Cannabis and the Cardiovascular system

(An extract from Cannabis: 'A General Survey of its Harmful Effects' Mary Brett updated January 2019

Comparatively little research has been done in this area, but there are sufficient published scientific papers to raise concern.

At first the intoxication produced by cannabis causes an increase in heart rate of between 20 and 50% (Huber et al 1988, Jones 1984). A rise in blood pressure occurs if the person is sitting or lying, but on standing up the pressure drops, in some cases causing the person to faint (Maykut 1984). A new and naive smoker may be concerned about these effects (Sidney 2002), but someone with a healthy heart is not thought to be at risk.

Cannabis affects the cardiovascular system in other ways as well. THC increases the production of chemicals called catecholamines which stimulate the heart, it also has analgesic properties which may lessen any chest pain and delay the seeking of treatment and the level of carboxyhaemoglobin is raised, decreasing the supply of oxygen to the heart, placing it under greater strain (Jones 1982 and 1984).

Older field studies involving chronic cannabis users in Costa Rica (Carter et al 1980), Greece (Stefanis et al 1977) and Jamaica (Rubin and Comitas 1975), found no evidence of cardiac toxicity even in subjects with existing heart disease. And electrocardiographic studies in both acute and prolonged administration have rarely revealed pathological changes (Benowitz and Jones1975, Jones 1984). So again it was concluded that young healthy adults using cannabis intermittently ran no major risk of a life-threatening cardiovascular event as may occur with a drug like cocaine. (Gawin, Ellinwood 1988).

However tolerance quickly develops to the acute cardiovascular effects of cannabis (Benowitz and Jones 1975, Jones and Benowitz 1976, Nowlan and Cohen 1977). And Jones (1984) showed that in people receiving daily high doses by mouth, tolerance develops in 7 to 10 days. This could possibly help to explain why toxic effects are sometimes not seen.

More recently though, there have been a number of papers documenting myocardial infarction and angina pectoris among young people using cannabis.

Podczeck and others 1990 reported 2 cases of myocardial infarction in very young healthy people and Choi and Perl 1989 and Perl and Choi 1992 found the same in young men, heavy users, with no history of heart disease. In 2000 Kosior and others wrote about 2 cases of cardiac arrhythmia (one of atrial fibrillation and one of recurrent paroxysmal tachycardia) in youngsters. Jones in 2002 reported transient ischaemic attacks and strokes in young and older people as well as deaths in young people from myocardial infarction.

Three teenagers, 15,16 and 17, who "binge smoked" cannabis suffered strokes, two died and one was left paralysed. In the two who died the stroke appeared to have been triggered by a clot in the brain or a constriction of the blood vessels over a wide area (Geller et al 2004). Professor John Henry of Imperial College said it was very disturbing, "I have seen cases of stroke due to cannabis use but fortunately none of my patients have died. One woman had all the signs of a stroke with paralysis down one side but fortunately recovered after several days".

A 36 year-old man suffered strokes on three separate occasions, at almost yearly intervals, shortly after smoking a large amount of cannabis. He had been an occasional cannabis user, did not use other drugs and drank only occasionally. He had no known risk factors for stroke and no narrowing or hardening of the arteries which may lead to strokes or heart attacks. Mateo et al in 2005 said, "…even if the side effect is rare, it is a serious one"

An item in The Crawley News (Trinity Mirror PLC) on 12/07/06 reported that a 23-year-old sales manager had collapsed and died from a brain haemorrhage. He was a fit, healthy man with no hardening of the brain arteries but had a history of cannabis abuse and had been complaining of headaches for some time. At the inquest, Dr Colin Hunter-Craig said, " He died of a brain haemorrhage

due to cannabis abuse…This is incredibly rare in young people, but in old people we would recognise this as a stroke".

Research in 2001 by Herning et al using Transcranial Doppler Sonography (Sound waves to measure cerebral artery blood flow resistance) found that prolonged marijuana use in 18 to 30 year olds increased the resistance in these arteries so restricting blood flow to the brain. 16 long-term male users were compared with 19 non-users. The deficit persisted for 4 weeks after abstinence. They compared the results to that of the brain of a 60 year old. Advancing age increases the chance of a stroke.

