

Marijuana Use in Cancer: Myths and Reality

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A little about me:

- Cleveland, OH
- Yeshiva University
- NYCOM -> NovaSE COM
- Wellington Florida
- HealthInternal

No, I'm not a "Pot head"

But, here I am with some "pot heads"



First and Foremost:

Cannabis/Marijuana is currently a **Schedule I drug**

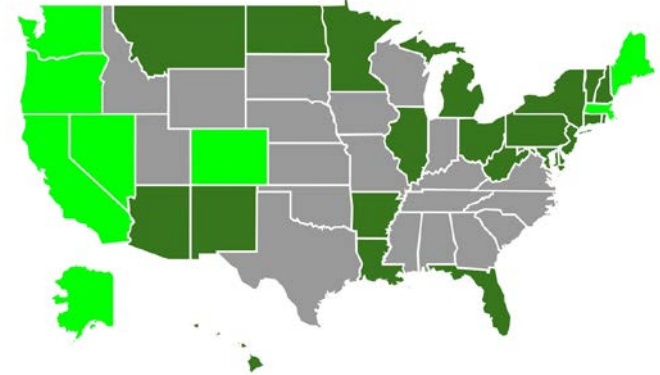
It is **federally** not legal to prescribe (as of 1970...)

30 states have laws allowing it

8 States (and DC where the laws are written...)

have recreational cannabis

Information is current as of Jan. 8, 2018.



Marijuana Legalization Status

- Medical marijuana broadly legalized
- Marijuana legalized for recreational use
- No broad laws legalizing marijuana

THIS LECTURE IS NOT TELLING PEOPLE TO BREAK THE LAW

Myth #1:

Pot is Pot, right?

cannabis, hashish, hemp, sinsemilla, dope, grass, weed, Mary Jane, bud, hash, bhang, keif, ganja, locoweed; reefer, doob, spliff, tokes, roach

What is Cannabis?

Kingdom: Plantae

Clade: Angiosperms

Clade: Eudicots

Clade: Rosids

Order: Rosales

Family: Cannabaceae

Genus: ***Cannabis***

Species

- *Cannabis sativa*
- *Cannabis indica*
- *Cannabis ruderalis*

Species



SATIVA

Cannabis Sativa Sativa is characterized by leaflets that are more narrow, branches that are farther apart, and coloration that tends more toward spring green. *Sativa Sativa* plants tend to be taller and produce fewer flowers.



INDICA

Cannabis Sativa Indica is characterized by broad leaflets that offer overlap, branches that are closer together, and coloration that tends more toward deep olive green. *Sativa Indica* plants tend to be shorter and bushier, producing fuller, denser flower buds.



RUDERALIS

Cannabis Ruderalis is characterized by varied leaflets in the mature leaves, a shorter stature and generally small size. This subspecies is used to create *S. Sativa* or *S. Indica* hybrids with select desired traits.

Cannabis-derived cannabinoids [edit]

The classical cannabinoids are concentrated in a viscous [resin](#) produced in structures known as glandular [trichomes](#). At least 113 different cannabinoids have been isolated from the *Cannabis* plant^[5] To the right, the main classes of cannabinoids from *Cannabis* are shown. The best studied cannabinoids include [tetrahydrocannabinol](#) (THC), [cannabidiol](#) (CBD) and [cannabinol](#) (CBN).

Types [edit]

All classes derive from [cannabigerol-type](#) (CBG) compounds and differ mainly in the way this precursor is cyclized.^[12] The classical cannabinoids are derived from their respective [2-carboxylic acids](#) (2-COOH) by [decarboxylation](#) (catalyzed by heat, light, or [alkaline](#) conditions).^[13]

- THC ([Tetrahydrocannabinol](#))
- THCA ([Tetrahydrocannabinolic acid](#))
- CBD ([Cannabidiol](#))
- CBDA ([Cannabidiolic Acid](#))
- CBN ([Cannabinol](#))
- CBG ([Cannabigerol](#))
- CBC ([Cannabichromene](#))
- CBL ([Cannabicyclol](#))
- CBV ([Cannabivarin](#))
- THCV ([Tetrahydrocannabivarin](#))
- CBDV ([Cannabidivarin](#))
- CBCV ([Cannabichromevarin](#))
- CBGV ([Cannabigerovarin](#))
- CBGM ([Cannabigerol Monomethyl Ether](#))
- CBE ([Cannabielsoin](#))
- CBT ([Cannabicitran](#))

Tetrahydrocannabinol [edit]

Main article: Tetrahydrocannabinol

Type	Skeleton	Cyclization
Cannabigerol-type CBG		
Cannabichromene-type CBC		
Cannabidiol-type CBD		
Tetrahydrocannabinol- and Cannabinol-type THC, CBN		
Cannabielsoin-type CBE		
<i>iso</i> - Tetrahydrocannabinol- type <i>iso</i> -THC		

What's in cannabis?

