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# A COMMON SENSE APPROACH TO MARIJUANA THERAPY

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## INTRODUCTION

A recent *Journal of the American Medical Association* study recorded a notable increase in the number of pregnant women using marijuana<sup>1</sup> during pregnancy, where some dispensaries may be encouraging using marijuana products for pregnancy-induced nausea.<sup>2</sup> Also, marijuana is often used by many as an effective daily/nightly sleep aid. Yet, are these practices safe? Unfortunately, tight restrictions on U.S. laboratory research on effects of marijuana use render medical information almost non-existent, creating a vacuum filled with casual information and conjecture, and leaving many ailing patients with little on which to base decisions on therapeutic marijuana use.

## THERAPEUTIC MARIJUANA FOR MORNING SICKNESS AND INSOMNIA

Individuals and their doctors should be making appropriate marijuana therapy determinations, but with that freedom comes some personal responsibility based on common sense when deciding to use marijuana for a given malady. A starting point is understanding what current medical and scientific research does and does not say about a few specific use cases of marijuana.

### *Pregnancy*

Early studies on the effects of marijuana use during pregnancy suggested that it resulted in lower birth weights and more preterm births.<sup>3</sup> However, these studies failed to truly isolate marijuana use as the causal factor, and once other factors were controlled for, such as alcohol and tobacco use, the relationship between marijuana and negative health effects disappeared. One meta study of the topic concluded that there were no identifiable patterns in negative health outcomes for mothers or babies who used marijuana.<sup>4</sup>

### *Sleep*

A 2017 meta-study of cannabis and sleep concluded that while the CBD component (the non-inebriating variety) of cannabis could benefit sleep, prolonged THC use (marijuana) could impair sleep quality long term, specifically by blocking the “dream” state of stage 5 rapid eye movement (REM) sleep.<sup>5</sup> However, the meta study provides many results that conflict with this assertion, and concludes that there are no clear and direct connections between marijuana and sleep disruption when other factors, such as attitudes and depression symptoms, were accounted for. And yet more new research suggests it may block critical REM sleep patterns, causing fatigue and a host of other health-related effects.<sup>6</sup>

## GENETICS AND THE INHERENT LIMITS OF RESEARCH

Many times in contemporary history, studies have claimed to know the health benefits or dangers of a substance, only to find later that the conclusions were false. One could point to government nutrition research from the 60s—that eating fat causes heart diseases and premature death—now accepted as patently false as perhaps the best example.<sup>7</sup> The list goes on: don’t eat too many eggs, caffeine causes heart disease, and so on.

The fact is that science is far from certain about what is healthy for our bodies to consume, and is an ongoing work in progress. A randomized control trial and its various subsets offer a fairly effective way of navigating these waters, but still have important drawbacks, like confounding factors, that limit their ability to make firm causal conclusions from situations like marijuana use in which only observational data are available due to the practical and ethical barriers to running truly experimental studies. Furthermore, many of these studies and their aggregate data fail to meet the important Bradford-Hill causality criteria<sup>8</sup> especially crucial in epidemiology, such as temporality, consistency, and biological gradient. Indeed, specifically as it relates to consistency, there may be a “crisis” of reproducibility in biomedical research; one journal was unable to reproduce some 70% of its results.<sup>9</sup>

At our current level of scientific ability, research on genetically complex subjects such as marijuana and human beings is far from the more solid knowledge we have of thermodynamics—and yet we act as if they are similar, perhaps through wishful thinking. The scientific findings of thermodynamics took decades of careful examination and repeated experience to establish, for example, that no matter which external factors change around in the world or how many different ways experiments are run, water will change its state relative to the temperature. All relevant factors are included in the experiment and the results are perfectly predictable every time. While few dispute physical truths such as this, even the “laws” of nature are up for revision. Newton’s theories of time were mathematically consistent with current observations until Einstein rewrote the laws of time with the theory of general relativity, and quantum mechanics still lurks with the potential to re-engineer fundamental theories of physics.

Unfortunately for social and biomedical scientists, both marijuana and humans, as scientific subjects to be studied like atoms, are more genetically complex and contain more internal heterogeneity that cause them to react to outside stimuli more unpredictably than a water molecule. Our knowledge of the complex system that is the human body is still quite limited, with the main electrochemical system that interacts with marijuana, the endocannabinoid system (ECS), being discovered only 30 years ago.<sup>10</sup>

We know that, at a minimum, marijuana activates the ECS by turning off or amplifying the brain receptors that regulate emotions like fear, excitement, and anxiety.<sup>11</sup> However, many important synapses of the brain remain unmapped, leaving a lot of guesswork for biomedical researchers not specifically trained in neuroscience and the rapid advancements occurring in that field. It is definitionally impossible to know what you don’t know and it is certain that some properties of the brain elude our knowledge. Anyone claiming to know the

full impact of marijuana on the brain has many unknown confounding factors to deal with that could very well invalidate their claims.

