Spring 2016

Legalizing Marijuana Medicinally to Help Weed Out Cancer

Richard Tafoya
Regis University

LEGALIZING MARIJUANA MEDICINALLY TO HELP WEED OUT CANCER

A thesis submitted to
Regis College
The Honors Program
in partial fulfillment of the requirements
for Graduation with Honors
by
Richard Tafoya
May 2016

Thesis written by
Richard Tafoya

Approved by

Catherine Kleier

_____

Thesis Advisor

Jay Campisi and Nicholas Kallan

_____

Thesis Reader or Co-Advisor

Accepted by

Thomas Howe

_____

Director, University Honors Program
Senior Thesis Handbook 21

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Acknowledgements

I would like to thank Dr. Campisi, Dr. Kallan, and Dr. Kleier for helping me complete this thesis. I would like to thank them for all of the hard work and dedication they put in to make sure that my thesis was well developed. I would also like to thank the Honors program and the Honors directors, Dr. Howe and Dr. Kleir, for making this all possible. Lastly, I would like to thank Regis University and all my friends and family for everything that they have done for me.

Abstract

Throughout the years, marijuana has been looked down upon with a negative connotation because of its label as a scheduled 1 drug, and because of this, it has not been given the chance to do good in the medical world. In areas where medicinal marijuana is illegal, testing with marijuana in hospitals is very strictly regulated, and this may be hindering the discovery of finding alternative treatments for diseases. Marijuana for the most part is only being used as a symptom management for cancer patients. This symptom management includes prevention of nausea, help to gain weight, and pain reduction for patients undergoing various cancer treatments in specific states in the U.S where medicinal marijuana is legal. Studies have shown that marijuana may be an anti-cancer drug and that the cannabinoids in marijuana may actually be able to inhibit cancer growth in humans. Cannabinoids in marijuana have also been shown to improve the quality of life for many patients with debilitating diseases. This may be the cancer treatment we have been looking for, but before one can confirm this assumption, more research and testing with marijuana needs to be allowed. Making testing and researching legal in hospitals throughout the U.S may help us fight off cancer and slow down its progression.

Marijuana also has the ability to improve the overall quality of a patient's life while they are undergoing cancer treatments. However, as we have seen with

legalizations of marijuana in certain states in the past, there are always going to be pros and cons with the implementation. Risks that come along with recreational marijuana are too high in terms of negatively affecting society and adolescent development, but medical legalization could work with tightly held regulations. Medical legalization would economically benefit society, and would make research on the drug easier. Medical marijuana should be made legal throughout the U.S. to help make research easier so that we can better understand the possibilities of using marijuana in various types of medical treatments including cancer treatments.

Chapter 1: An Introduction to Marijuana and its Reputation in Society

The government has extremely mixed feelings when it comes to the topic of legalizing marijuana. For several decades, marijuana has been looked at as a scheduled 1 drug as well as a gateway drug that does not benefit society. A gateway drug is a drug that leads to harder and more dangerous drugs that could severely damage someone's life as well as others lives. Often times, people overlook gateway drugs and just think that people are being ridiculous and overcautious, but gateway drugs are a real thing and they do lead to dangerous decisions with extreme consequences. Some of these consequences that may come with the legalizing of marijuana include increased crime rates, increased drug trafficking, and increased drug use (Morris, 2006). There have been several studies that show that gateway drugs impair the user's decision making which can lead to using illicit drugs that can do severe damage. The use of marijuana in adolescents has been correlated with the use of harder and more dangerous drugs in these people when they become young adults (Morris, 2006). They become comfortable with the drug of marijuana which makes them more comfortable to expand their horizon to other drugs. Sometimes these drugs are worse and sometimes they aren't, but the point is that when people become comfortable using one drug it makes them think that other drugs aren't as bad as the government says they are. In turn, harder drugs are used after one consistently uses the gateway drug marijuana. This is why the governmental and societal outlook

towards marijuana is a negative one. Because of this outlook, medicinal marijuana and its possible treatments have suffered.

However, even though marijuana has a bad reputation with a lot of society and the government, marijuana can help us in many areas when it comes to healthcare. Medical marijuana is actually very useful. It can drastically improve certain patient's symptoms and pain. Marijuana has the potential to help treat several different diseases that other drugs are unable to do. But because marijuana is a schedule 1 drug, medical researchers and hospitals have been unable to tap into this possible phenomenon that marijuana has to offer in terms of treating deadly diseases such as cancer, AIDS, HIV, and many others. Hospitals in Canada and other countries are allowed to do research on this drug and there have been signs that it could be used as an extremely positive treatment for many diseases. There are many positive effects that can come about from marijuana, and more research in terms of cannabinoids as a cancer antagonist in the U.S needs to be applied to better understand its pathways and mechanisms. Marijuana has an unknown world to offer, but one must be able to tap into this world to see its benefits and risks. Research has shown that marijuana can inhibit the spreading of cancer cells. This could change current cancer treatment options because the current therapies are not ideal for patients for many reasons. Marijuana could be the answer for a more ideal option.

Marijuana has been legalized to perform research on humans to learn about medical uses for cannabinoids. According to Clinical Trials.gov, there are currently at least 20 studies that have occurred in the U.S dealing with testing the effect of cannabinoids on cancer in humans. Several of these studies were terminated for

governmental reasons before results were obtained. However, almost all of these clinical trials are using cannabinoids for more of a symptom management drug, specifically to alleviate pain and nausea, rather than an actual cancer antagonist. Researching the effect marijuana has on humans is a step in the right direction, and several studies have shown that marijuana does a fine job at helping with the symptoms that most cancer patients express. It is great that testing of cannabinoids for symptom management is happening, but there may be more that cannabinoids can bring to the table against cancer. There have been studies that show cannabinoids may actually be able to kill cancer cells, and I believe that we need to switch paths that research on cannabinoids is going towards. Instead of just testing cannabinoids on cancer as a symptom management drug, we need to investigate how cannabinoids can affect the cancer cells themselves. Clinical trials using cannabinoids as a symptom management drug is a start, but more testing needs to be done in the area of cannabinoids as a cancer antagonist.

Chapter 2: Cancer and its Properties

Cancer cells are very different than other cells because they grow and spread uncontrollably, and they do not die off over time. Instead of dying off, they continue to grow and form new, abnormal cells. Secondly, cancer attacks and invades our normal tissues and cells which allows them to be very evasive from our immune system (Kerr, 1994). Basically the only way to kill of the cancer is through some form of cancer treatment, and often times those don't even work. This is why cancer is so harmful and dangerous to our bodies.

Cancer is a very dangerous disease, and often times it develops from DNA (deoxyribonucleic acid) damage. DNA is the basis of our existence and is everywhere in our body, and it is very vital that it repairs itself so that our body functions correctly without any hitches. Normally DNA repairs itself correctly or gets degraded. But when this does not happen due to some mishap or mutation in the body, cancer cells come about. These cells then continue to replicate out of control and quickly start to spread. These cells then sometimes clump together and form dangerous tumors in our body. The tumors begin to crowd healthy tissues causing grave harm to our bodies (Knudsen, 1971). Eventually the cancer in our bodies will kill us if current cancer treatments don't get rid of the harmful cells. This is why cancer is so dangerous. It is very difficult for our bodies to try and control the spreading and dividing of these cancerous cells, and even the current treatment options often fail in the targeting and destroying of cancer. A new

treatment needs to be researched to control cancer more effectively and improve the quality of life for patients.

Chapter 3: Cancer and Current Treatments

One of the most common forms of cancer treatment involves chemotherapy. Chemotherapy is a fairly effective treatment for inhibiting cancer, but it is not the most ideal therapy in terms of how the patient feels while undergoing this process. Chemotherapy is often used with many other treatments such as radiation. Radiation and chemotherapy attempt to target, shrink and kill cancerous cells to prevent them from uncontrollably dividing and spreading throughout the body. When cancer cells uncontrollably divide and spread they start to form harmful and painful tumors. Preventing this spreading and dividing helps relieve pain in the patients from the cancerous tumors. The radiation and chemotherapy kill off good useful cells in the body and this comes with several negative side effects such as fatigue, sickness, nausea, and loss of appetite. Other side effects that may occur in patients include mood disturbance, sleep disturbance, and various types of pain (Cheng, 2013). All of these side effects are very serious and need to be taken into consideration when prescribing cancer treatments. Undergoing these treatments for many patients is often times unbearable and the quality of life during treatment is not very ideal.

The current treatments are the best ones that we have for the atrocious disease of cancer and alternative treatments are being researched every day to find better options. Current treatments come with several consequences, and this is why research of marijuana on cancer cells needs to be allowed. Signs have shown that marijuana could

help, and now we must take hold of these signs and put marijuana's potential abilities to use. Marijuana may be a better alternative treatment to fight cancer, or at the least could be used medicinally to help improve the quality of life for the patient by lessening symptoms from current cancer treatments.

Chapter 4: How Marijuana and Cannabinoids Trigger Body Functions

Marijuana is a very interesting option for a treatment that needs to be further researched. It is a very interesting drug that has very unique characteristics that make for a possible treatment to fight cancer. It is capable of perfroming these tasks because it can bind to cannabinoid receptors in the body. This binding induces certain pathways to activate in the body.

The system in our body that is affected by marijuana is the endocannabinoid system. This system consists of endocannabinoids (endogenous ligands), cell signals, cannabinoid receptors, and neurons. The cannabinoid receptors are CB1 (cannabinoid-1) and CB2 (cannabinoid-2), and these receptors are located all throughout our bodies. CB1 is in the central nervous system and CB2 receptors are primarily in peripheral tissues and central immune cells. On each of these CB receptors, several endocannabinoids are synthesized to act on these receptors as mediators for cannabinoid effects in the body. These endocannabinoids are formed within neurons and other cells by the multiple biosynthetic pathways. They are produced on demand from membranous fatty acids from the activity of phosphodiesterase enzymes. This occurs after cellular stimulation from certain signals, and this causes the release of active endocannabinoids. After the endocannabinoids are released they can bind to the cannabinoid receptor, or they are degraded if they are not needed. Once they bind to the extracellular portion of the CB receptor, they then send out signals to neurons throughout the body that stimulate several

senses. These signals control appetite, sleep, memory, immune function, energy, stress response and several other functions throughout the body (Seamon, 2007).

When one smokes or ingests marijuana, the endocannabinoid system is activated. Marijuana is the crude product of the plant *Cannabis sativa* and *Cannabis indica* and contains over 460 active chemicals of which many of them are cannabinoids. The major active ingredient in marijuana is THC (Tetrahydrocannabinol), and it is primarily responsible for the therapeutic effects triggered in the body. Also the quantity of THC determines how intense the effects will be. When smoked or ingested, THC passes rapidly from the lungs into the bloodstream to a number of bodily organs. This causes CB receptors to become overloaded with an abundance of cannabinoids that are acting as endocannabinoids. This causes an increase of signaling in the endocannabinoid system which causes certain effects to take place such as appetite stimulation, energy change, and many other effects. Other common effects include anti-inflammatory and antinociceptor responses, and this is why patients that receive marijuana treatment feel less pain when they are sick or undergo certain treatments. Also because of the fact that cannabinoid receptors are all over our body, one experiences a wide range of side effects from marijuana in various regions of the body. Not only will it alleviate inflammation and pain-like symptoms from the cancer, marijuana will also alleviate pain induced from the chemotherapy, radiation therapy, and other current cancer treatments offered to patients in today's hospitals. Marijuana could be added on to other current treatments to improve the quality of life for cancer patients by improving their overall mood, increasing their appetite, and alleviating pain. Improving the quality of patient's life is

one of the most important aspects in the medical industry, and this is why research on marijuana needs to be done so that one can see how much marijuana would improve the quality of a patient's life.

