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ADOPTING THE UNESCO ETHICS MODEL TO CRITIQUE DISEASE
MONGERING

A Dissertation

Submitted to the McAnulty College and Graduate School of Liberal Arts

Duquesne University

In partial fulfillment of the requirements for
the degree of Doctor of Philosophy

By

Barbara A. Postol

May 2016

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Barbara A. Postol

2016

ADOPTING THE UNESCO ETHICS MODEL TO CRITIQUE DISEASE

MONGERING

By

Barbara A. Postol

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ABSTRACT

ADOPTING THE UNESCO ETHICS MODEL TO CRITIQUE DISEASE MONGERING

By

Barbara A. Postol

May 2016

Dissertation supervised by Dr. Henk ten Have, MD, PhD

The question this dissertation seeks to address is if the process of disease mongering can be ethically assessed. Chapter one provides a broad scope of the ethical challenge of disease mongering, UNESCO model framework, ADHD and PMDD. Chapter two examines disease mongering and its driving forces in detail. Chapter three provides an overview of the UNESCO model framework. Chapter four ethically examines disease mongering in conjunction with Attention Deficit Hyperactivity Disorder (ADHD). Chapter five examines disease mongering in association with Premenstrual Dysphoric Disorder (PMDD). Chapter six concludes that examined through the UNESCO model ethical framework disease mongering is occurring for both ADHD and PMDD, and provides remarks for the addressing this in the future.

DEDICATION

For you, Mom and in memory of you, Dad; thank you for everything.

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Chapter 1: Introduction

1.1 Background

When posed with the question, what is disease; answers seem intuitively to be clear-cut. Disease includes cancer or tuberculosis, we believe to know what disease is when we see it; but a proper articulation of what precisely defines disease is more elusive. The distinction between disease, human behavior or characteristics that are troubling proves to be difficult.¹

This ambiguity blurs the lines between conditions that are serious, simply annoying, mild, or just a natural part of the human condition. Additionally, this raises questions such as which of these conditions require pharmaceutical treatment and who makes this decision. The average individual may assume drugs are created in response to a medical need, but examined deeper, this often does not appear to be the case.

There is an ethical concern regarding what role the pharmaceutical industry has in determining and defining disease. The concern is that the industry is actively involved in a process known as disease mongering.² Disease mongering takes many different forms and none of them are ethical because the intent is not to treat illness but rather benefit from the process financially.

There is concern that diseases are being created to coincide with drugs that are developed. A new clinical diagnosis can have the possibility for more financial incentive.³ This practice is clearly unethical when framed by incentivizing the treatment of various problems for financial gain.

Overtreatment is the essence of disease mongering. People who are not sick or who are not sick enough receive drugs unnecessarily. These types of practices are

transforming more people into patients and exposing them to drug treatments which may be unnecessary or even potentially harmful.⁴ Disease mongering is propelled by a wide variety of methods used to sell the industry's goods. These include off-label drug use, ghostwriting, and seedling trials which are promotional in nature. Disease mongering also is evident in thresholds of diagnostic criteria that become lowered, risk factors become labeled as potential disease that requires intervention, and the pharmaceutical industry works to create, maintain, and expand markets for the very definition of what it means to be ill. Critics of disease mongering argue that all of these methods subordinate the practice of sound science in favor of commercial means.⁵

At issue is not that certain conditions do not exist or that they do not cause unpleasant symptoms but rather the concern is that the process of disease mongering widens the boundaries of "disease" to include and treat as many people as possible and to sell as much medication as possible. The mere presence of a cluster of symptoms does not mean that these are abnormal or requiring medical intervention. Expanding conditions creates problems such as unnecessary concern of mild symptoms; excessive use of medical technologies and services; wasting medical resources on trivial conditions at the expense of serious disease; and exposing patients to unnecessary risk. This makes disease mongering a serious threat to public health.⁶

The process of disease mongering medicalizes normal life experiences.⁷ The literature on disease mongering currently focuses on descriptive reports and commentary of cases of suspected disease mongering, as well as critique of drug company promotion tactics.⁸ Little literature exists on the prevalence rates at which disease mongering is suspected to occur. Disease mongering has only recently been gaining a growing

scholarly concern; therefore to date most literature is focusing on explaining the phenomenon rather than tracking the rate of occurrence.⁹

Disease mongering exposes patients to potentially unnecessary treatment and the practice is driven by a wide variety of methods. This makes it difficult to gauge when disease mongering may be a factor in healthcare. These apprehensions make disease mongering a unique and growing area of concerns in bioethics, but to date disease mongering has never been subjected to proper ethical assessment. For example, a variety of conditions are often connected to disease mongering, particularly in mental health. The sole treatment of mental health diagnoses are often drug therapy treatments and meeting the criteria for some mental health conditions may be subjective. Attention Deficit Hyperactivity Disorder (ADHD) and Premenstrual Dysmorphic Disorder (PMDD) are two such conditions which are associated with various forms of disease mongering.

What is lacking is an ethical framework which can be used in the assessment of the process of disease mongering. There is growing literature suggesting that disease mongering is occurring. But, in order to actually determine its occurrence, a normative framework must be in place to function as a lens through which to examine the phenomenon. Therefore, the method of the analysis of disease mongering will be the UNESCO ethics model framework. The UNESCO model provides the necessary tool that can be used in the assessment of disease mongering on many different levels.

The UNESCO model is a global framework which is best suited to analyze disease mongering, which is not only an individual but also a global problem. Disease mongering has far-reaching impacts ranging from research to treatment of disease and many areas throughout healthcare. The UNESCO model will be used to examine

Attention Deficit Hyperactivity Disorder and Premenstrual Dysmorphic Disorder. Upon analyzing these two conditions with the UNESCO model the conclusion is that several principles of the framework are violated which suggests occurrence of disease mongering and these violations have impacts on various domains of health. The thesis of this study therefore is: How can the process of disease mongering be ethically assessed? Broadly, the thesis statement will be explored in five chapters beginning in chapter 2 through conclusions of results in chapter 6.

