

Figura 2.1.7 - Percentuale delle sostanze stupefacenti detenute dalle persone segnalate per violazione Art.75 DPR n.309/1990 per genere delle persone segnalate

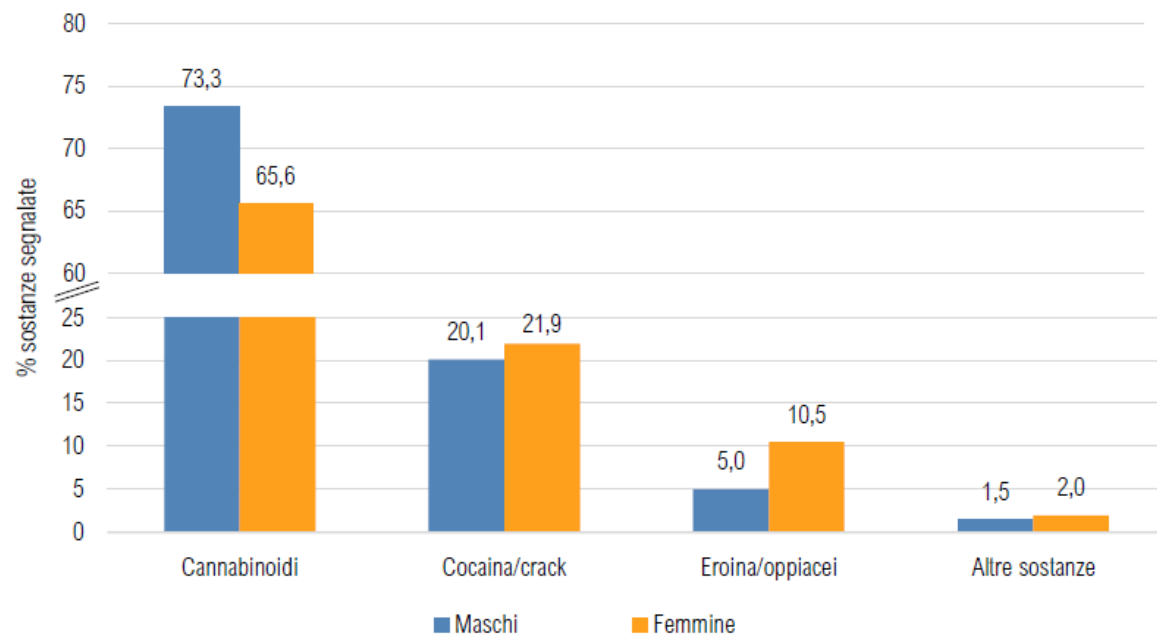
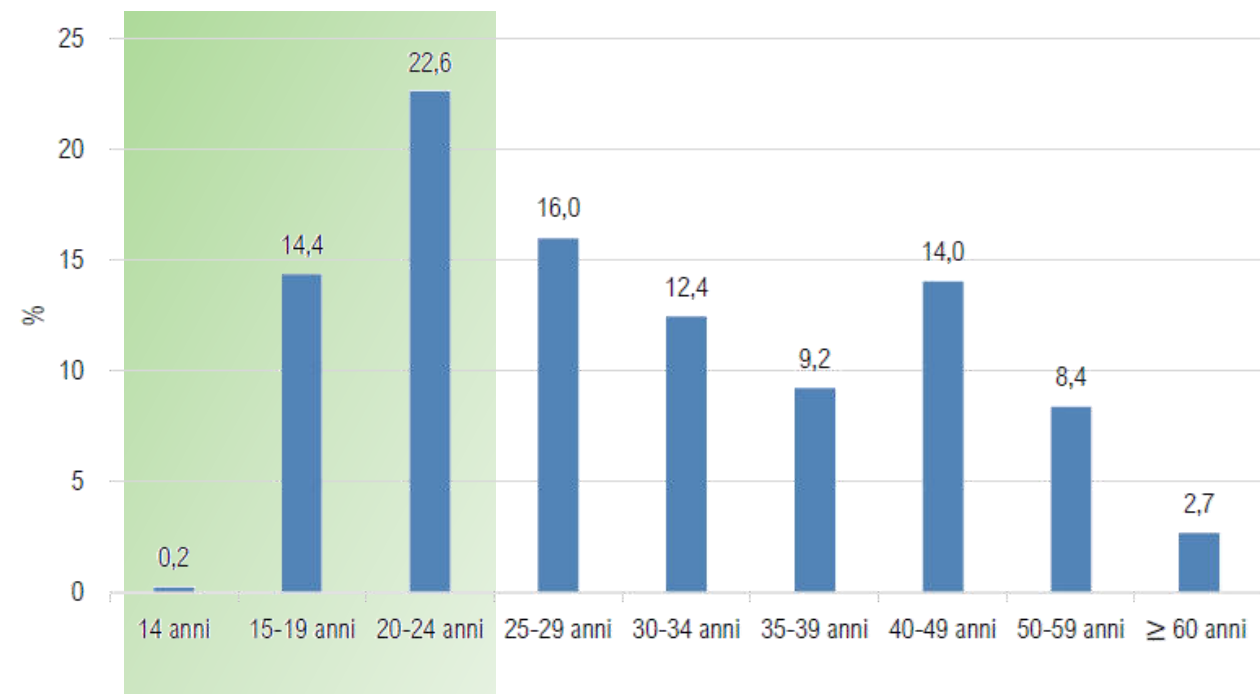
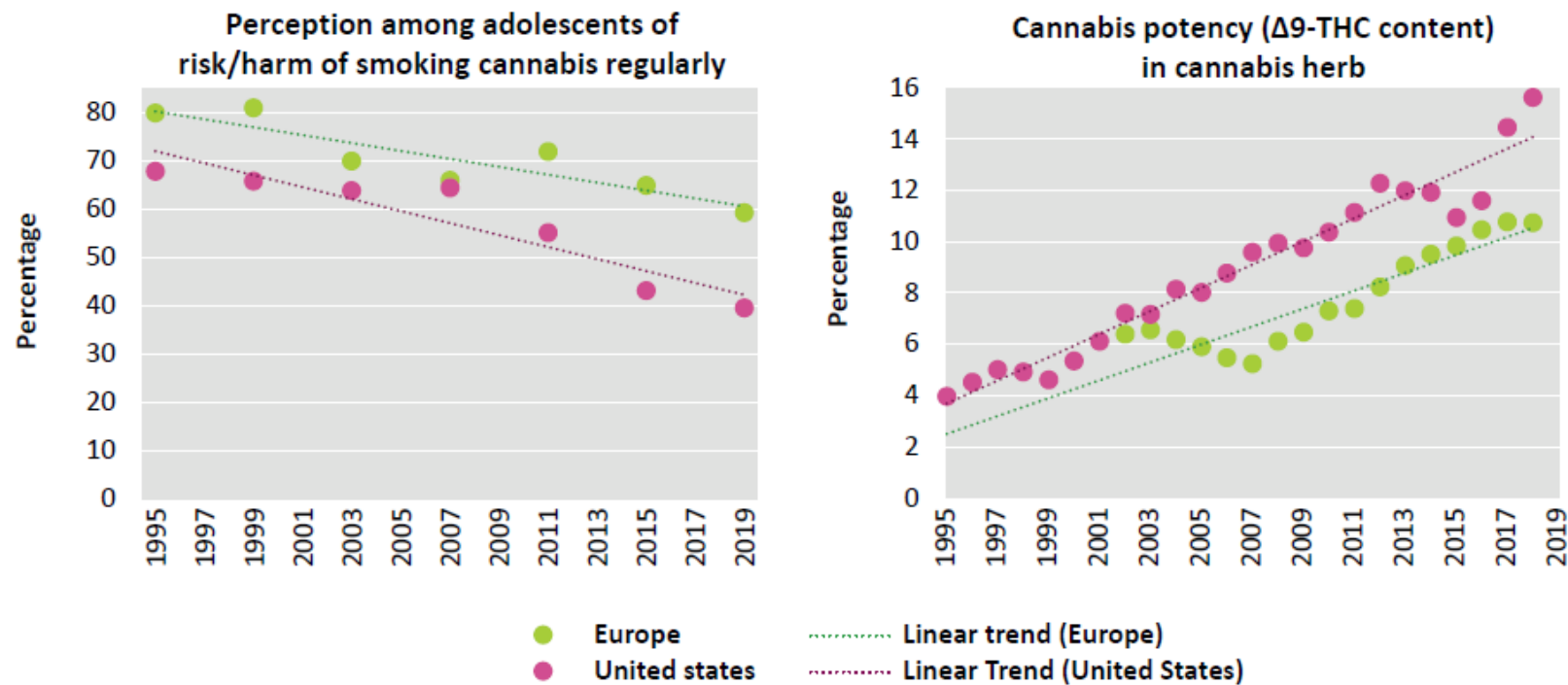


Figura 2.2.14 - Percentuale denunce per reati cannabis-correlati per classi di età



CANNABIS: INCREMENTO DELLA POTENZA ($\Delta 9$ -THC)

FIG. 27 Potency of cannabis and perception of risk from cannabis use among adolescents, Europe and United States, 1995–2019

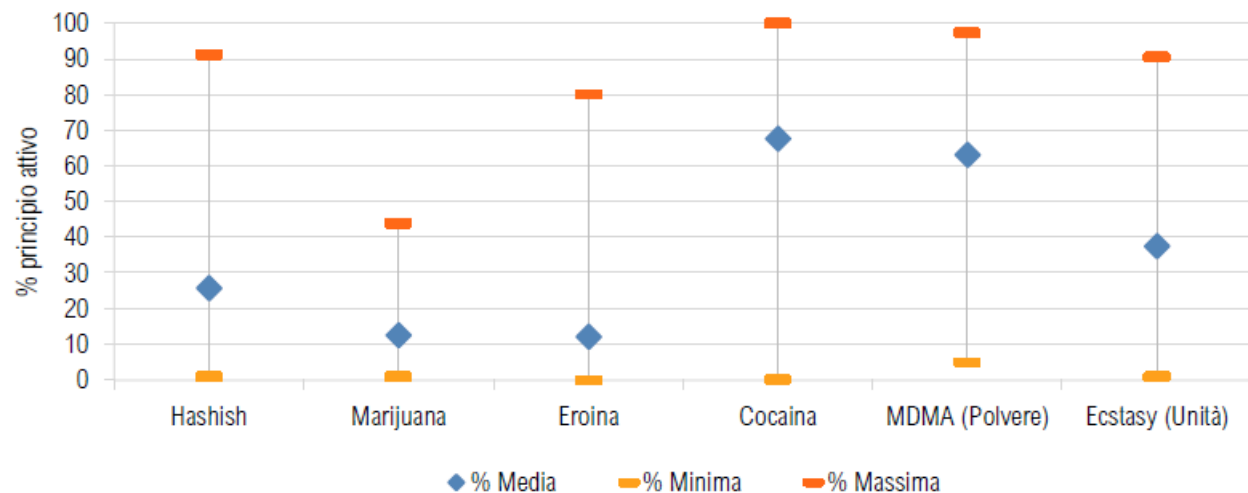


Cannabis resin samples from police seizures in England, 2016.