483 chemicals

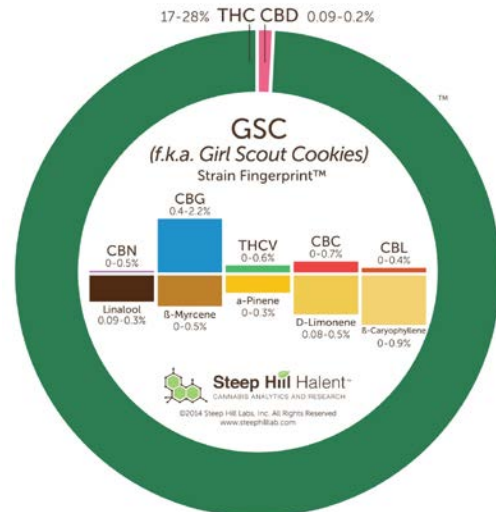
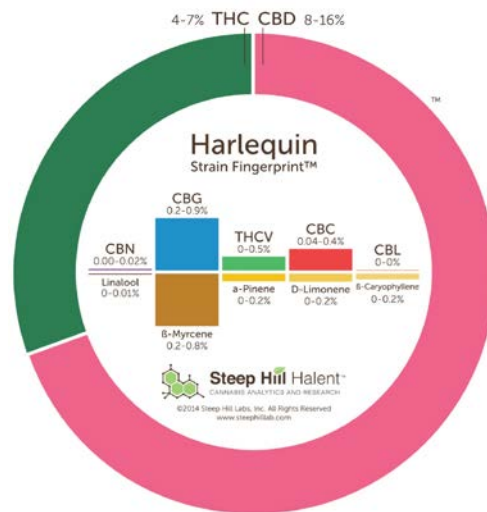
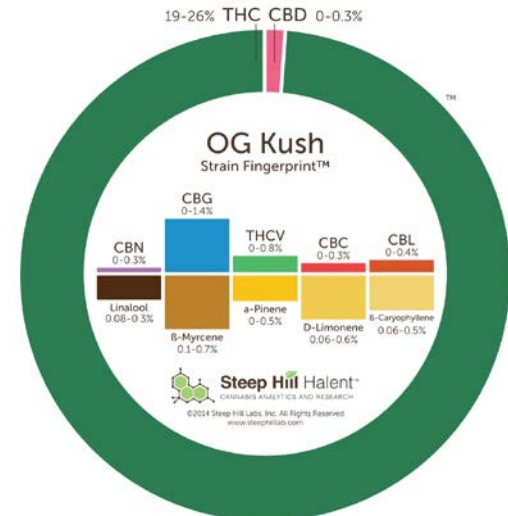
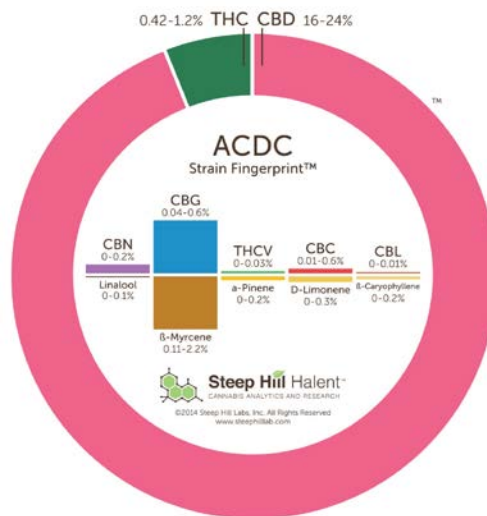
113 phytocannabinoids

Terpenoids

Trichomes

Flavonoids

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What we are really talking about

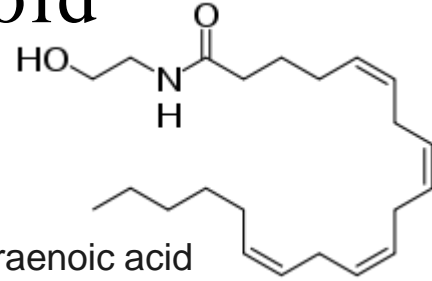
Chemicals that affect receptors:

CB1 - neural/central: acts as a neuromodulator to inhibit release of glutamate and GABA

CB2 - immune/peripheral: including immune suppression, induction of apoptosis, and induction of cell migration.

