

# The Negative Side-Effects of Prescription Drugs

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**Abstract:** In modern medicine, the prescribing of medication has become the full norm when it comes to treating patients. However, one must note the long-term side-effects of such prescription drugs. It should also be noted that most or if not every prescription drug is produced and manufactured with chemicals evasive to the human body. Thus, many negative long-term effects can take place, although the medication can alleviate the pain in a short and prompt period of time. An example of this can be seen in the usage of ADHD medication. Although ADHD drugs can help relieve the child's brain of hyperactive activity, constant medication can cause risks of inducing cardiovascular diseases. Another example is the prescription of benzodiazepines, which is a chemical that helps reduce sharp pain. While benzodiazepines medication has helped with bodily pains, studies have shown it to cause depression, high anxiety, and emotional irregularities. However, this does not mean that prescription medicine should be dismissed altogether. Rather, medication should be prescribed in a few doses and on a strict schedule until the patient does not have to be dependent upon the drug. Prescribing the right medication for patients is important as well since there are many cases in which patients have been prescribed the wrong medicine. Also, considering alternative medication with lighter chemicals as well as therapy should be considered.

**Keywords:** Side-effects of prescription and medication, ADHD drugs and cardiovascular diseases, opioid medication and mental health disorders, drug adherence scheduling, pharmacotherapy and soft music treatment for depression, alternative medication.

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## I. INTRODUCTION

Both the lack of acceptance for alternative medication and the mainstream acceptance of prescription medicine have caused many long-lasting problems for patients with chronic illnesses. Such problems have ironically stemmed from the medication that have been prescribed to the patients, as such medication has caused negative long-term effects. The purpose of this paper is to highlight such negative side-effects, but to also explore alternative medication which have been showing promising results. In order to do so, risks and side effects seen in ADHD medication, opioid PTSD medication, antipsychotic medication, and nasal medication will be explored. Second, various alternative medications will be explored as well. Such medications listed are medication adherence, alternative relievers for asthma, acupuncture, CAM, CIM, Korean integrative medicine, and music therapy.

## II. BACKGROUND

### A. Negative Side-effects of Prescription Medication

Vincent M. Figueredo, in The American Journal of Medicine, investigates the negative effects of both prescribed and non prescribed drugs on the heart. To start off, the non prescribed drugs that may induce cardiomyopathy are alcohol and cocaine. For alcohol, although moderate alcohol consumption may bring positive effects against cardiovascular diseases, alcohol abuse can result in dilated cardiomyopathy. Then, for cocaine, it is largely associated with multiple cardiovascular complications including chest pain, aortic dissection, and stroke. Left ventricular function can significantly improve with abstinence from cocaine. Moving on to the prescribed medicine, there are 9 medications mentioned in this article in order to discuss the negative effects on the heart. First, there is anabolic steroid-induced cardiomyopathy. In a recent study, it reported that 12 of 34 anabolic steroid abusers showed cardiac pathology, proving that prolonged use of anabolic steroid can irreversibly reduce compliance of the left ventricle. Second case is amphetamine-induced cardiomyopathy. In a real case of cardiomyopathy, after 7 days of abstinence of this drug, left ventricular dilation and ejection fraction showed a

significant improvement. On the flip side, “Anabolic steroids can cause alterations in heart structure, including left ventricular hypertrophy and dilation, and impaired contraction and relaxation.<sup>24,25</sup> Potential sequelae include hypertension, arrhythmias, heart failure, myocardial infarction, and sudden death.” (Figueredo, 2010). Third, there is Ephedra-induced cardiomyopathy. Ephedra is also known as ma huang, containing 2 alkaloids, ephedrine, and pseudoephedrine. They also note, “Prolonged catecholamine excess with long-term ma huang use is one likely underlying mechanism for cardiomyopathy.” (Figueredo, 2010). It is greatly related to stroke, sudden death, and cardiomyopathy. Next, 3, 4-Methylenedioxyamphetamine can also cause cardiomyopathy. It is also known as ecstasy. Animal studies have clearly proven that repeated use of this medication can cause eccentric left ventricular dilation and diastolic dysfunction. For the fifth, there is anthracycline-induced cardiomyopathy. This is likely multifactorial. Anthracyclines promote generation of free radicals and oxidative stress that correlates with cellular injury. And, “Other anthracycline-induced mechanisms of cell injury may include apoptosis, elevated calcium accumulation in mitochondria, and modulation of cardiac gene expression.<sup>38-40</sup>” (Figueredo, 2010). Also, there are other antineoplastic drugs causing cardiomyopathy, such as sunitinib, which has rates of cardiac toxicity, as high as 11%. Moving on to seventh, medication, chloroquine can also induce cardiomyopathy by conducting disturbances such as complete heart block. Then, there is clozapine myocarditis related to cardiomyopathy. This medication was initially only approved for treatment-resistant schizophrenia, but numerous cases of myocarditis have occurred, leading some of the cases to the degree of fatal condition. Lastly, Methylphenidate can induce cardiomyopathy. In a test with rats, this altered myocardial ultrastructure in them. In conclusion, the heart was a target of injury for both prescribed and non prescribed chemical drugs. The discussion regarding potential risk of cardiomyopathy is essential before taking the medicine.