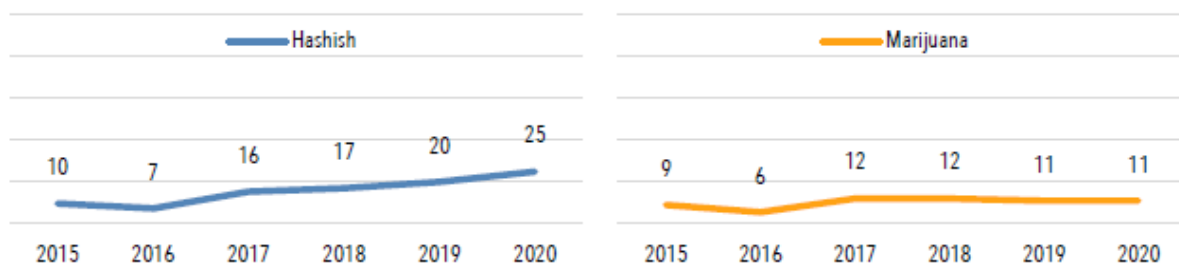
CANNABIS: INCREMENTO DELLA POTENZA ($\Delta 9$ -THC)

Figura 1.2.2 - Percentuale media, minima e massima di principio attivo rilevata nelle sostanze stupefacenti analizzate provenienti dal mercato dello spaccio

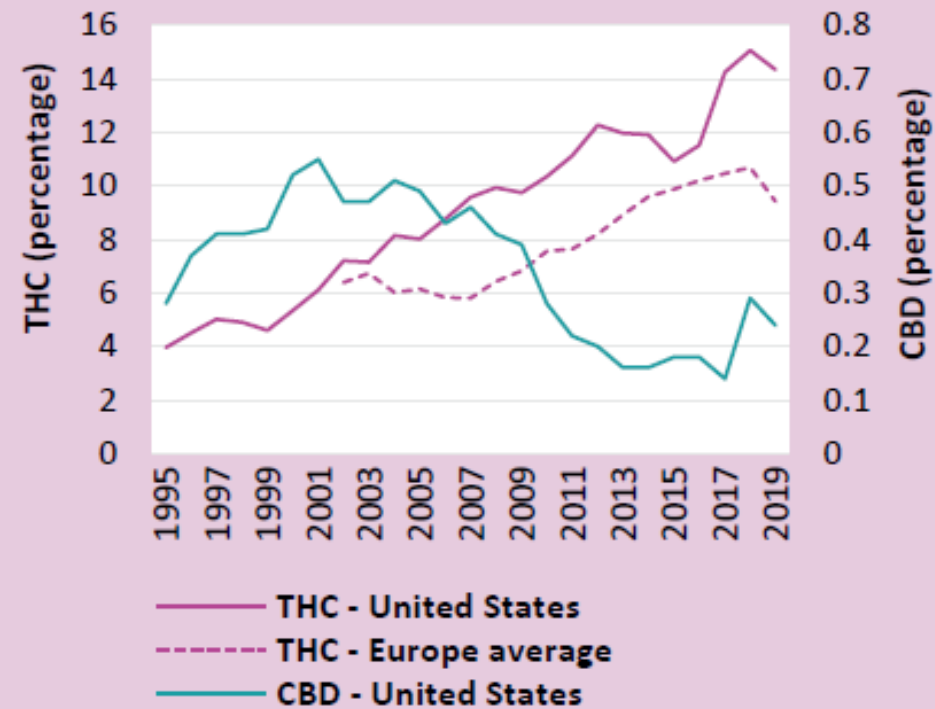


Fonte: Ministero della Difesa - Raggruppamento Carabinieri Investigazioni Scientifiche - Anno 2021

Figura 1.3.2 - Percentuali di principio attivo rilevate sulle sostanze stupefacenti analizzate

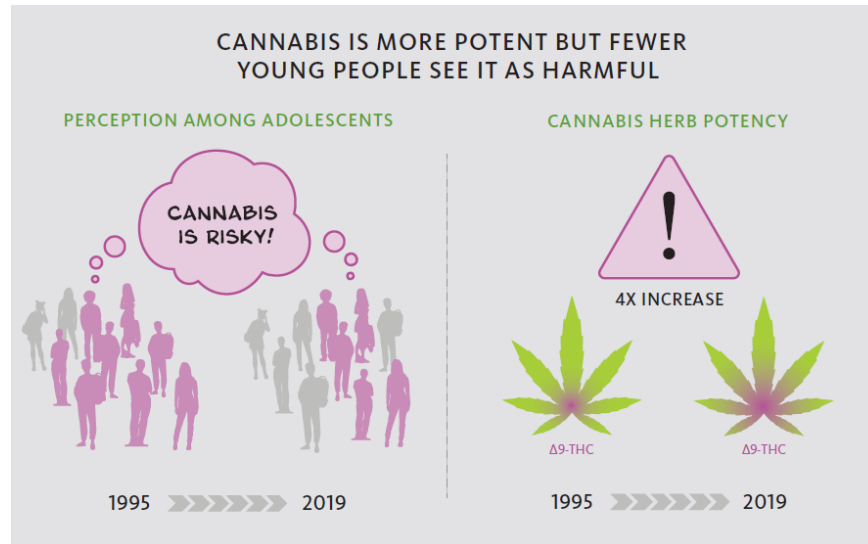
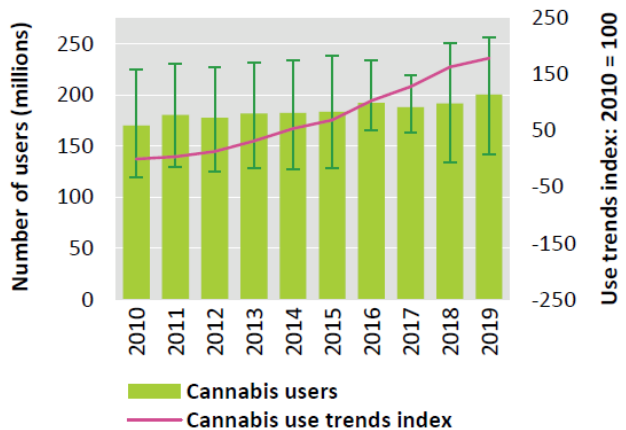


Cannabis potency ($\Delta 9$ -THC content) and CBD in cannabis herb in Europe and the United States



CANNABIS: IMPATTO DELLE NUOVE TENDENZE

FIG. 11 Trends in the global number of people who use cannabis and reported trends in cannabis use, 2010–2019



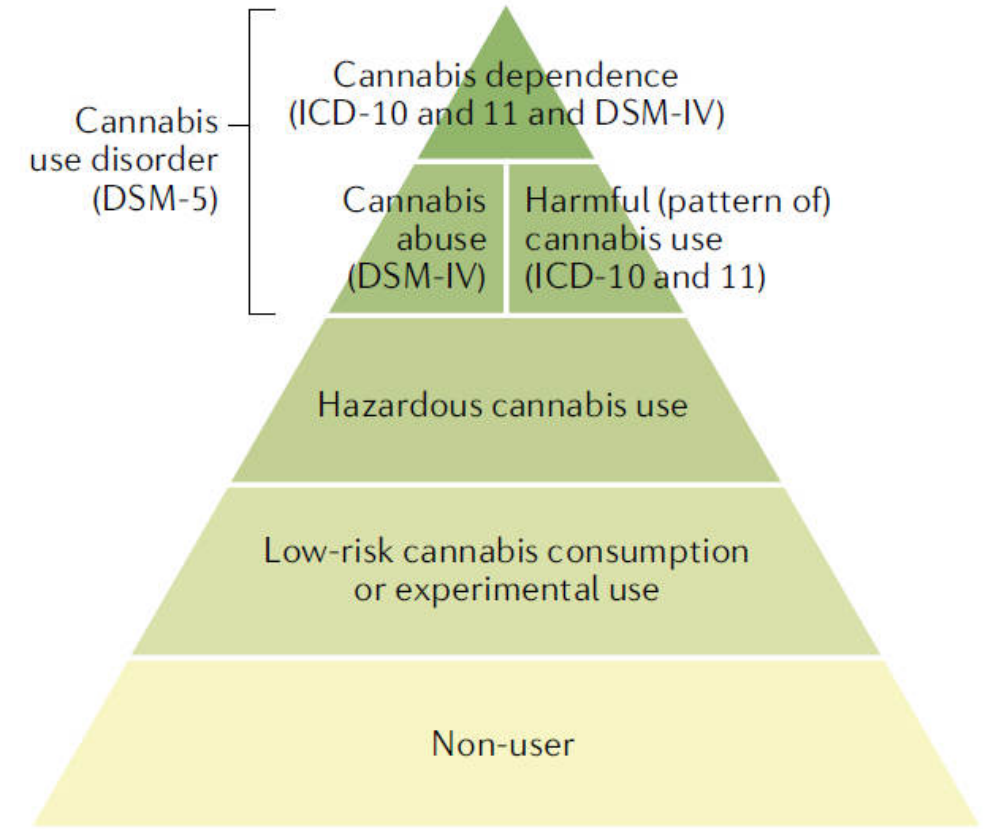
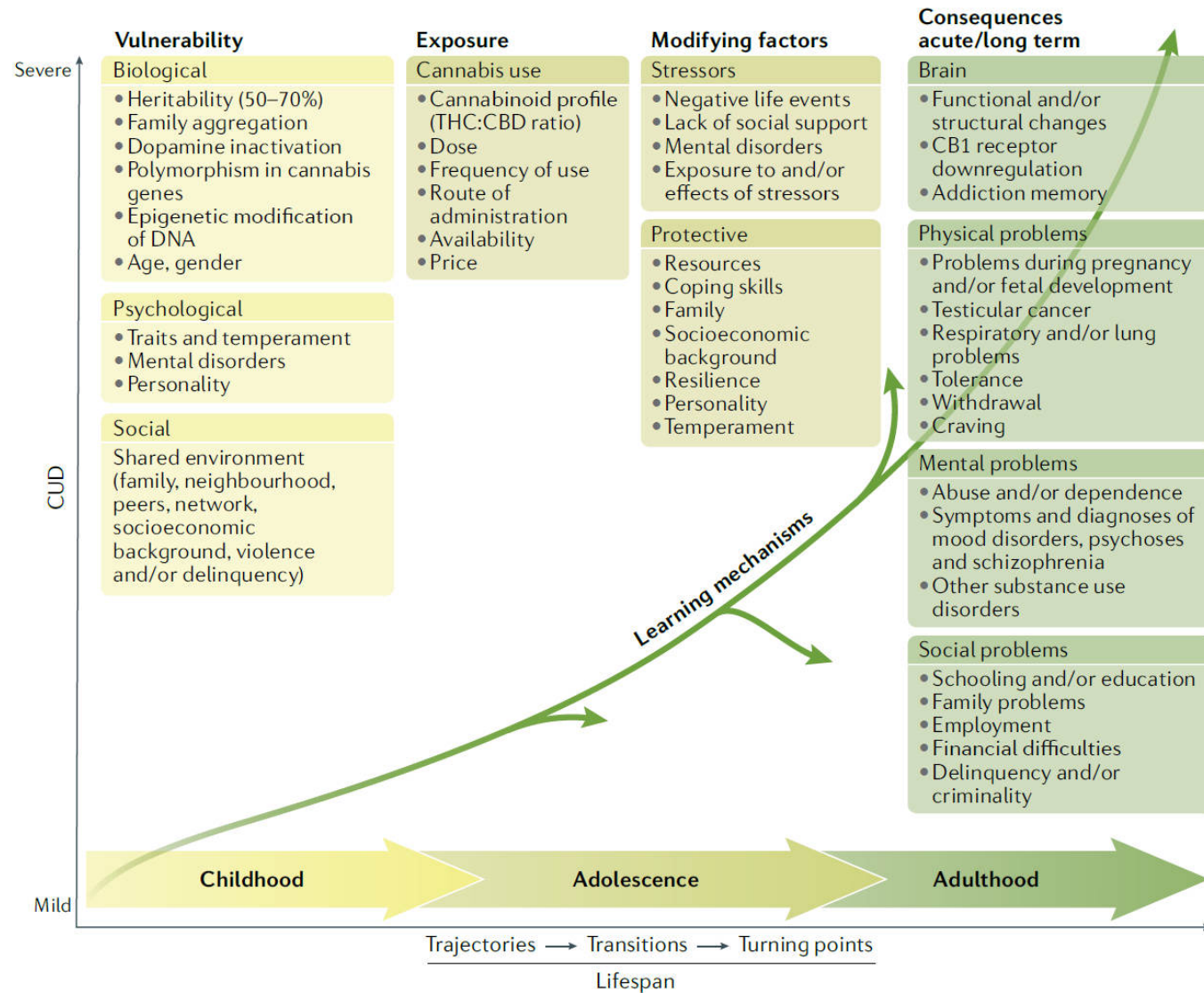
INCREMENTO
DEI CONSUMI

