commentary and correspondence

How Flimsy Can a Study Get?

Dunedin, a small city on New Zealand's Southern Island, has been the scene of a long-term data-collection effort focused on public health.

"Heavy Pot Use Tied to IQ Drop," is how *MedPage Today* played a recent study published online in *Proceedings of the National Academy of Sciences*. Many more headlines blare out the conclusions of the research team led by Madeline Meier, PhD, of Duke University. *MedPage Today* provides two "action points" at the top of their coverage for busy healthcare providers and bureaucrats whose attention span can't handle more than a summary of a summary

"• Individuals repeatedly diagnosed with cannabis dependence during young adulthood had noticeable declines in IQ scores by age 38, especially when the heavy use started in their teens.

"• Note that the study findings are consistent with speculation that cannabis use in adolescence, when the brain is undergoing critical development, may have neurotoxic effects."

The study by Meier *et al* involved a grand total of 23 individuals who had been diagnosed as "cannabis dependent" at least three times before age 18 (!)

The researchers compared scores from IQ tests taken before adolescence (ages 7 through 13) and again at age 38. They found that those who used heavily before age 18 lost an average of about eight IQ points by age 38, whereas those whose heavy use began after 18 lost almost zip.

The heavy users had been identified by the Dunedin Multidisciplinary Health and Development Study, which has tracked 1, 037 individuals born between April 1972 and March 1973 in a southern New Zealand City. Everyone in the Dunedin cohort gets interviewed every five years. In this process, 242 never reported cannabis use; 479 reported use but were not diagnosed with "dependence;" 80 were diagnosed with dependence once, 35 twice, and 38 three or more times.

"Adult-onset cannabis users did not appear to experience IQ decline as a function of persistent cannabis use," according to the investigators. They describe their findings as "consistent with speculation that cannabis use in adolescence, when the brain is undergoing critical development, may have neurotoxic effects."

Meier *et al* are confident their findings about heavy users who start early are valid, and expect the Corporate State Propaganda Machine to warn the masses. "Prevention and policy efforts should focus on delivering to the public the message that cannabis use during adolescence can have harmful effects on neuropsychological functioning, delaying the onset of cannabis use at least until adulthood, and encouraging cessation of cannabis use particularly for those who began using cannabis in adolescence," they advise.

Duke's press release was unrestrained: "Adolescent pot use leaves lasting mental deficits," said the headline. "The persistent, dependent use of marijuana before age 18 has been shown to cause lasting harm to a person's intelligence, attention and memory" declared the lead.

A paper in the *Proceedings of the National Academy of Sciences* by Dr. Ole Rogeberg criticizes Meier *et al* for failing to control in their study for socio-economic status. Rogeberg suggests that poorer kids were getting an initial boost in IQ when they first went to school but that this declined over time... We suggest that by age 38 the early-heavy-using dudes and dudettes of Dunedin could no longer take seriously the inane testing ritual. Maybe with every joint they had gotten not less intelligent but more cynical, more alienated.

John Harvard, Cambridge, Massachusetts

Pot Partisans Ponder The Significance Of Sequencing the Genome of Cannabis

"Unnecessary"

"From my point of view" said a plant breeder who requested anonymity, "genetic modification is unnecessary. We can do almost anything we want without resorting to actual genetic modification.

"Elucidating the genome to see what compounds the plant produces by what pathways, and how everything is synthesized and regulated, will maybe, eventually, enable drug companies to tweak a step in the process so that plants produce a lot of something that they previously produced only in small amounts.

"But isn't that what conventional (albeit high-tech) plant breeders have done? We find a plant that has an unusually high amount of, say, CBC. We breed it with our next best plant and keep doing so for generations —or until we find the rare plant that lacks the enzyme to go further than CBC.

"We can also 'self' a plant of interest— give it hormones so that it becomes a hermaphrodite. The CBC-rich female plant makes pollen, fertilizes itself, and produces some seeds with a much higher CBC content. Plants from those seeds, having been inbred, tend to be weak. They might produce more cannabichromene but have a poor growth habit, few flowers. So you cross them back with something that's vigorous and has lots of trichomes. The progeny include plants that are both vigorous and produce a high quantity of CBC."

GMO Cannabis

Genetically modified organisms (GMOs) are created by inserting genes from another organism to create what the experimenter considers desirable traits. According to our most respected source, the prospect of "GMO Cannabis" is something to start thinking about.

"The great danger is, you never can tell the ramifications. Monsanto has genetically engineered the Bt protein into corn plants. [*Bacillus thuringiensis* produces a pest-killing crystal.] So every cell in the corn plant is now producing its little cache of toxins. The corn borers will bore in and eat these cells. Fine for Monsanto.

For me as an organic vegetable gardener I've relied on Bt, using it very selectively. When the bugworms are coming out, that's when I spray —and there's never been any resistance to Bt.

"But now you've got vast acreages of corn producing Bt all the time and that selects for resistant organisms. It's just a matter of time before organic gardeners are going to lose their best weapon against corn borers. It's almost like a rear-guard sabotage action against organic farmers. That same borer also attacks cannabis. So maybe people will decide to monkey with the plant and introduce traits that they think are desirable..."

GMO cannabis seems sort of disrespectful. The plant has provided so many variants on its own.

How Seriously Should We Take the USC Study Linking Cannabis use to Testicular Cancer?