While the human genome project was declared complete in 2003, some researchers claim that up to 8% still remains to be coded.<sup>12</sup> That may not sound significant, but when considering that apes and humans are approximately 90%-95% genetically similar, that 8% could contain sequences that are key to our understanding of disease and human physiology. Researchers know that CB1, the main receptor of the psychoactive ingredient of marijuana, is found in both the ECS and the central nervous system (CNS) where it is one of the most abundant receptors.<sup>13</sup> The category of p450 enzymes and specifically CYP2C9 have recently been found to be vitally important in the metabolization and oxidation of many drugs, including marijuana.<sup>14</sup>

It may be tempting to think about the human body as a static thing to be studied like atoms and molecules, but more careful examination shows that we are undergoing chemical and genetic changes all the time that are not fully understood or properly recorded. This is acutely important for drug-metabolizing enzymes, “numerous variants of drug-metabolizing enzymes have been discovered since the completion of the human genome project... establishing the impact of the newly identified genetic variants from genomic studies on drug therapy remains a major challenge.”<sup>15</sup> Indeed, genetic research has re-shaped part of our understanding of the largest health debate of the 20<sup>th</sup> century: tobacco smoking. Ronald Fisher, one of the godfathers of modern statistics, was wrong about tobacco smoke—it certainly does increase the risk of cancer. But he was right about the fact that pharmacogenetics plays an important role in epidemiology, something not commonly accepted in his time.

In the late 2000s several studies began to converge on a few gene variations that appeared to motivate the initiation of smoking and cause the same kind of cancer as tobacco smoking. By 2012 and several meta studies later, it was concluded that the genes could cause the cancer without ever smoking, but even more interesting was the finding that, “carriers of the higher risk variant... are exposed to more nicotine and toxins than those who don’t carry the variant... For the same number of cigarettes smoked, these high-risk individuals are at even higher risk.”<sup>16</sup> The study estimates that 56% of people carry one or two of the gene variations, and that the risk of cancer is roughly 70% higher for those carrying both variants. This does not change the fact that smoking tobacco at all is a risk, but has helped epidemiologists determine how individual genetic heterogeneity scales the level of risk. The amount of tobacco smoke a human body can process without causing disease has a large degree of variation, meaning there is an unknown range of people who can smoke

significant amounts of tobacco with little to no health consequences all the way to those who smoke very little and contract diseases. Good studies inform us of facts like these but cannot inform a given individual on their situation, and we risk committing the ecological fallacy by attempting to universalize the findings of studies down to the level of the individual.

One more example makes the point clearer—lactose intolerance. Genetic research shows that up to 95% of northern Europeans can tolerate lactose, meaning their body naturally produces an enzyme called lactase which digests milk. Some estimates reverse that number for those of east Asian and African descent—around 90% are intolerant.<sup>17</sup> This is all a result of genetic variation over time, and humans aren't the only ones changing. One can see the challenge laid out for biomedical researchers—trying to ascertain a universal effect of drugs on subjects that are not universally similar across geography and time.

Cannabis varieties themselves are similarly unique. For example, informal knowledge suggests that indica-based strains of marijuana induce a sleepy, relaxation response while sativa-based strains induce more uplifting but possibly stress-inducing responses. But is this scientifically true? Some experts correctly point out that genetic testing of the chemical compounds in marijuana do not provide the clear sativa versus indica distinction, but show hundreds of compounds that exist along a spectrum, creating a variety of different marijuana plants with varying genetic structures and potential physiological effects. These experts contend that, for future marijuana products to maximize safety and efficacy, full chemical profiles should be delivered with every product to maximize our understanding of how marijuana interacts with humans.<sup>18</sup> A much-improved understanding has been forged through the Open Cannabis Project and Sunrise Genetics,<sup>19</sup> but perhaps we are still in the infant stages of understanding the true chemical and therapeutic nature of cannabis.

Nearly every biomedical study of cannabis to this point has failed to fully incorporate both genetic varieties into the model, leaving large confounding factors outside statistical modeling, and will continue to do so until we incorporate the genetics of both subjects. This discrepancy holds true for THC and non-THC varieties of cannabis as well. Indeed, studies find THC's psychological effect on humans is highly individualized.<sup>20</sup> CBD's therapeutic effects have been much talked about and there is developing evidence that it may effectively treat seizures as well as general pain and nausea, perhaps not by "curing the pain" rather by simply blocking or disrupting neuron pathways, but the majority of research shows no conclusive causal effects—good or bad.<sup>21</sup> It is incredibly unlikely that CBD positively treats as many ailments as many claim it does.<sup>22</sup>

Genes are powerful in shaping our physiology but are far from being the only factor. Many other non-genetic factors impact our response to drugs, including but not limited to food/drug interactions, drug/disease interaction, drug/drug interaction, age, environment, and many others. When we incorporate these factors, the number of potential results expands exponentially (thus explaining why there are so many conflicting and non-reproducible biomedical studies with varying outcomes.) The resulting logic is that there is no “effect of marijuana on humans” stated plainly and universally. So if we cannot always make universal claims about causal health outcomes of marijuana use, how do we make policy decisions about people’s choices?