RIDUZIONE
PERCEZIONE
DEL RISCHIO

INCREMENTO
DELLA
POTENZA

AUMENTO
PREVALENZA
DISTURBO DA USO
DI CANNABIS

CUD: MODELLO MULTIFATTORIALE E GERARCHIA DIAGNOSTICA

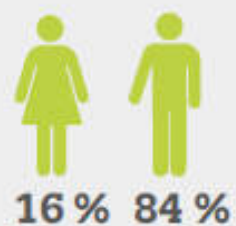


DISTURBO DA USO DI CANNABIS: RICHIESTA DI TRATTAMENTO



Consumatori di cannabis che si sottopongono a trattamento

Caratteristiche



Età media al primo consumo **17**

Età media all'inizio del primo trattamento **25**

62 000
Utenti presi in carico per la prima volta
56 %



28 000
Utenti già in carico
25 %

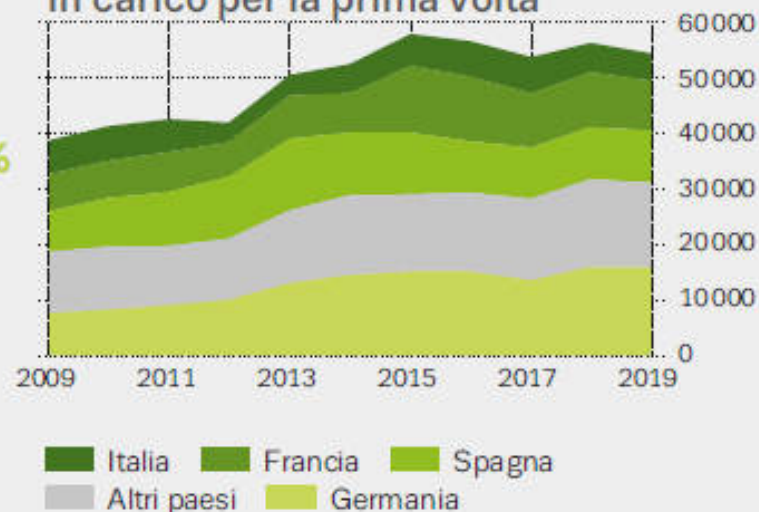
21 000
Status sconosciuto
19 %

Frequenza di consumo nell'ultimo mese

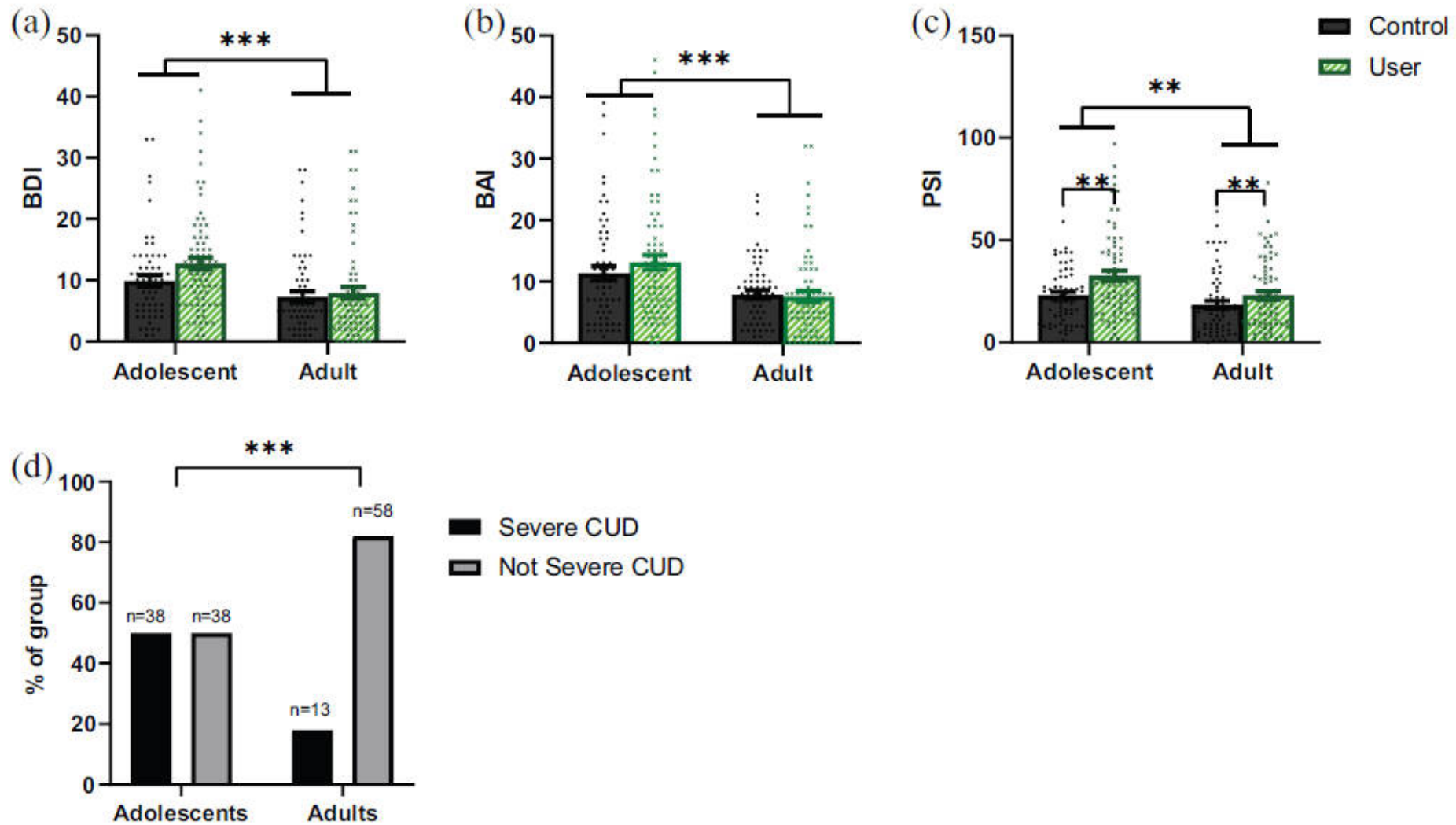
Consumo medio di 5,2 giorni alla settimana



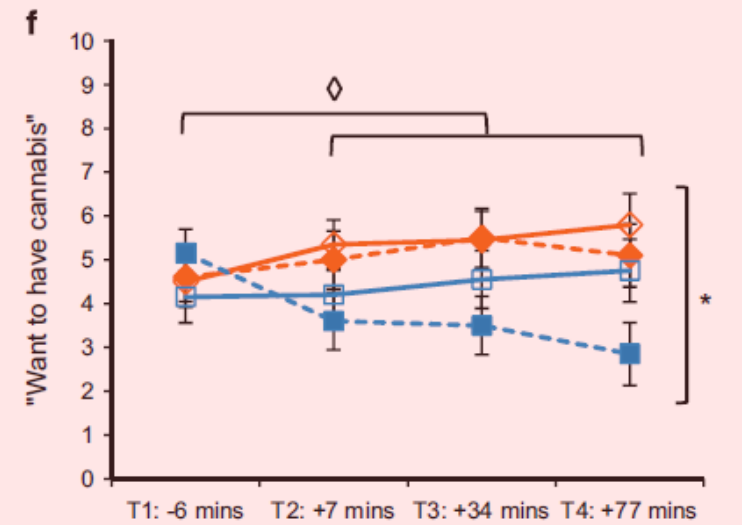
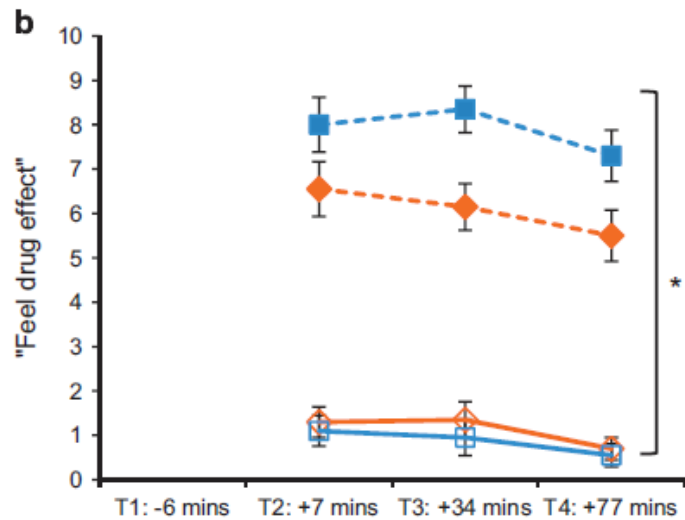
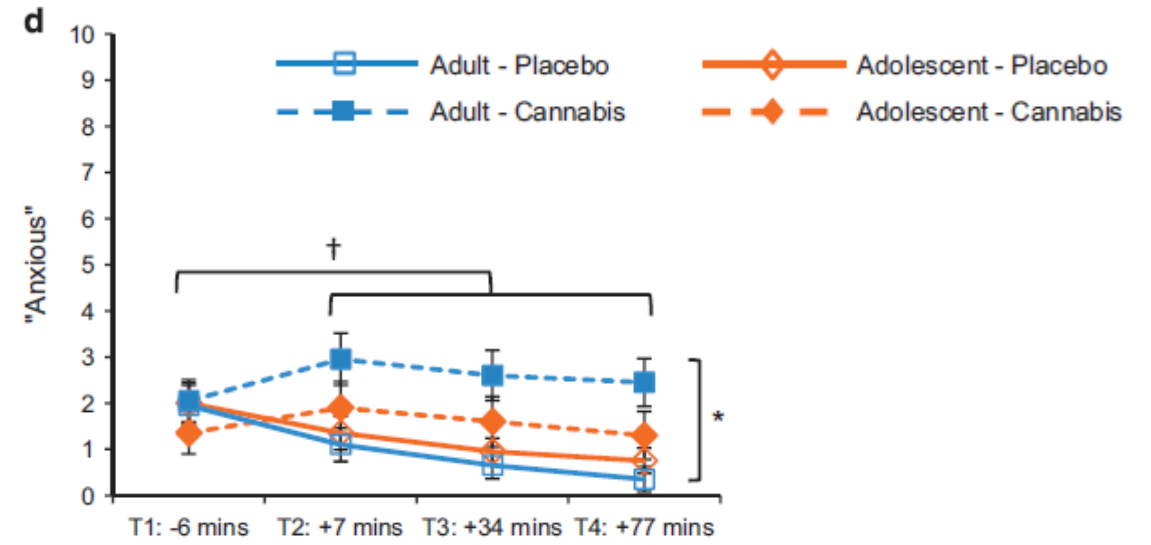
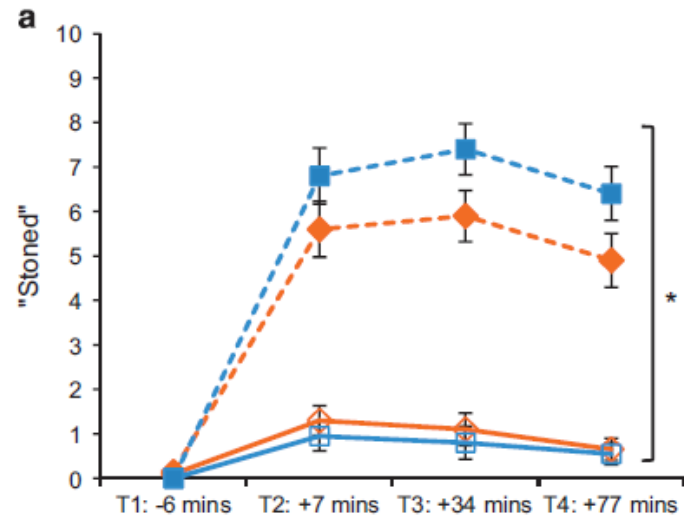
Tendenze relative agli utenti presi in carico per la prima volta