1.2 Chapter 2

Chapter 2 introduces the concept of disease mongering. Disease mongering is a term given to the possible creation or expansion of illness by the pharmaceutical industry in order to sell prescription drugs to consumers. The chapter will examine if disease mongering is ethically valid because medications may not be necessary, which places consumer health in jeopardy. Moynihan, Doran, and Henry examine the global debate on disease mongering as well as illustrate the pharmaceutical industry tactics which promote disease mongering.¹⁰ The mission of pharmaceutical companies has changed from discovering beneficial drugs to more of a machine used to market medications.¹¹

Chapter 2 also provides the overview of the reasons why disease mongering occurs in examining its various driving forces. The mechanisms that promote disease mongering include: expansion and creation of disease criteria, lax definitions of disease, construction of disease, business market procedures, manipulation of diagnostic criteria, and appeal of autonomous choice conveyed through advertising.

Disease is often loosely defined, this is especially the case in psychiatry. The Diagnostic and Statistical Manual (DSM), published by the American Psychiatric Association (APA) leaves different forms of mental illness susceptible to disease mongering due to its almost narrative definitions of what is disease.¹² For ADHD and PMDD, this is especially relevant, as well as industry ties to the DSM. Doran and Henry discuss how disease mongering expands the boundaries of treatable disease because of strong commercial interest involved.¹³ Self-diagnosis is becoming more prevalent in medicine, due to in part the strong marketing practice of direct to consumer advertising.¹⁴ Data on direct to consumer marketing suggests there is benefit to advertising. This marketing is beneficial to the pharmaceutical industry because for each dollar spent in advertising, over four dollars in profit are earned, making it a lucrative practice.¹⁵

Medicalization is also examined in this chapter. Medicalization illustrates that drugs can harm the healthy when administered to patients unnecessarily. Conditions that may never cause harm are being aggressively treated, a practice that may pose harm.¹⁶ Also, Brody and Light state there is concern that medicalization may become a public safety threat. This is because of drug marketing techniques that reduce disease threshold, use surrogate endpoints, exaggerate safety and efficacy claims, as well as create new diseases, and encourage unapproved drug use.¹⁷ Williams, Martin, and Gabe explain why new health “problems” often have pharmaceutical “solutions” and the authors also identify how medicalization of illness takes place in various dimensions. These include the following: Redefining health problems as having a pharmaceutical solution, globalization and pharmaceutical research, the role of media, and patients and consumers being redefined as expert partners along with their physicians.¹⁸ Since the 1970s the

process of medicalization has been most driven by commercial interest.¹⁹ Moynihan and Cassels detail specifically medicalization of PMDD and ADHD.²⁰

1.3 Chapter 3

Chapter three involves employing an ethical framework in which disease mongering may be assessed. Especially in the United States, autonomy serves as the guiding principle whether or not one chooses to take medications. However, while the individual's right exists to take the medication, autonomous choice doesn't address the broader issue of whether disease mongering is happening in the first place. The drug treatment may be unnecessary or based on flawed information; therefore it is not truly an informed decision to make if disease mongering has occurred leading to treatments. Therefore, the ethical framework which will be used is the Universal Declaration on Bioethics and Human Rights adopted by member states of UNESCO. The framework will be explored and the benefit of a global model emphasized in analysing instance of disease mongering.

The UNESCO model appeals to more considerations that are not addressed based solely on an individual perspective. The scope of the principles and the aims make the UNESCO model the best fit to analyze disease mongering because it is not assessing disease mongering at only the individual level but also on a wider, universal level. A need to focus not only on individual rights but also to include obligations to community is necessary when discussing the topic of disease mongering.²¹ A global approach is beneficial, to address not only well known ethical issues, such as autonomy, but to address the great health disparities that exist in the world such as socio-economic

inequality, and the duty not to harm, which are of special importance in regards to disease mongering.²² Whitehouse states the need for this broad approach in bioethics.²³ As stated in ten Have, Van Rensselaer Potter's notion of global bioethics is increasing in value and is in part illustrated by bioethical activities in UN agencies.²⁴

Set forth by the United Nations Educational, Scientific and Cultural Organization normative standards for global bioethics were developed. Also noteworthy is that the UNESCO model is an international model. The key aim is to provide a universal framework of procedure and policy, which facilitates in this case, the ethical assessment of disease mongering.²⁵

The declaration uses 15 principles: Human dignity and human rights; benefit and harm; autonomy and individual responsibility; consent; persons without the capacity to consent; respect for human vulnerability and personal integrity; privacy and confidentiality; equality, justice and equity; non-discrimination and non-stigmatization; respect for cultural diversity and pluralism; solidarity and cooperation; sharing of benefits; and protection of the environment, the biosphere and biodiversity. Solbakk notes the need for the UNESCO Articles 8, 13, and 15 (human vulnerability and personal integrity; equality, justice, and equity; and solidarity and cooperation) to be of special value in research. These too will be key in the analysis of disease mongering because disease mongering impacts both the individual (vulnerability) and the greater population (equality, justice, and equity; and solidarity).²⁶ Andorno states that the Declaration principles are intentionally general. The Declaration is a combination of academic theory and practical means which can be applied by governments. Lastly, unlike law, the declaration encourages states to abide, rather than force application.²⁷ In order to assess

disease mongering, questionable diseases will be examined within the UNESCO framework beginning with ADHD.