G-Protein coupled receptors

Anandamide - endogenous Cannabinoid



Is a fatty acid neurotransmitter derived from the non-oxidative metabolism of eicosatetraenoic acid (arachidonic acid) an essential ω -6 polyunsaturated fatty acid.

Anandamide is the precursor of a class of physiologically active substances, the prostamides.

The acute beneficial effects of exercise (termed as *runner's high*) seem to be mediated by anandamide in mice.

Anandamide is found in chocolate together with two substances that might mimic the effects of anandamide, *N*-oleoylethanolamine and *N*-linoleoylethanolamine.

Anandamide inhibits human breast cancer cell proliferation.

Anandamide is also important for implantation of the early stage embryo in its blastocyst form into the uterus.

Myth #1:

Pot is Pot, right?

No, different strains have different chemical compositions.

Different chemicals will have different effects.

Myth #2, Its for pain, right?

Uses of Cannabinoids: A brief History

- The earliest recorded history of Cannabis 3rd millennium BCE: Chinese Emperor Shen Nong - according to legend - discovered the healing properties of “Ma”, (and ginseng and ephedra)
- The Venidad, One of the books of the Zend-Avesta (by Zoroaster) records its medical Uses
- In Sanskrit its called “Ganja”
- Used to treat leprosy in Indian Medicine 600 BC
- Herodotus (484-425 BCE) Greek - describe the Scythians (a nomadic tribe in Asia) inhaling the smoke of “kanabis”
- The Greeks use it for earache, edema and inflammation.

1 AD - Ancient Chinese Text Recommends Marijuana for More Than 100 Ailments



Chinese ideogram for marijuana ("ma")

Source: *Marijuana as Medicine: Beyond the Controversy*, 2000

"In a compendium of drug recipes compiled in 1 AD [*Pen Ts'ao Ching*], based on traditions from the time of Shen Nung, marijuana is depicted as an ideogram [pictorial symbol] of plants drying in a shed. This ancient text... recommends marijuana for more than 100 ailments, including gout, rheumatism, malaria, and absentmindedness."

Janet Joy, PhD ★★☆☆ Alison Mack ★ *Marijuana as Medicine: Beyond the Controversy*, 2001

Uses of Cannabinoids: A brief History

Roman Medical Text *Pedanius Dioscorides* (70 CE) - describes both using the plant for rope as well as juice that was used to treat earache and suppress sexual longing (Martin Booth)

1500s Muslim Doctors used it to reduce sexuality (Mia Touw)

William Turner, the first English Botanist (1538) describes the plant as central to any Herbalists medicine cabinet. (M Booth)

Uses of Cannabinoids: A brief History

- English Clergyman and Oxford Scholar Robert Burton suggests Cannabis as a treatment for depression in his book **“The Anatomy of Melancholy”**, 1621
- 1799 Napoleon brought the Rosetta Stone and Cannabis back to France
- 1840 Brought to Europe from India by Sir William Brooke O’Shaghnessy, an Irish Doctor Studying in India, used to treat stomach pain and vomiting in cholera patients
- This was used by Queen Victoria to treat menstrual cramps
- Dr Joseph Moreau, a French Psychiatrist writes in 1840s how Marijuana suppressed headaches, increased appetites and aided people in sleep.