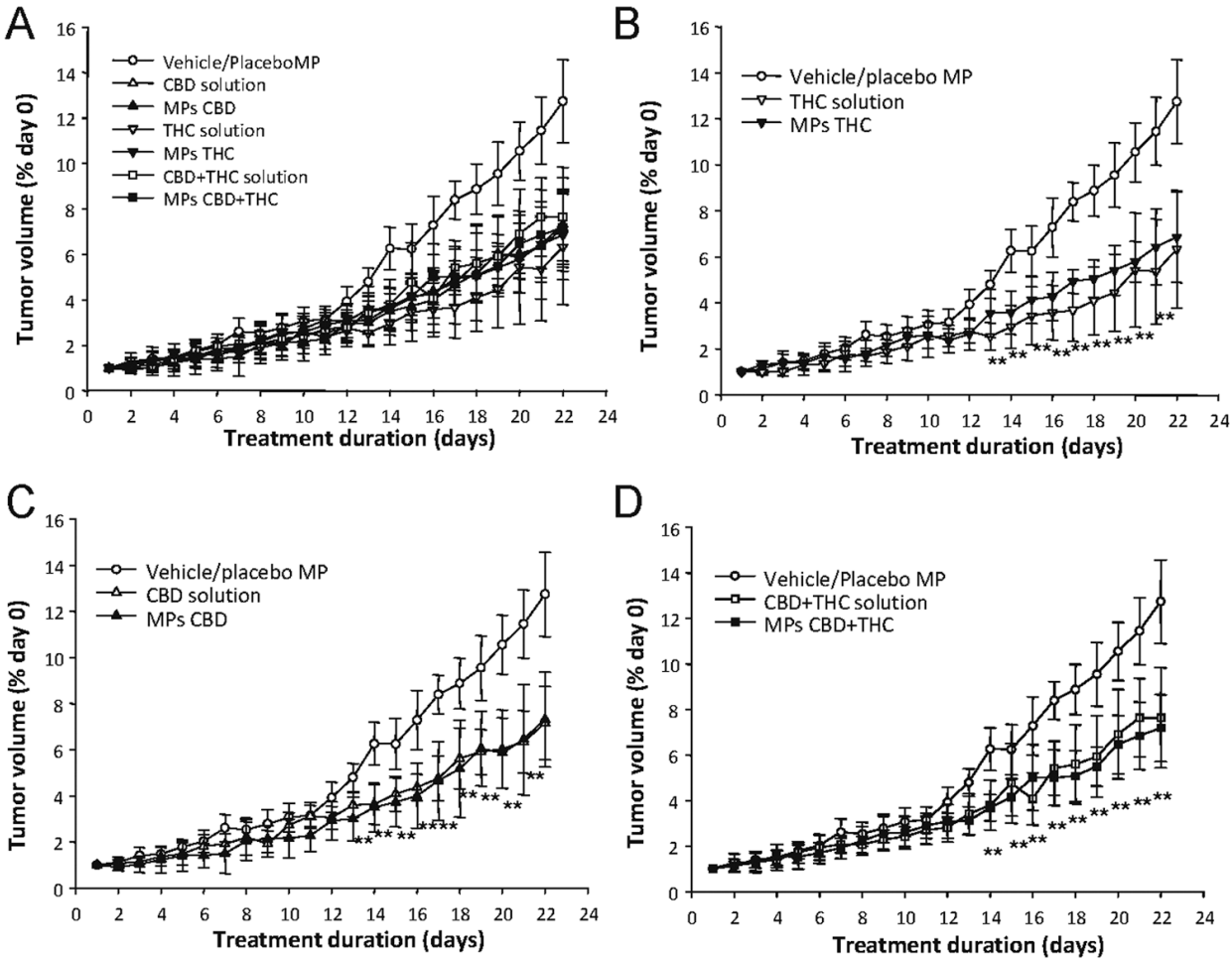
Marijuana could potentially improve the quality of the patient's life while they are undergoing cancer treatments in several ways. First of all, cannabinoids have been shown to be able to cooperate and not inhibit current cancer treatments. Cannabinoid tests on cancer in animals have shown they do not produce any toxic effects in the tissues that would limit the effectiveness of chemotherapy (Bifulco, 2002). Second of all, cannabinoids can alleviate pain and decrease nausea in chemotherapy patients which would allow the patient to feel more comfortable increasing their overall happiness. They will be relieved from the miserable state that the pain and sickness put them in (Borgelt, 2013). Third of all, the patients undergoing chemotherapy will obtain an increased appetite which will allow them to eat more and will turn give them more energy to undergo the seemingly endless battle with cancer (Pacher, 2013). Lastly, marijuana has been shown to alleviate stress like symptoms which is also a good thing. Being stressed adds to emotional and physical distress of the patient, and alleviating some of this stress will improve the patient's quality of life (McRae-Clark, 2013). Even if marijuana can't be used as an anti-cancer treatment, it still can be used with current treatments to improve the quality of the patient's life. The fact that marijuana can be used to improve the patient's mood and appetite while decreasing their sickness form the current treatments should be enough to consider the testing and researching of marijuana

on cancer patients and cancer cells. Marijuana can alleviate many symptoms and has many positive effects that need to be taken advantage of.

Marijuana can improve the quality of how a patient feels while undergoing cancer treatments, and may even be able to fight off the cancer itself. Several studies have been done on marijuana and animals in the U.S, and there have been mixed feelings on whether or not marijuana will prevent cancer in the human body. Some studies argue that marijuana inhibits cancer cells and tumor growth, and some studies argue that marijuana proliferates cancer cells and tumor growth. This alone shows the uncertainty of how marijuana works and how its pathways could affect cancer. Because no one really knows for sure if marijuana could prevent cancer, more research needs to be done. Just the fact that there is a possibility of preventing cancer should tell the government that this needs to be researched.

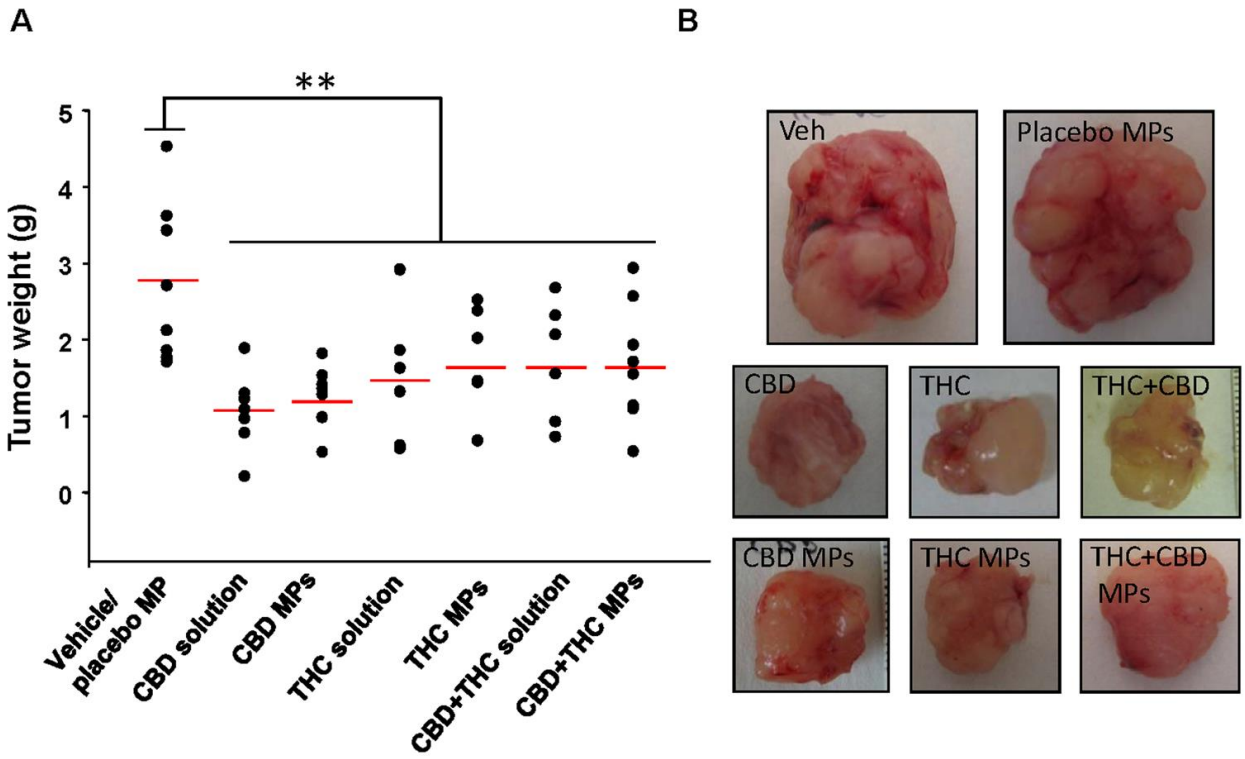
Clinical evidence by de la Ossa et al. (2013) shows that the cannabinoids in marijuana can slow down cancer growth and the spreading of cancer in mice and rats. The specific cannabinoids in this study were THC (Tetrahydrocannabinol) and CBD (Cannabidiol). The mechanism of how these two cannabinoids reduce cancer growth as well as tumor growth is not completely understood and more research needs to be done to better understand the biochemical pathways in how they interact with the body. However, for the time being, it is thought that these cannabinoids play a role in induced apoptosis somehow that is reliant on a high production of reactive oxygen species, and this mechanism is also in glioma cells which cause cancer. Both of these cannabinoids were tested to treat rats and mice in this study to see if these cannabinoids are actually

effective in preventing cancer growth (de la Ossa, 2013). Microencapsulated cannabinoids containing THC and CBD were prepared and injected into the cancerous sections of the mice. The capsules containing these two cannabinoids effectively counteracted the cancer growth in the mice. The microsphere capsules permitted the cannabinoids to be released into the cancerous sites effectively without being degraded. This is important because a lot of alternative cancer treatments are degraded by water and bodily chemicals before getting to the desired cancer site. This study suggests that putting these two cannabinoids into microcapsules enable effective concentrations of cannabinoids to fight off the cancer and results of tumor size reduction can be seen in Figure 1 and 2 below. If the cannabinoids can get to the desired site safely, their anticancer effects can effectively take action (de la Ossa, 2013). The results and conclusion of this study show that in vivo administration of these two cannabinoids does effectively reduce cancer, and it can and should be used as an anti-cancer treatment of some form. Testing and research of this treatment needs to be done to see if marijuana will be useful against cancer cells in the human body.



de la Ossa, D. r., Lorente, M., Gil-Alegre, M. E., Torres, S. a., García-Taboada, E., Aberturas, M. R., & ... Torres-Suárez, A. I. (2013). Local Delivery of Cannabinoid-Loaded Microparticles Inhibits Tumor Growth in a Murine Xenograft Model of Glioblastoma Multiforme. Plos ONE, 8(1), 1-8. doi:10.1371/journal.pone.0054795

Figure 1: This figure shows how microencapsulated cannabinoids injected into cancerous areas in mice slowed down the progression of cancer growth. They also decreased the size of the tumors in the specific areas over the course of twenty-four days.



de la Ossa, D. r., Lorente, M., Gil-Alegre, M. E., Torres, S. a., García-Taboada, E., Aberturas, M. R., & ... Torres-Suárez, A. I. (2013). Local Delivery of Cannabinoid-Loaded Microparticles Inhibits Tumor Growth in a Murine Xenograft Model of Glioblastoma Multiforme. Plos ONE, 8(1), 1-8. doi:10.1371/journal.pone.0054795

Figure 2: This figure also showed that microencapsulated cannabinoids were able to decrease the size of the tumor in the mice.