### III. RISKS OF ADHD MEDICATION

Dr. Steven E. Nissen, the interim chairman of the Department of Cardiovascular Medicine at the Cleveland Clinic, discovers a cardiovascular risk induced by ADHD drugs in order to emphasize the FDA’s recommendation regarding this drug. The drug safety and risk management advisory committee of the Food and Drug Administration described the cardiovascular risks of ADHD drugs, including amphetamines and methylphenidate. Despite their long-proven efficiencies through the treatment of German soldiers during the WWII, medical use of this agent is now limited. Commonly, ADHD is diagnosed in school-age boys, characterized by inability to concentrate and poor academic performances. Also, “In a placebo-controlled trial, mixed amphetamine salts (Adderall) administered to adults increased systolic blood pressure by about 5 mm Hg; similar effects were found with methylphenidate formulations.” (Nissen, 2006). The FDA indicated that 2.5 million U.S. children take stimulants, but signified that these agents are much less prevalent in Europe, as well. And, “The administration of these drugs produces persistent increases in heart rate, inducing chronic heart failure in animal models of dilated cardiomyopathy” (Nissen, 2006). However, the problem revealed in the research was that these drugs increase the risk of cardiovascular diseases, as shown in the symptoms like increased heart rate and blood pressure. A review regarding the regulatory history of this class of drugs clearly shows why the advisory committee took a decisive action. Within this class of drugs, there is a dietary supplement ephedra, which is widely used by millions of Americans to assist in weight loss. However, this drug was determined risky and the federal officials planned to ban it immediately due to its catastrophic outcomes, shown by the death of 23-year-old Steve Bechler. Similarly, there was another action trying to ban this class of drugs. Namely, “The FDA’s action followed many years of concern about the potential of PPA products to cause hemorrhagic stroke” (Nissen, 2006).

Cases of Sudden Death Reported to the FDA Advisory Committee from the AERS Database.*				
Patients	Amphetamines		Methylphenidate	
	Unadjudicated Sudden Deaths	Cases Meeting WHO Criteria for Sudden Death	Unadjudicated Sudden Deaths	Cases Meeting WHO Criteria for Sudden Death
		<i>number</i>		
Age, 1–18 yr		12		7
Age, >18 yr		5		1
Total	28	17	16	8

\* Data are from the Adverse Event Reporting System (AERS) of the Food and Drug Administration (FDA).<sup>1</sup> Amphetamines include mixed amphetamine salts (Adderall), amphetamine, biphentamine, and dextroamphetamine. WHO denotes World Health Organization.

**Figure 1: Sudden death reports due to cardiovascular attack correlated with ADHD prescribed medicine (Nissen, 2006).**

Most importantly, the review showed 25 cases of sudden death of children who take these drugs for the treatment of ADHD. Therefore, the advisory committee recommended the strong regulation of the two members of the class (ephedra and PPA), which might lead to serious adverse effects.

Elisa Cascade, Amir H. Kalali, and Sharon B. Wigal, three psychiatrists who collected data regarding ADHD in order to provide statistical information for medical centers, did research on the side effects of ADHD medication. They state, "Also evident with these clinical benefits is the associated pattern of relatively common adverse events (AEs) that may impact, and even impair, short- and long-term outcomes" (Cascade, 2010). This article contains and tabulates information regarding the patient-reported side effects from ADHD medications, including dextroamphetamine, atomoxetine, dexamethylphenidate, lisdexamfetamine, and methylphenidate. From the sample of 325 patients, 48% of them reported that they have experienced side effects. Only 21% of side effects were classified as bothersome or very bothersome. However, regardless of how bothersome the side effects were, only 20% of patients reported their side effects to their prescribing physicians. It should be noted, "AEs are typically dose-dependent and mild-to-moderate in severity, yet they often may be the reason why patients discontinue treatment" (Cascade, 2010). The survey was proceeded through a medication monitoring service, iGuard.org, randomly choosing enrolled members. Medical treatment of ADHD is characterized by significant therapeutic outcomes across many different symptoms. The clinical benefit is also associated with adverse events (AEs), and such AEs can vary with patient's ages. For example, preschool aged children tend to have more intensive adverse events than the older group. Several key issues related to AEs may be addressed more precisely in the future.