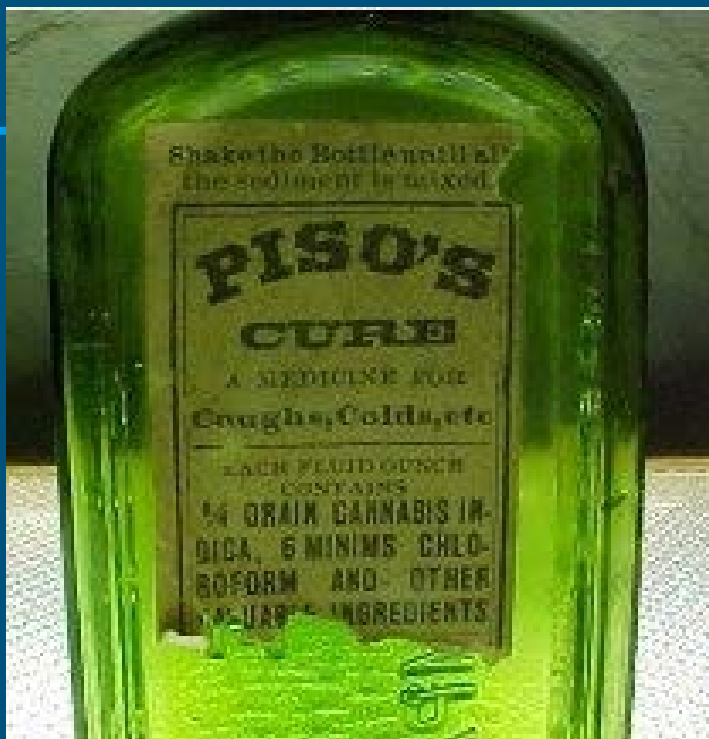
Uses of Cannabinoids: A brief History

1850 - Cannabis added to the US Pharmacopia

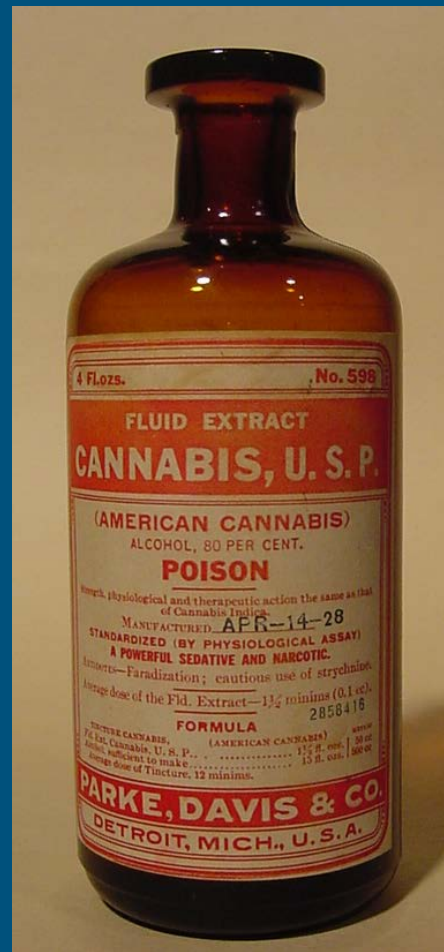
Indications: Neuralgia, Tetanus, Cholera, Rabies, Dysentary, Alcoholism, Opiate addiction, Anthrax, Leprosy, Incontinence, Gout, Convulsive Disorders, Tonsillitis, Insanity, Excessive Menstrual Bleeding, Uterine Bleeding, Etc.

- Boire, Feeny: Medical Marijuana Law 2007

1899 Lancet article by Dr EA Birch describe how to use cannabis for Opium and Chloral hydrate addictions



1906 Bottle



1930s Bottle

Beware! Young and Old—People in All Walks of Life!

This  may be handed you

by the friendly stranger. It contains the Ki
"Marihuana"—a powerful narcotic in whi
Murder! Insanity! D



WARNING!

Dope peddlers are shrewd! T
put some of this drug in the
in the or in the tobacco c

WRITE FOR DETAILED INFORMATION, ENCLOSED 12 CENTS IN POSTAGE—MAN

Address: **THE INTER-STATE NARCOTIC ASS**
(Incorporated not for profit)
53 W. Jackson Blvd. Chicago, Illinois

FULL CAST AND CREW

TRIVIA

USER REVIEWS

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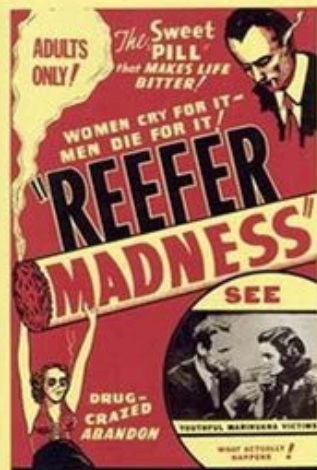
Reefer Madness (1936)

★ 3.8 / 10
6,653

★ Rate This

Tell Your Children (*original title*)

PG | 1h 6min | Drama, Thriller | 1938 (USA)



Cautionary tale features a fictionalized and highly exaggerated take on the use of marijuana. A trio of drug dealers lead innocent teenagers to become addicted to "reefer" cigarettes by holding wild parties with jazz music.