Some other clinical evidence has been done on mice that suggested a way in which THC acts as an anti-tumor agent. A study done by Lorente et al. (2011) suggested that cannabinoids activate the endoplasmic reticulum stress-related signaling route that leads to the activation of several co-factors. The stimulation of this pathway promotes apoptotic events and antitumoral actions. THC does inhibit tumors and cancer growth, but glioma cells in our bodies initiate a problem for a cancer treatment based on cannabinoid reagents. This study shows that many glioma cells are resistant to THC effects and therefore cancer will not be killed or suppressed by THC's effects. Some glioma cells will be killed based on their resistance towards cannabinoids, but some will not be killed. This is a problem. One found that the gene Mdk (midkine) inhibits THC's effects and adds to the resistance of the cancer. If one could silence this gene, or temporarily delete it, THC could run its course and inhibit the growth of the harmful cancerous cells (Lorente, 2011). This is still a viable option, and in this study it was proven to still be effective. They silenced the gene MDK, and THC was able to suppress the glioma cells and inhibit the growth of cancer proving that it can be used as an anti-tumoral agent. This again shows that more research needs to be done on medical marijuana and its effects on cancer because this has shown that marijuana can be very beneficial in reducing the effects of cancer in patients.

Chapter 5: Cannabinoids against Common Types of Cancer Across the U.S.

Weeding out Breast Cancer

Cannabinoids from marijuana may be therapeutic for many different types of cancer patients. Cannabinoids are a group of compounds from the *Cannabis sativa* plant. In 1990, the first cannabis membrane was observed in the body. This observation started a boom in the medical research. However, due to this drug's "power", clinical use for medicine has remained limited to this day. THC is already used in some forms of cancer treatment, but these forms all deal with symptom management. Basically the only way that marijuana can be used to help cancer patients is by helping increase their appetite and decrease the feeling of nausea. This sense of medical management is very helpful, but this drug may be able to provide even more help in the war between humans and cancer. There has been evidence that these compounds derived from marijuana can have antitumor effects in many different cancers. This action can take place by blockade of the tumor progression. They can inhibit cancer cell proliferation and induce apoptosis in the cells. But because they have been seen to prevent the spread of cancer in many different areas of the body, it is thought that marijuana has more generalized effects against cancer rather than specific effects (Behrend, 2013). Because it is thought that it has more generalized effects, I believe that the cannabinoids in marijuana could be very beneficial for patients with common types of cancer. The most common types of cancer

in the U.S. are breast cancer, prostate cancer, and lung cancer. The estimated amount of people diagnosed for specific types of cancer, and the estimated amount of people that died from a specific cancer can be seen in Table 1 below. These estimations were made using years of cancer trends and cancer statistics. The estimations are made for the year of 2016.

Table 1: This table demonstrates the main types of cancer diagnosis in the U.S. This table illustrates the estimated amount of people diagnosed with specific types of cancer as well as and estimation of how many people died from that specific form of cancer. These numbers were based on previous years of cancer statistics. These estimations are for 2016. It illustrates that the more common types of cancer are breast cancer, prostate cancer, and lung cancer.

Cancer Type	Estimated New Cases	Estimated Deaths
Bladder	74,000	16,000
Breast (Female – Male)	231,840 – 2,350	40,290 – 440
Colon and Rectal (Combined)	132,700	49,700
Endometrial	54,870	10,170
Kidney (Renal Cell and Renal Pelvis) Cancer	61,560	14,080
Leukemia (All Types)	54,270	24,450
Lung (Including Bronchus)	221,200	158,040
Melanoma	73,870	9,940
Non-Hodgkin Lymphoma	71,850	19,790
Pancreatic	48,960	40,560
Prostate	220,800	27,540
Thyroid	62,450	1,950

There are several ideas that have been proposed concerning the effect cannabinoids have on breast cancer. This proposal discusses how cannabinoids are involved in the control of the cancer's cell fate. A cells life is based on the cell cycle. The cell cycle decides whether or not a cell will proliferate, differentiate, or die off. Cannabinoids may affect the way the cell cycle occurs for breast cancer cells. Cannabinoids when bound to their receptors have multiple effects on the body. One of the effects is through modulating mitogen-activated protein kinases and

phosphatidylinositol 3-kinase/Akt survival pathway, which plays a vital role in the control of the cell cycle and the cells future conditions. Researchers tested this by using breast cancer cell lines. After performing several tests and analyzing the effects of cannabinoids on the cell line, cancer cell proliferation was decreased. This was due to the blockade of the G2-M transition in the cell cycle. THC was seen to decrease the total levels of Cdc2, the major CDK controlling the entrance of cells in mitosis after finishing G2 events. Also the p21, a CDK inhibitor was also enhanced in the presence of THC which helps prevent cells continuing past the G2 phase. This is why the cancer cells were not able to complete the stages after G2 in the cell cycle. Because many of the cancer cells couldn't complete the later stages in the cycle, the cancer cells decreased in number. Next, the effect of apoptosis was looked at. It was seen that cannabinoids did increase cancer cell apoptosis, but the majority of the cells that underwent apoptosis were the cells that were unable to go past the G2 phase in the cell cycle due to the fact that THC prevented them from entering later stages in the cell cycle as the information in this paragraph previously stated. Lastly, the reason THC can affect breast cancer cells and breast cancer tumors is the fact that CB1 and CB2 receptors are present on the cells and tumors. Without the necessary receptors cannabinoids would be useless. But because the receptors are there, cannabinoids can have an extremely positive affect on breast cancer as well as many other cancers (Caffarel, 2006).

Breast cancer is one of the most common types of malignancy among women and although mortality rates have dropped significantly over the recent years due to early screening and prevention, breast cancer is still one of the most common types of cancer in

the U.S. (Behrend, 2013). Breast cancer takes account for about 30% of newly diagnosed cancers each year (Caffarel, 2010). There are several types of breast cancer tumors that are resistant to conventional cancer treatments, and because of this there is a dire need to develop new therapeutic strategies to help patients with this disease (Behrend, 2013). The cancer cell tumors become unresponsive to conventional treatments, and most of these patients that are treated with the normal cancer reagents used today begin to develop metastases. Because 75% of the patients with this sort of breast cancer are not helped from current cancer treatments, urges for new alternative treatments are needed (Caffarel, 2010). Cannabinoids were used against these resistant breast cancer cells, and the results showed that the cannabinoids were able to modulate key estrogen and progesterone receptors that were positive for breast cancer cells. They also were able to slow down the migration and invasive nature of the cancer (Behrend, 2013).

There is another type of breast cancer tumor that expresses tyrosine kinase receptors HER2. Cannabinoids have also been shown to help these patients that have these tumors. THC and a CB2 selective agonist was injected into mice with these tumors to see if any positive effects would take place. THC as well as the agonists showed tumor suppression evidence. Tumor blood cells were decreased and the size of the tumor was decreases showing that cannabinoids also positively can affect this type of breast cancer in reduction and slowing down cancer growth (Behrend, 2013).

But, although there have been many findings where cannabinoids may be able to help cure and prevent breast cancer, there are some cases where evidence contradicts these findings. There have also been tests that suggest cannabinoids actually enhance the

breast cancers that do not have CB receptors present. Every form of cancer is different, and some cancers do not have CB receptors. So when thinking about using cannabinoids as a cancer treatment, one has to make sure that the risks do not outweigh the rewards. If there is more cancer present without CB receptors then one may not want to use cannabinoids. More research needs to be done to see why some cancers have the receptors and why some cancers do not have the CB receptors. Knowing which cancers have CB receptors is vital in using cannabinoids as a treatment. There are also the rare cases where cancers with CB receptors are enhanced with the use of cannabinoid treatment. The mechanism behind how cannabinoids affect cancer is still not fully understood and more research needs to be done to understand exactly how the cannabinoids interact with cancer. One thing is for sure though, cannabinoids do work against many forms of cancer, and the importance of understanding the cannabinoid pathways is vital to making the drug the new possible treatment (Sarfaraz, 2008).

If cannabinoids cannot be used as a main reagent against cancer, they should at least be used in a combination treatment. There has been clinical evidence where the combination approach not only reduces negative symptoms of the treatments, but also increases the positive effects in a synergistic way (Caffarel, 2012). One example of this being true was the use of temozolomide (the standard therapy for glioma patients) exerted an anti-tumor effect in animal models that was profoundly improved by the combination with cannabinoids (Caffarel, 2012). This correlation held true for many other clinical trials as well including several breast cancer treatment trials. There is compelling

evidence that cannabinoids can have an extremely positive effecst against cancer and the evidence for using cannabinoids continues to grow every day.

Breast cancer affects approximately 1 in every 10 women at some point in their lives. Many forms of breast cancer cause tumors that are resistant to current treatments, and this is why alternative treatments are being tested every day. Cannabinoids have been suggested to be one of these new alternative treatment ideas. Cannabinoids have been shown to inhibit breast cancer in many forms, and have a high ceiling potential to be the cancer drug of the future. Synthetic cannabinoids have been tested in different types of breast cancer, and almost all of the results concluded with an inhibition of cancer cell proliferation and angiogenesis. Lastly, cannabinoids may prove to be very useful against cancer due to the fact that the compound has very low toxicity as well as a high safety profile for patients (Behrend, 2013). Cannabinoids in THC may just be the fire power we've needed to beat breast cancer. Breast cancer has ruined so many people's lives and is so prevalent in the world today. Cannabinoids have the potential to help us out and they need to be allowed to help save the lives of the women on this earth. With more research, maybe this drug could be regulated to help the cause of so many women in the world.

Weeding out Prostate Cancer

Prostate cancer ranks as the most common malignancy and the second leading cause of cancer-related deaths in American males. The major cause of mortality due to this disease is from metastasis of hormone refractory cancer cells that fail to respond to hormone ablation therapy. Surgery for this type of cancer is not an effective treatment. Because this type of cancer is so hard to get rid of, novel therapy drugs are being researched to see if a new and better treatment can be found (Safaraz, 2006.).

One of the new therapeutic drugs that has drawn major interest from researchers working with cancer is marijuana. The components of *Cannabis sativa* in marijuana have diverse pharmacologic activities that may be helpful in fighting prostate cancer. Studies have shown that the expression levels of cannabinoid receptors in cancer prostate cells are actually higher than normal prostate cells which may show that cannabinoids can have more powerful affects against prostate cancer than in other parts of the body (Saffaraz, 2005).