Mittleman and others in 2001 interviewed 3882 patients with heart attacks. He concluded that the risk of onset of myocardial infarction rose by almost 5 times in the hour following the smoking of a joint.

2002 Clinical Cardiology carried an article by McLeod L et al on myocardial infarction in a young man following the combined use of cannabis and viagra. Viagra is metabolised predominantly by cytochrome P450 3A4 isoenzyme. Cannabis is a known inhibitor of this isoenzyme. Caution is needed in prescribing viagra in cases where the person has cardiovascular disease because of the vasodilatory effects of viagra.

In January 2004 an article in Neurologist by Moussouttas reviewed all reported cases of presumed cannabis related cerebral ischemic events in the medical literature, as well as pertinent human and animal experimental studies on the cardiovascular and cerebrovascular effects of cannabis. His conclusion was "Cannabis use seems to have been causally related to several instances of cerebral ischaemia and infarction. Proposed etiologic mechanisms have included cerebral vasospasm, cardio-embolization and systematic hypotension with impaired cerebral auto-regulation, but most of the available data points to a vaso-spastic process. The exact relation to cerebro-vascular disease remains to be determined".

We still do not know the long term effects of exposure to cannabis smoke on the cardiovascular system over several years but our experiences with the problems of tobacco smoke should make us very cautious. Jones (1984) suggested that, "after years of repeated exposure, there may be lasting, perhaps even permanent alterations of the cardiovascular system function". He says, " There are enough similarities between THC and nicotine's cardiovascular effects to make the possibility plausible".

One paper in 2004 involving a study on genetically modified mice found that THC helped prevent atherosclerosis, a "furring up" of the arteries caused by plaques of protein and other material. The study was headed by Francois Mach a cardiologist, and published in Nature. He warned that smoking cannabis would not be the answer as oxygen levels are reduced and THC increases the heart rate and interferes with blood pressure as previously described. He called for THC (already available as a medicine, Nabilone) or other cannabinoid derivates to be investigated for this role. This is in line with all licensed medicines that must be pure single chemicals and subjected to standard clinical testing. This request was repeated in another paper by Mach and Steffens in January 2006.

In 2005 a letter to the editor of The International Journal of Cardiology was sent by Lindsay et al. It described 2 distinct cases giving cause for concern. In the first, "cannabis use precipitated a malignant arrhythmia in a patient with critical ischaemia from long-standing coronary artery disease. In the second, a young patient presented with an acute myocardial infarction that had started while smoking marijuana; subsequently diffuse coronary artery disease was found at angiography despite the patient's low risk factor status".

A case of paroxysmal artrial fibrillation (AF), a common condition usually triggered by alcohol use, was documented when a young female 22 year old presented herself. She had normal echocardiography but was a regular daily (1-2 joints) cannabis smoker. The author, Charbonney in 2005, warned that marijuana was a unusual trigger but should be checked for in young people after alcohol consumption had been ruled out.

The Irish Examiner on 3rd May 2007 reported the sudden death of a 21 year-old fit young father. Tiny traces of cannabis were found in his system. Assistant state pathologist, Dr Margaret Bolster said David Kelly died because the rhythmical electrical pulse in his heart misfired, causing it to stop. She pointed to a growing body of medical evidence which shows links between the triggering of similar heart

conditions and the use of drugs like cannabis and cocaine. The individual may have had an underlying genetic cardiac problem, this happens in almost a quarter of such cases.

A study in February 2008 on atrial fibrillation and marijuana smoking by Korantzopoulos et al links atrial fibrillation with marijuana smoking. Only healthy young male smokers took part and it was found that "Compelling evidence is accumulating that cannabis has significant haemodynamic (change in blood pressure) and electrophysiological (tachycardia and atrial fibrillation) effects on the cardiovascular system". The authors concluded that atrial fibrillation should be included in the cardiovascular complications of marijuana smoking. Its incidence in the general population is probably underestimated.