#### IV. RISKS OF OPIOID PTSD MEDICATION

Karen H. Seal, Ying Shi, Gregory Cohen, Beth E. Cohen, Shira Maguen, Erin E. Krebs, and Thomas C. Neylan from San Francisco Veterans Affairs Medical Center studied the relationship between mental health disorders with prescription opioids as well as the conventional use of opioids in US veterans of Iraq and Afghanistan. They write, "Among veterans prescribed opioids, the absolute risk of all adverse clinical outcomes, except for wounds and injuries, was greatest for the PTSD group than for veterans without a mental health diagnosis or mental health diagnoses other than PTSD" (Seal, 2012). In recent years, the use of opioid analgesics has almost doubled since 1994 as the importance of relieving pain is more clearly recognized. However, because of this reason, the rate of prescription opioid misuse and overdose has also increased accordingly, now becoming a leading cause of death in the USA. Especially veterans from Iraq and Afghanistan are at high risk of prescription misuse due to their PTSD. This article presents the association of opioid medication and mental disorder as well as clinical outcomes. In conclusion, "Unfortunately, treatments with opioids among patients with mental health problems may result in or exacerbate substance abuse and worsening of mental health symptoms over time." (Seal, 2012). The sample population of the study mostly contains veterans from Iraq and Afghanistan who received a new non-cancer pain diagnosis within a year of VA healthcare system entry, and they were observed if they have experienced adverse clinical outcomes during the following 1 year. For a result, of 291,205 veterans who entered VA health care from 2005 through 2008, during 1 year of follow-up, 48% received at least 1 pain-related diagnosis, and the majority (66%) had received 2 or more different pain diagnoses. To associate with Opioid medication prescription, the veterans with PTSD or mental health diagnosis other than PTSD were more likely to receive opioid than those who do not have PTSD diagnosis, though there was no significant interaction by sex, race, or military rank. Also, veterans who have PTSD were more likely to receive opioid for a longer period than median duration. Most significantly, those who got prescribed opioid, especially the ones who had PTSD, showed a higher prevalence of all adverse clinical outcomes, including accidents resulting in wounds, opioid related accidents, alcohol- and non-opioid drug related accidents, and violence related injuries. Veterans with mental health problems have barriers to seeking treatment and preferentially use VA primary care. Unfortunately, their clinicians lack specialized training in the management of comorbid pain and PTSD. With the same context, there was a report about increasing use of chronic opioid in younger combat veterans, prescribed in primary care. It is very problematic since the prescription of opioid can also increase the risk of central nervous system depression and overdose. This study supports further efforts to improve care of patients with comorbid pain and PTSD because of the high risk of self-medication with opioids, which may cause interpersonal functioning. Integrated treatment that targets both mental health and pain simultaneously would be effective and may decrease potential harms resulting from opioid therapy.

Dr. Jeremy Gauntlett from the Department of Psychology of the Bath Centre investigated the effects of both opioids and benzodiazepines, and further analyzed the efficiency of benzodiazepine, which potentially may be more harmful than opioids. Unlike the opioid prescription, which its dependency and medical side effects are well known, a little is emphasized regarding the potency that benzodiazepine has as well as dependency and side effects. In this study, the goal is to address both opioid and benzodiazepine use together in chronic pain. It is widely agreed that greater than 120mg/d are hard to justify in noncancer pain and greatly increase the risk of overdose. Long term opioids use may cause immune system deficiency, endocrine dysfunction, and hyperalgesia. Despite its dependency and potential possibility of different adverse selections, opioids are still prescribed with high doses, which found to be associated with greater pain, depression, and health service use. While much guidance is provided with opioid prescription, the pain literature infrequently engages with the issues of benzodiazepines. Doctors have even noted, "There is no positive evidence for the use of benzodiazepines in any area of long-term chronic pain, yet nearly a third of our participants were taking them, and were in a worse state than those without these medications" (Gauntlett-Gilbert, 2016). Benzodiazepines are often prescribed as muscle relaxants in cases of acute back pains. However, there are ongoing concerns regarding its broader medical side effects and comprehensive Z-drugs. The guidance is to restrict its use for anxiety and insomnia to only 2 to maximum 4 weeks because of its dependency. Nevertheless, it was proven that long term users have cognitive impairment due to the benzodiazepine, it is uncertain that patients with chronic pain strictly control themselves as bound by the 2-4 week prescriptions. Also, oftentimes both opioid and benzodiazepine are prescribed concurrently, showing that there may be no clear evidence that benzodiazepines reduce the core symptoms of chronic pain. Furthermore, "Rather, in our sample, being on an opioid at all was associated with worse physical functioning and less success in leading a valued life" (Gauntlett-Gilbert, 2016). During the research, higher doses of ME and DE were proven wrong to be associated with better functioning or reduced distress. The results for benzodiazepines were much clearer. Higher doses were rather responsible for worse outcomes in most of the situations than actually lowering the chronic pain. On top of that, the effects of benzodiazepines were associated with worse depression and pain-related fear, and higher doses associated with a poorer ability to accept emotions, or pain in general. Therefore, this proves that the pain literature needs a modification to benzodiazepine's recommendation as well as restriction guidance.