A treatment of LNCaP cells with a mix of CB1 and CB2 agonists were analyzed in an experiment to see how cannabinoids affect prostate cancer cells. LNCaP cell lines are human cells that are commonly used in the field of oncology. These cells are androgen-sensitive prostate adenocarcinoma cells derived from the left supraclavicular lymph node metastasis (Safaraz, 2006). Basically, LNCaP cells are cultured prostate cancer cells that are commonly used to see how new treatments could attack prostate cancer cells. The treatment resulted in inhibition of cell growth in the prostate, and results also showed an induction of cancer cell apoptosis. Treatment of the LNCaP cells resulted in the prevention of the cancer cells to proceed in the cell cycle (Safaraz, 2006). This prevention occurred in the G0 to G1 phase. This means that the cancer cells were unable to proceed through the necessary growth cycle to continue growing. Because they couldn't proceed past the G1 phase in the cell cycle, they were unable to proliferate and accompanying mechanisms activated apoptotic events within the cells. The mechanisms underlying these series of events are not completely understood though, and more research needs to be done to see exactly how the cannabinoids stunted the growth of the

cancer cells and induced apoptotic events. When an antagonist was used instead of an agonist for cannabinoids, the cell growth of the cancer thrived (Safaraz, 2006).

Just as we saw in the breast cancer cell lines, cannabinoids were able to stunt the cancer growth and slow down the spreading. Although the mechanisms underlying the events were not completely understood, there is evidence that shows cannabinoids could possibly be used as some form of treatment. Cannabinoids were able to stop cancer cells progression through the cell cycle, and they were also able to induce a series of apoptotic events. More research needs to be done to see exactly how the cannabinoids in marijuana can alter prostate cancer, but current research shows some promising results against prostate cancer cell lines that could be beneficial to many patients that suffer from prostate cancer.

Weeding out Lung Cancer

Lung cancer is a major concern in the world today because it is one of the most difficult diseases to treat which makes it one of the deadliest diseases. Specifically, Non-small lung cancer is one of the more serious forms of lung cancer. Non-small lung cancer (NSCLC) is the leading cause of cancer deaths worldwide because the treatments for this type of cancer are so limited. NSCLC accounts for about 85% of all lung cancer cases, and fewer than 15% of patients with the disease survive more than 5 years after

being diagnosed (Preet, 2011). Most times there is an overexpression of epidermal growth factor receptor (EGFR) that accompanies the disease, and this contributes to the cancer cells being able to proliferate and survive. Most of these patients receive a combination of current cancer treatments, but they develop a resistance to the treatments. This resistance is thought to be due to abnormal transduction pathways and a high EGFR expression level. EGFR inhibitors were used on patients, but the cancer found different pathways to proliferate through, and these pathways are not completely understood (Preet, 2011). Because there is such a need for a new option, the role of cannabinoid receptors as therapeutic target agents for NSCLC was investigated.

In most of the patients that had NSCLC, an expression of CB1 receptors (24%) and CB2 receptors (55%) was observed. These receptors were then introduced to cannabinoid agonists and the effects of the receptors being bound were observed (Preet, 2011). Once the agonists bound to the CB receptors, positive effects occurred in the patients. Significant reduction in focal adhesion complex was seen to take place. This complex plays a big role in allowing the cancer to be able to migrate. With reducing the focal adhesion complex, the migration of the cancer was also reduced. With the agonists present there was also inhibition of tumors in the area. The tumors were reduced in size, and the amount of tumors was also reduced. Reduced cancer cell proliferation and cancer cell induced apoptosis was also seen. The mechanism was not completely understood, but it was seen that the agonists inhibited phosphorylation of AKT, which is a signaling molecule controlling survival, migration, and apoptosis. These results suggested that

CB1 and CB2 agonists could be used as novel therapeutic targets against NSCLC (Preet, 2011).

Conclusion Concerning the Medicinal use of Cannabinoids against Cancer

To wrap things up, marijuana can in fact be used as an anti-cancer agent. There have been several studies done that show that cannabinoids do in fact inhibit the growth of cancer cells and tumors. However, the mechanism of how marijuana inhibits the cells is not fully understood. It is also not fully understood why some dosage levels inhibit cancer while others promote cancer. This is a big problem and this needs to be

understood before a viable treatment option can be performed. There are several ways in which these cannabinoids can be used to treat patients, and the most effective way needs to be found. It can be implemented by a spray, smoke, and oral treatment, but before marijuana can actually be used as a cancer treatment more research needs to be done. The limitations of research literature and human testing of cannabinoids hinders our ability to understand the pathways in which cannabinoids work in terms of cancer (Temple, 2011). Marijuana could change the way medicine is used forever, but first one must perform clinical trials using cannabinoids as a cancer antagonist instead of focusing on using cannabinoids as a symptom management drug for cancer patients.

Chapter 6: Social implications on Youth and Development

Marijuana and its Influence on Adolescent Development

Even though a lot of good could come from marijuana, legalization of marijuana throughout the U.S. comes with some major concerns. The chemicals in marijuana have potential to serve many medical purposes, but these chemical effects could be dangerous if not used properly. According to BMJ, use of marijuana has serious negative effects on

adolescents, and legalization would increase the use of the drug in adolescents which could be very detrimental (BMJ, 2002). Legalizing marijuana medically and possibly recreationally can have extremely positive effects on the economy in certain areas, but the negative effects that come along with legalization can't be overlooked. The major concerns with legalizing marijuana in different states are the negative effects on adolescents, possible increase of criminal activities, and use of other drugs (BMJ, 2002).

For a long time now, marijuana and is legal status have been a vigorously debated topic. Advocates of legalizing marijuana argue that marihuana allowed and permitted to individuals in small amounts would not be dangerous. They also argue that current criminal sanctions against small personal use and possession of the drug are excessively harsh and unnecessary. The current penalties and restrictions placed on the drug are driving marijuana underground which is more dangerous for societies than strict legalizing policies would be. The last major idea that advocates argue is that current legalized drugs such as tobacco and alcohol cause far more damage to society than marijuana does. Alcohol and tobacco cause more mortality and economic costs associated with the use of these drugs trump the societal costs that marijuana would bring forth with its legalization. The opposing party for legalizing marijuana argues that marijuana shares some dangerous chemical features with other illicit drugs that would in fact cause harm to society. They argue that legalization of the drug would trigger a substantial boom in its use and would cause foreseeable consequences. They believe that it is too risky to legalize the drug (BMJ, 2002).

One of the major concerns for legalizing marijuana in terms of medicine and research is the effect that it will have on adolescents. The adolescents in the world will be the ones that make up the future and people are afraid that the supportive laws that come with legalizing marijuana for research and medicine will be detrimental for adolescents and their future.

How Marijuana affects Development in Adolescents

The regular use of marijuana during adolescents is a major concern when talking about medical marijuana and recreational marijuana legalization in the United States. One of the major concerns is due to the increased likelihood of deleterious consequences

in development as well as other risks that come along with usage of marijuana during adolescents (Volkow, 2014).

One of the first major side effects of using marijuana at an early age is the risk of addiction. Many argue that marijuana is not addictive, but science has clearly shown that long term use of marijuana most likely will lead to addiction. Roughly 9% of those who experiment with marijuana become addicted to the drug. This percentage increases if it is used during the adolescent period. This number increases to about 1 in every 6 if they start using marijuana as a teenager. It goes up even higher from 25-50% for those that smoke daily. According to Valkow et al, "About 2.7 million people 12 years and older met the criterion to be termed dependent on the substance" (Volkow, 2014). Once they have become dependent on the drug they experience several withdrawal symptoms. These include irritability, sleeping difficulties, anxiety, memory issues, etc. A lot of these withdrawal symptoms are more extreme if one was using marijuana during adolescents because of the fact that the brain undergoes major development. The endocannabinoid system also undergoes active development during adolescents which plays a role in the addiction and adolescent development. Adolescents frequently using marijuana are 2 to 4 times more likely to become addicted to marijuana and experiences withdrawal symptoms within 2 years of first using the drug than marijuana users that start using in adulthood (Volkow, 2014).

The use of marijuana during adolescents plays a crucial role in brain development because the brain undergoes crucial development until one reaches approximately 22 years of age. During these years, the brain is very vulnerable and the effects of chemicals

such as THC and other ingredients in marijuana are more severe. Early exposure to THC can recalibrate the sensitivity of the "reward system" in the brain and can also affect cytoskeleton dynamics which are critical for the establishment of axonal connections between neurons. This early exposure can affect how the brain makes connections with certain stimuli and affects how the individual responds in certain conditions. Adults that smoked marijuana regularly during adolescents have impaired neural connectivity in specific brain regions as a result. These regions include the precuneus, which is a node that is involved in functions that require a high degree of integration. This deals with alertness, self consciousness, and awareness. Another region affected is the fimbria which is an area in the hippocampus that deals with memory. Reduced connectivity in the pre-frontal networks and the subcortical networks have also been observed. These deal with habits and routines. The pre-frontal cortex has also been seen to be affected by adolescent usage. This deals with decision making and whether or not a certain action is right or wrong. Lower IQ's are also seen in frequent adolescent users which is a direct correlation to marijuana inhibiting the development of the adolescent brain. This shows that the altering of the cannabinoid system changes how the brain develops. The cannabinoid system is thought to play a crucial role in synapse formation during brain development due to these findings as well as other sources of research (Volkow, 2014).

Another concern about the increase of adolescents using marijuana is the possibility of marijuana as a gateway drug. Many studies suggest that marijuana influences addictive behaviors in adulthood. It has been shown that in adolescent rats exposed to marijuana have a decreased reactivity of dopamine neurons that modulate the

brains reward regions. This exposure alters the developmental regulation of the dopamine system, and this could explain the increased susceptibility to drug abuse and addiction to other drugs later on in life (Volkow, 2014).

Regular marijuana use during adolescents is also a concern for development of a mental illness. The metal illnesses of major concern are anxiety and depression. Although it is thought that marijuana may increase the risk for both of these diseases, a definite link can't really be made because of the vast amount of factors that have to be accounted for when it comes to mental illness. One can make assumptions when it comes to the relationship between marijuana and mental illness, but it is very difficult to confidently attribute a correlation between the two (Volkow, 2014).

School performance and professional achievements is another concern when it comes to adolescents using marijuana. Is has been shown that about 6% of high school students use marijuana daily, and this is most likely low balling the situation. Marijuana impairs cognitive functions during intoxication as well as days after intoxication. This naturally lowers student's ability to learn and perform well in school. Failure to perform well in school leads to failure to advancing ones education. Failure to advance one's education leads to more difficulty in finding a prestigious job (Volkow, 2014).

Motor vehicle accidents are another big issue with adolescents using marijuana. It has been shown that both immediate and long term exposure to marijuana impair driving ability. Marijuana is the illicit drug that is reported the most in connection with impaired accidents as well as fatal accidents. It has been shown that the involvement of

an accident increases by a factor of two when a person drives under the influence of marijuana (Volkow, 2014).

The increased risk of cancer and lung damage is also a concern with the use of marijuana and adolescents. The increased risk of lung cancer due to marijuana is not clear, but one can assume that marijuana is not good for the lungs. It is associated with inflammation of large airways, and has been shown to increase airway resistance making it harder for the individual to breathe. Bronchitis has been a common report for those that chronically use marijuana. However, the effects of low marijuana usage appear to be insignificant (Volkow, 2014).

The negative effects on adolescent development from the possible increase in use of marijuana in teens are a major concern with legalizing the drug. The effects of early use in marijuana is correlated to a very wide range of effects as listed in the above paragraphs, and one can see some of the consequences of using marijuana at an early age in Table 2 below.

Table 2: This table illustrates some of the negative consequences that come with using marijuana during adolescent years. The table illustrates results from using marijuana over a short period of time (a couple of months) as well as some of the results that could come with using marijuana over a long period of time (at least one year) (Volkow, 2014).