In early September a University Of Southern California research group led by Victoria K. Cortessis MSPH, PhD, reported —according to the headlines summarizing their study— that there is a doubling of the risk of testicular cancer in young men who consume cannabis. The study itself, "Population-based case-control study of recreational drug use and testis cancer risk confirms an association between marijuana use and nonseminoma risk," was published online by the journal *Cancer.*

Cortessis *et al* analyzed data from 163 young men who had been diagnosed with testicular cancer in Los Angeles County and 290 controls. Both groups had been interviewed about their health and drug use between December 1986 and April 1991. Among those who developed testicular cancer, 81 percent were found to have used marijuana at some point in their lives. Among the controls, 70 percent had used marijuana.

The paper concluded, "The current results warrant mechanistic studies of marijuana's effect on the endocannabinoid system and [testicular cancer] risk and caution that recreational and therapeutic use of cannabinoids by young men may confer malignant potential to testicular germ cells."

Cortessis was not modest about the import of her findings. "It is hard to imagine a scenario whereby it is due to chance and I can't think of a systematic bias that would cause this," she told the media. "I will feel very confident that this is cause and effect once we have worked out the biology... This is the third study consistently demonstrating a greater-than-doubling of risk of this particularly undesirable subtype of testicular cancer among young men with marijuana use... I myself feel like we need to take this seriously now."

Dr. Frankel's Perspective

We asked Allan Frankel, MD (whose daughter, BTW, recently graduated from USC medical school) how seriously he took the paper in *Cancer*. He replied:

1. The study group was way, way too small. How can you have a control group of less than 150 men for a study like this, when the incidence of Testicular Cancer is 0.4% or 1 in 280! In my opinion, this alone makes the report useless.

2. It is reported that the higher-dose users of cannabis did NOT have an increased incidence of testicular cancer. In fact, heavy users actually had a reduced likelihood of developing testicular cancer. It makes no sense that the alleged tumor-causing effect would not be dose-related.

3. There are significant differences in the two cohort groups they studied. With a study in young males there are many issues that must be controlled for, including which soft drinks they consume, the level and nature of their activities (sports, sitting at the computer, etc.), their sexual patterns, whether they'd been breast fed, and so forth.

4. This type of simple retrospective "survey" study cannot establish cause and effect. According to the medical establishment's own criteria, the only studies that can show cause and effect are prospective controlled studies.

5. "The people who had been diagnosed with Testicular Cancer were less likely than controls to report religious affiliation." This is a direct quote. Are they suggesting that church activities somehow protect against testicular cancer?

6. Another absurd finding was that cocaine "protected" against testicular cancer. This seems as unlikely as cannabis inducing it..

7. With increasing frequency, sound scientific studies documenting the anti-cancer properties of CBD and THC are being published in peer-reviewed journals. If I had testicular cancer, I would take CBD + THC in as large a dose I could tolerate, which would probably be a lot.

8. A reader of my blog noted that Northern Europeans have a higher rate for that particular cancer. And 70% of the group who didn't have cancer used marijuana. I believe all the survey proved is that 70-to-80% of young American adult males use marijuana.

Contaminants influencing data?

Jeffrey Raber, PhD of The WercShop suggests that "some of these apparently cannabis-based adverse causes might be coming from contaminants in the supply. With what we have seen in terms of contamination, it would appear far more likely that pesticides are the culprit, as they are known to be carcinogenic."

Dr. Abrams Comments:

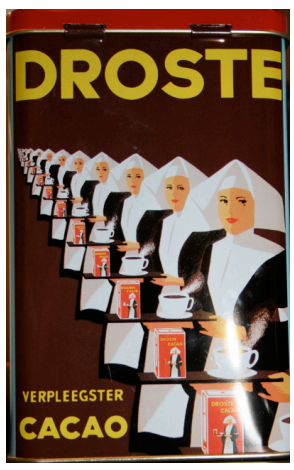
This is the third study to suggest the same association. Is it just that cannabis is used by young men and they are also the ones who get testicular cancer? Matching by age, etc. should take care of that.

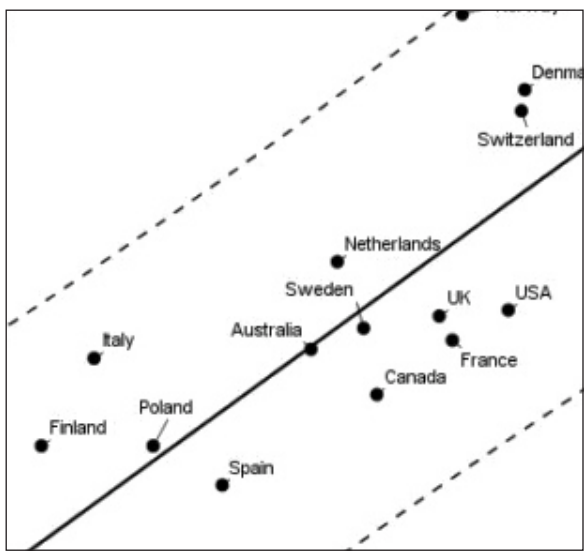
The Los Angeles study did not really match all that well. None of the odds ratios were significant unless the findings were adjusted. And even when adjusted, the odds ratios were all less than 2.0, which suggests that the association is not that robust.

Plus, there is really little biologic explanation as to why there would be this association even though the authors try to make a case.

Finally, what about Jamaica? Where's the association between testicular cancer and marijuana use in Jamaica?

I came across an article that shows that testicular cancer rates around the world are directly correlated to the amount of cocoa consumed, so go figure.





Cocoa consumption and testicular cancer rates were correlated in a 2009 study by Fabrizio Giannandrea. Vertical scale shows incidence of testicular cancer per 100,000 18-24 year olds. Horizontal scale shows cocoa consumption per capita in kilograms per year. Data was gathered from 18 countries. Rates were highest in Germany and Denmark, lowest in China and India. Source: *Int J Environ Res Public Health. 2009 February.*