1.4 Chapter 4

Chapter 4 examines Attention Deficit Hyperactivity Disorder and will use the UNESCO framework to ethically assess the process of disease mongering. ADHD was chosen due to its vast prevalence. ADHD is often a condition in which suspected disease mongering takes place. The background of ADHD will be examined. ADHD rates in 6-17 year olds were approximately 0.5% in prevalence and drug use to treat ADHD from 2011-2012 was at 16% of patients.²⁸ ADHD is second to bipolar disorder as the most common mental health diagnosis. School teachers play a critical role in the determination of ADHD in the classroom. Criticism is drawn because of the aim of the pharmaceutical companies which target teachers through “educational” websites and similar resources.²⁹

ADHD is often in question in regards to disease mongering due to the ever increasing number of children who are diagnosed with the condition.³⁰ Moynihan and Cassels state that concern exists because beginning in the 1990s, candidates for ADHD are now across a much wider age range; children exhibit less impairment, and also exhibit fewer problems. The expansion of the number of ADHD candidates is suggestive of broadening the definition of ADHD and the possibility of disease mongering. Likewise by including more children (and adults) meeting criteria ADHD, this increases the number of potential patients. This also can be suspect of disease mongering.³¹

All of this combined draws critical views. Classic ADHD, which may affect a smaller proportion of the population, is expanding. Now, minor symptoms, such as

forgetfulness are being medicalized and therefore being treated with drugs. Since 2002, the usage of stimulant medications, which are used in the treatment of ADHD, have more than quintupled. The new market of adult ADHD may even surpass these figures. This is suggestive of the critical distinguishing factors between genuine disease and overly aggressive pharmaceutical campaigns.³² The determination of whether and what forms of disease mongering occurring within ADHD are necessary. Another condition will then be analyzed within the UNESCO framework, PMDD.

1.5 Chapter 5

Chapter 5 examines Premenstrual Dysphoric Dysfunction (PMDD) and will use the UNESCO framework to ethically assess the process of disease mongering in PMDD. PMDD is now included in the DSM-5 as a mood disorder, which was not the case in previous versions of the DSM. The concern is that PMDD medicalizes premenstrual syndrome.³³

Industry involvement in PMDD is not without worry. In 2006, 100% of the people on two DSM panels (Schizophrenia and Psychotic Disorders and Mood Disorders) had financial ties to industry. These types of connections raise red flags because as with all mood disorders, treatment is primarily drug therapy. PMDD is treated with selective serotonin reuptake inhibitors (SSRI) medications. Speculation exists that Eli Lilly launched treatment for this condition in the United States because their patent protection for their medication, Prozac, was soon to expire. This coincided with the introduction of their medication used to treat PMDD, called Sarafem, which was fluoxetine. The European Medicine Evaluation Agency refused to approve medication to treat PMDD. The

reasoning behind this refusal what that women who were not severely affected by this disorder would be needlessly treated with fluoxetine. The medication is approved for use in the United States and in Australia, however not covered by insurance in Australia. In the United States, the Food and Drug Administration (FDA) cited violations in the advertising of this medication because it was not clear enough in distinguishing PMDD from PMS.³⁴

Sufrin and Ross examine how the pharmaceutical industry uses marketing in regards to women's health issues by creating new consumers and as well as targeting physicians through the use of sampling, detailing, and offering continuing medical education credits. It is necessary to examine if disease mongering has occurred with PMDD because it is a relatively new condition. PMDD raises questions about financial conflicts of interest due to industry ties and the birth of the condition as well as the unknown impact of medicalizing symptoms that are part of the female menstrual cycle.³⁵

1.6 Chapter 6

Lastly, chapter 6 is the conclusion. The conclusion summary includes risks to individual consumers and the general public by pharmaceutical industry practices that promote disease mongering. Chapter 6 also provides the ethical summaries and future considerations.

The conclusion summarizes that PMDD and ADHD both have aspects which fall under disease mongering (expansion and creation of disease criteria, lax definitions of disease, construction of disease, business market procedures, manipulation of diagnostic criteria, and appeal of autonomous choice.) This conclusion illustrates that individual

autonomy of choice alone is not a sufficient framework to assess disease mongering but rather the UNESCO framework provides the best platform. The framework is able to be applied to a variety of steps in the process of suspected examples of disease mongering, from clinical trials to drugs on the market.

The UNESCO model principles bring forth instance of disease mongering for ADHD and PMDD. Examples of disease mongering are clear when examined within the framework. It is important to ethically assess the process because of the profound impacts disease mongering has on medicine and patients. There is an impact that the medicalization by the pharmaceutical industry has on society.³⁶

The pharmaceutical industry is changing medicine; how it is practiced, driven, and this affects the health of consumers.³⁷ The industry is increasingly combining pharmaceutical science and corporate power. The result of this combination is impacting the very definition of health and illness and elevating more and more conditions appropriate to pharmaceutical intervention.³⁸ Doran and Hogue state consumers have anxiety about risk; they trust medical explanations and have preference for quick and easy solutions when it comes to health. Consumers are framed as vulnerable in the sense they are open to the suggestion that there is a medication to fix every life problem.³⁹ There is a multitude of ways that industry influence has impacted all aspects of medicine.⁴⁰ The practice of disease mongering, which extends throughout healthcare and involves the industry, physicians, and patients is a challenge in medicine.⁴¹

Disease mongering is a widespread and multi-faced problem that is not likely to decrease. A framework for analysis provides aid in the detection and may be beneficial in exposing the adverse impacts it has on health care.

Chapter 2: Disease mongering and the mechanisms that drive it

Disease mongering is a term that is associated with the pharmaceutical industry's strong influence in the creation or expansion of illness. Disease mongering takes many forms such as expanding the criteria of a disease so that more people are included or the invention of new, vague medical conditions that have a drug available as treatment or otherwise normal functions are rebranded as disease.