SVILUPPO DI CUD: ADOLESCENTI vs ADULTI



SVILUPPO DI CUD: ADOLESCENTI vs ADULTI



CUD: DIMENSIONI DEL FENOMENO

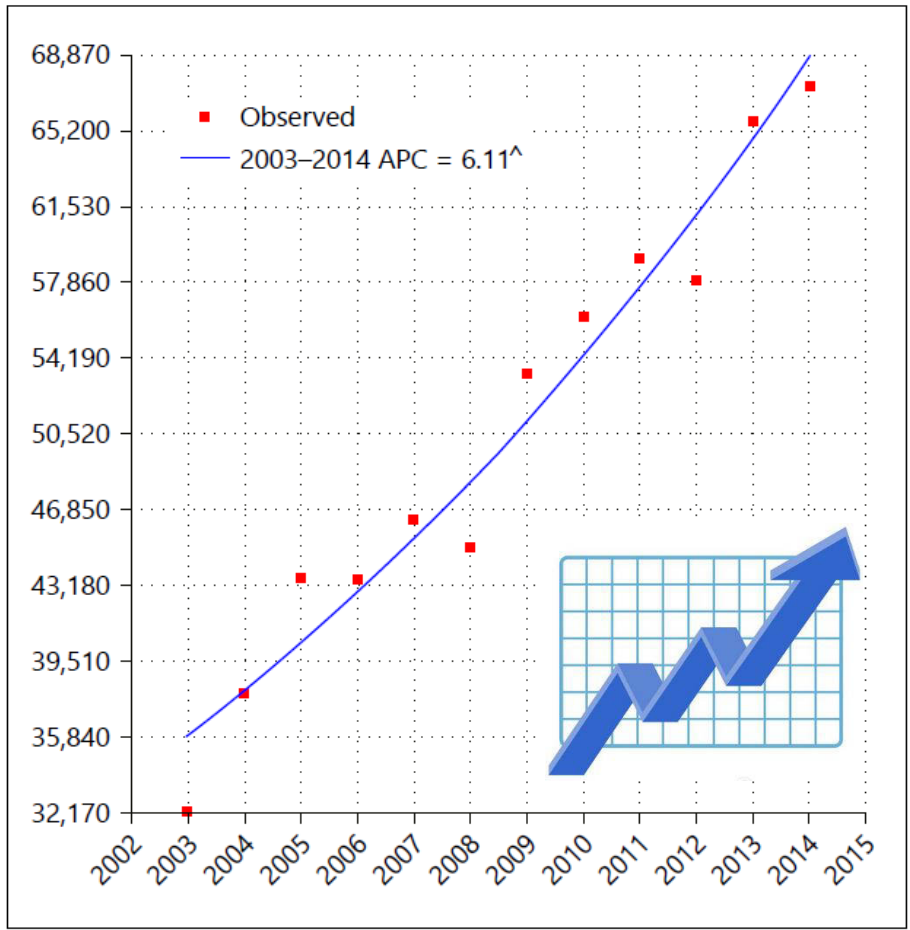
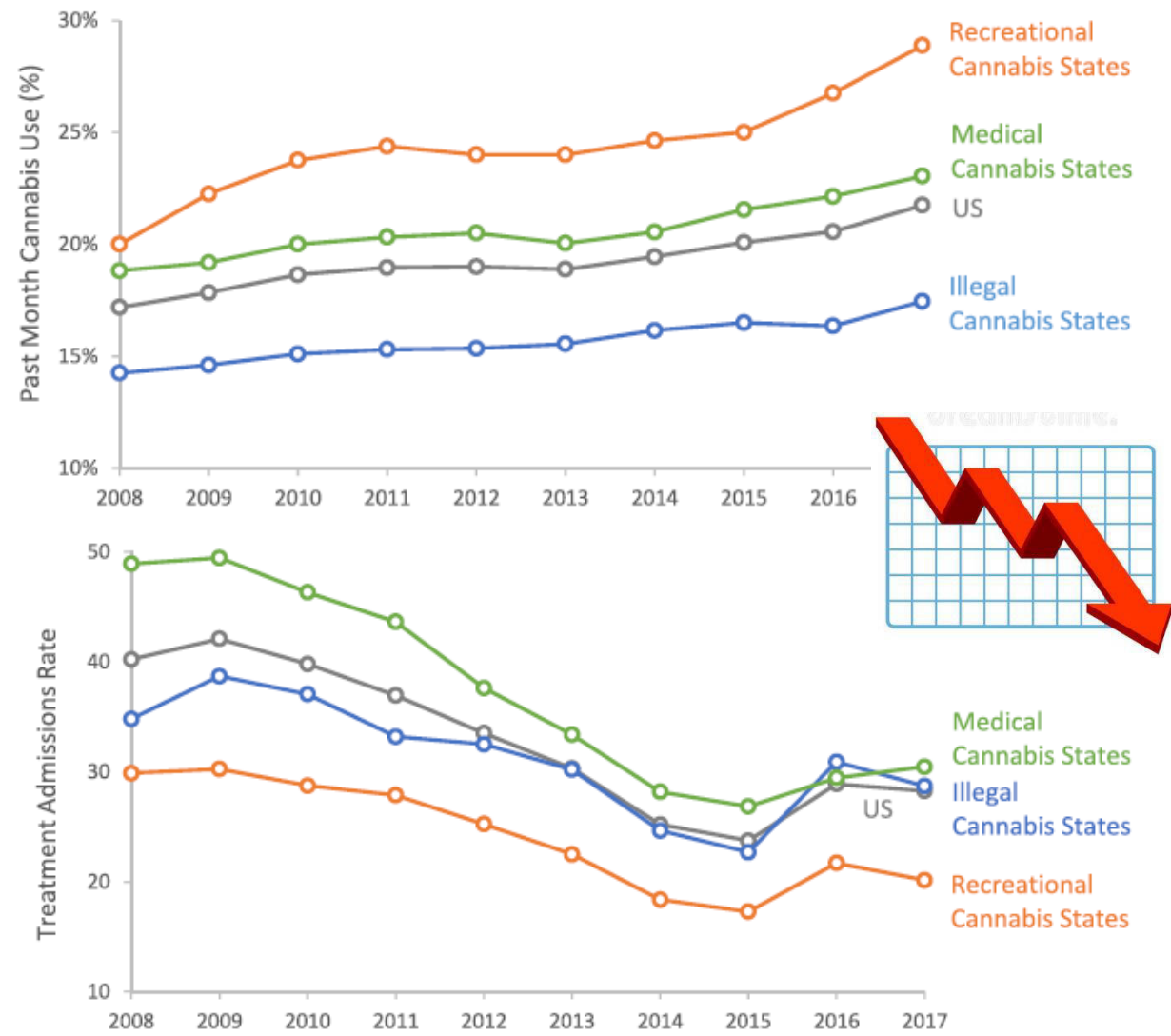


Fig. 1. Trends in the number of first-time cannabis treatment admission in Eu-22 – jointpoint regression outcome, 2003–2014. APC, annual percent change – observed.



Montanari L et al. Cannabis Use among People Entering Drug Treatment in Europe: A Growing Phenomenon? *Eur Addict Res.* 2017;23(3):113-121
 Mennis J et al. Young adult cannabis use disorder treatment admissions declined as past month cannabis use increased in the U.S.: An analysis of states by year, 2008-2017. *Addict Behav.* 2021 Dec;123

DISTURBO DA USO DI CANNABIS: RICHIESTA DI TRATTAMENTO



Figura 6.1.5 - Distribuzione degli utenti trattati nei SerD per sostanza primaria

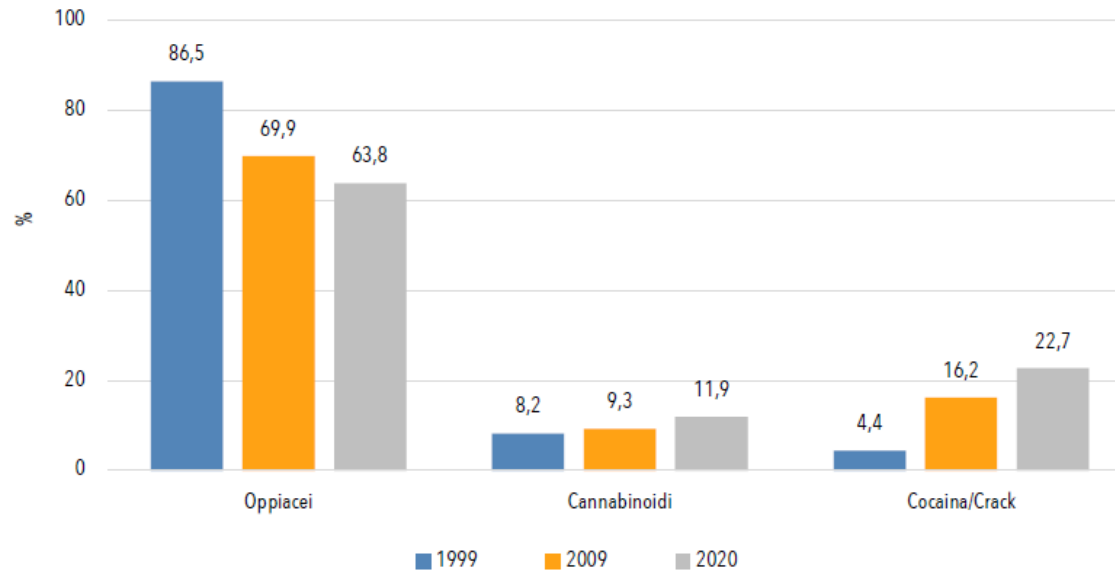
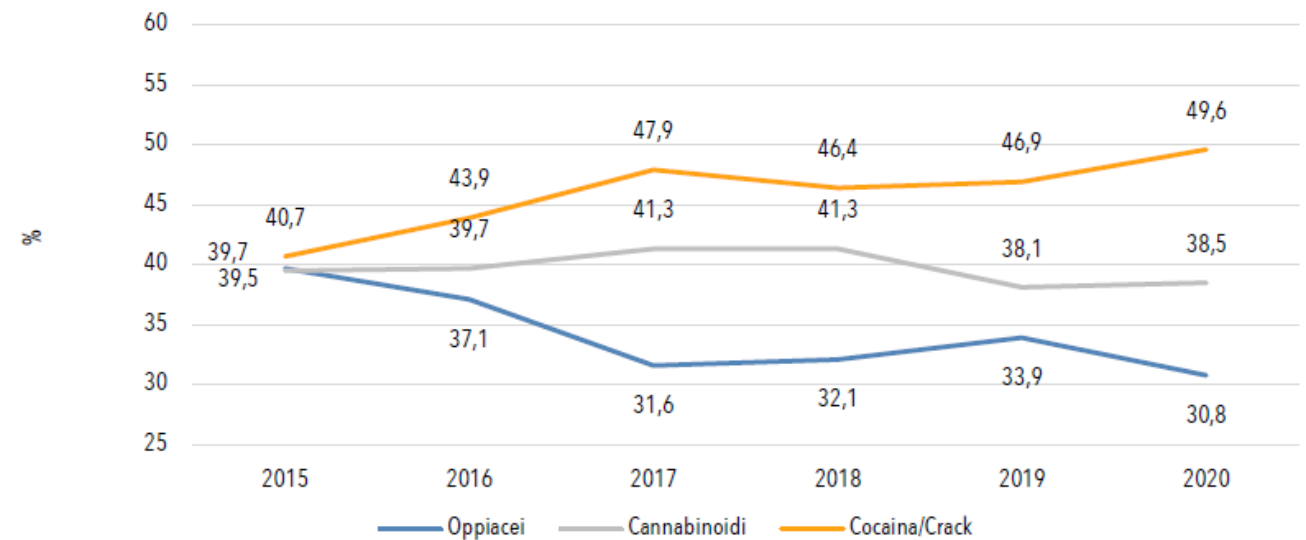


Figura 6.1.7 - Andamento temporale dei nuovi utenti trattati nei SerD per sostanza (primaria o secondaria)