Director: [Louis J. Gasnier](#) (as Louis Gasnier)

Writers: [Lawrence Meade](#) (original story), [Arthur Hoerl](#) (screenplay) | [1 more credit](#) »

Stars: [Dorothy Short](#), [Kenneth Craig](#), [Lillian Miles](#) | [See full cast & crew](#) »

Reviews

115 user | 67 critic



Watch Now
With Prime Video



WATCH NOW



ON DISC

The tide turned...

Nov 24th 1976 Federal Court Rules that Robert Randall, afflicted by glaucoma, employed the (then) little used doctrine of medical Necessity. All charges dropped.

1978 - Federal Government starts Investigational New Drug - supplying cannabis to certain patients under “Compassionate Use”

1980 - Marinol (6 states sponsored studies comparing to smoking regular Marijuana: Thousands found marijuana safer and more effective, but FDA greenlights it anyway) - Schedule III

Tangent...(cough, cough) we're here about cancer....

J Natl Cancer Inst. 1975 Sep;55(3):597-602.

Antineoplastic activity of cannabinoids.

Munson AE, Harris LS, Friedman MA, Dewey WL, Carchman RA.

Abstract

Lewis lung adenocarcinoma growth was retarded by the oral administration of delta9-tetrahydrocannabinol (delta9-THC), delta8-tetrahydrocannabinol (delta8-THC), and cannabiniol (CBN), but not cannabidiol (CBD). Animals treated for 10 consecutive days with delta9-THC, beginning the day after tumor implantation, demonstrated a dose-dependent action of retarded tumor growth. Mice treated for 20 consecutive days with delta8-THC and CBN had reduced primary tumor size. CBD showed no inhibitory effect on tumor growth at 14, 21, or 28 days. Delta9-THC, delta8-THC, and CBN increased the mean survival time (36% at 100 mg/kg, 25% at 200 mg/kg, and 27% at 50 mg/kg, respectively), whereas CBD did not. Delta9-THC administered orally daily until death in doses of 50, 100, or 200 mg/kg did not increase the life-spans of (C57BL/6 times DBA/2)F1 (BDF1) mice hosting the L1210 murine leukemia. However, delta9-THC administered daily for 10 days significantly inhibited Friend leukemia virus-induced splenomegaly by 71% at 200 mg/kg as compared to 90.2% for actinomycin D. Experiments with bone marrow and isolated Lewis lung cells incubated in vitro with delta9-THC and delta8-THC showed a dose-dependent (10(-4)-10(-7)) inhibition (80-20%, respectively) of tritiated thymidine and 14C-uridine uptake into these cells. CBD was active only in high concentrations (10(-4)).

PMID: 1159836

[Indexed for MEDLINE]

Publication types, MeSH terms, Substances



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Similar articles

The inhibition of DNA synthesis by cannabinoids. [Cancer Res. 1976]

Effects of cannabinoids on L1210 [Res Commun Chem Pathol Pharmacol. 1977]

Delta9-THC as a discriminative cue in pigeons [Arch Int Pharmacodyn Ther. 1977]

Review Does Cannabis Composition Matter? Different [Curr Addict Rep. 2017]

Review Neuroprotection in Experimental Neuroinflammation [J Neuroimmune Pharmacol. 2015]

See reviews...

See all...

Cited by 25 PubMed Central articles

Review A user's guide to cannabinoid therapies in oncology. [Curr Oncol. 2016]

Review Endocannabinoid system as a regulator of tumor growth [Onco Targets Ther. 2016]

Guzman 1998 - Δ 9-THC induces apoptosis in C6 glioma cells

2000 - in vivo in Windsor Rats, 2003 - inhibition of angiogenesis, inhibition of endothelial migration and survival.

Massei - 2004 - CBD does this too

Blazques - 2004 - inhibition of VEGF system

Caffarel 2006 - Δ 9-THC arrests cells in G2-M via downregulation of Cdc2, CB2 receptor which was not seen in non-tumor breast tissue

- 2010: ErbB2-driven breast cancer progression through Akt inhibition

Carracedo - 2006 - apoptosis of pancreatic tumor cells via a CB2 receptor and de novo synthesized ceramide-dependent up-regulation of p8 and the endoplasmic reticulum stress-related genes ATF-4 and TRB3

Petrocellis - 2012 - prostate CA: in vivo and in vitro apoptosis via down-regulation of AR, p53 activation and elevation of reactive oxygen species.