A 2008 paper by Mukamal et al found that marijuana use was associated with a 3-fold greater mortality after acute myocardial infarction. This suggests there may be particular risks for people with established cardiovascular disease.

A possible connection between marijuana abuse and stokes or heart attacks was found in a paper in 2008 (May) by Jayanthi and others. Abnormalities in proteins caused by heavy marijuana use were investigated. A protein, apoC -111 (apolipoprotein C-111) showed significant increases in marijuana users. This is associated with increases in triglycerides. This may be one reason why some marijuana users have an increased risk of stroke and heart attack.

2010 Jouanjus et al looked at cannabis-related hospitalizations among 200 patients admitted to the public hospitals of the Toulouse area of France between Jan 2004 and Dec 2007. They found that one of the adverse events (AE) was lethal. Psychiatric disorders occurred in 57.7%, leading to 18.2% of AEs, central and peripheral nervous system disorders, 15.8%, acute intoxication 12.1%, respiratory system disorders 11.1%, and cardiovascular disorders 9.5%.

2011 April Wolff et al examined 48 consecutive young patients admitted for acute ischemic stroke. They found multi-focal intra-cranial stenosis associated with cannabis use in 21% (10 patients), and concluded that multi-focal angiopathy associated with cannabis consumption could be an important cause of ischemic stroke in young people.

2013 February Wolff, after a new literature review, concluded that cannabis-related stroke is not a myth and cannabis use should be considered as a risk factor inducing ischemic stroke. She said, 'most cannabis users are young , patients under 45 years of age presenting with symptoms of stroke should be asked about cannabis use and their urine tested for cannabinoids. 59 cases of cannabis-related stroke (mean age 33) were described mostly male ratio male to female 4.9:1. Of the 59, 46 were classified as ischemic stroke, 5 were transient ischemic attacks, one a haeorrhagic stroke and in 4 patients a diagnosis of stroke was suspected but no neuro-imaging was done. In many cases they occurred while smoking or within half an hour.

2013 February 6th Dr Alan Barber (University of Auckland) presented his findings to The American Stroke Association annual meeting in Honolulu. He studied 160 controls and 160 stroke patients, 150 of them with ischemic strokes. 16% of stroke patients had positive cannabis screens compared with only 8% of the controls. This is a doubling of the risk. They were more likely to be male (84%) and tobacco smokers (88%). This is a doubling of the risk for cannabis users.

2013 Professor Joseph Harbison told Dublin Coroner's Court that St James's Hospital had seen 5 or 6 cases of young people having strokes following the use of herbal cannabis in the last 3 years. He thought it may be due to the higher strength.

2014 Thomas et al determined what cardiologists need to know. 200 million use cannabis worldwide. Since cannabis is now legal in 2 American States and medical cannabis is available in around 20 others, it is important that cardiologists are aware of the increase in health problems that may occur. These are: myocardial infarction, sudden cardiac death, cardiomyopathy, stroke, transient ischemic attacks, and cannabis arteritis.

2014 Singh and others Looked at a case of atrial fibrillation in an eighteen year old adolescent. An 18 year old with a structurally normal heart presented with prolonged atrial fibrillation (AF) precipitated by new-onset generalised tonic-clonic convulsions and marijuana abuse. This is an interesting

association and a unique pathophysiology between generalised toni-clonic convulsions , marijuana abuse and AF. Seizures and marijuana abuse should be considered in the differential diagnosis of the etiology of AF in children.

2014 Daldrup et al found that 2 young men had died unexpectedly after smoking cannabis. A 23 year old had a serious undetected heart problem and the 28 year old had abused alcohol, amphetamine and cocaine in the past. 'To our knowledge these are the first cases of suspected fatal cannabis intoxications where full post-mortem investigations…… were carried out'.