## V. SIDE-EFFECTS OF ANTIPSYCHOTIC MEDICATION

A. Tschoner, J. Engl, M. Laimer, S. Kaser, M. Rettenbacher, W. W. Fleischhacker, J. R. Patsch, and C. F. Ebenbichler wrote a review journal in the International Journal of Clinical Practice regarding the metabolic problems induced by antipsychotic medication. The metabolic issues, such as diabetes, weight loss, and weight gain, are largely associated with the use of antipsychotic medications. Among these side effects, especially obesity may lead to a serious long term consequence since it is the main modifiable risk factor for type 2 diabetes mellitus. The second generation antipsychotics, in particular, are related to a significant insulin resistance and an atherogenic lipid profile, and there is a guideline recommending baseline screening and follow-up monitoring of patients. For the exact data, the NHIS revealed that 42 percent of schizophrenic patients have higher BMI than 27 compared to approximately 25 percent of the general population. Weight gain reduces the quality of life and social retreat. On top of that, it also increases the risk of development of cardiovascular diseases as fat is deposited in the visceral adipose tissue. The prevalence of metabolic syndrome was significantly higher in patients with chronic psychiatric diseases. Doctors have noticed, "Clozapine and olanzapine cause weight gain that continues over a prolonged period" (Tschoner, 2007). The antipsychotic medication has proven to have severe metabolic side effects including weight gain through many different ways. First of all, the medication changes glucose homeostasis. This induces the new onset of diabetes during antipsychotic therapy as it increases the insulin resistance which is critical for diabetes. Second, the medication disturbs lipid metabolism. Also, "Additionally to weight gain and diabetes, some SGAs cause hypertriglyceridaemia, which is an independent risk factor of coronary arteriosclerosis" (Tschoner, 2007). The medication is very problematic since it can also develop the risk of coronary arteriosclerosis. In another study, antipsychotic medication resulted in greatly elevated triglyceride levels and a reduction of HDL cholesterol. In response to these problems, this journal suggests switching antipsychotic medication for alternatives, such as newer SGAs like aripiprazole or ziprasidone which have lesser risk. Overall, the medication-induced weight gain is a serious side effect of many commonly used psychotropic drugs. This study suggests that the psychotropic medications should be taken into account when planning the therapeutic practice.

**Table 1** Atypical antipsychotics and metabolic side effects

Atypical antipsychotic	Weight gain	Risk for diabetes	Dyslipidaemia
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	IR	IR
Quetiapine	++	IR	IR
Aripiprazole	+/-	-	-
Ziprasidone	+/-	-	-
Amisulpride	-	-	-

+, increasing effect; -, no effect; IR, inconclusive results.  
Reproduced and modified from ref. no. (2).

**Figure 2: List of chemicals within antipsychotic medication associated with diabetes risk (Tschoner, 2007).**

Bruce L. Lambert, Francesca E. Cunningham, Donald R. Miller, Gregory W. Dalack, and Kwan Hur conducted a study in a national sample of US veterans Health Administration patients with schizophrenia. As widely accepted, the new generation of antipsychotic drugs has been recognized as an important advance in treating schizophrenia with less side effects. However, some of the newer drugs are associated with new problems, metabolic disturbance, including weight gain and new-onset diabetes mellitus. Thus, “In most of these, observers reported diabetic ketoacidosis, new-onset diabetes, or hyperglycemia among patients initiating either clozapine (26–33, 65) or olanzapine, the two second-generation antipsychotic agents that have been on the market for the longest time and have most often been associated with weight gain” (Lambert, 2006). This research is designed to determine the risk of new-onset type 2 diabetes related to the use of single-agent antipsychotic medications among US veterans. And, “Compared with conventional antipsychotic agents, clozapine has been associated with more than a twofold increased risk of diabetes in younger patients (ages 20–34 years) with schizophrenia” (Lambert, 2006). The authors studied 15,767 patients who initiated the use of antipsychotic medications, such as olanzapine, risperidone, quetiapine, or haloperidol after at least 3 months with no antipsychotic prescriptions. According to the research, there is growing evidence of metabolic side effects, especially weight gain, which increases the risk of type 2 diabetes. However, the mechanism appears to be very complex, possibly involving direct effects of the agents on insulin sensitivity and serotonin receptor activity. Also, while a possible risk is proven to be right, the increase in risk is relatively small. Overall, approximately one third of new cases of diabetes may be attributed to use of olanzapine, risperidone, and quetiapine in patients taking these medications. The study suggests patients to be mindful of diabetes risks when treating patients with schizophrenia.

## VI. SIDE-EFFECTS OF NASAL MEDICATION

### A. Inhalers for Children

David P. Skoner from Temple University of Medicine, wrote an article regarding the negative effects of inhaled steroid controlled medication. This article discusses the relationship between inhaled steroid controller and final adult height of the children with asthma across 8 clinical centers in the US and Canada. This study was conducted by comparing two groups of randomly selected children, having one group use a real steroid inhaler and the other group use nedocromil or placebo effect. Skoner notes, “A larger daily dose of inhaled glucocorticoid in the first 2 years was associated with a lower adult height” (Skoner, 2007). The result clearly showed that the mean adult height was 1.2 cm lower in the budesonide group than in the placebo group, and it was also 0.2 cm lower in the nedocromil group than in the placebo group. The initial decrease in attained height related to the use of inhaled steroid controllers in children proved as a reduction in final height, even though this reduction was nothing progressive or cumulative. Overall, the growth effect was proven right, even with low doses. The position of the US FDA is that prolonged treatment with ICS should be weighed against clinical benefits and the availability of safe and effective noncorticosteroid alternatives. However, the risk is manageable and does not further discourage patients from using ICS.