Cannabinoidi



SOSTANZA PRIMARIA

14.968

11,9

SOSTANZA SECONDARIA

19.565

15,6

TOTALE

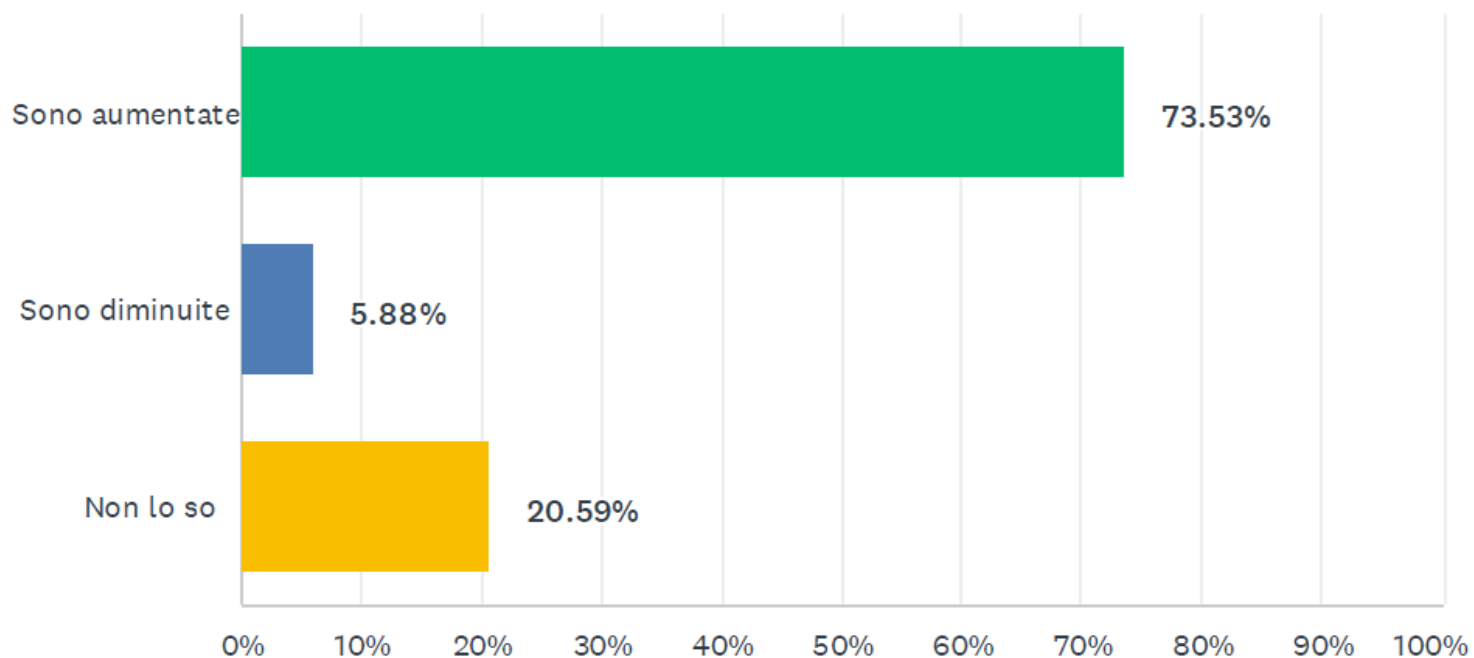
34.533

27,5



D1 Negli ultimi anni le richieste di presa in carico per Disturbo da Uso di Cannabis nel tuo Servizio:

Risposte: 136 Saltate: 2



DISTURBO DA USO DI CANNABIS (CUD)

Broad domain	DSM-5 CUD 'diagnostic criteria' ⁴	ICD-11 Cannabis dependence 'description' ⁵
Impaired control	1 ^a Cannabis is taken in larger amounts or over longer periods than intended	"Cannabis dependence is a disorder of regulation of cannabis use arising from repeated or continuous use of cannabis. The characteristic feature is a strong internal drive to use cannabis, which is manifested by impaired ability to control use..."
	2 ^a There is a persistent desire or unsuccessful attempts to cut down or control cannabis use	
	3 ^a A great deal of time spent in activities necessary to obtain cannabis, use cannabis or recover from its effects	
	4 Craving, or a strong desire or urge to use cannabis	
Increasing priority resulting in social and physical risk	5 Recurrent cannabis use resulting in a failure to fulfil major role obligations at work, school or home	"...and persistence of use despite harm or negative consequences."
	6 Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis	"...and persistence of use despite harm or negative consequences."
	7 ^a Important social, occupational, or recreational activities are given up or reduced because of cannabis use	"...increasing priority given to use over other activities..."
	8 Recurrent cannabis use in situations in which it is physically hazardous	"...and persistence of use despite harm or negative consequences."
	9 ^a Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis	"...and persistence of use despite harm or negative consequences."
Physiological dependence	10 ^a Tolerance, as evidenced by a markedly diminished effect	"Physiological features of dependence may also be present, including tolerance to the effects of cannabis, withdrawal symptoms following cessation or reduction in use of cannabis, or repeated use of cannabis or pharmacologically similar substances to prevent or alleviate withdrawal symptoms."
	11 ^a Withdrawal syndrome, or drinking to prevent withdrawal	

Un pattern problematico di uso di cannabis che porta a disagio o compromissione clinicamente significativi, come manifestato da almeno due delle seguenti condizioni, che si verificano entro un periodo di 12 mesi

Gravità CUD

- CUD lieve: 2–3 condizioni
- CUD moderato: 4–5 condizioni
- CUD grave: ≥6 condizioni

DSM-5 specificatori

- Remissione precoce: 3–12 mesi
- Remissione protratta: >12 mesi

CUD: ASTINENZA

Criteria diagnostici

- A. Cessazione dell'uso di cannabis che è stato pesante e prolungato.
- B. Tre (o più) dei seguenti segni e sintomi, che si sviluppano approssimativamente entro 1 settimana dopo il Criterio A:
 - 1. Irritabilità, rabbia, aggressività
 - 2. Nervosismo, ansia
 - 3. Difficoltà del sonno (per es., insonnia, sogni inquietanti)
 - 4. Diminuzione dell'appetito o perdita di peso
 - 5. Irrequietezza
 - 6. Umore depresso
 - 7. Almeno uno dei seguenti sintomi fisici causa malessere significativo: dolori addominali, instabilità/tremori, sudorazione, febbre, brividi, cefalea
- C. I segni o sintomi causano disagio clinicamente significativo o compromissione del funzionamento in ambito sociale, lavorativo o in altre aree importanti.
- D. I segni o sintomi non sono attribuibili a un'altra condizione medica e non sono meglio spiegati da un altro disturbo mentale.

CUD: INTOSSICAZIONE ACUTA

Criteria diagnostici

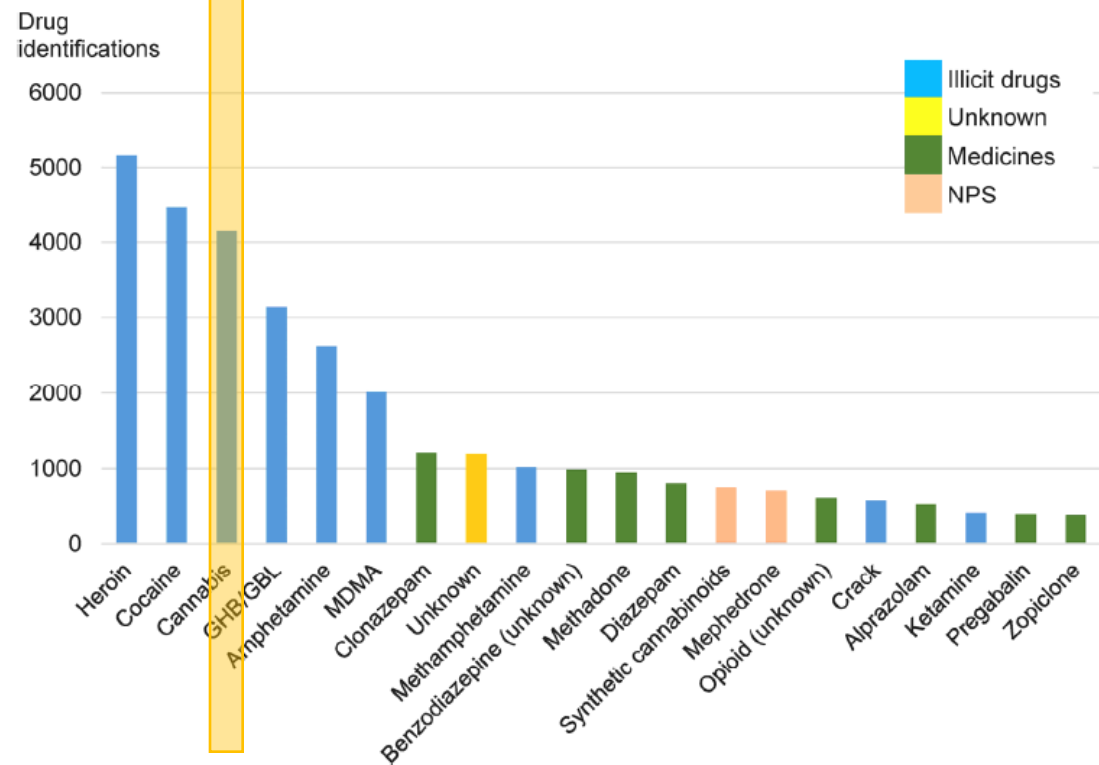
- A. Recente uso di cannabis.
- B. Comportamento problematico clinicamente significativo o cambiamenti psicologici (per es., coordinazione motoria compromessa, euforia, ansia, sensazione di rallentamento del tempo, capacità critica compromessa, isolamento sociale) che si sviluppano durante, o subito dopo, l'uso della cannabis.
- C. Due (o più) dei seguenti segni o sintomi, che si sviluppano entro 2 ore dall'uso della cannabis:
 - 1. Iperemia congiuntivale.
 - 2. Aumento dell'appetito.
 - 3. Secchezza delle fauci.
 - 4. Tachicardia.
- D. I segni o sintomi non sono attribuibili a un'altra condizione medica e non sono meglio spiegati da un altro disturbo mentale, compresa intossicazione da altra sostanza.

Specificare se:

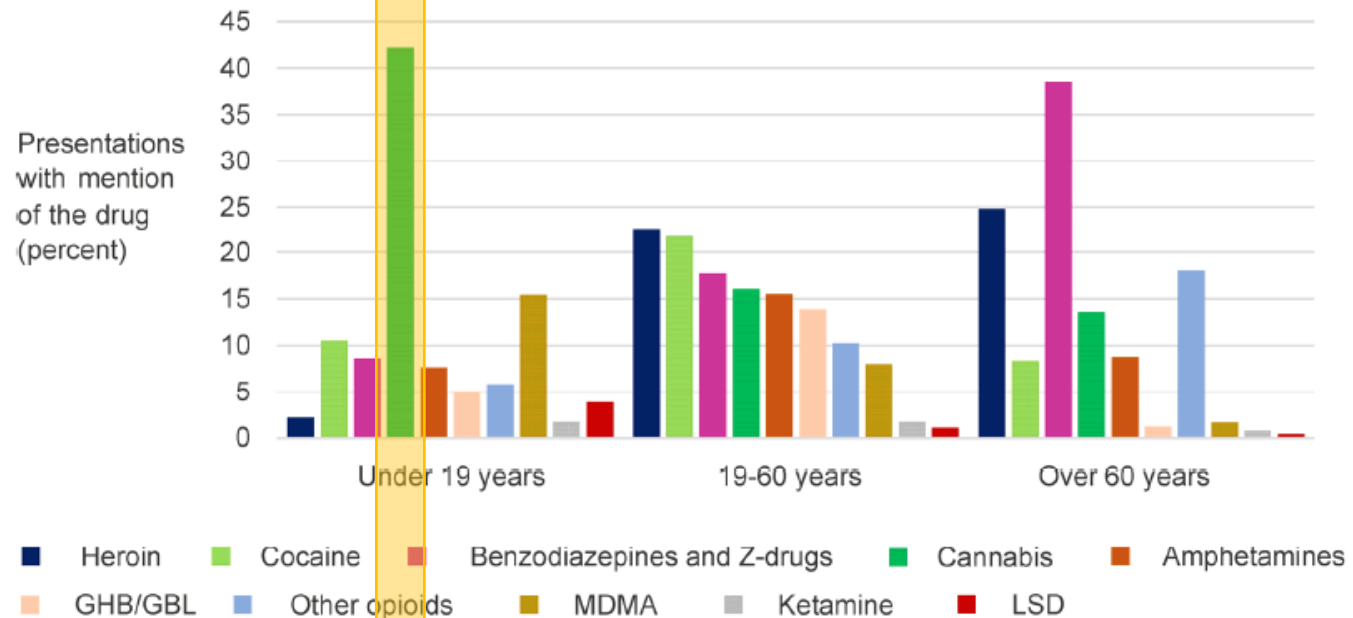
Con alterazioni percettive: Allucinazioni con esame di realtà integro o illusioni uditive, visive o tattili che si verificano in assenza di un delirium.