## A CAUTIOUS, COMMON-SENSE APPROACH

For morning sickness, would mothers prefer to take marijuana, Ondansetron, or the FDA-approved Diclegis, the latter of which was banned in 1983 but is now back after a handful of studies? Nine out of ten women already take some kind of drug during pregnancy.<sup>23</sup> Would those with insomnia rather use marijuana, Butisol, or Zolpidem? Zolpidem directly caused over 19,000 hospital visits in 2010, up from 5,000 visits in 2005, and is still on the market.<sup>24</sup> The long-term effects of these drugs are as unknown as marijuana itself.

Or should pregnant women abstain from all drugs and suffer whatever health conditions may arise during pregnancy to make it as “natural” as possible? For insomniacs, what is more deleterious to health: suffering the long-term health effects of sleep deprivation or the long-term effects of marijuana and drug use?

These questions bear out the conclusion that there is not, and should not be, a universal answer that applies to everyone, especially not one that is applied with the force of government. There is no completely disinterested third party who is so intimate with another’s genetic and chemical biology, environmental factors, and the drug in question, that they could read an academic journal and tell them exactly what and what not to do, except perhaps a physician. Decisions to consume or not consume carry risk, whether they are known, unknown, endorsed by science and the government or not. Even if marijuana is a “natural” substance, natural substances, like harmful chemicals, can still be abused, and it is certainly true that marijuana affects biology even if the extent of these impacts, good or bad, short or long term, remain unknown.

However, instead of laws restricting choice, consumers should be encouraged to exercise some logic and common sense in their approach to marijuana therapy. To ensure that pregnancy, sleep, and biology remain absolutely unaffected by marijuana and other drugs, abstinence is the only true option. This applies to any drug or substance, such as the smoking and cancer example. Minimizing the chance of lung cancer demands abstinence from smoked tobacco. Yet there are many people for whom mild tobacco use represents little to no risk yet brings much personal enjoyment. There is a massive gap between the scientific conclusion that zero tobacco smoke is the safest option and the government absconding the right to buy and use tobacco as the individual deems acceptable. Yet even in the absence of such knowledge with marijuana, governments have readily abused this individual liberty.

With all our advancement in medicine and drug knowledge, it is also true that abstinence from drugs is a risk in and of itself. Persistent lack of sleep and constant vomiting during pregnancy could be worse from a health perspective than therapeutically using marijuana. Could light marijuana use during pregnancy be safe for some women? Could it be that the form of marijuana administration, primarily smoking, which displaces oxygen in the body and across the placenta, is what is causing negative health findings? What if all these studies were replicated to administer subjects a CBD/THC oil or pill instead of smoking? Could marijuana harm some, not affect others, and help others?

All of these outcomes are entirely possible, but unknown. Ideally, a full genetic profile of the patient as well as the plant would be available wherein physicians could know beforehand whether a patient's genetics were compatible with the type of marijuana being administered. But this reality is far from present capability. Consumers and policymakers are thus operating in a place void of firm scientific knowledge, meaning there should not be any firm restrictions on adult marijuana use that claim to be based on public health.

## CONCLUSION

Expectant mothers in legal states should still have the option to use medical marijuana should they desire, without continuing to face the litany of criminal charges and penalties put forth for mothers who test positive for THC.<sup>25</sup> However, they should also be aware that the science being put forth by marijuana advocates could be as shaky as the science that created the anti-marijuana movement. Marijuana may effectively abate nightly insomnia, but patients and users should not be fooled into thinking additional sleepiness from consuming marijuana is the extent of the effect on the body and brain. Given the structural

flaws in marijuana research, there is simply very little that we can claim about the way it impacts individuals. Government should not endorse the science on either side of the issue, but rather encourage more research on the topic so that the void of knowledge is diminished as much as is possible, and allow patients and their doctors the freedom to decide what is best in their unique circumstances without imposing injurious penalties.

## ABOUT THE AUTHOR

**Spence Purnell** is a policy analyst at the Reason Foundation, where he works on pension reform, Florida policy issues and economic development. Spence has worked on cannabis policy for the last two years with a focus on market design, taxes, and expungement. His work is being featured in Florida, Colorado and Michigan.

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*For more on cannabis policy, see [reason.org/topics/drugpolicy](https://reason.org/topics/drugpolicy)*





# ENDNOTES

- <sup>1</sup> A variety of cannabis plant, marijuana contains tetrahydrocannabinol (THC), which is an inebriating substance. Cannabis also has varieties with little or no THC, some of which are used to produce therapeutic CBD creams, oils or other products containing the non-inebriating “cannabidiol.”
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- <sup>7</sup> Garcia, Alexis. “How Big Government Backed Bad Science and Made Americans Fat.” *Reason Magazine.* May 2018.
- <sup>8</sup> The “Bradford Hill Criteria”—a set of nine criteria—have become the most frequently cited framework for causal inference in epidemiologic studies.

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<https://www.nydailynews.com/new-york/weed-dozen-city-maternity-wards-regularly-test-new-mothers-marijuana-drugs-article-1.1227292>