### ***B. Calcineurin Inhibitors***

Felix M. Arellano, Charles E. Wentworth, Alejandro Arana, Carlos Fernandez, and Carle F. Paul wrote an article revealing the risk of lymphoma exposure to calcineurin inhibitors and topical steroids among patients with atopic dermatitis. Over the last 30 years, there was a moderate increase in the prevalence of atopic dermatitis (AD) in western countries. The symptoms, including itch, loss of sleep, bleeding from skin, and skin infection can be extremely painful and disturbing. Research shows, “High exposure to topical medications (topical steroids and/or topical calcineurin inhibitors remained associated with an increased risk of lymphoma (OR 2.30;95% CI 1.17–4.51).” (Arellano, 2006) For this reason, a number of patients are prescribed intermittent treatment with topical immunomodulatory drugs, which are topical corticosteroids or topical inhibitors. This is why, “The use of systemic corticosteroids has previously been associated with an increased risk of lymphoma” (Arellano, 2006). In this study, the authors did research with patients with atopic dermatitis who used calcineurin inhibitors in order to analyze its effect on the risk of lymphoma. Throughout the research, although the increased risk of lymphoma with people using calcineurin inhibitors was not proven, the authors mentioned that it may vary with longer exposures. Additionally, the higher OR (Odd ratio) was reported for topical calcineurin inhibitors concurrently with the use of topical steroids. This signifies the need for future research regarding the relationship between topical calcineurin and lymphoma. However, during the study, severity of AD is found to be associated with an increase in the risk of lymphoma. It is plausible that this result can be multifactorial, but this outcome was consistent with the fact that other inflammatory diseases are closely related to the increased risk of lymphoma.

## **VII. ALTERNATIVES TO MEDICATION**

### ***A. Medication Adherence***

Sonke Arlt, Reinhard Linder, Alexander Rosler, and Wolfgang von RentelnKruse wrote a comprehensive review paper about medication adherence in patients with dementia. Medication adherence is one of the most crucial parts in treating elderly with multiple diseases, especially dementia. Currently, the study regarding this issue is scarce, but there is increasing knowledge about those factors that influences prescription adherence in older patients. Non-adherence is very problematic since the drugs are not used by patients as directed, which may lead to poor therapeutic outcomes, treatment failure, and increased risk for negative side effects. In this study, the authors analyzed the factors associated with non-adherence in elderly patients. First, patients tend to discontinue the drug with cognitive impairment and functional disabilities. For instance, some of the patients who did not adhere with medication are found to have impaired memory as well as forgetfulness. The authors explain that elderly patients often easily forget to take the medicine, according to the self-reported reason for medication non adherence. Monitoring also helps as, “Studies using electronic medication monitoring in different practice settings and in drug trials have revealed partial compliance with various once-daily medications in young and old patients” (Arlt, 2008). In order to solve this problem, the importance of social support is emphasized. The author also explains, “Reduced ability to self-administer medication has been identified as a predictor of assisted-living placement” (Arlt, 2008). For the second factor, depressive symptoms have been proven as an important risk factor for non-adherence. Therefore, detection and treatment of depression may increase the quality of life as well as improve medicine adherence. Third, the authors identified some intra- and interpersonal problems as factors for non-adherence of medicine. It is possible that the patients discontinue with medication because of their personality trait, health beliefs, or other clinical variables. The author states, “Strategies for facilitating medication adherence in patients with dementia include prescribing as few medicines as necessary, tailoring dose regimens to personal habits, and coordinating all drug dosing schedules as much as possible.” (Arlt, 2008). So for the solution of this problem, the authors supposed some strategies when treating older patients, including prescribing as few medicines as necessary, adjusting doses to personal habits, and coordinating the drug dosing schedules as much as possible.

### ***B. Alternative Relievers for Asthma Medication***

Keng Sheng Chew, Hamizah Kamarudin, and Che Wan Hashim did a comprehensive trial on the use of budesonide/formoterol as an alternative medication for mild to moderate asthmatic attacks. Asthma is described as an inflammatory disorder with wheezing, breathlessness, chest tightness, and nocturnal or early morning cough. Although the conventional medication for asthma is a nebulized SABA (short-acting b<sub>2</sub> agonist) because of its convenience and effectiveness, following the worldwide respiratory pandemics including H1N1 or SARS, it was discouraged due to its association with air-borne infection. In this research, the authors identified the formoterol as an alternative since it can exhibit onset as rapidly as the conventional ones. Moreover, there are a few benefits with formoterol, such as stabilizing the mast cells, which causes immediate allergic reactions, or reducing the release of reactive oxygen species through

neutrophils, which can affect the function of neighboring cells. In this trial, a total of 32 patients enrolled, and measured patients' symptoms rated from relief as 1 to much better as 5. As a result, "In this study, both nebulized salbutamol and Symbicort® demonstrated objective and subjective clinical improvements in the first 15 min" (Sheng Chew, 2016). The alternative medication used here was symbicort. In conclusion, the alternative, symbicort, clearly demonstrated clinical improvements in relieving asthmatic attacks. And, "If an alternative agent that combines both reliever and maintenance medications could be used, this would simplify treatment and provide a more convenient and effective way in which to deliver medications to the endobronchial tree" (Sheng Chew, 2016). To wrap up, one of the biggest problems in treating asthma is the non-adherence of ICS (inhaled corticosteroid) therapy, which can result in development of severe exacerbation. For future researches, it will be a great alternative agent if it is possible to combine reliever and maintenance medication.