Disease mongering is mainly propelled by business methods such direct to consumer advertising that frames ads as educational or promoting the choice of treatment to the medical consumer. Essentially, the goal is to teach consumers to self-diagnose a possible problem and talk to his or her doctor for treatment options. Drug companies also strongly target physicians with sales representatives who seek to inform about new conditions and drugs. Pharmaceutical companies also try to influence indirectly by sponsoring events or conferences. Throughout medicine, the presence of the pharmaceutical industry is strong. However, the connection of pharmaceutical companies and healthcare creates ethical problems.

Because the definition of disease is vague, new conditions can arise that may be mild or even normal, but can become medicalized requiring treatment. Once a condition is framed as a problem, it can be treated medically. However, was a drug created in response to a true problem, or did a drug come along that needed a condition for which it could be used to treat is a question involved in examining disease mongering. Ethical concerns of unnecessary treatment include the risk that may cause to patients. Taking drugs have the risk of side effects or adverse events, which is especially concerning if these drugs are not medically necessary. This is especially true in mental health because

the conditions are all mainly treated with drugs, and lack any form of a biological diagnostic exam. The focus appears to be centered on selling more medications for profit and overlooking diseases that are life threatening. Treating all problems medically also ignores other variables that can contribute or exacerbate symptoms. This allows for social conditions that let problems flourish to continue and places all responsibility on the individual. Disease mongering also places a burden on health care by treating conditions that are minor or unnecessary.

Because so many other countries around the world turn to the US model for medicine, a dangerous precedent can be set. Chapter one explored all facets of disease mongering, the forces that drive it and why disease mongering is a problem. How the lax definitions of disease contributes to more conditions becoming medicalized is also a topic included in this chapter. The impacts that this can have globally is examined as well. To begin, disease mongering as a concept is detailed.

2.1 Disease mongering

Medication is considered aid in the treatment of the sick; however when the goal shifts from a focus on targeting to cure the ill to developing and promoting drugs for the healthy, the concept of disease mongering arises. There is a growing concern that too many people are being over-treated, overdosed, and over-diagnosed.⁴² Disease mongering turns common ailments into problems, mild symptoms are viewed as serious, personal problems become medical ones, and risks turn into diseases. Disease mongering opportunistically exploits fears in the name of innovation.⁴³ Disease mongering makes the treatment legitimate for conditions in the past which were never considered to be

disease. This expansion is harmful because it generates unnecessary concerns, unnecessary use of medical services and technologies, wastes precious resources on trivial conditions at the expense of serious disease, places patients at risk unnecessarily, and narrows the treatment options to those which are products that may be sold. The encouragement of such practices makes this a serious public health problem.⁴⁴

Disease mongering is most often exemplified by pharmaceutical companies and disease awareness campaigns which intend more to sell drugs than genuinely educate about health maintenance and the prevention of illness. It is difficult to provide an operational definition of disease mongering. There are some individuals with severe forms of illness who will benefit from new drugs and awareness. For example, industry-funded HIV awareness campaigns were very beneficial. Depending on whether or not an observer has industry ties or is independent from industry lends to different perspectives, conditions such as PMDD for example, can be considered a serious illness for industry associates or a non-existent condition to those with no industry ties. There is a variety of activities to expand definitions of disease in order to reach more markets.⁴⁵

Medicine is hailed as being evidence based, which is a moral ideal, however the reality is currently one of marketing-based medicine. Negative data is suppressed, ghostwriting is used as a tool to manage medical journal articles to highlight products, and physicians are used in a context to optimize sales. All of which is less suggestive of good science but rather good marketing.⁴⁶

The process of disease mongering includes pharmaceutical companies developing and manipulating drugs to prevent, cure, or treat symptoms. Then, the medications are marketed to recoup their initial investment as well as please company shareholders. This

cycle is argued to invent diseases to match existing medications all in the name of profit.⁴⁷ Disease mongering as further defined as selling sickness that widens the boundaries of illness because this creates a new market for treatments. The process of disease mongering turns people who are otherwise healthy into new patients. Disease mongering wastes resources and introduces people to harm otherwise not experienced if not for the medication. In part, disease mongering is driven by corporate interest.⁴⁸



Figure 1. Source: www.havidol.com, used with permission.

Disease mongering may be best illustrated by the work of Justine Cooper, an Australian artist who created artwork (see Figure 1) as a parody of the pharmaceutical industry and disease mongering. Her fictional condition was called Dysphoric Social

Attention Consumption Deficit Anxiety Disorder (DSACDAD) and the fictional drug used to treat is called Havidol (pronounced, have-it-all).⁴⁹

The “ads” represent all of the characteristics of most industry marketing campaigns for new diseases. The tagline reads, “When more is not enough”, and the quest for being better than just well is promoted. Industry tactics such as fear is illustrated with insets indicating the condition may get worse over time, a mock self-assessment quiz is even included. And of course, the ubiquitous expression of “talk to your doctor” is included.⁵⁰

The term disease mongering was coined in 1992 by Lynn Payer, stating that disease mongering tries to convince otherwise healthy people that they are sick, or those who are somewhat ill that they are extremely sick. Payer went on to state that consumers and physicians must be convinced that patients *are* sick to use the product. Disease mongering is so menacing because it takes the form of medical education in the form of advertising. Disease mongering informs society of a disease, implies there is a high instance of the disease by citing large numbers of people who have the disease or by citing universal and normal symptoms, such as fatigue, to individuals to wonder if they perhaps have this condition.⁵¹

The concept was given attention by Ivan Illich stating that life itself was becoming “medicalized” and making too many people into patients.⁵² Illness was once socially constructed, medical conditions were deemed abnormal by society and therefore labeled as a disease. The concept of disease mongering is also stated as the manipulation of disease and disease boundaries to expand markets for medical products. Disease mongering symbolizes the entanglement of medicine and commercial interest and it

shapes physicians' understanding of the boundaries of treatable illness.⁵³ The process puts patients at risk of iatrogenic harm and raises considerations whether the cures to these diseases are worth the harm patients may face as the result of treatment. Adverse drug events, medication side effects or other harms should be balanced against the benefits of taking the drugs. However, drug promotion often undermines the proper risk benefit ratio of a new drug.⁵⁴