CUD: INTOSSICAZIONE ACUTA

Top 20 drugs involved (number of reports) in Euro-DEN Plus presentations, 2014-2017



Proportions of people within each age group reporting each drug in Euro-DEN Plus presentations, for selected substances, 2014-17



CUD: INTOSSICAZIONE ACUTA

Most common clinical features in the cases with cannabis alone (N = 186).

Clinical feature	Occurrence as the only clinical feature	Occurrence with other clinical features	Total occurrence
<i>Cardiovascular symptoms</i>			
Tachycardia (HR ≥ 100 bpm) on arrival	6	60	66
Palpitations	3	44	47
Chest pain	2	25	27
Nausea / vomiting	5	43	48
Anxiety	1	41	42
Dizziness	0	27	27
Impaired consciousness (GCS 8-14/"drowsy") on arrival	5	16	21
Agitation / aggression	1	18	19
<i>Respiratory symptoms</i>			
Dyspnoea	2	17	19
Hyperventilation	0	17	17
Panic attack	0	14	14
Psychosis	1	11	12
Mydriasis	0	11	11
Seizures	2	7	9
Hallucinations	0	7	7

Number of patients presenting with the clinical features in descending order of frequency. HR: heart rate; bpm: beats per minute; GCS: Glasgow Coma Score.

Substances reported or analytically detected in combination with cannabis (n).

Substances	Reported	Analytically detected
alcohol	238	219
cocaine	121	77
amphetamine/methamphetamine	45	39
benzodiazepines/sedatives	40	72
MDMA/ecstasy	30	
heroin	23	
LSD	21	2
opioids other than heroin or methadone	12	
methadone	9	22
opiates		31
methylphenidate	7	1
psychedelic mushrooms	5	
neuroleptics	4	3
ketamine	3	1
poppers	2	
antidepressants	2	6
antihistamines	1	
laughing gas	1	
dextromethorphan	1	
testosterone	1	
sildenafil	1	
bupropion	1	
tizanidine	1	
clomethiazole	1	
caffeine	1	
melatonin (self-reported as "melanin")	1	
self-reported "smileys"	1	
self-reported "synthetic drugs"	1	
unknown substance	10	

CUD: INTOSSICAZIONE ACUTA

Hospital outcomes for AMI by significant substance abuse

Variable	Cannabis abuse	Amphetamine abuse	Cocaine abuse
Severity of illness (%)			
Minor	40.1	60.0	38.2
Moderate	45.2	31.7	52.9
Major	14.7	8.3	8.8
Length of stay and charge			
Mean length of stay (\pm SD), days	2.8 (\pm 2.29)	2.5 (\pm 1.47)	3.2 (\pm 5.29)
Mean total charge (\pm SD), \$	53,608 (\pm 63,092)	43,720 (\pm 35,939)	49,979 (\pm 88,493)
Therapeutic procedure (%)			
Angiography	55.6	25.0	77.5
PTCA	19.4	8.3	0
CABG	2.0	0	0
Disposition of patient (%)			
Routine	86.2	100	95.1
Short-term hospital	4.0	0	0
SNF/INF	0	0	4.9
Home health care	4.0	0	0
Against medical advice	4.0	0	0
Inpatient death	2.0	0	0



CANNABINOID HYPEREMESIS SYNDROME (CSH)



Frequent vomiting from use of cannabis (pot/marijuana)

2,2 – 13,3/100.000 ED visits annually

CHS - Cannabinoid Hyperemesis Syndrome



If you are vomiting more than 5 times per day, for a day or longer, immediately contact your health care provider or go to the nearest emergency department.



If you continue to experience CHS symptoms and are not improving as expected, talk with your health care provider.

What is CHS?

People with cannabinoid hyperemesis syndrome (CHS) experience persistent nausea and stomach pain that can lead to frequent and repetitive vomiting and weight loss. Frequent use of cannabis (at least once a week for more than a year) can increase the risk.

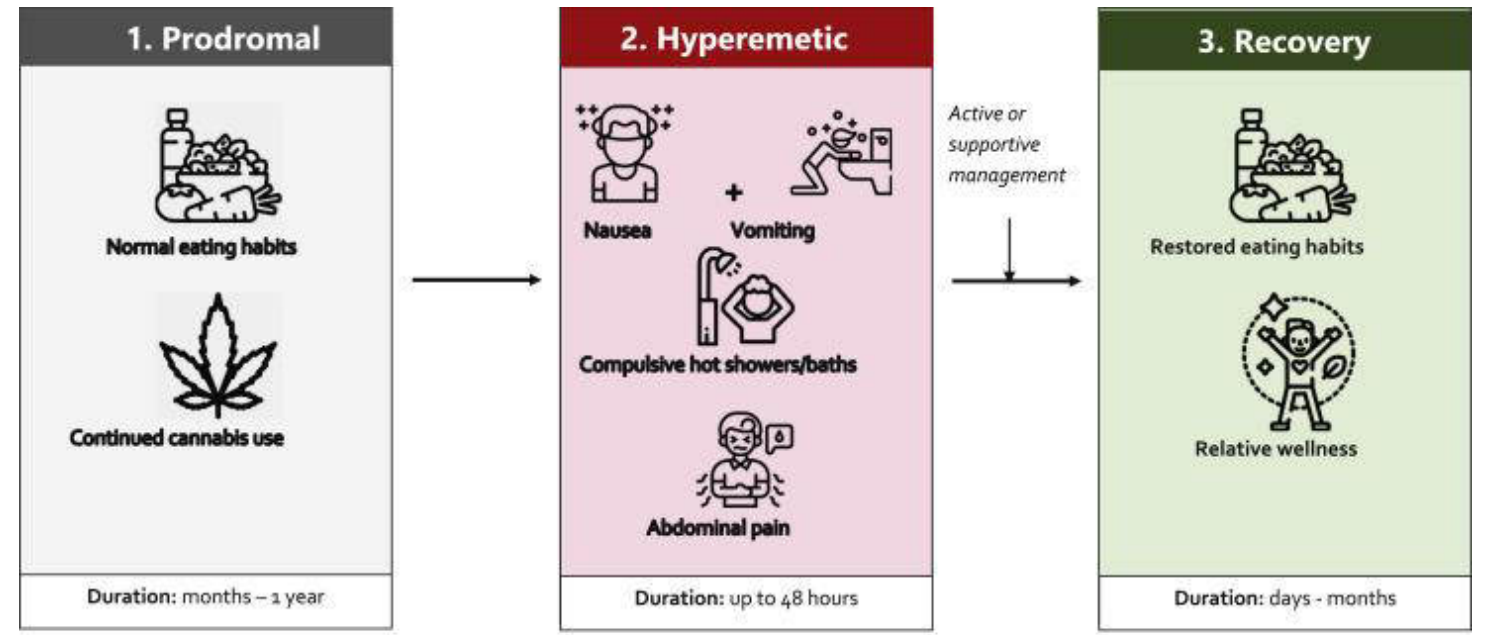
Treatment

- People with CHS may take a hot shower or bath to help temporarily relieve their symptoms. Caution should be taken as these can cause dehydration or scald/burn the skin.
- Capsaicin cream (brand name Zostrix) may be prescribed to help reduce the symptoms of CHS. The cream is to be applied to your stomach, back, or arms.
- Other medications may be prescribed to relieve nausea and vomiting.
- If you go to the emergency department, let your health care provider know if you are using cannabis to manage a medical condition. Your health care provider may do some blood tests. You may be given fluids intravenously to keep you hydrated and help you feel better.

Prevention

Choosing not to use cannabis is the only way to completely avoid CHS. If CHS does occur, the symptoms will usually resolve within 2 weeks after you stop using cannabis. **However, if you've had CHS once, even a small amount of cannabis can cause the symptoms to come back.** If this happens, talk to your health care provider about treatment options or programs for stopping cannabis use.

Reduce your risk of CHS by following "[Cannabis & Your Health: 10 WAYS to Reduce Risks When Using](https://bit.ly/lcugphac)". <https://bit.ly/lcugphac>



For more information visit: www.ccsa.ca/cannabis

To access a PDF of this handout visit: safemedicationuse.ca/tools_resources/tips.html



CANNABINOID HYPEREMESIS SYNDROME (CHS)

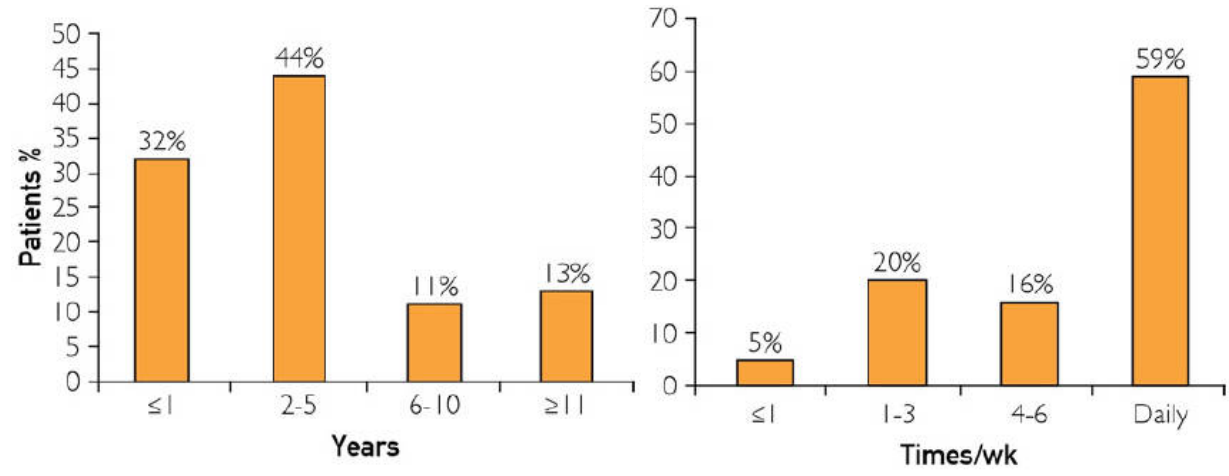


Table 1
Rome IV criteria for CHS diagnosis

Category	Features
Essential	Stereotypical episodic vomiting resembling CVS in terms of onset, duration, and frequency Presentation after prolonged, excessive cannabis use Relief of vomiting episodes by sustained cessation of cannabis use
Supportive remarks	May be associated with pathologic bathing behavior (prolonged hot baths or showers)