### ***C. Acupuncture***

Ji-Yeon Park, Hi-Joon Park, You Yeon Choi, Mi Hye Kim, Seung-Nam Kim, and Woong Mo Yang wrote a research article in the Creative Commons Attribution License regarding the evidence based Complementary and Alternative Medicine for the treatment of 1-chloro-2,4-dinitrochlorobenzene-induced atopic dermatitis. The purpose of this research article is to determine the yet uncertain mechanism of acupuncture for a treatment of atopic dermatitis. To begin with, allergic contact dermatitis (ACD) is a chronic inflammatory skin disease which developed increasingly in industrial countries. Conventionally, ACD has been treated with medications including steroid therapy and immunosuppressive agents. Despite its effectiveness, these agents may induce various side effects, and thus require a careful treatment. In order to address this problem, the alternative method, Acupuncture, became increasingly popular. Acupuncture has been a nonpharmacologic technique widely used in the treatment of skin diseases such as inflammation. They also state, "In several studies, acupuncture has been shown to reduce experimental itch, allergen-induced basophil activation, and eczema in atopic dermatitis" (Park, 2013). Its effectiveness is also proven through several studies, clearly indicating the reduced experimental itch and eczema in atopic dermatitis. However, despite its clinical outcomes, the mechanism behind it remained poorly understood for long. To address its accurate mechanism, the authors employed a 1-chloro-2,4-dinitrobenzene- (DNCB) induced model of ACD in mice. In the meantime, they treated it with acupuncture and observed the body condition of mice if it showed a pro-inflammatory expression. The measurement was divided into 5 sections: histological changes, serum IgE levels, cytokine levels, NF- $\kappa$ B Expression, and MAPKs in the Skin. In the conclusion of the research, "These results demonstrate that acupuncture may be a useful treatment for the treatment of ACD. Further investigation would be necessary to clarify its molecular mechanisms of action" (Park, 2013). As a result, the authors could observe that acupuncture treatment on the LI11 meridian point is an effective method to reduce dorsal skin hyperplasia and serum IgE levels in ACD. Acupuncture also affected the level of pro-inflammatory cytokines and proteins which regulates the symptoms. As described above, the authors demonstrated the usefulness of acupuncture on atopic dermatitis and suggested further research on its molecular mechanism.

### ***D. Complementary Alternative Medicine***

Farida Islahudin, Intan Azura Shahdan, and Suzani Mohamad-Samuri wrote an original review regarding the relationship between belief and attitude toward preference of CAM (complementary alternative medicine). Recently, more and more people started to use complementary and alternative medicine without informing their health care provider. In this research, questionnaires were distributed in Malaysian respondents older than 18 years. Those included 3 different sections including demographic and health data, complementary alternative medicine health beliefs, and attitude toward the use of CAM. Research has shown, "Use of supplements on the other hand was also believed to improve health and was similarly popular as a more natural substitute or adjunct to conventional medicine in both Asian and Western populations" (Islahudin, 2017). As a result, among 1,009 respondents, it was proven that CAM became increasingly popular due to its holistic approach following the failure of several conventional medicines to treat chronic diseases. Another reason for its popularity included its lack of side effects, too. The results are promising as, "Interestingly, the current work among the Malaysia public attitude varied, with most of the respondents agreeing to CAM due to the lack of side effects compared to conventional medicine and natural approach to health" (Islahudin, 2017). Obviously, the use of CAM was positively correlated with positive beliefs and attitude especially in patients with chronic illness. To conclude, it is very important to inform health care providers when using a CAM since it can lead to serious clinical outcomes. Therefore, a more comprehensive understanding of complementary and alternative medication should be identified in the future.

### E. Complementary and Integrative Medicine

Moshe Frenkel, Victor Sierpina, and Kenneth Sapire wrote an article as a part of the *Integrative Care* in order to address the usage of complementary and integrative medicine (CIM) among cancer patients and survivors. Cancer survivorship is getting a growing interest to the public in the last few years. Despite the good care from conventional medication and follow-up care, many patients still require assistance due to the physical and emotional unsettlement, including fatigue, cognitive dysfunction, heart failure, and kidney failure as well as the fear of recurrence. In this case, complementary and integrative medicine can help cancer survivors with a holistic approach, including mind-body interventions, better nutrition, and physical activities along with other CIM methods such as acupuncture. During the research, it was observed that cancer patients or survivors are constantly looking for CIM for their unmet needs, which can also imply that CIM use may indicate the psychological distress. This is why doctors exhort, “Although additional studies are needed to confirm these findings, given the low cost of these CIM interventions, their minimal risk, and the potential magnitude of their effects, these approaches might be considered as additional important tools to integrate into cancer survivorship care plans” (Frenkel, 2015). Although there are prevalent concerns regarding the effectiveness of CIM, thinking that it is a “false hope”, recent studies proved that this integrative approach can demonstrate approved quality of life and improve the survival of patients affected by cancer. In conclusion, to address constant unmet physical, social, employment, financial, emotional, and spiritual needs. Which shows, “In most instances, patients who use CIM are not disappointed in or dissatisfied with conventional medicine but want to do everything possible to regain their health and improve their quality of life” (Frenkel, 2015). CIM intervention may positively influence patients as a “lifestyle medicine” and even lower the risk of recurrence. Given the low cost of treatment, minimal side effects unlike the conventional medication, and mind-body intervention approach, the authors asserted that CIM can be an additional significant tool when treating cancer patients.