A 2014 study consisted of interviews of 18 experts in the topic of disease mongering who were either academics, authors, or activists (many were all three).⁵⁵ The experts were asked questions such as the following: how they would define disease mongering, why it happens, the consequences, and disease mongering's efficacy. The results yielded common accounts among the experts. Disease mongering was described as the nonsense that surrounded the sale of drugs. The experts described that any poorly defined, but measurable condition can become subject to disease mongering and that boundaries are pushed. The participants did not deny conditions may cause a patient to suffer (such as PMS) however, broad spectrum disorders, poorly defined conditions, and those easily confused with normal life function are the ripest for disease mongering. All agreed that the "sowing" of the discontent of everyday life is what misleads people towards medical treatments, thus exposes them to unclear benefit and potential harm. The industry was portrayed by the experts as a business with a goal to sell, putting profit first, stating that companies are in the market to make money. The role of the prescriber was another factor the experts discussed. Physicians came across as well-intended, however easily manipulated. The experts stated that because doctors view themselves as not being vulnerable to the industry tactics they are blinded to the possibility that they are being

misled. Marketing claims are presented to physicians as scientifically valid to quell their skepticism and shift their line of thought to one in which all complaints warrant treatment. Lastly are the consumers, who the experts deemed as being vulnerable and open to infinite suggestion and who they called easy prey. The experts state consumers are not good evaluators of risk, especially when it comes to their own health and consumers are always open to the possibility that medicine offers a way to live a wonderful life, now and in the future. The notion of having their problems legitimized is also a theme amongst consumers. Being messy, for example may not be a positive personality trait for an individual, but if it is not one's fault and the result of a disease (such as ADHD), it is able to be fixed. Quick and easy solutions like drugs are more attractive than lifestyle changes. The interviewees stated they even considered themselves to be vulnerable. In sum, the industry is viewed as corrupt, the consumer as gullible, and physicians are seen as being too confident. The experts state disease mongering plays upon the dissatisfaction of humans and seeks to exacerbate it.⁵⁶

The pharmaceutical industry argues that it looks for cures and not diseases and it is the responsibility of the medical community to develop diagnostic tools and to evaluate responses of the patient. The industry states that drugs are approved based on evidence from clinical trials.⁵⁷ However, when this is examined critically, growing evidence which proves to be troubling in many areas, suggests profit has a strong impact on the development of prescription drugs and the practice of medicine.

2.2 Why disease mongering is problematic

The health care industry differs from other markets for various reasons, one of which is that when life itself is at stake, issues are framed by more emotional than rational responses. This makes the health care market susceptible to corruption. Disease mongering creates a battle between private enterprise and public health. It is argued that the interests of the industry are not always in support of public health.⁵⁸ Disease mongering exploits the fear of death or illness and makes claims to improve health with drugs. Significant amounts of money is made by the marketing of pharmaceutical solutions as remedies for disease and even more money is generated through the marketing of the prevention of risk factors for disease.⁵⁹ The pharmaceutical industry is a business, and like most businesses profits are increased when a market is expanded. In other forms of industry this may be good free market economics but healthcare is different. The practice of expanding a market to otherwise healthy people to consider themselves sick has risks such as unnecessary exposure to side effects of medication that may not be beneficial to the patient and be burdensome to health care systems.⁶⁰

The pharmaceutical industry's focus on research and development of beneficial drugs has had a dramatic shift from developing beneficial treatment to now marketing medication for questionable conditions, arguably in order to sell more drugs. Many of these drugs offer suspect benefits.⁶¹

The fact that drugs are heavily marketed leads to the assumption that new drugs are safer and more effective than older drugs and that having FDA approval prevents marketing of ineffective or unsafe medications. In the past decade many new drugs were discovered to be less safe or less effective than originally believed. It is argued that the

marketing arm of pharmaceutical companies extends the use of drugs beyond their evidence base. The marketing push is done in six ways: 1. The thresholds for diagnosing disease are reduced. 2. The use of surrogate endpoints (such as bone density testing) in lieu of a clinical endpoint (such as fracture). 3. Safety claims are exaggerated. This is illustrated by the marketing of newer drugs, such as atypical antipsychotics, as safer than older equivalents. This is an erroneous claim, yet, physicians are more at ease to prescribe the newer drugs to patients who in the past would have not even been treated with the first generation drug. 4. Efficacy claims are exaggerated, often in conjunction with safety. 5. Marketing of new diseases. For example, the creation of social phobia, and a new treatment with selective serotonin reuptake inhibitors (SSRI) drugs. 6.

Encouraging unapproved uses of drugs. It is illegal to market drugs other than for approved use. However when companies are fined for doing this illegal activity it brings light onto the fact it is occurring. Off-label use, based on federal allegations for the drug quetiapine for example, include physicians giving talks encouraging off-label use of the drug and sponsoring ghostwritten articles for off-label use as well.⁶²

The driving force behind disease mongering is profit. The pharmaceutical industry profits more than most other sectors of industry.⁶³ When the perceived risk or occurrence of disease is increased, more drugs can be sold. Profit driving disease mongering is illustrated by the enormous amounts of money allocated to marketing drugs. Pfizer's cholesterol lowering medication Lipitor is the best -drug of all time.⁶⁴ Lipitor had a marketing budget of 1.3 billion dollars in 2002. The same amount of money was spent by the National Institute of Health for researching Alzheimer's disease, epilepsy, autism, arthritis, influenza, multiple sclerosis, sickle cell disease, and spinal

cord injury collectively.⁶⁵ Lipitor is a drug which has long term use. Medicines that need to be taken for a long time are dubbed blockbuster drugs, as they are quite profitable. Long term use drugs are therefore desirable.⁶⁶ Disease mongering typically takes place in vague and wide ranging symptoms, anywhere from mild to severe. Then these symptoms are marketed for treatment in one of two ways, by labeling the normal as now pathological and expanding upon a condition to include either earlier, milder, or pre-symptomatic forms of illness.⁶⁷ These forms of disease mongering will next be discussed.