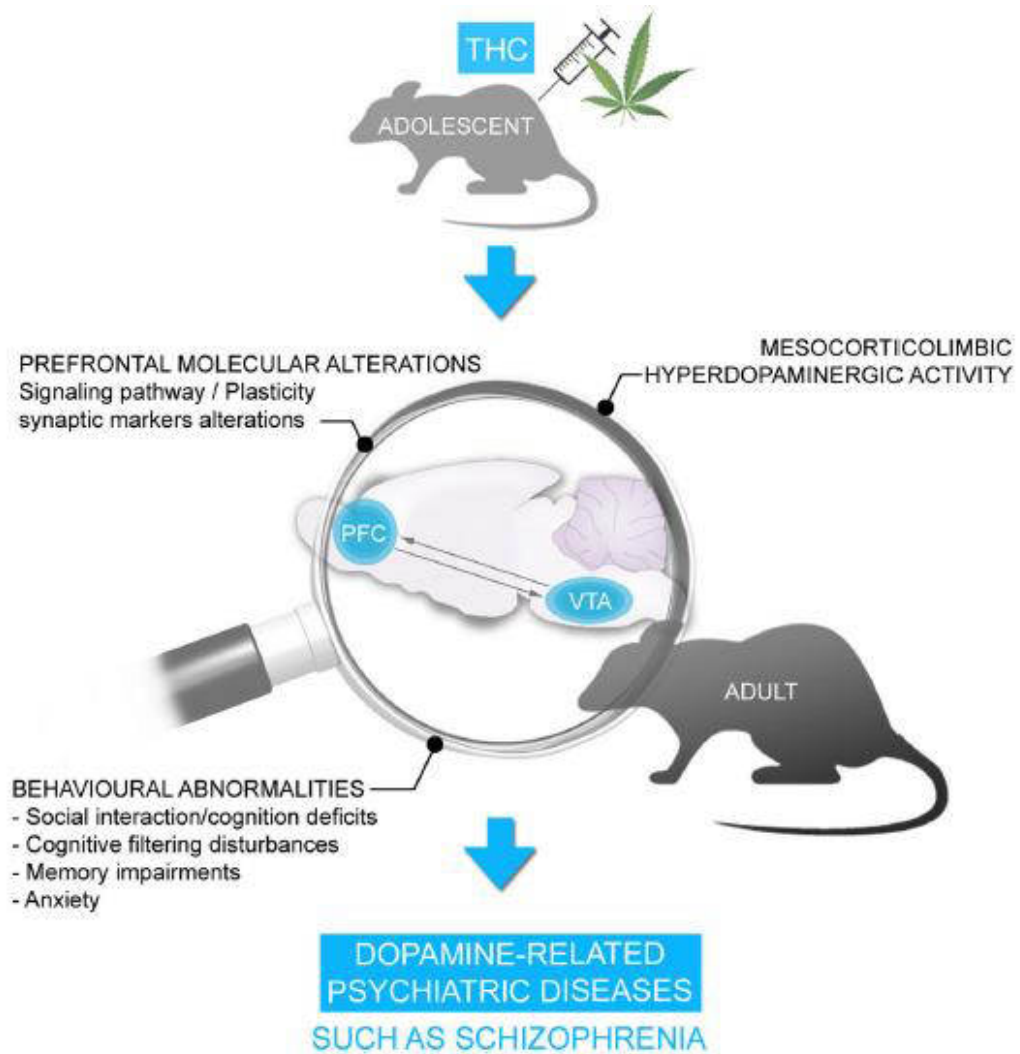
CHS = cannabinoid hyperemesis syndrome; CVS = cyclic vomiting syndrome.

Mechanism

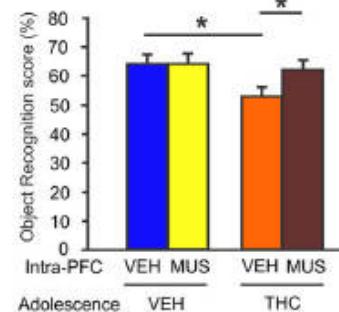
GRADE rating

- The emetogenic and anti-emetic effects of $\Delta 9$ -THC and its analogs are mediated through CB-1 receptors (CB1r) and thus underlie the syndrome of CHS [106, 135] Very low
- Cannabinoids may bind to CB-1 receptors in the gastrointestinal tract and decrease GI motility and gastric emptying, which may override brainstem-mediated antiemetic effects and precipitate hyperemesis [9, 92, 95, 132] Very low
- Chronic cannabis use may lead to paradoxical and plastic changes in expression and downstream effects of cannabinoid receptors [133] Very low
- Chronic cannabis use leads to desensitization and downregulation of CB1 receptors that ordinarily have peripheral antiemetic effects, causing rebound vomiting and spasmodic pain that abates with abstinence and corresponding recovery of CB-1 receptor activity [98, 136, 185] Very low
- In chronic cannabis users, cannabinoid metabolites may accumulate in the brain and fatty tissues inducing a toxic effect [90, 94] Very low
- CHS may be caused by a non-THC, cannabinoid-like structure within *Cannabis sativa*, such as cannabidiol [96, 186] Very low
- Patients susceptible to developing CHS may have genetic variation in their metabolic enzymes resulting in toxic levels of cannabinoid metabolites [131] Very low
- $\Delta 9$ -THC may act as a partial agonist on CB1 receptors and thus relatively antagonize the effects of full endogenous agonists on these receptors, thus precipitating sudden withdrawal and hyperemesis in sensitive patients [97, 105] Very low
- THC causes dilation of splanchnic vasculature, resulting in CHS. Hot bathing leads to peripheral venodilation and shunts blood away from the splanchnic bed, resulting in symptom improvement [102, 137] Very low

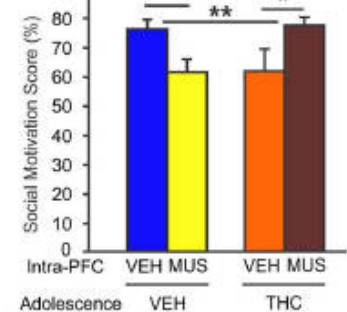
CUD E PATOLOGIE PSICHIATRICHE



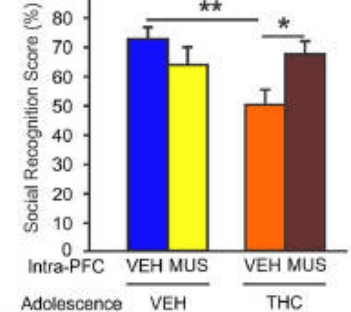
A Object Recognition Index (%)



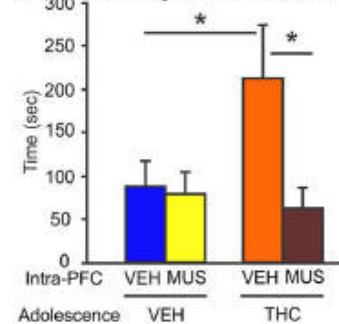
B Social Motivation Score (%)



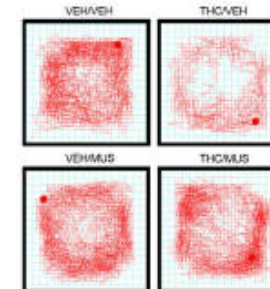
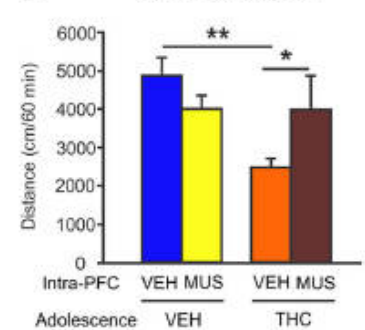
Social Recognition Score (%)



C Latency to first transition



D Distance travelled



CUD E PATOLOGIE PSICHIATRICHE



Figure 2. Forest Plot Showing Adjusted Odds Ratio (OR) and 95% CIs for Depression and Anxiety in Young Adulthood According to Cannabis Use in Individual Studies

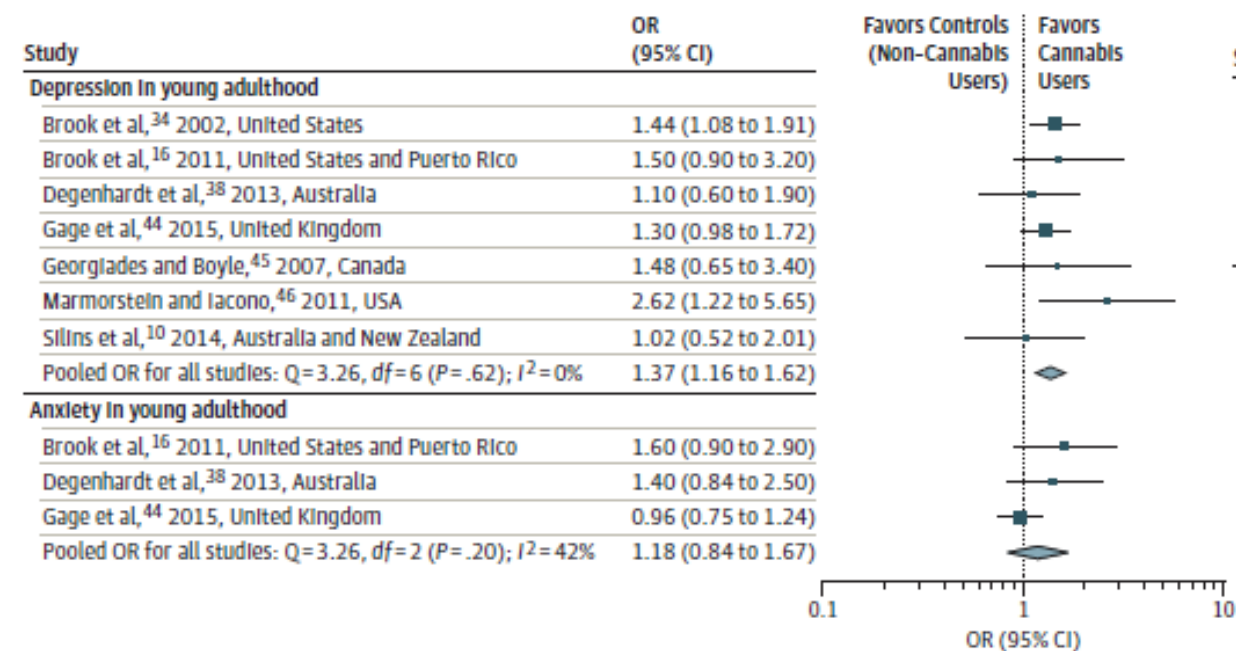
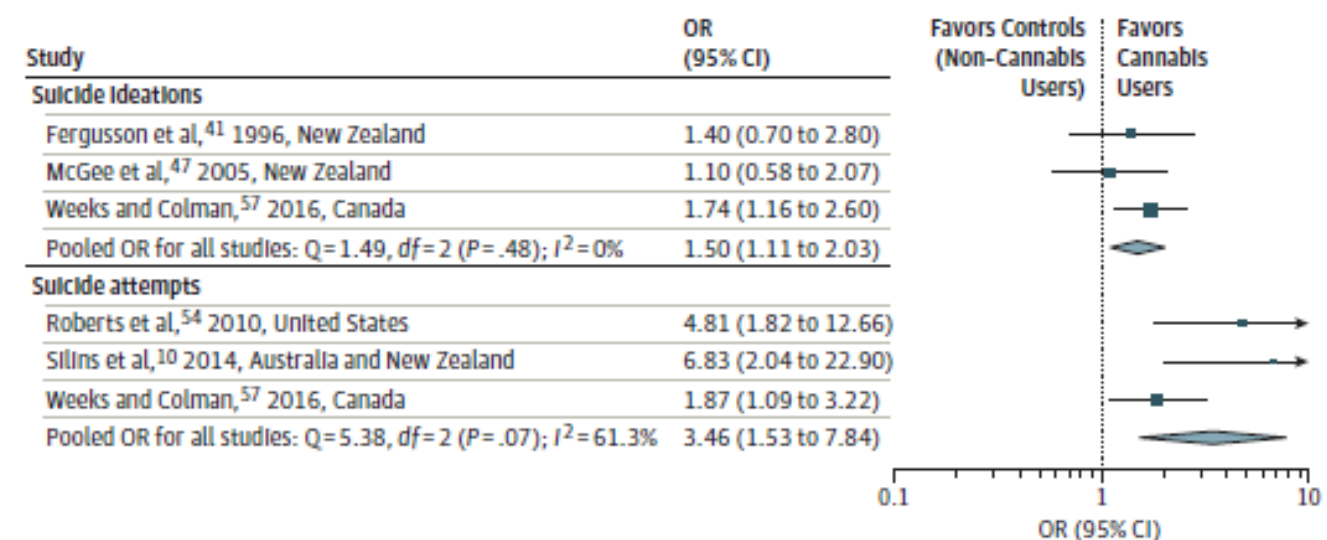
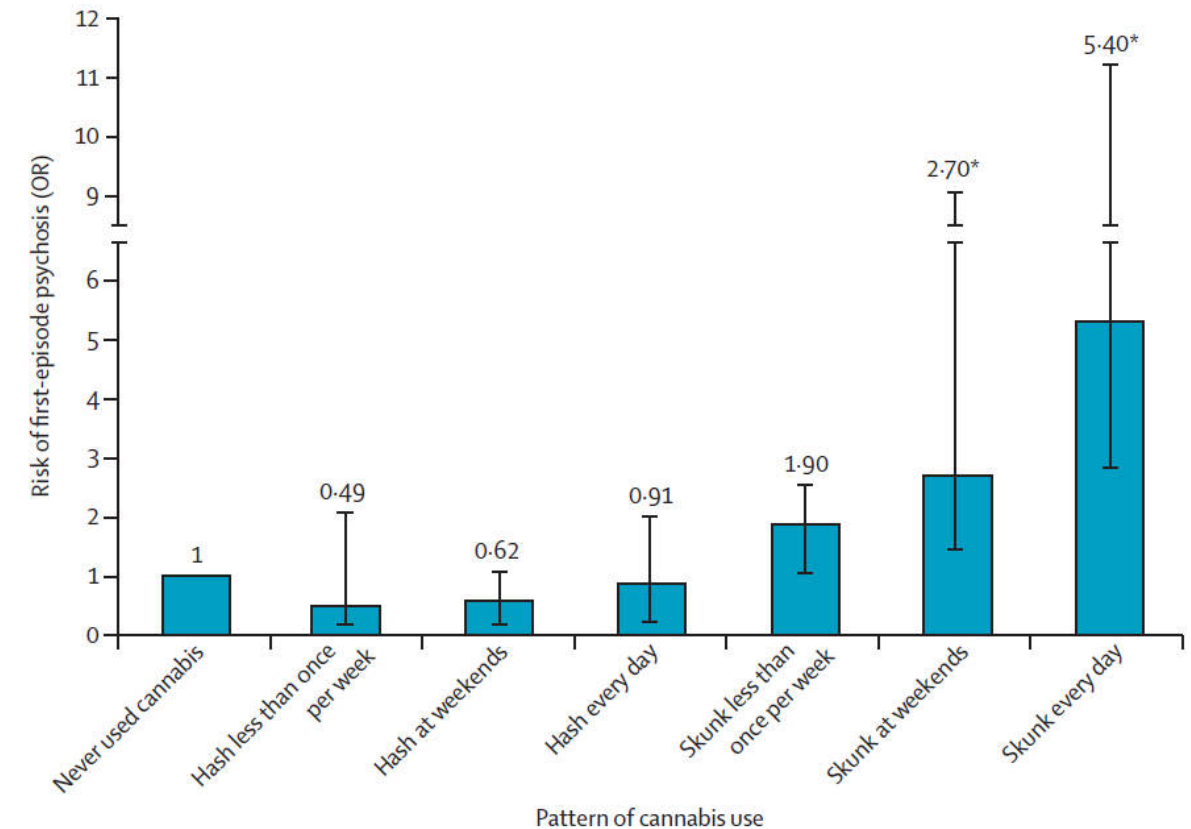
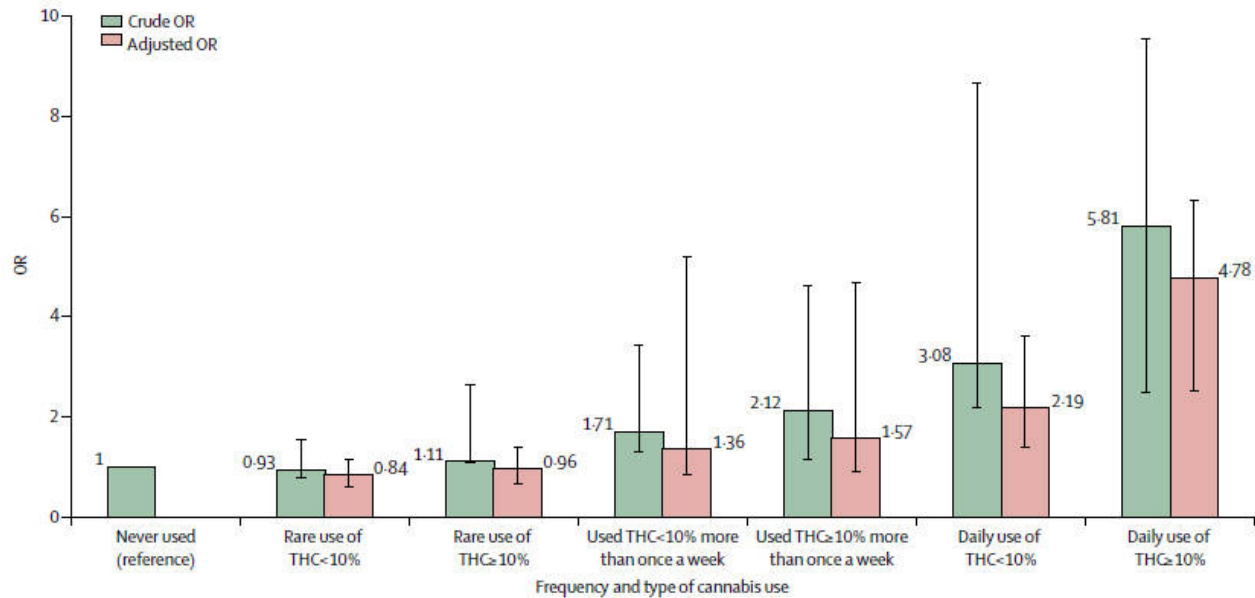