Effects of short-term use
Impaired short-term memory, making it difficult to learn and to retain information
Impaired motor coordination, interfering with driving skills and increasing the risk of injuries
Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases
In high doses, paranoia and psychosis
Effects of long-term or heavy use
Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*
Altered brain development*
Poor educational outcome, with increased likelihood of dropping out of school*
Cognitive impairment, with lower IQ among those who were frequent users during adolescence*
Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*
Symptoms of chronic bronchitis
Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

* The effect is strongly associated with initial marijuana use early in adolescence.

Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. (2014). Adverse health effects of marijuana use. *New England Journal of Medicine,370*(23), 2219-2227.

Since there is so much concern surrounding adolescents, a lot of research has been done to see how the chemicals in marijuana affect the body. Scientists have shown that there are withdrawal symptoms from marijuana linked to corticotrophin releasing factor, the same chemical that is linked to anxiety and stress during withdrawal from alcohol and cocaine. More reports show that THC, the active ingredient in marijuana, stimulates

release of dopamine in the brain which increases the dependence on the drug showing that people can become addicted to marijuana. There are also some consequences that come with over use and dependence on the drug. Short term memory, concentration, attention span, motivation, problem solving, coordination, judgement, reaction time, and tracking ability are all worsened if dependence on the drug occurs. One major concern with all of this is that these are the major negative effects from the drug that have substantially contributed to unintentional deaths and injuries in adolescents in the past when the drug was still illegal. These studies showed that there is a negative effect correlated to the use of marijuana and mental development in adolescents (BMJ, 2002).

The adolescents in this study were of the age of 15-18 years old, and the sample size was 1037 adolescents in total. 494 of the adolescents reported that they had never used marijuana at the ages of 15-18 years old. 236 of the adolescents reported that they had used marijuana at least three times at the age of 18. 29 of the adolescents said that they had used marijuana at least three times by the age of 15. Later the subjects were then analyzed at the age of 26 to see how the use of marijuana affected their development as well to see if they now had any symptoms from using the drug. The results can be seen below in Table 3. The results showed that early use of marijuana at the age of 15 increased the likelihood of negative symptoms and development of schizophrenia was four times greater than those who never used marijuana (BMJ, 2002).

Table 3: This table shows a correlation marijuana use and certain mental illnesses. This table illustrates that if one starts using marijuana at the age of 15, they are much more likely to develop a mental illness then people that start using marijuana at the age of 18 or older. This shows that if one starts to regularly use marijuana at an early age, they are more likely to develop a mental disorder due to the fact that they are still undergoing very crucial developmental stages (BMJ, 2002).

		Schizophrenia outcomes				Depression outcomes			
		Schizophrenia symptoms (scores 0-58)		Schizophreniform disorder (n=25; 3.3%)		Depressive symptoms (scores 0-54)		Depressive disorder (n=118; 15.5%)	
Model*	Predictor	B¶ (SE)	P value	Odds ratio (95% CI)	P value	B§ (SE)	P value	Odds ratio (95% CI)	P value
1†	Cannabis users by age 15	6.91 (0.91)	0.001	4.50 (1.11 to 18.21)	0.035	0.25 (1.93)	0.897	1.02 (0.34 to 3.04)	0.971
	Cannabis users by age 18	1.04 (0.40)	0.009	1.65 (0.65 to 4.18)	0.293	1.98 (0.84)	0.018	1.62 (1.06 to 2.49)	0.028
2‡	Weak psychotic symptoms at age 11	0.68 (0.53)	0.201	4.65 (1.84 to 11.78)	0.001	1.60 (1.13)	0.159	1.45 (0.82 to 2.56)	0.203
	Strong psychotic symptoms at age 11	5.16 (1.39)	0.001	15.97 (3.38 to 75.47)	0.001	−0.55 (2.96)	0.852	0.54 (0.07 to 4.25)	0.554
	Cannabis users by age 15	6.56 (0.91)	0.001	3.12 (0.73 to 13.29)	0.124	0.13 (1.94)	0.946	1.01 (0.34 to 3.02)	0.987
	Cannabis users by age 18	1.03 (0.39)	0.009	1.42 (0.54 to 3.74)	0.473	1.96 (0.84)	0.020	1.61 (1.05 to 2.47)	0.031
3§	Other drug users at age 15 to 18	−0.3 (0.69)	0.615	0.30 (0.05 to 1.62)	0.160	2.48 (1.45)	0.086	1.23 (0.55 to 2.32)	0.743
	Cannabis users by age 15	7.2 (1.07)	0.001	11.38 (1.84 to 70.45)	0.009	−1.75 (2.26)	0.438	0.93 (0.27 to 3.17)	0.905
	Cannabis users by age 18	1.1 (0.42)	0.008	1.95 (0.76 to 5.01)	0.167	1.55 (0.88)	0.078	1.59 (1.01 to 2.49)	0.043

BMJ 2002; 325 doi: http://dx.doi.org/10.1136/bmj.325.7374.1212 (Published 23 November 2002)Cite this as: BMJ 2002;325:1212

Even though there is a log of evidence showing correlations between adolescent marijuana use and negative developmental symptoms, there are some studies that show that these correlations may be due to other factors. According to a study by Joffe et al, a twin study showed that marijuana didn't have significant developmental consequences. However, this study used a small sample size of 56 cotwins which may have limited their results.

In the study by Joffe et al, the twins that were eligible had to pass certain criterion. The first was that they had to be monozygotic twins, which means that they were identical twins. The second was that one twin had to smoke marijuana at least once a week for a minimum of one year, and the other twin could only have smoked marijuana five times or less in their life. The marijuana smoking twin had to have smoked at least one month prior to this interview showing that they were still smoking marijuana. Neither sibling could report the use of using any other illicit drugs, nor could either sibling could repot that they ever experienced withdrawal symptoms from alcohol. 117 twins were then invited to the study to see the effects of marijuana use, but only 62 twins agreed to be examined and were given a stipend of 200 dollars for their participation. The research to be performed was explained to each participant and confirmed consent was obtained by the institutional review board of Harvard University and Washington University Schools of medicine. Then differences between the twins concerning tobacco and alcohol use were determined. There was no significant difference between the use of marijuana and the use of those two drugs. Then differences in health assessments were determined throughout their lives, and no statistical difference was observed. This showed that marijuana abuse didn't really have any effect on the twins in terms of alcohol abuse and health concerns. The results from this study can be seen in the Table 4 and Table 5 below (Joffe, 2004).

Table 4: This table compares the non-marijuana using twin and the marijuana using twin. It illustrates that there wasn't much of a difference in either of the twins in terms of using abusing tobacco or alcohol later on in their life (Joffe, 2004).

Alcohol or nicotine use	*Marijuana users*	*Non-marijuana users*	*Statistics*	*P*
Alcohol use				
Life-time alcohol abuse/dependence[ab] (56)[c]				
No abuse/dependence	35.7%	48.2%	2.13[d]	0.14
Abuse/dependence	64.3%	51.8%		
Current drinker (54)[c]				
Former drinker	29.6%	33.3%	0.25[d]	0.62
Current drinker	70.4%	66.7%		
Duration of drinking (years)[e] (50)[c]	23.3 (8.8)[f]	22.7 (9.0)	0.47[g]	0.64
Average number of drinks/day in past year[e] (47)[c]	0.9 (1.1)	0.6 (0.7)	1.57[g]	0.12
Nicotine use				
Life-time nicotine abuse/dependence[ab] (56)[c]				
No nicotine abuse/dependence	48.2%	44.7%	0.60[d]	0.44
Nicotine abuse/dependence	51.8%	55.4%		
Current smoker (53)[c]				
Former smoker	66.0%	71.7%	0.82[d]	0.37
Current smoker	34.0%	28.3%		

Joffe, A., & Yancy, W. S. (2004). Legalization of marijuana: potential impact on youth. *Pediatrics, 113*(6), e632-e638.

Table 5: This table compares medical aspects of the non-marijuana using twin and the marijuana using twin. This illustrates that there was not a significant difference in terms developing a disease or abusing alcohol. It also shows that there is no significant difference in terms of seeing a physician more often for various problems (Joffe, 2004).

Health-care utilization	*Marijuana user mean (SD)*[d]	*Non-marijuana user mean (SD)*	*Statistics*	*P*
Seen by physician[a] (yes/no)	57.1%	62.5%	0.27[b]	0.60
Number of physician visits for				
Specified diseases[a]	5.05 (10.51)	6.32 (10.91)	–0.68[c]	0.50
Minor problems or routine checkups	4.49 (5.57)	4.94 (7.03)	–0.46[c]	0.65
Number of ER visits for				
Specified diseases[a]	0.38 (0.96)	0.18 (0.43)	1.47[c]	0.15
Accidents	0.38 (0.65)	0.39 (0.65)	–0.14[c]	0.89
Number of hospitalizations for				
Specified diseases[a]	0.29 (0.78)	0.16 (0.53)	0.98[c]	0.33
Accidents	0.11 (0.57)	0.06 (0.41)	0.57[c]	0.57
Total medical health services use for specified diseases[a]				
Physician and ER visits and hospitalization	5.71 (10.80)	6.66 (11.24)	–0.50[c]	0.62
Used prescribed medication[a]	41.1%	42.9%	0.04[b]	0.85
Mental health professional visits[e] for				
Non-alcohol-related drug problems	0.00 (0.00)	0.00 (0.00)	–	–
Non-alcohol-related psychological problems[f]	0.32 (2.04)	0.54 (2.57)	–0.48[c]	0.63
Family, marriage, or relationship problems	1.93 (7.2)	3.55 (15.09)	–0.78[c]	0.44
Mental health hospitalizations for				
Non-alcohol-related drug problems	0.00 (0.00)	0.00 (0.00)	–	–
Non-alcohol-related psychological problems[f]	0.13 (0.95)	0.00 (0.00)	1.00[c]	0.32

Joffe, A., & Yancy, W. S. (2004). Legalization of marijuana: potential impact on youth. *Pediatrics*, *113*(6), e632-e638.

Even though the sample size for this study was very limited and small, the outcomes of the research can't be ignored. A large portion of the evidence that marijuana is associated with long term residual adverse health effects is very limited and controversial. The research in this type of area is very complicated and difficult because of all the different variables that can come into play. One has to make sure that all the

variables are put into play to come up with the most accurate outcome possible. When analyzing how marijuana affects certain subjects, all characteristics need to be accounted for to obtain reliable data. Education level, tobacco use, alcohol use, illicit drug use, social demographic, social status, and many other variables all play a role in determining how marijuana affects society. This study shows that marijuana and its negative effects may not happen to everyone. Maybe the reason that marijuana has shown such negative effects in past studies is due to the fact that the subjects had an "unhealthy" lifestyle. These subjects used in this study had very similar lifestyles and had the same genetic material as their twin, and no significant difference was seen in health characteristics. It is important to consider this study when it comes to seeing marijuana as only producing negative effects for people's health (Joffe, 2004).