### F. Integrative Korean Medicine

Jisu Kim, Jungjae Cho, Dongwoo Nam, Jung Won Kang, and Seunghoon Lee wrote an article regarding the integrative Korean medicine for a treatment of mild cervical spondylotic myelopathy (CSM), which is a common spinal cord disorder in older patients, instead of conventional methods such as surgery. CSM is related to advancing age, and the most prevalent and traditional way to treat it is surgery. Despite this, having a surgery is highly risky especially for elderly with multiple diseases due to many different postoperative complications. Korean Medicine (MD) has been widely accepted as a nonsurgical option in South Korea. In this research, the authors investigated the effectiveness and safety of this option. An 81-year-old male with CSM was the case the authors investigated. His symptoms included hand weakness and inability to perform fine movements with tingling and dull pain in fingers. Also, he used a wheelchair due to his right leg weakness. After 12 weeks of KM treatment, the finger escape sign of the left hand and right hand, the grip and release test number and grasp power gradually increased. Kim also noted, “However, treatment with KM improved his gastrointestinal health, and his bowel movements were regularized” (Kim, 2018). The MRI showed no aggravation of lesion of the C-spine.

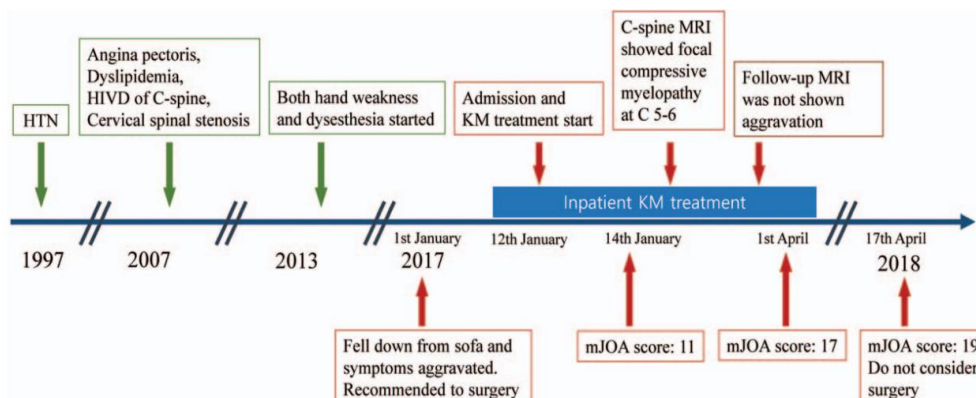


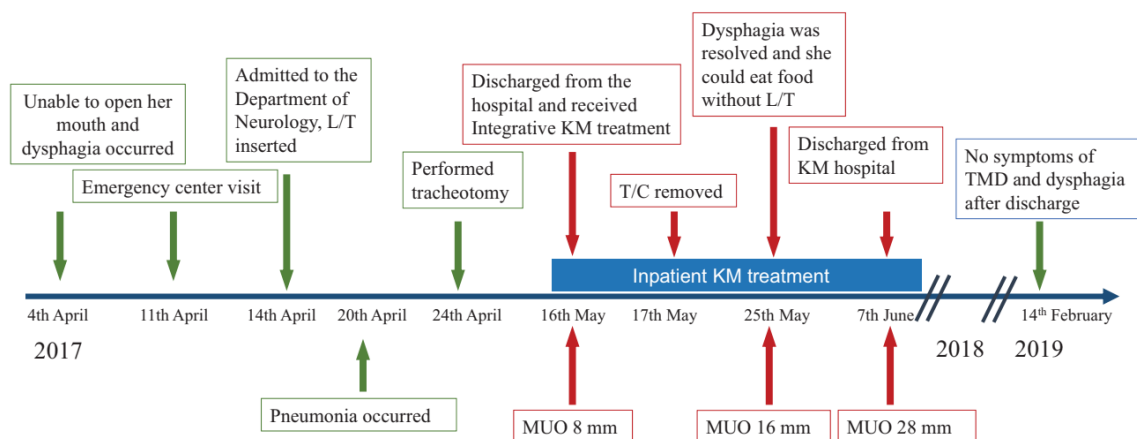
Figure 2. Timeline. HIVD of C-Spine=herniated intervertebral disk of cervical spine, HTN=hypertension, KM=Korean medicine, mJOA=modified Japanese orthopedic score, MRI=magnetic resonance imaging.