2.3 Some examples of disease mongering

Disease mongering includes unnecessary treatment of conditions which are deemed problematic by the pharmaceutical industry. Unhappiness, thinning of the bones, boredom, and stomach aches once common conditions are now being redefined. This redefinition classifies these conditions as diseases: mild depression, osteoporosis, Attention Deficit Hyperactivity Disorder (ADHD) and irritable bowel syndrome. Drugs once used to treat impairing illness such as major depressive episodes, for example are now being used to treat the slightest form of a mild depression. There is ambiguity where mild symptoms turn into a serious problem warranting medical intervention. Shyness was once marked by fears of eating in front of others or public speaking. GlaxoSmithKlein's drug Paxil had gained approval to treat a new condition, called social anxiety disorder, an extreme form of shyness. With the birth of social anxiety disorder came claims that Glaxo invented the condition to expand use of its drug Paxil.⁶⁸

A blockbuster drug, Prozac, was introduced in 1987 as a new form of antidepressant known as a Selective Serotonin Reuptake Inhibitor (SSRI). Prozac was

presented as having better efficacy than older drugs and having fewer adverse effects. The sales were profound; in 2003 US sales were \$10.9 billion, making SSRI drugs the third best-selling class of drugs. There were already many SSRI drugs on the market when Paxil arrived in 1996, so Glaxo sought FDA approval to target the drug to the market for the treatment of some lesser known anxiety disorders, Social Phobia and Generalized Anxiety Disorder. Before Paxil, these were very vague diagnoses in the DSM, but since the approval of Paxil to be used in the treatment of Social Phobia and Generalized Anxiety Disorder these once minor problems became more common. The 2005 rates suggest prevalence between 3 to 13 percent of the population.⁶⁹

Millions of dollars were spent marketing Generalized Anxiety Disorder and Social Phobia to give them a more public visibility. This ranged from television ads, to self-diagnostic websites, which led the public to determine if they may have these conditions. The marketing was successful. Paxil was one of the top three most widely recognized drugs in 2002; in 2005 it was the sixth ranked prescription medication with US sales at \$2.1 billion and globally at \$2.7 billion. Now, Generalized Anxiety Disorder and Social Phobia are common terms which most people know. Glaxo's Paxil campaign is a successful example of medicalizing the problems of shyness and worrying and framing them as medical problems and a drug, Paxil, as the correct treatment. Another example, is the condition adult ADHD. Ritalin has been approved to treat ADHD in children since the 1970s, but it is not FDA approved for adult use. Beginning in the 1990s the trend for adult ADHD began with more adults seeking medical solutions for this problem and requesting evaluation. Because the drug is not FDA approved for adults, physicians may prescribe it for off-label use but the drug companies cannot directly

promote use in adults. Industry heavily funds one well-known group, Children and Adults with Attention Deficit and Hyperactivity Disorder (CHADD), who strongly advocates for adults seeking treatment for ADHD. It is argued the group has helped medicalize underperformance in adults.⁷⁰ Strattera, was developed for the treatment of ADHD for children and also for the first time, treating adults. Marketing for the drug made use of ads of stressed, distracted, or disorganized adults stating that adult ADHD can go undiagnosed and be mistaken for a stressful life. There was suspicion that adult ADHD was an industry creation. Disease mongering that promotes common life conditions and raises them to disease status may be illustrated by adult ADHD. ADHD was a condition thought to only affect children defined as a childhood disorder, but along with the drug was the birth of a new condition called adult-ADHD.⁷¹

A mode of disease mongering illustrating the form of “disease prevention” is the use of hormone replacement therapy for women going through menopause. The pretense is that women are at an increased risk to have damaging effects to their bodies in menopause which could be prevented with hormone replacement therapy. These menopausal symptoms include hot flashes, change in mood and memory, difficulty with sleeping and bladder control, and sexual changes. Yet, the risk of taking hormone replacement therapy includes stroke, heart attack, pulmonary emboli, and even precursors to dementia. Consideration must be given whether the risks of these medications are worth treating symptoms of menopause.⁷²

The process of setting guidelines to determine whether or not one has a condition is often influenced by the pharmaceutical companies.⁷³ Using and influencing guidelines can promote another form of disease mongering. Guidelines can expand the domain of

illnesses in order to target broader populations, so that the coverage of existing medications can be enlarged to treat more people. The cutoffs for hypertension, for example, may be a level that the pharmaceutical industry closely sets. The difference of 140/90 as a reading and 130/80 seems as if it should be based on an individual and the individual's specific needs. But the difference to a pharmaceutical company is profit. If a patient has a blood pressure of 130/80 this may not classify as hypertension, adjusting the criteria, which is influenced by the drug manufacturers, suddenly expands the market because more people will meet criteria for hypertension. There is a profit which may be made having a reading that warrants the use of medication.⁷⁴

Medications used to treat high cholesterol, for example, have recently had expanded so that many more people may now be treated with statin drugs. It is controversial because the drugs are not targeted for those with already extremely high LDL cholesterol, those who have had a heart attack, or who have diabetes but for those individuals who are otherwise healthy. The new guidelines would also include many of these individuals taking statins to prevent perceived future risk. Expanding boundaries leaves more room for more people to be treated within the new guidelines.⁷⁵ Lowering treatment thresholds is common, but there are few reports on potential harm of including more people into a disease category. Lowering thresholds that leads to earlier diagnosis can be beneficial for some conditions such as treating hypertension. However, the increase of medicalization brings harm when people with only mild problems are treated unnecessarily.⁷⁶