2014 Jouanjus et al, looked at all spontaneous reports of cardiovascular complications related to cannabis use collected by the French Addictovigilance Network from 2006 to 2010. 1.8% of all cannabis-related reports (35/1979) were cardiovascular complications, with patients being mostly men (85.7%) and of an average age of 34.3 years. There were 22 cardiac complications (20 acute coronary syndromes), 10 peripheral complications (lower limb or juvenile arteriopathies and Buerger-like diseases), and 3 cerebral complications (acute cerebral angiopathy, transient cortical blindness, and spasm of cerebral artery). In 9 cases, the event led to patient death.

2014 April Casier et al reported cases of 3 patients where recent and/or chronic use of marijuana lead to severe cardiac function. All 3 collapsed at home and needed CPR with initial restoration of spontaneous circulation (ROSC). All 3 had used cannabis and no other drug. They concluded: ' Cannabis use can lead to severe cardiovascular problems and sudden death, not only in people at increased cardiovascular risk but also in young people without any medical history or risk factors'.

2014 Lee found migratory superficial thrombophlebitis in a cannabis smoker. A 28-year old man had a 5-year history of recurrent painful subcutaneous nodules in various parts of his body. He developed a 1cm nodule in his right calf which progressed over 2 days to 4cm. This was repeated once/every few weeks in diffeent locations. This was Buerger disease. Tobacco smoking is often considered essential but he denied smoking. A few cases associated with cannabis have been repported.

2014 Wolff and others looked at the high frequency of intracranial arterial stenosis and cannabis use in ischaemic stroke in the young. 159 patients (18-45) admitted for acute ischaemic stroke from Oct 2005 to Dec 2010 were studied. Conclusion: Intracranial arterial stenosis may be an important mechanism of stroke in young patients and should be systematically investigated using vascular imaging. Patients should be strongly questioned about cannabis use. Cannabis use may be associated with critical consequences such as stroke.

2014 Gunawardena et al reported a case of myocardial infarction following cannabis induced vasospasm. A 29 year old man (Sri Lanka) presented with acute coronary syndrome following consumption of 'Kerala Ganja', a much more potent form than the local ganja (marijuana). A diagnosis was made of vasospasm causinf myocardial infarction, most likely to have been triggered by cannabis consumption.

2014 Wang et al looked at the damage to blood vessels by secondhand marijuana smoke. Anaesthetised rats were exposed to marijuana SHS (Secondhand smoke). They concluded that marijuana and tobacco SHS impair endothelial function similarly under comparible exposure conditions. Public exposure should be avoided whether tobacco or marijuana smoke.

2015 Hackam investigated cannabis and strokes. Case reports on cannabis and cerebro-vascular events were retrieved. There were 34 case reports on 64 patients. Most of them (81%)exhibited a temporal relationship between cannabis exposure and the index event. In 70% the evaluation was sufficiently comprehensive to exclude other sources for stroke. 22% of the patients had another stroke after subsequent re-exposure to cannabis. Finally half the patients had concominant stroke risk factors, most commonly tobacco (34%) and alcohol (11%) consumption. They concluded that many case reports support a causal link between cannabis and cerebro-vascular events.

2015 Rumalla et al looked at hospitalizations for aneurismal sub-arachnoid haemorrhage (aSAH). The Nationwide Inpatient Sample, 2004-2011 was used. They concluded that 'Our analysis suggests that recreational cannabis use is independently associated with an 18% increase likelihood of asAH'. It was more frequent in younger male patients.

2016 Wang et al looked at second-hand marijuana smoke (SHS) exposure and vascular endothelium functioning. Endothelial function was measured as femoral artery flow-mediated dilation (FMD) in rats. One minute of exposure to SHS of marijuana impaired FMD to a comparable extent as impairment from equal concentrations of tobacco SHS but recovery was considerably slower.