Figure 3: Timeline and results showing of Korean medication (Kim, 2018)



Overall, the patient clearly showed an improvement in both CSM and his daily life. Kim even writes, “During the integrative KM treatment, the Mini-Mental State Examination-Korean score evaluating the patient’s cognitive function increased from 22 to 24 and resulted in fluency.” (Kim, 2018). As a result, this research demonstrated that although surgery should be considered in cases of moderate to severe CSM, the KM is a possible alternative option without surgical complications for mild CSM. The authors recommend that further research should be continued with a longer follow-up period.

Ji Eun Park and Seunghoon Lee wrote an article about implementing Integrative Korean Medicine treatment for temporomandibular joint disorder (TMD) -induced dysphagia. Temporomandibular joint disorder includes a wide range of disorders around the temporomandibular joint (TMJ). It is multifactorial, which can be genetic, hormonal, and anatomical in origin, and quite prevalent around the world with 5% among adults in the US, and 3.1% in Korea. This can impair eating, drinking, and swallowing. However more importantly, severe TMD may induce dysphagia, which can be connected to aspiration pneumonia. For its treatment, Integrated Korean Medicine (KM) is suggested. The results are promising as, “Several studies have reported the effects of acupuncture on TMD and suggested that acupuncture improves pain in TMD and could improve mouth opening and jaw movement” (Park, 2019). In this study, the authors report a case of a 76-year-old female with severe TMD who developed dysphagia which causes aspiration pneumonia. When she first visited the clinic, she experienced difficulty opening her jaw, and in the following period, she received KM treatment. For a clinical outcome, both left and right lateral movement increased and the pain of the left temporomandibular joint as well as temporalis muscle significantly decreased.



**Figure 6.** Timeline of the case. KM=Korean medicine, L/T=Levin tube, T/C=tracheotomy, TMD=temporomandibular disorder, MUO=maximum unassisted opening.

#### Figure 4: Results and timeline of KM treatment (Park, 2019).

Physicians integrating Korean medicine treatment have stated, “We performed CMT to provide a TMJ space for disc reduction. CMT could equalize the length of the sarcomeres in the involved MTrPs, causing reactive hyperemia in that region or a spinal reflex mechanism that relieves muscle spasm” (Park, 2019). Finally at the end of the treatment, the authors confirmed that TMD symptoms and dysphagia are absent. To sum up, this research demonstrated the effectiveness of KM. Nevertheless, future rigorous research is expected with a long-term follow-up period and larger sample population in order to further solidify its effectiveness.

#### G. Music Therapy

Wei-Chi Hsu and Hui-Ling Lai created a study in order to analyze the effect of soft music in treatment of major depression in Kaohsiung City, Taiwan. Recently, major depression was recognized as one of the most important causes worldwide of loss in disability-adjusted life-years, and it is as prevalent as 5% in the general population has it. Nonetheless, depression is very problematic since it can result in severe personal problems and social and economic cost through patient’s pain including disability and self harm. The main therapies for major depressions are the following: pharmacotherapy, psychotherapy, and electroconvulsive therapy, which all utilizes antidepressant medication. Yet, these conventional medications are proven to have some extent of side effects which can lower the quality of life depending on

individuals. Therefore, depression has been one of the largest areas in medicine that complementary and alternative medicine was used concurrently. In this research, as well, evaluated the effect of music on depression. The sample population was recruited through referral by the psychiatric physicians. Then, they listened to the song of their choices for 2 weeks, and several factors that define depression were measured by authors through global depressive score. Interestingly, “Even among patients who show improvement with short-term antidepressant use, there is a significant risk for relapse within 1 year after treatment termination. Therefore, nonpharmacological methods that promote a mind-body interaction without side effects should be tested to reduce depression in MDD patients.” (Hsu, 2004). As a result, the participants showed a great improvement in the global depressive score during the research, proving its effectiveness and that the music therapy is actually a valid treatment for major depressive disorder, and this research became the extension of the previous ones. Moreover, the positive effects of music therapy was not limited in depression, but it improved the overall quality of mental health. Psychiatrists have wrote, “Based on a psychophysiological theory synthesized from the literature, certain type of music induces relaxation and please responses, which reduce activity in the neuroendocrine and sympathetic nervous systems, resulting in decreased anxiety, heart rate, respiratory rate, and blood pressure” (Hsu, 2004). In the end of the article, the authors mention the need for further research in order to continue exploring the effect of music therapy for a longer period of time to see if there are any more improvements with extended duration. Overall, the findings in this research proved the effectiveness of music therapy in treatment to major depressive disorder.

### VIII. CONCLUSION

The results are promising as seen in the alternatives for prescription medication. The American Journal of Medicine has shown alarming rates of negative effects seen in the constant prescribing of medication. Such effects can be seen in ADHD medication, PTSD medication, and so forth. Thus, it is important to both explore and support the existing alternatives that have shown positive long term effects contrast to prescription medicine. Alternative such as CAM, CIM, Korean integrative medicine, and a treatment as niche as music therapy have positively treated patients without negative ramifications. Hopefully, once alternatives to medication are becoming more normally prescribed, one can see many more patients becoming healthy again without having to worry about further health issues.

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