Excessively widening of disease boundaries and increasing the treatment threshold to a lower point may expose many more people to harmful effects of drugs. As

more and more people are included with fewer symptoms, the potential risk of harm from drug treatment climbs. When the diagnostic criteria for disease is constantly changing, especially among older adults, there can almost always be a guarantee of at least one chronic condition present. Once asymptomatic conditions that carry a risk of adverse effects from treatment (such as osteoporosis for those at low risk for fracture) or conditions which otherwise had common associated difficulties (for example, female sexual dysfunction) become classified as disease. These changes to criteria of disease are often made by panels of experts who have ties to the drug companies that benefit from a broader population of individuals receiving treatment. There is cultural belief that more is better amongst patients. Evidence suggests patients are more satisfied to have access to more tests and treatments even though these may do more harm than good for them.⁷⁷

Where to draw the boundaries between conditions warranting treatment or not is a query that can produce another form of disease mongering. The distinction between mild symptom or a disease is not easy to determine. Some conditions that are often viewed critically such as Post Traumatic Stress Disorder (PTSD) had a dramatic shift in their validity once they received industry support. For example, when the drug Zoloft was approved for the treatment of PTSD, the validity of the condition was solidified. Now, PTSD is no longer questioned. Once a threshold is determined there is an incentive to even further market the relevant drugs to the whole population.⁷⁸

Pharmaceutical companies are often involved in litigation for practices covered under the umbrella of disease mongering. Court cases involving large monetary settlements have become increasingly more common. But, in contrast to the profits that the drugs generate, the fines are comparatively small. For example, in 2012,

GlaxoSmithKlein settled criminal and civil complaints in regards to illegal marketing of Paxil and Wellbutrin and for not reporting safety data for the drug rosiglitazone.

However, the company generated at least 28 billion dollars of profit for the years covered by the settlement. Other recent large settlements include examples such as occurred in 2013 with Johnson & Johnson's drug, Risperal. The company was charged with off-label drug marketing and reached a settlement of 2.2 billion dollars. In 2012, GlaxoSmithKlein reached a settlement for 3 billion dollars for off-label marketing, kickbacks, and suppressing safety risk for the drugs Paxil, Wellbutrin, and Avandia.⁷⁹ There are many settlements, by many companies, for large sums of money for partaking in illegal practices.

This overview provides an illustration of how disease mongering takes many different forms. Drugs used to treat diseases are often hailed as wonderful or innovative science with empirical support but powerful governing bodies. This leads to the perception that all drugs on the market must be safe and effective or they would not be there. However, even this assumption may be suspect upon examination.

2.4 The impact of disease mongering on research and medicine

The industry creating new medications is promoted as medical innovation in the United States, but true innovation is questionable. In the past 20 years, research and development has increased yet there are not enough new drugs to take the place of those coming off patent. The majority of new drugs fail in the development phase for lack of efficacy.⁸⁰ The discovery of new molecular entities⁸⁰ has not declined but the therapeutic advancement of them has declined. Most new medications offer minor clinical advantage

over existing drugs. Since the mid-90s, independent reviews concluded that roughly 80-90 percent of all new drugs provide little advantage to patients. Yet, the FDA granted priority status to approximately 44 percent of new drug applications from 2000-2010. The increase began in 1992, when pharmaceutical industries began to contribute funds to the FDA approval process.⁸¹ To remain vital in the health care segment, the pharmaceutical industry needed new strategies, including creation of new disease and care models and develop drugs for healthy people, and exploit the idea originated from managed care to turn patients into consumers. The industry successfully lobbied for changes. At the regulatory level there were changes in the US to allow a business model to be propelled. For example, increasing the number of products on the market was in part greatly helped with the creation of the Prescription Drug User Fee Act.⁸²

2.4.1 Prescription Drug User Fee Act

The Prescription Drug User Fee Act (PDUFA) was enacted in 1992 and renewed in 1997 (PDUFA II), 2002 (PDUFA III), 2007 (PDUFA IV), and 2012 (PDUFA V). It authorizes FDA to collect fees from companies that produce certain human drug and biological products. Since the passage of PDUFA, user fees have played an important role in expediting the drug approval process.⁸³ The problem is that most research and development produces only minor differences on existing drugs and most new drugs are not better on clinical measures.⁸⁴ After the PDUFA was adopted, new approvals were issued like never before and review times were at their lowest. Beneficial medications targeting heart disease and AIDS were developed during this time. But, many medications that were lifestyle drugs and either not useful, not new, or even harmful were

also released. Argentina and Brazil would later follow this FDA model of drug approval, including enacting a fee for pharmaceutical companies to initiate approval, in 1993 and 1999, respectively.⁸⁵

2.4.2 The Bayh-Dole Act

In 1980 the Bayh-Dole act was passed, this act allowed universities and its researchers intellectual property rights to the findings of their research funded with federal dollars. In turn, the universities and researchers could sell this to outside industry. The Bayh-Dole act largely led to research to become more commercialized. This was an act created with good intentions meant to push the process of commercializing research forward so that these discoveries created new markets and industries. However an unintended consequence of this became distrust from the public regarding medical research.⁸⁶ How drugs are approved in the US is the next area.