2016 Singh et al found that marijuana use may be linked to temporarily weakened heart muscle. 'Active marijuana use may double the risk of stress cardiomyopathy , an uncommon heart muscle malfunction that can mimic heart attack symptoms'. The heart's ability to pump leads to chest pain, shortness of breath, dizziness and sometimes fainting. 33,343 people hospitalised with the condition from 2003-2011 in the USA were studied. Less than 1% were cannabis users (210). These users were significantly more likely to go into cardiac arrest (2.4% v 0.8% (non-users), and require a defibrillator. "Marijuana users were more likely than non-users to have a history of depression (32.9 percent vs. 14.5 percent), psychosis (11.9 percent vs. 3.8 percent), anxiety disorder (28.4 percent vs. 16.2 percent), alcoholism (13.3 percent vs. 2.8 percent), tobacco use (73.3 percent vs. 28.6 percent) and multiple substance abuse (11.4 percent vs. 0.3 percent). Because some of these can increase the risk of stress cardiomyopathy, the researchers adjusted for known risk factors to investigate the association between marijuana use and stress cardiomyopathy."

2016 Reece and others looked at cannabis exposure as an interactive cardiovascular risk factor and accelerant of organismal ageing. 11 cannabis-only smokers, 504 tobacco-only users, 114 tobacco and cannabis users and 534 non-smokers were studied over a 5 year period. They discovered that long-term use of cannabis increased the biological age of those studied by 11% due to the impact of hardening of the arteries e.g. a thirty year old would have a biological age of 33. Associate Professor Stuart Reece said that the results showed that, 'not only does it age you, it increases ageing at an exponential rate over time which is alarming'.

2016 Draz et al Looked at marijuana use in acute coronary syndromes. 138 male patients, around 40 years of age with acute myocardial infarction were studied. Urine samples were submitted for toxicological analysis. None of group 1(cannabis positive only) had normal coronaries. Significant changes in echocardiography and angiography were found between group 1 and the other groups – group 2 (patients positive for other substance abuse) and group 3 (Negative for any substance abuse). 'Cannabis smoking could be a potential risk factor for the development of cardiac ischemia'.

2017 Kalla et al found that cannabis users have a 26% higher chance of suffering a stroke and 10% higher chance of suffering a heart attack than non-users. Confounding factors like obesity, alcohol and tobacco smoking were accounted for. Previous research in cell culture has shown that heart muscle has cannabis receptors relevant to contractility or squeezing ability which may be one mechanism whereby marijuana use could affect the cardiovascular system. More than 20 million records of young and middle-age patients between 18 and 55 discharged from 1,000 hospitals in 2009 and 2010 when marijuana use was illegal in most states were studied. 1.5% were marijuana users.

2017 Atchaneeyasakul et al found that a large amount of cannabis ingestion results in spontaneous intracerebral haemorrhage. Abstract: Although multiple cases of cannabis-associated ischemic stroke have been reported, there are only 2 reported cases of hemorrhagic stroke with an associated cerebral vasoconstriction. To our knowledge, we present the first case of basal ganglia hemorrhage after a large-volume oral ingestion of cannabis without other identified risk factors. In our case, cerebral digital subtraction angiography within 24 hours of presentation did not reveal vasoconstriction leading to a possible alternative explanation for hemorrhagic stroke, including cannabis-induced transient arterial hypertension and auto-regulation disruption'.

2017 Wolff et al found that strokes are possible combinations of cannabinoid use. Ninety eight patients were described as cannabinoid-related stroke, 85 after cannabis use and 13 after synthetic cannabinoids. The mean age of patients was 32.3 years and ratio of male to female was 3.7:1. In 66% of cases cannabis was smoked with tobacco. Most with cannabinoid strokes were chronic (81%) cannabis users and for 18% of them there had been an increase in consumption of cannabis in the days before the stroke. The prognosis was favourable in 46% of cases, but 5 patients died. As of today, reversible cerebral vasoconstriction triggered by cannabinoid use may be a convincing mechanism of stroke in 27% of all cases.