What has been studied

Glioma, Breast, Colon, Prostate, Lung, SCC and NSSLCA

Skin: Basal

Leukemia: T Cell, AML, ALL

Cervical CA cells, Colangocarcinoma, Head and neck CA, Urological cancer

And more

NORML: <http://norml.org/library/item/gliomascancer>

Myth #2, Its for pain, right?

- Ok for “pain”
 - **A selective review of medical cannabis in cancer pain management.** [Ann Palliat Med.](#) 2017 Dec;6(Suppl 2):S215-S222. 2017 Aug 23.
 - Dose/Route
 - Strain not studied, receptors not studied
-
- Good in neuropathic pain (HIV/Parkinsons/MS)
 - Symptoms (nausea, anorexia) control

Myth #3: so you prescribe them a joint, right?

- Ground Flower
- Vaping
- Oral: Pills
- Edibles
- SL:Tincture
- Nasal Spray
- Rectal
- Dermal/Transdermal



Myth# 4: Schedule I drug

The federal government has classified marijuana as a Schedule I controlled substance.

Schedule I substances are defined, in part, as having:

- (1) a high potential for abuse;
- (2) no currently accepted medical use in treatment in the United States; and
- (3) a lack of accepted safety for use under medical supervision.

Federal law prohibits the manufacture, distribution and possession of marijuana even in states, such as Florida, which have modified their state laws to treat marijuana as a medicine.

1938 -NYC Mayor Fiorello LaGuardia requests the NY Academy of medicine
Conduct an investigation on Marijuana.

1944 - “The marihuana Problem in the City of New York” concludes that many
claims are exaggerated or untrue.

“The practice of smoking Marihuana does not lead to addiction in the medical
sense of the word...The use of marihuana does not lead to morphine or heroin or
cocaine addiction and no effort is made to create a market for these narcotics by
stimulating the practice of marihuana smoking..[It] is not the determining factor
in the commission of major crimes ...The publicity concerning the catastrophic
effects of marihuana smoking in New york City is unfounded.”

1970 - Controlled Substance Act - signed by Nixon - Repealed the Tax Act and listed it (along with Heroin and LSD) as a “Schedule I Drug: no medical uses, high abuse potential”

1972 - National Commission (Schafer Commission) released a report recommending “Partial Prohibition” and lowered penalties - Nixon and others ignored this.

1988 - DEA Judge Francis Young

5...there are simply no credible medical reports to suggest that consuming marijuana has caused a single death.

6. By contrast aspirin, a commonly used, over-the-counter medicine, causes hundreds of deaths each year.

7. Drugs used in medicine are routinely given what is called an LD-50...

8. At present it is estimated that marijuana's LD-50 is around 1:20,000 or 1:40,000. **[one] would theoretically have to consume nearly 1,500 pounds of marijuana within about fifteen minutes to induce a lethal response.**

15. In strict medical terms marijuana is far safer than many foods we commonly consume. For example, eating ten raw potatoes can result in a toxic response. By comparison, it is physically impossible to eat enough marijuana to induce death.

16. Marijuana, in its natural form, is one of the safest therapeutically active substances known to man. By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care."



Around
46
PEOPLE

die every day from overdoses involving prescription opioids.

Comparative risk

Deaths: In 2016, there were more than 63,600 drug overdose deaths in the United States.

Opioids: 42,000 in 2016

ETOH: Drinking too much can harm your health. Excessive alcohol use led to approximately **88,000** deaths and **2.5 million** years of potential life lost (YPLL) each year in the United States from 2006 – 2010, shortening the lives of those who died by an average of **30** years. Jan 3, 2018

Benzo: 12,000

Cannabis: 0

Motor vehicle - can double to triple the risk of crashing, no increase in deaths though...

Negatives

AMS

Addiction?

CYP450 inhibition

Can increase bleeding, can increase heart rate, can drop blood pressure: may lead to stroke

Myth #5: Everyone should be on it

- Just like putting antibiotics in the water, not a good idea.
- Lets not turn this into the next pill-mill
- Qualified doctors
- Proper Training - THERE IS NONE
- Reimbursement - ITS FEDERALLY ILLEGAL: you can't charge for it, you can't mention it in your notes or Medicare or other payers may take the \$ back
- Find a doctor who you trust to do the right thing

Thanks

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