Given this somewhat contradicting information, there is still no certain answer to how certain legalizations of marijuana would affect adolescents in society in terms of health and development. But due to the fact that there have been some studies that show marijuana can have negative effects on adolescents and their development, it is still a big concern for the U.S to think about legalizing it to advance medical research. One way of predicting how changing the status of marijuana could affect adolescents is by examining the county's experience with drugs over the past 200 years. In the 19th century opium drugs were legal, and easily accessible. Morphine and cocaine were also legal at one time. The opiate addiction rate increased from .72 per 100 in 184 to 4.59 per 100 in the 1890's. In the mid 1960's the enforcement of marijuana became very lenient, and adolescents began to think that the drug wasn't dangerous (Joffe, 2004). The authorities

were more concerned about fighting the battle against heroin at the time. The penalties for marijuana began to be less severe, and basically were gone altogether if it was just a small amount caught with. In 1975, 6% of seniors in high school reported using marijuana daily, and by 1978 the percentage of seniors in high school reporting daily use increased to 10.7% (Joffe, 2004). This evidence shows that if marijuana does become illegal it is evident that there will be more use in adolescents. The drug will not be seen as an illegal criminalizing drug, and it will be seen as no longer dangerous. How much of a usage increase is unknown, but there would be undoubtedly an increase in use for adolescents which raises concern. Marijuana has been correlated to hurt the development in adolescents and an increase in usage must be accounted for when considering legalizing the drug. In legalizing marijuana to advance research on its properties, we must first know how serious the effects will be adolescents, and analyze whether or not the benefits of research outweigh the risks to society.

Legalization of Marijuana and Possible Effects on Adolescents

Because there is so much concern for adolescents using marijuana, one needs to see how law changes will affect usage rate in adolescents in the U.S. According to Joffe et al, if adolescents live in societies where drugs are supported they will use them more often (Joffe, 2004). If marijuana laws come across as more supportive of the drug this

may change how adolescents view the drug, and it may change their views on using it. It has been shown that in the past decriminalizing a drug has resulted in the increased use of the drug.

Marijuana is the most frequently used illicit substance in the United States, and supportive law changes may increase that use even more so. Cerda et al tested the relationship between state level legalization of medical marijuana and marijuana use, abuse, and dependence. They used a survey to test the relationship for 68,000 individuals of age 12+. States with medical marijuana laws had higher odds of marijuana use and marijuana abuse than states without laws. However, the abuse and dependence of the drug among the users was not higher in states with laws suggesting that the higher risk of abuse and dependence in these states was accounted from the higher usage rates in general (Cerda, 2012). More research needs to be done to see why the usage rate is higher. Is it due to community norms, supportive legislature, and the fact that it is easier to obtain?

It has been shown that an individual living in areas where marijuana is legal makes the individual more likely to use it because it is socially acceptable. Social norms have a big influence on how individuals behave in a society, and this study shows that if marijuana is socially acceptable the usage rate will be higher (Cerda, 2012).

Advertisement and its Influences on Society

Legalizing marijuana is mainly focused around adults, but the change in legalization and decriminalization will have some effect on adolescents. Alcohol and tobacco had rules and regulations put on them, and they are the most widely psychoactive substances abused by adolescents. Granted they are "safer" than drugs such as meth and heroin, but they are still abused more than any other drug and still have serious

consequences if not used responsibly (Joffe, 2004). If marijuana is legalized it will most likely result in advertising in many different campaigns.

Some of these campaigns may even be "directed" towards adolescents. Controlling advertisement directed towards only adults would be very difficult and would be nearly impossible to implement for many reasons. Companies in the past that advertised tobacco and alcohol have been guilty of advertising to adolescents even though they argue that they did no such thing. But in reality it is enticing towards adolescents and makes adolescents want to buy their product. The same concept is seen in the alcohol industry. Alcohol industries portray drinking in ways that are very appealing to younger people. They portray it as sexy, popular, fun, and socially acceptable (Joffe, 2004). These characteristics are extremely desired by adolescents especially in the years when they are trying to find who they are and where they fit in. This most likely would happen the same way with marijuana and its marketing. This would not be as big of a problem if there was evidence that adolescents' abuse of tobacco and alcohol was decreasing, but it is quite the opposite.

It is not certain how advertisements of legal marijuana for adults would affect adolescents, but it is assumed that the advertisements that would be used for marijuana would entice younger people to obtain the product. If the authorities aren't controlling abuse of tobacco and alcohol in adolescents why would they be able to control the abuse of marijuana? The newer advertisements of marijuana would then change the way adolescents perceive the drug, and recent studies have been shown that it would increase the use in adolescents due to in no longer being illegal for adults. Since it wouldn't be

illegal for adults younger people would see it as less dangerous. The use of marijuana is inversely correlated to the perceived risk associated with it. This can be seen in the graph below. To avoid more drug abuse of adolescents, authorities need to do a better job to ensure that adolescents are not able to obtain the drug. Also advertisement rules need to be stricter to that they are not targeting younger adults. Doing this will not only prevent abuse of marijuana if it is legalized, but will also lower the abuse of tobacco and alcohol in future adolescent generations (Joffe, 2004).

Our focus shouldn't be on keeping marijuana illegal, it should be on enforcing laws on current drugs such as alcohol and tobacco. We need to be worried about the current problems we have with adolescent drug abuse instead of worrying about problems that may or may not be in our near future. If we can control the current drug abuse in adolescents due to advertisements and lacking enforcement, than we could probably control the drug abuse of marijuana if it was legalized in the future. I think with the correct procedures and actions drug abuse could be reduced and there would be fewer concerns with legalizing marijuana in the future, but one must take care of the current problems in society today.

Chapter 7: Recreational and Medical Marijuana Legalizations in Colorado

Medical Marijuana in Colorado

Colorado voters first legalized marijuana in 2000, when they passed Amendment 20 which permitted a qualifying patient and/or caregiver of a patient to possess up to 2 ounces of marijuana and allowed them to grow up to six marijuana plants for medical purposes. It also provided identification cards for those individuals with a doctor's recommendation to use the drug. For a patient to obtain medical marijuana they had to go through the following process: they had to have a prescription from a physician, they

had to have a debilitating disease, and they had to obtain a medical marijuana card (Rocky Mountain High Intensity Drug Trafficking Area, 2014). When medical marijuana was first legalized medically in Colorado in 2000, everyone was wondering how this would influence the everyday lives of members in Colorado.

In the first couple years of medical legalization form 2001 to 2008, there were only 5,993 patient applications received and only 55 percent of those designated a primary caregiver. During that time, the average was three patients per caregiver and there were no known retail stores selling medical marijuana ("dispensaries"). Dispensaries were not an issue because the Colorado Department of Public Health and Environment (CDPHE) placed regulations that limited a caregiver to no more than five patients. Over the first couple of years, crime rates, traffic arrests, and traffic DUID's related to marijuana did not really increase, and crime related to marijuana actually decreased (Rocky Mountain High Intensity Drug Trafficking Area, 2014). Everything seemed like medical marijuana was going to work without any major issues. However, this soon changed when commercialization of the product became more prevalent. Commercialization made more people want this medical treatment even though they really didn't need it (Rocky Mountain High Intensity Drug Trafficking Area, 2014).

The first major change took place in a Denver court, when a patient that was unable to attain marijuana fought to get their prescription. The Denver District Judge who, in late 2007, ruled that CDPHE violated the state's open meeting requirement when setting a five-patient-to-one-caregiver ratio, and overturned the rule concerning the small ratio of patient to caregiver. This new rule made it much easier to get prescribed medical

marijuana and opened the door for caregivers to claim an unlimited number of patients for whom they were providing and growing marijuana for (Rocky Mountain High Intensity Drug Trafficking Area, 2014). This opened the floodgates for medical marijuana use by the average citizen. This is when medical marijuana abuse started to happen in Colorado.

Later in July of 2009, the Colorado Board of Health tried to regain control of medical marijuana but failed to do so once again in court. The failure to keep the ratio low for the amount of medical marijuana patients to one physician made it extremely hard on caregivers. Some primary caregivers had as many as 1,200 patients instead of 5 patients. Because caregivers and physicians had so many patients now, it was hard to keep track of how each patient's health was progressing. The patients became more of a number to the physicians. The commercialization companies and the federal government did not regulate the use of marijuana at all and as a consequence medical marijuana was abused. Almost anyone could get medical marijuana if they really wanted it (Rocky Mountain High Intensity Drug Trafficking Area, 2014).

After abuse of medical marijuana occurred, marijuana became more prevalent in the market and DUID's and other incidents sky rocketed. The use of marijuana in adolescents and the incidents of marijuana related DUID's almost doubled. This may be because marijuana was now easier to obtain, or they switched from using other drugs to using marijuana because society made it more "legal" in a sense. Over the years of medical marijuana being legal there have been increases in marijuana use throughout Colorado as one can expect. Even though the negative incidences of adolescent use and

traffic incidence boomed after commercialization, they have now leveled off and haven't increased too much from 2010-2013 due to tighter regulations on the drug (Rocky Mountain High Intensity Drug Trafficking Area, 2014). I believe that if tight regulations are placed on medical marijuana and laws are put into place to prevent abuse of the drug, medical marijuana can be very beneficial to society. Over the first couple of years when regulations were held tightly on the drug, Colorado didn't see any major issues. It was when these regulations became lax that medical marijuana was abused. Medical marijuana can help with many debilitating diseases and provides a better quality of life for many patients. Also if medical marijuana is legalized throughout the U.S., every state could perform medical research on the drug more easily which would help us understand its unique medical properties. Medical legalizations would improve quality life for patients, and it would improve the amount of research that can be done on the drug to assess its medical possibilities.

Recreational Marijuana in Colorado

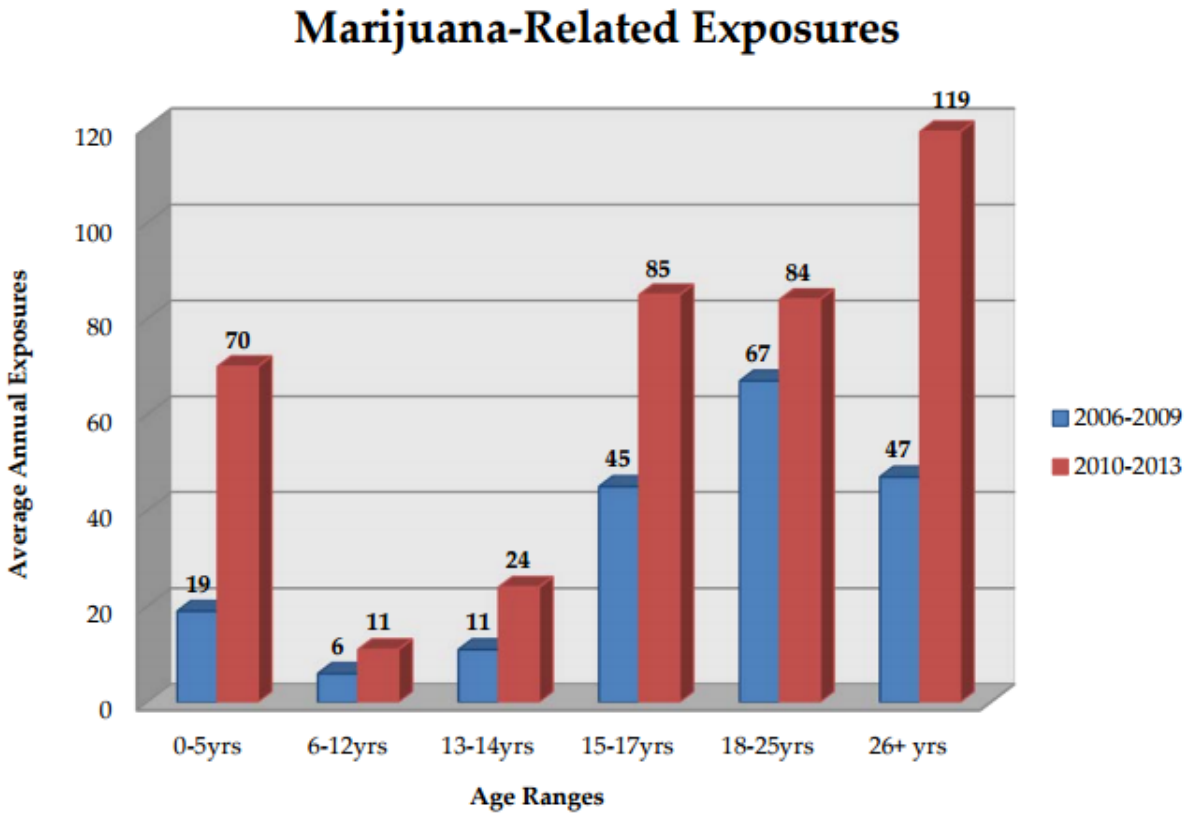
Recreational marijuana was first legalized in Colorado in 2012 when voters passed Amendment 64. This stated that an individual could possess up to 1 ounce of weed at a time if that individual was at least 21 years old. It also stated that an individual could purchase up to$1/4^{th}$ of an ounce of cannabis at a time. Lastly, the individual was only to consume the product in private locations or designated area (Room, 2014). This legalization created a major buzz around the Colorado, and has brought many changes to the city of Denver in particular. Although it has only been a couple of years since the legalization has occurred, there have been many changes that have come along with the

legalization. Some of these changes have been positive for society, but some of these changes have been correlated to negative consequences in society as well.