2017 Yankee et al looked at the effect of marijuana use on cardiovascular and cerebrovascular mortality. ‘The design of this study was based on a mortality follow-up. Method We linked participants aged 20 years and above, who responded to questions on marijuana use during the 2005 US National Health and Nutrition Examination Survey to data from the 2011 public-use linked mortality file of the National Center for Health Statistics, Centers for Disease Control and Prevention. Only participants eligible for mortality follow-up were included. We conducted Cox proportional hazards regression analyses to estimate hazard ratios for hypertension, heart disease, and cerebrovascular mortality due to marijuana use. We controlled for cigarette smoking and other relevant variables. Results Of the 1213 eligible participants 72.5% were presumed to be alive. The total follow-up time was 19,569 person-years. Adjusted hazard ratios for death from hypertension among marijuana users compared to non-marijuana users was 3.42 (95% confidence interval: 1.20-9.79) and for each year of marijuana use was 1.04 (95% confidence interval: 1.00-1.07). Conclusion From our results, marijuana use may increase the risk for hypertension mortality. Increased duration of marijuana use is associated with increased risk of death from hypertension. Recreational marijuana use potentially has cardiovascular adverse effects which needs further investigation’.

2017 Volcon et al looked at multiple cerebral infarcts in a young patient associated with marijuana use. ‘ Cerebrovascular events associated with marijuana use have been reported previously. This association is plausible, but not well-established yet. A 14-year-old girl, long-term heavy cannabis user, presented with generalized tonic-clonic seizures and decreased level of consciousness a few hours after smoking cannabis. Brain magnetic resonance imaging showed multiple areas of acute, subacute and chronic ischemic lesions in the left frontal lobe, basal ganglia, and corpus callosum. History of other illicit drug use and other known causes of stroke were ruled out. Cannabis might cause stroke through direct effects on the cerebral blood circulation, orthostatic hypotension, vasculitis, vasospasm, and atrial fibrillation. Long-term daily use of marijuana in young people may cause serious damage to the cerebrovascular system’.

2017 Rickner et al looked at a case report of neuro-and cardiotoxicity following use of cannabis concentrates. ‘A 17-year-old athletic man developed agitation requiring sedation and intubation for safety, with peak systolic blood pressures in the 190s and hyperthermia (to 102 °F). He developed elevated serum troponins with persistent tachycardia despite sedation and no clear non-intoxicant etiology. It was discovered that the patient had recently been "dabbing"; an exhaustive search of his home found a sample of the "dabs" which was analyzed along with a comprehensive urine drug screen by tandem liquid mass spectroscopy (t-LCMS) for confirmation.Tetrahydrocannabinol (THC) has been increasingly associated with agitation and cardiotoxicity, while cannabidiol (CBD) has been associated with neuroprotective, inhibitory states. We propose that increasing concentrations of THC as well as THC:CBD ratios seen in cannabis concentrates such as "dabs" may cause agitation and end-organ damage through sympathomimetic and serotonergic pathways.

2017 Gomez-Ochoa investigated stroke and cannabis use in patients with no cardiovascular risk factors. ‘A systematic literature review was conducted through Medline, EBSCOhost, EMBASE, Lilacs, and Scielo to gather case reports published before 13 May 2016 presenting patients with a diagnosis of CVD or transient ischaemic attack, a history of cannabinoid use, and no other cardiovascular risk factors A total of 18 case reports were selected from the 566 references found.There is a wide variety of reports of stroke associated with cannabis use in patients with no other risk factors. Noteworthy findings were presentation at young age and a strong temporal association, which place cannabis use as a potential risk factor for this population in line with the epidemiological and pathophysiological studies in this area.

2017 Abouk et al looked at the relationship between medical cannabis laws and cardiovascular deaths in the US. ‘We analyze cardiac-related mortality data from the U.S. National Vital Statistics System for 1990-2014. We use difference-in-difference fixed-effects models to assess whether there are increased rates of cardiac-related mortality following passage of medical cannabis programs. We also analyze whether states with more liberal rules on dispensing cannabis show higher mortality rates. For men, there is a statistically significant 2.3% increase in the rate of cardiac death following passage. For women, there is a 1.3% increase that is also statistically significant. he effects increase or both men and women with age. The effects are also stronger in states with more a lax approach to cannabis dispensing’.