Figure 3. Forest Plot Showing Adjusted Odds Ratio (OR) and 95% CIs for Suicidal Ideations and Attempts According to Cannabis Use in Individual Studies



PATTERN DI CONSUMO E PATOLOGIE PSICHIATRICHE



Di Forti M et al; EU-GEI WP2 Group. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *Lancet Psychiatry*. 2019 May;6(5):427-436; Di Forti M et al. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *Lancet Psychiatry*. 2015 Mar;2(3):233-8

CUD: TRATTAMENTO FARMACOLOGICO

TABLE 3 Summary of Placebo-Controlled Clinical Trials of Medications for CUD Treatment

Medication(s)	Mechanism of action	Reasoning for CUD treatment	Utility in CUD treatment	Publications
Bupropion	NE+DA reuptake inhibition	Withdrawal Cannabis use	Limited, if any	Haney <i>et al</i> , 2001 (L) Carpentar <i>et al</i> , 2009 (T) Penetar <i>et al</i> , 2012 (T)
Nefazodone	NE reuptake inhibition	Withdrawal Cannabis use	Limited, if any; no longer available in the United States	Haney <i>et al</i> , 2003 (L) Carpentar <i>et al</i> , 2009 (T)
Atomoxetine ^a	NE+DA reuptake inhibition	Cognitive symptoms (similarities with ADHD), +ADHD	Limited, if any	McRae-Clark <i>et al</i> (2010) (T)
Venlafaxine ^a	NE+5HT reuptake inhibition	CUD+MDD	Limited, potentially exacerbates cannabis use	Levin <i>et al</i> , 2013 (T)
Mirtazepine	NE+5HT reuptake inhibition	Withdrawal Cannabis use	Specific withdrawal symptoms of insomnia and food intake	Haney <i>et al</i> , 2010 (L)
Bupirone	5HT 1A partial agonist	Cannabis use, anxiety	Limited, if any, particularly in women	McRae-Clark <i>et al</i> , 2009 (T) McRae-Clark <i>et al</i> , 2015 (T)
Escitalopram	5HT reuptake inhibition	Cannabis use, withdrawal, anxiety, depression	Limited, if any	Weinstein <i>et al</i> , 2014 (T)
Vilazodone	5HT 1A partial agonist+5HT reuptake inhibition	Cannabis use	Limited, if any	McRae-Clark <i>et al</i> , 2016 (T)
Divalproex	Blocks voltage-dependent Na channels, increases GABA	Withdrawal, irritability Cannabis use	Limited, if any	Haney <i>et al</i> , 2004 (L) Levin <i>et al</i> , 2004 (L)
Lithium carbonate	Not fully known, mood stabilizer with impact of depression, stimulates oxytocin release	Withdrawal Treatment completion	Limited, if any	Johnston <i>et al</i> , 2014 (T/I)
Quetiapine	5HT _{2A} , DA ₂ , H ₁ , α ₁ , α ₂ antagonism; 5HT _{1A} partial agonism; NE reuptake inhibition	Withdrawal Cannabis use	Specific withdrawal symptoms, including sleep, food intake, and weight loss; concerns about increases in craving need to be considered	Cooper <i>et al</i> , 2013 (L)
Badofen	GABA-B agonism	Withdrawal Cannabis use	Limited, if any	Haney <i>et al</i> , 2010 (L)
Zolpidem	GABA-A agonism	Withdrawal, insomnia	Withdrawal-related sleep disturbances	Vandrey <i>et al</i> , 2011 (L)

CUD: TRATTAMENTO FARMACOLOGICO

Gabapentin	Blocks $\alpha_2\delta$ subunit on voltage gated Na channels, indirect GABA modulator; restores brain CRF-mediated homeostasis	Withdrawal, cognitive performance, cannabis use, problems secondary to cannabis	Encouraging for use in withdrawal, reductions, craving, cognitive functioning, and improvement in problems	Mason <i>et al</i> , 2012 (T)
Topiramate	Blocks Na and Ca channels, potentiates GABA-A; AMPA/kinate glutamate antagonism	Cannabis use	Encouraging for its reduced use in adolescents, not well tolerated, slower titration may help	Miranda <i>et al</i> , 2016 (T)
Dronabinol	CB-1 agonist	Withdrawal Cannabis use	Encouraging for reductions in global withdrawal symptoms	Haney <i>et al</i> , 2004 (L) Budney <i>et al</i> , 2007 (L) Levin <i>et al</i> , 2011 (T)
Dronabinol +lofexidine	CB-1 agonist+ α_2 agonist	Withdrawal Cannabis use	Lofexidine adds no benefit and is poorly tolerated to dronabinol monotherapy	Haney <i>et al</i> , 2008 (L) Levin <i>et al</i> , 2016 (T)
Nabilone	CB-1 agonist	Withdrawal Cannabis use	Encouraging for its reductions in withdrawal and cannabis use	Haney, 2013b (L)
Nabilone +zolpidem	CB-1 agonist+GABA-A activity	Withdrawal, withdrawal-related sleep disturbance, cannabis use	Encouraging for reductions in withdrawal and cannabis use	Hermann <i>et al</i> , 2016 (L)
Nabixmols	CB-1 agonist+multi functions (through CBD)	Withdrawal Cannabis use	Encouraging for use in withdrawal	Allsop <i>et al</i> , 2014 (T/I)
Cannabidiol	Multifunctional	Cannabis use	Limited, if any	Haney <i>et al</i> , 2016 (L)
Rimonabant	CB-1 antagonism	Cannabis use	Limited if any due to discontinued use/safety risk	Huestis <i>et al</i> , 2001 (L) Huestis <i>et al</i> , 2007 (L)
Naltrexone	Mu opioid antagonism	Cannabis use	Encouraging for reductions in use when chronically dosed	Cooper and Haney, 2010 (L) Haney <i>et al</i> , 2015 (L)
N-acetylcysteine	Cysteine prodrug (cysteine–glutamate exchanger)	Cannabis use	Encouraging for reductions in use in adolescents; limited use in adults	Gray <i>et al</i> , 2012 (T) Gray, 2017 (T)
Oxytocin	Neural roles in prosocial behavior	Cannabis use (indirectly by enhancing psychosocial treatment)	Encouraging for enhancement of psychosocial treatment	Sherman <i>et al</i> , 2017 (T)

CUD: TRATTAMENTO FARMACOLOGICO



Cochrane Database of Systematic Reviews

Pharmacotherapies for cannabis dependence (Review)

Nielsen S, Gowing L, Sabioni P, Le Foll B

AUTHORS' CONCLUSIONS

Implications for practice

Studies undertaken to date on pharmacotherapies for cannabis dependence are insufficient to guide clinical practice. There is incomplete evidence for all of the pharmacotherapies investigated in this review.

At this point in time, psychological approaches such as MET and cognitive-behavioural therapy remain the mainstay of treatment for cannabis use disorders.

CONSUMO E DISTURBO DA USO DI CANNABIS: CONCLUSIONI



Fenomeno in incremento e in mutamento
Nuove modalità di consumo

Necessità di indagare il poliabuso

Quadri clinici aspecifici e di gravità variabile

Rete assistenziale?

Traiettorie psico-patologiche

Strumenti di prevenzione e trattamento



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