Negative Effects on Adolescents from Recreational Marijuana Legalization in Colorado

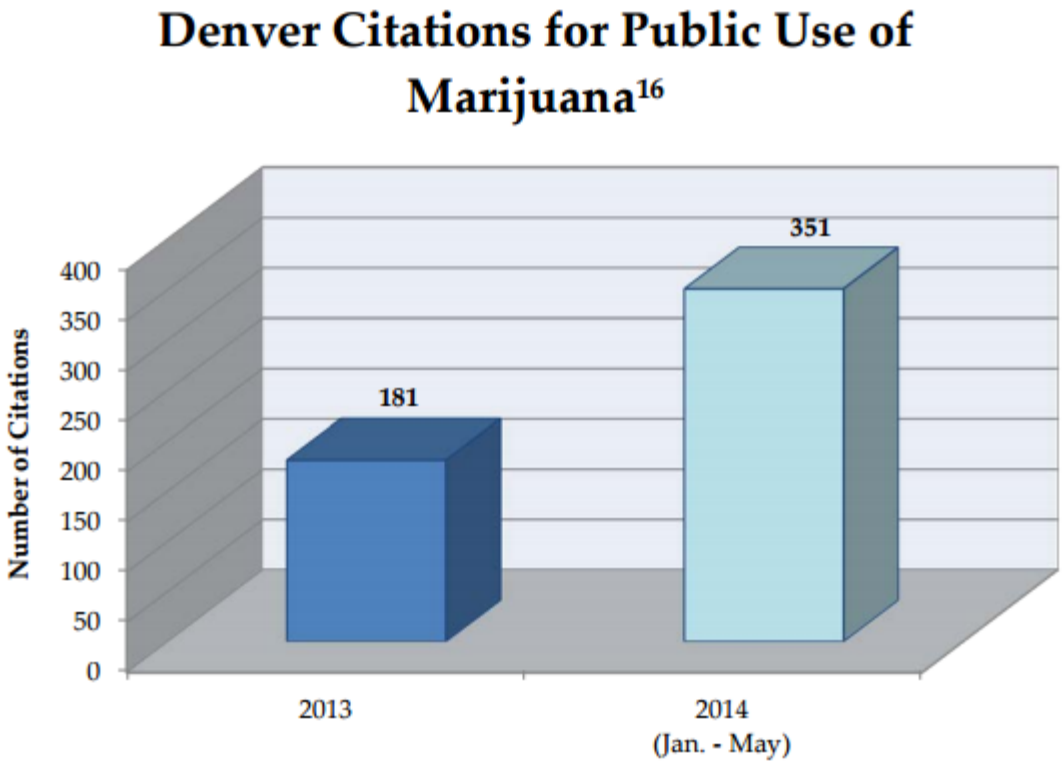
When it comes to recreational marijuana, there are both pros and cons to the implementation. With legalization comes more positive stigmas to society, and sometimes these positive stigmas can have negative influences on society if they are not correctly educated about the drug. If society is not correctly educated about the drug they will most likely use it irresponsibly. This is especially true for adolescents. We have seen this before with medical marijuana. Adolescents and adults will have easier access to it, and adolescents are exposed to the drug much more frequently. The increased

exposure rate due to legalizations can be seen in Figure 3 and 4 below. Because of the higher exposure frequency, they see the drug as less dangerous and eventually abuse it. The increase in use in adolescents can be seen in Figure 5 below. If they abuse marijuana they will see many negative consequences such as being suspended from school, getting in trouble with the law, getting into traffic accidents, health problems, etc., and some of these can be seen in Figure 6 below. These are some of the possible negative consequences from recreational marijuana if society is not properly educated. However, when they are educated more properly these negative consequences have been seen to go down. It is extremely important to educate society, especially adolescents if recreational marijuana is to have more positive effects than negative effects on society.



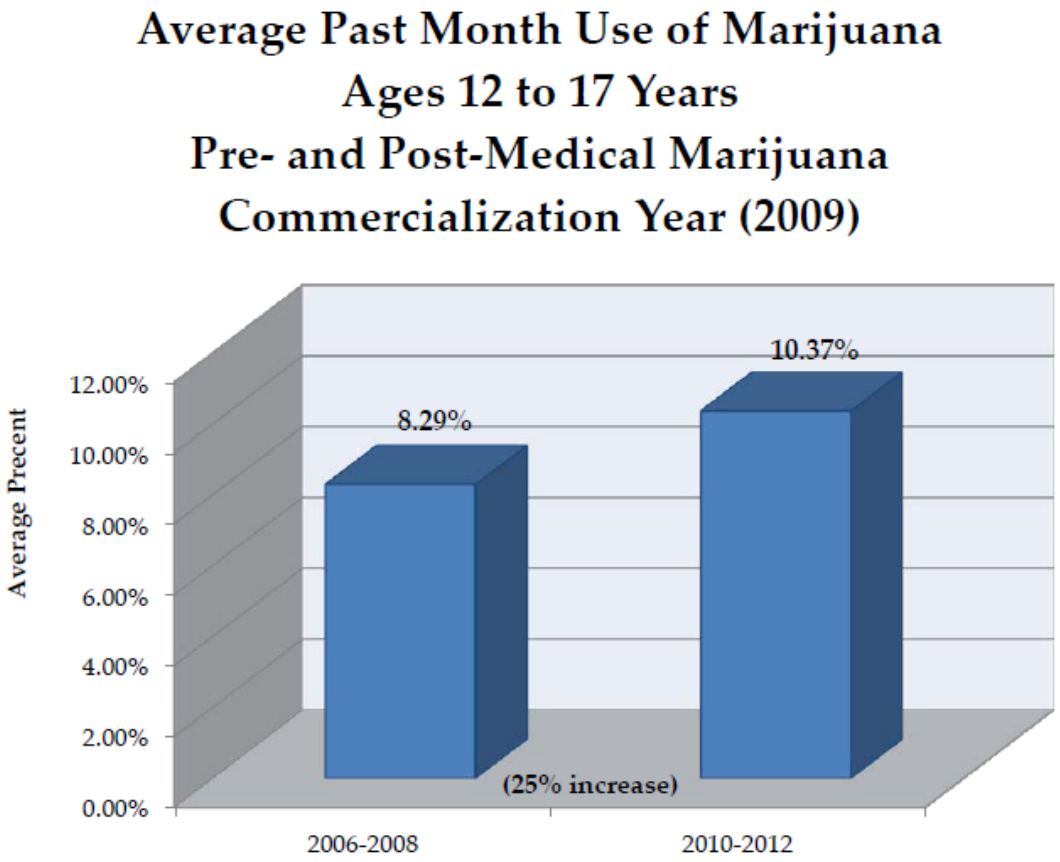
Rocky Mountain High Intensity Drug Trafficking Area. (2014). The Legalization of Marijuana in Colorado: The Impact.

Figure 3: This figure shows how the exposure rates of marijuana have increased after recreational marijuana was legalized. The exposure rates have almost doubled in every age group listed in the figure below. This shows that adolescents are being exposed to the drug much more frequently which can change the way they perceive the drug. If their parents and friends are using the drug, they will not see the drug has potentially harmful to their health. This could be a major influence as to why adolescents are more likely to abuse the drug if it is legalized.



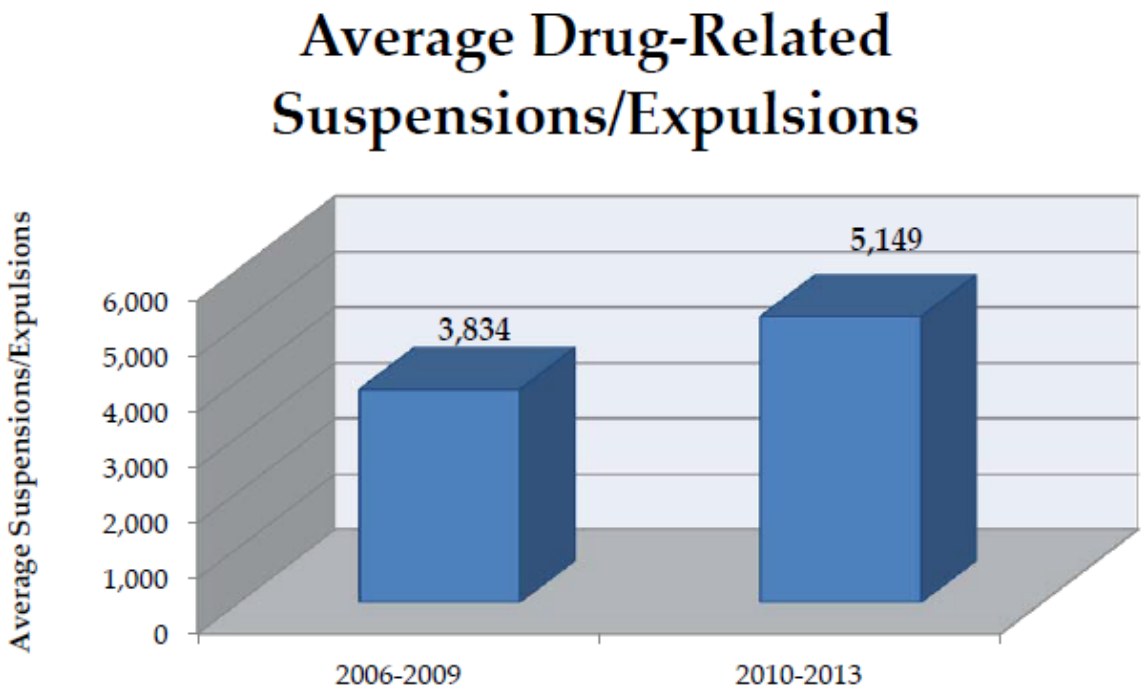
Rocky Mountain High Intensity Drug Trafficking Area. (2014). The Legalization of Marijuana in Colorado: The Impact.