2017 Singh et al looked at cardiovascular complications with marijuana and other substances. ‘Absract: The recreational use of cannabis has sharply increased in recent years in parallel with its legalization and decriminalization in several countries. Commonly, the traditional cannabis has been replaced by

potent synthetic cannabinoids and cannabimimetics in various forms. Despite overwhelming public perception of the safety of these substances, an increasing number of serious cardiovascular adverse events have been reported in temporal relation to recreational cannabis use. These have included sudden cardiac death, vascular (coronary, cerebral and peripheral) events, arrhythmias and stress cardiomyopathy among others. Many of the victims of these events are relatively young men with few if any cardiovascular risk factors. However, there are reasons to believe that older individuals and those with risk factors for or established cardiovascular disease are at even higher danger of such events following exposure to cannabis. The pathophysiological basis of these events is not fully understood and likely encompasses a complex interaction between the active ingredients (particularly the major cannabinoid, Δ9-tetrahydrocannabinol), and the endo-cannabinoid system, autonomic nervous system, as well as other receptor and non-receptor mediated pathways. Other complicating factors include opposing physiologic effects of other cannabinoids (predominantly cannabidiol), presence of regulatory proteins that act as metabolizing enzymes, binding molecules, or ligands, as well as functional polymorphisms of target receptors. Tolerance to the effects of cannabis may also develop on repeated exposures at least in part due to receptor downregulation or desensitization. Moreover, effects of cannabis may be enhanced or altered by concomitant use of other illicit drugs or medications used for treatment of established cardiovascular diseases. Regardless of these considerations, it is expected that the current cannabis epidemic would add significantly to the universal burden of cardiovascular diseases'.

2018 Desai et al looked at recreational marijuana use and myocardial infarction. Abstract: To our knowledge, this is the first ever study analyzing the lifetime odds of acute myocardial infarction (AMI) with marijuana use and the outcomes in AMI patients with versus without marijuana use. We queried the 2010-2014 National Inpatient Sample (NIS) database for 11-70-year-old AMI patients. Pearson Chi-square test for categorical variables and Student T-test for continuous variables were used to compare the baseline demographic and hospital characteristics between two groups (without vs. with marijuana) of AMI patients. The univariate and multivariate analyses were used to assess and compare the clinical outcomes between two groups. We used Cochran-Armitage test to measure the trends. All statistical analyses were executed by IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY). We used weighted data to produce national estimates in our study. Results Out of 2,451,933 weighted hospitalized AMI patients, 35,771 patients with a history of marijuana and 2,416,162 patients without a history of marijuana use were identified. The AMI-marijuana group consisted more of younger, male, African American patients. The length of stay and mortality rate were lower in the AMI-marijuana group with more patients being discharged against medical advice. Multivariable analysis showed that marijuana use was a significant risk factor for AMI development when adjusted for age, sex, race (adjusted OR 1.079, 95% CI 1.065-1.093, p<0.001); adjusted for age, female, race, smoking, cocaine abuse (adjusted OR 1.041, 95% CI 1.027-1.054, p<0.001); and also when adjusted for age, female, race, payer status, smoking, cocaine abuse, amphetamine abuse and alcohol abuse (adjusted OR: 1.031, 95% CI: 1.018-1.045, p<0.001). Complications such as respiratory failure (OR 18.9, CI 15.6-23.0, p<0.001), cerebrovascular disease (OR 9.0, CI 7.0-11.7, p<0.001), cardiogenic shock (OR 6.0, CI 4.9-7.4, p<0.001), septicemia (OR 1.8, CI 1.5-2.2, p<0.001), and dysrhythmia (OR 1.8, CI 1.5-2.1, p<0.001) were independent predictors of mortality in AMI-marijuana group. Conclusion The lifetime AMI odds were increased in recreational marijuana users. Overall odds of mortality were not increased significantly in AMI-marijuana group. However, marijuana users showed higher trends of AMI prevalence and related mortality from 2010-2014. It is crucial to assess cardiovascular effects related to marijuana overuse and educate patients for the same.