Figure 4: This figure goes along with the exposure rate figure above. This just shows how people in the city of Denver aren't seeing the drug as potentially harmful as they used to see it. They also aren't following the laws stating that marijuana is only supposed ot be used in private areas. Because they are using the drug in public, adolescents are being exposed to it more often and think that it is no dangerous to use. This also shows that abuse of marijuana is taking place and the laws are not being tightly regulated.



Rocky Mountain High Intensity Drug Trafficking Area. (2014). The Legalization of Marijuana in Colorado: The Impact.

Figure 5: This figure shows how the use of marijuana has increased since recreational marijuana has been legalized. It also shows how the commercialization of marijuana influenced the use of marijuana in adolescents. The reason that may be attributed to the increase in marijuana use by adolescents may be the fact that legalizations bring a more positive light on the drug. Since it is legal, adolescents don't see the drug as dangerous as they did before it was legal. Being exposed to the drug more frequently also is likely to account for the increase in use by adolescents.



Rocky Mountain High Intensity Drug Trafficking Area. (2014). The Legalization of Marijuana in Colorado: The Impact.

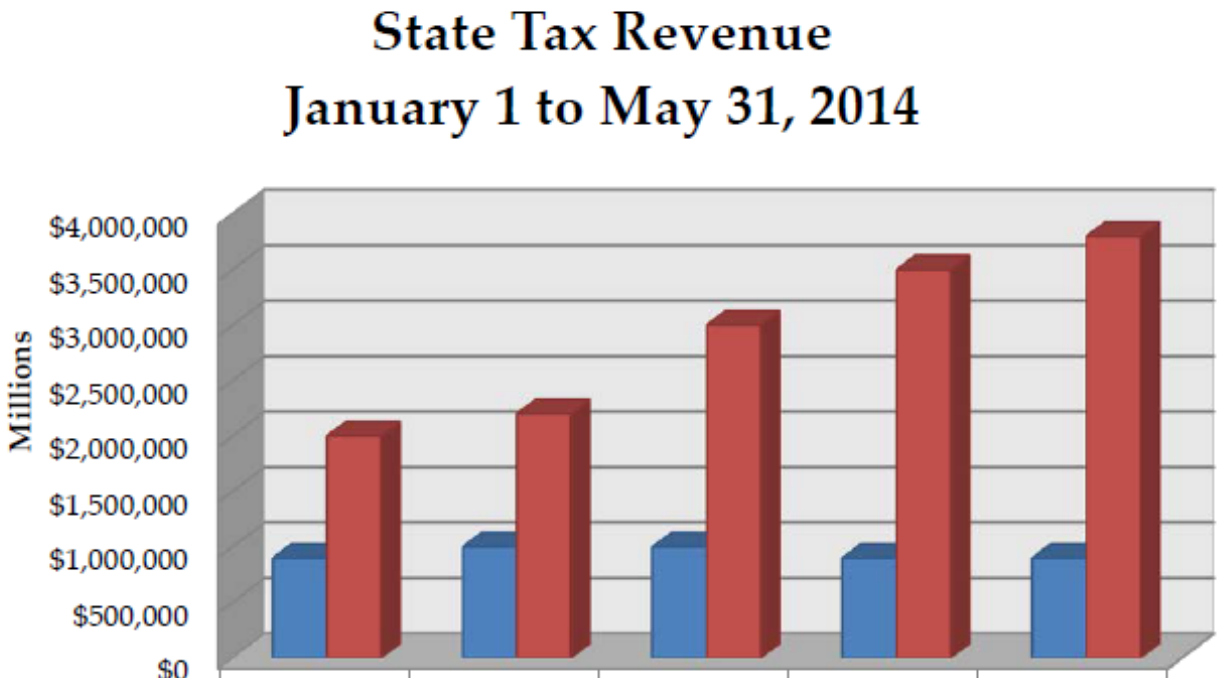
Figure 6: This figure shows how the increase in marijuana use in adolescents is correlated with negative outcomes in school. The negative outcomes in school have almost doubled since marijuana was legalized recreationally. This may be due to the fact that marijuana affects crucial brain development in adolescents and makes them less motivated to pursue higher education.

Positive Effects from Recreational Marijuana Legalization in Colorado

Even though there are a lot of negative consequences that can come with legalizing marijuana, there are also a lot of benefits that can come with it. These benefits can outweigh the consequences if the legalization is implemented corrects and society is correctly educated. Since the first retail marijuana stores opened on January 1st, 2014, the state of Colorado has benefitted from a decrease in crime rates, traffic fatalities, and an increase in tax revenue and economic output from retail marijuana sales and an increase in jobs.

According to the data from the Colorado Court System, marijuana possession arrests have dropped 84% since 2010. In 2010, 9,011 people were arrested for possession, and in 2014 there were 1,464 arrests for possession. Due to the decreasing arrests, the state is saving millions in adjudicatory costs for possession cases. Along with these decreases are the decreases in distributing arrests. The arrests from distribution have dropped about 90%. Property crime and violent crime in the city of Denver has also decreased. Violent crime went down about 2.2% in first 11 months of legalization. Burglaries and overall crime also decreased by about 9%. The tax revenue from the marijuana sales amounted to about $40.9 million between January 2014 and October 2014. This didn't include sales from medicinal marijuana. $2.5 million was set aside to increase the number of health professionals in Colorado Public Schools. Decreases in traffic fatalities went down about 3%. It went from about 449 fatalities to 436. Colorado has the fastest growing economy in the U.S now and its unemployment rates are the lowest they have been for six years. This area of Revenue supplied 16,000 jobs for

people by December 31,2014. The state has also allocated more than $8 million in retail marijuana revenue for youth prevention and education. $2.5 million helped fund youth programs and mentoring programs that focused on drug prevention and school retention. Over $4.3 million was used to fund school based outreach programs for students using marijuana (Alliance, 2015). The tax revenue from sales of recreational and medicinal marijuana can be seen in Figure 5 below.



	January 2014	February 2014	March 2014	April 2014	May 2014
Medical	$900,000	$1,000,000	$1,000,000	$900,000	$900,000
Recreational	$2,000,000	$2,200,000	$3,000,000	$3,500,000	$3,800,000

Rocky Mountain High Intensity Drug Trafficking Area. (2014). The Legalization of Marijuana in Colorado: The Impact.

Figure 7: This figure shows the tax revenue that Colorado has profited from the sales of medicinal and recreational marijuana over a couple of months in 2014. This shows how much of an economic boom legalizing marijuana has brought to Colorado. Not only has recreational and medical marijuana provided a lot of jobs for many people, but it has brought in a lot of money just from sales tax alone (Rocky Mountain High Intensity Drug

Trafficking Area, 2014). The money from these taxes has greatly benefited Colorado in many ways, and it will only continue to benefit Colorado in the coming future.

But, because it has only been a couple years since legalization the data isn't necessarily sufficient because the time period is too short. Although, this may show that advertisement and education on the drug has been made more aware to society due to better knowledge of the drug and its effects. Advertising and making the negative side effects of the drug aware to society may be more important than making the drug legal or illegal. One of the main reasons that there was a boom in usage and negative societal incidences after the 2009 commercialization of medical marijuana is because advertising companies did not do a good job in portraying the possible negative consequences. Also society was very uneducated in the topic of marijuana. The reason why crime rates and traffic incidents have gone down after the legalization of recreational marijuana may be accredited more so to the state of Denver and commercialization companies being better educated in the topic of marijuana use (Rocky Mountain High Intensity Drug Trafficking Area, 2014).

Reflection

While writing this thesis, my position on this topic flip-flopped several times. I originally was pro legalization for recreational and medical marijuana consumption throughout the U.S. The reason I chose this original position was because legalization throughout the U.S. would make research easier and would produce a large sum of money for schools and education programs. Legalization would make research easier and more accessible throughout the U.S. which would vastly increase the amount of knowledge that we currently have about the drug. This increased knowledge would help us better understand its medical properties and would help us know exactly what mechanisms it affects in the body. Obtaining this information could help us understand the various effects of cannabinoids in patients with debilitating and chronic diseases such as cancer and other ailments.

Furthermore, I chose to support legalization because of the positive effects that it would have on the economy. Recreational and medical marijuana would bring in millions of dollars just off of tax revenue. This tax revenue could be used to help fund schools and education programs. The money could also be used to raise awareness about the drug and fund research to help understand its medical properties. But, bringing in money for schools and various programs isn't the only thing that legalization would do. Legalization would also provide thousands of jobs for people around the U.S., and would drastically help decrease the unemployment level nationwide. Recreational and medical marijuana would create an economic boom that would drastically help our country in many positive ways.

However, when I started to do more research in this area of topic, my position slightly change from being all in for recreational legalization to being against recreational legalization. I started to look at stats about exposure rates in adolescents to marijuana in Colorado after legalization, and this statistic was concerning. I also looked into the detrimental effects that marijuana can have on adolescents that consume the drug. I became hesitant in supporting the legalization of marijuana after I looked at the possible side effects resulting from the drastic increase of adolescent consumption. This change in adolescent consumption was daunting, and it made me change my original position on the topic. I do believe that recreational marijuana has a lot of positive benefits, but I do not believe that these benefits are worth risking the health of our youth. I believe that the negative effects that could possibly come with recreational legalization are a little too risky. This is why I changed my position from pro-recreational marijuana.

Even though I am no longer pro-recreational marijuana, I am still pro-medical marijuana. I believe the cannabinoids in marijuana can be very beneficial to many patients, and they can drastically increase the overall quality of life for patients with debilitating diseases. Currently, where medical marijuana has been legalized, it is used to help alleviate various negative symptoms from cancer treatments in many patients. It has been seen to help these patients live a more comfortable life. Legalizing medical marijuana throughout the U.S. would give cancer patients and other patients with debilitating diseases the option of using medical marijuana to help alleviate the negative symptoms they have to deal with while undergoing their current treatments. Just using marijuana as a symptom management reagent could help improve the quality of life in

many patients during their treatment without any serious consequences. There is also new evidence that has shown marijuana may be able to fight cancer directly.

The cannabinoids in marijuana have now been shown to have some anti-cancer properties. These cannabinoids have been seen to decrease the size of cancerous tumors and slow down the progression of cancer throughout the body. They have also been seen to induce apoptotic events in the cancer which cause the cancer cells to die off. Cannabinoids also have low toxicity in the body and do not inhibit the effects of other cancer treatments such as chemotherapy. This evidence suggests that the cannabinoids in marijuana may be able to work with other cancer treatments to help fight cancer and its negative properties. Legalizing marijuana would allow us to better understand the effects cannabinoids have against cancer, and may actually show that marijuana should be used as a form of cancer treatment. I believe that cannabinoids could be used to fight cancer, and given the evidence deserve a chance to be used medically for many reasons.

Finally, I believe that medical marijuana should be legalized throughout the U.S. This legalization would make research on the drug easier and would help us understand its medical properties. I also believe that medical marijuana greatly improves the quality of life for many patients, and may also be able to slow down the growth of cancer in many patients. Medical marijuana also has stricter policies on it that make it less accessible to adolescents which would help prevent the detrimental effects that come with adolescent consumption. Lastly, medical marijuana would still help out the economy. It would still provide a lot of jobs throughout the U.S., and it still would bring in a large sum of money that could be used to help schools or disease research. In my opinion, the

benefits of medical marijuana outweigh the negative consequences of its legalization. Because of this I believe that medical marijuana should be legalized throughout the U.S. and its medical properties should be put into play.

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