2018 Defilippis et al investigated cocaine and marijuana use among young adults presenting with myocardial infarction. Abstract: We retrospectively analyzed records of patients presenting with a Type 1 MI at ≤50 years at two academic hospitals from 2000-2016. Substance abuse was determined by review of records for either patient-reported substance abuse during the week prior to MI or detection on toxicology screen. Vital status was identified by the Social Security Administration's Death Masterfile. Cause of death was adjudicated using electronic health records and death certificates. Cox modeling was performed for survival free from all-cause and cardiovascular death. 2097 patients had Type 1 MI (mean age 44±5.1 years, 19.3% female, 73% white) with median follow-up of 11.2 years (interquartile range: 7.3-14.2). Use of cocaine and/or marijuana was present in 224 (10.7%) patients; cocaine in 99 (4.7%) patients and marijuana in 125 (6.0%). Individuals with substance use had significantly lower rates of diabetes (14.7% versus 20.4%, p = 0.05) and hyperlipidemia (45.7% versus 60.8%, p < 0.001), but were significantly more likely to use tobacco (70.3% versus 49.1%, p < 0.001). The use of cocaine and/or marijuana was associated with significantly higher cardiovascular (HR 2.22;

95% CI 1.27 – 3.7, p=0.005) and all-cause mortality (HR 1.99; 95% CI 1.35 – 2.97, p=0.001) after adjusting for baseline covariates.Cocaine and/or marijuana use is present in 10% of patients with an MI at age ≤50 years and is associated with worse all-cause and cardiovascular mortality.

2018 Pacher et al looked at the cardiovascular effects of marijuana and synthetic cannabinoids. Abstract: Dysregulation of the endogenous lipid mediators endocannabinoids and their G-protein-coupled cannabinoid receptors 1 and 2 (CB1R and CB2R) has been implicated in a variety of cardiovascular pathologies. Activation of CB1R facilitates the development of cardiometabolic disease, whereas activation of CB2R (expressed primarily in immune cells) exerts anti-inflammatory effects. The psychoactive constituent of marijuana, Δ9-tetrahydrocannabinol (THC), is an agonist of both CB1R and CB2R, and exerts its psychoactive and adverse cardiovascular effects through the activation of CB1R in the central nervous and cardiovascular systems. The past decade has seen a nearly tenfold increase in the THC content of marijuana as well as the increased availability of highly potent synthetic cannabinoids for recreational use. These changes have been accompanied by the emergence of serious adverse cardiovascular events, including myocardial infarction, cardiomyopathy, arrhythmias, stroke, and cardiac arrest. In this Review, we summarize the role of the endocannabinoid system in cardiovascular disease, and critically discuss the cardiovascular consequences of marijuana and synthetic cannabinoid use. With the legalization of marijuana for medicinal purposes and/or recreational use in many countries, physicians should be alert to the possibility that the use of marijuana or its potent synthetic analogues might be the underlying cause of severe cardiovascular events and pathologies.

2018 August. Desai et al looked at the burden of arrhythmia in recreational cannabis users. Absract: Marijuana or Cannabis is extensively used as a recreational substance globally. Case reports have reported cardiac arrhythmias immediately following recreational marijuana use. However, the burden of arrhythmias in hospitalized marijuana users have not been evaluated through prospective or cross-sectional studies. Therefore, we planned to measure temporal trends of the frequency of arrhythmias in hospitalized marijuana users using National Inpatient Sample (NIS) database in the United States. Highlights:

- •Total of 2.7% of recreational marijuana users developed arrhythmia with a steadily increasing trend from 2010 through 2014.
- •Atrial fibrillation was the most common subtype arrhythmia among hospitalized marijuana users.
- •The incidence of arrhythmia in male and female marijuana users nearly increased two-fold between 2010 and 2014.
- •The all-cause in-hospital mortality in marijuana users with arrhythmias increased from 3.7% in 2010 to 4.4% in 2014.

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