2.4.3 Drug approval process

The FDA drug approval process takes the following steps: First, preclinical animal trials are done. Next, an Investigational New Drug (IND) application is submitted which details the intent of the drug for human clinical trials testing. Next are trials; phase one studies involve approximately 20-80 people; phase two a few dozen to around 300 people; phase three several hundred to approximately 3,000 people. After the phases, but before the application step is a common time for the FDA and study sponsor to meet. The next step is submission of a new drug application (NDA), considering the drug for marketing approval. The FDA has 60 days to decide if it should be filed for review. If the

NDA is filed, an FDA review team studies safety and efficacy of the drug. The FDA reviews what will go on the drug label such as usage indications, and may inspect manufacturing facilities as part of the approval process too. Lastly, FDA reviewers approve the application or issue a complete response letter.⁸⁷

The US drug approval process is similar in all western European countries. There must be two studies submitted to the FDA. One that indicates that the drug is better than placebo (that it is effective) and another study indicating the drug does not have adverse effects (that it is safe.) As many studies as are necessary may be completed to prove safety and efficacy of the drug. If a drug is already on the market to treat the same condition, the new drug does not need to be more effective to be approved; data for any trials failing to meet efficacy do not need to be supplied to the FDA. Once approved by the FDA, a drug can be marketed.⁸⁸

The European Medicines Agency (EMA) approves 74% of all new applications based on company designed trials, and safety and efficacy is kept private. Of new drugs approved by the EMA, 29 percent received a safety warning within their first 10 years on the market. European Union countries, too, are thought to be paying much more than necessary for drugs that provide little gain as new drugs are not being proportionally processed along with their clinical value.⁸⁹

A concern is that the pharmaceutical industry tests the drugs it develops in trials that could not be well designed, based on small and poorly selected participants. Drug studies that are funded by the manufacture tend to yield favorable results compared to studies conducted of the drug without industry ties. A main reason is that the industry is not required to publish negative results. Internal versus public data are different. For

example, the antipsychotic drug, Seroquel was a second generation antipsychotic and its older counterpart, haloperidol, was deemed the lesser of the two drugs at a 2000 American Psychological Association (APA) conference. Marketing materials all hailed the benefits of Seroquel as being better at treating patients who had schizophrenia. The APA presentation included data of a meta-analysis of four studies. However, during litigation, documents released showed that the results of the research indicated that Seroquel had weaker efficacy. This information was known before the APA presentation, as well. Another comparative trial, known as Study 15, reported favorable results for the older drug as well. There were negative results which were not published, however cherry picking of data occurred. Thus, the favorable results were published on measures of improved cognitive functioning in which Seroquel was indeed superior, but there was no mention of increased risk of psychotic relapse and poorer scores on symptom measurements for the new drug Seroquel.⁹⁰

Publications can be selective by suppressing or misrepresenting trial results. The industry is the largest sponsor of clinical trial research and because of this, selective reporting has a great impact on medical literature. The pharmaceutical industry decides which, if any, data to submit for publication, final content of the article, and the analyses included. Even in cases where the industry is working in collaboration with academic institutions, the industry drafts articles and makes decisions on content half of the time. Some trials are selectively not published. Comparing published trials with reports submitted to the FDA for review indicates that 31 percent of antidepressant trials were not published. Ross et al indicated in a 2012 analysis of the Clinical-Trials.gov database, which is publically accessible, showed that of registered trials posted, fewer than half had

been published and industry sponsored trials had amongst the lowest number of publications.⁹¹ One of the most famous cases of questionable research is the case of the drug VIOXX.

2.4.4 The case of VIOXX

The pharmaceutical industry has a profound impact on the medical profession in the areas of research, clinical practice and education. An example of data manipulation in the promotion of Merck & Co, Inc, product, Vioxx (rofecoxib) illustrates these dangers. The following information became public during litigation. Clinical trial and review articles for the drug were ghostwritten by employees of for-profit information industries with often primary authorship given to academics who had little if any, affiliation to the company or did not disclose financial ties. Merck may have misrepresented the risk-benefit profile of a trial involving patients with dementia or Alzheimer's. Reports to the FDA appeared to minimize mortality risks. One trial had no data and safety monitoring board in place potentially placing patients in harm's way.⁹²

The case of Vioxx brought attention to poor industry strategies. In 2000, the results of Merck's Vioxx Gastrointestinal Outcomes Research study (VIGOR) were published in the *New England Journal of Medicine*. Vioxx was associated with fewer gastrointestinal complications than naproxen. Naproxen is standard nonsteroidal anti-inflammatory drug (NSAID). However, the VIGOR study also showed that the patients who were given Vioxx had four times as many myocardial infarctions compared to those given naproxen. After a 2004 placebo-controlled study confirmed its risk Vioxx was removed from the market. More than 100 million prescriptions had been filled in the

United States and tens of millions of these prescriptions were for people who had a low or even very low risk of gastro-intestinal problems in the meantime. Merck instructed its drug reps in regards to physicians inquiring about cardiovascular implications be given what was called “The Cardiovascular Card”. This was a pamphlet in essence designed to quiet physician concerns. The card included no data from the VIGOR study. The Cardiovascular Card was misleading and included preapproval studies. Most these studies were of low doses of Vioxx that was used for a short period of time; none of these studies were designed to assess cardiovascular safety and none included cardiovascular events. In 2001, the Arthritis Drugs Advisory Committee of the Food and Drug Administration heard evidence from the VIGOR study. There was disparity between the evidence-based perspective provided by scientific journals and expert committees and with the company’s sales pitches. Merck representatives were instructed to provide only certain approved study results to doctors, for example. Approved studies were defined as those that provided evidence why doctors should prescribe Merck products to appropriate patients and in comparison studies that raised concerns regarding the drug’s safety were considered to be background studies. It was a violation of Merck’s company policy to distribute the results of these background studies.⁹³ Sponsored research often raises concerns.

2.4.5 Sponsored research

Research indicates that industry sponsorship has impacts on how study outcome is presented. Authors who have financial conflicts of interest often report results favorable in respect to the study intervention compared to authors who do not have financial ties.

For example, drug studies on SSRI's effectiveness were often viewed as superior to other drugs such as tricyclic antidepressants, when there was industrial sponsorship compared to those non-industry sponsored trials.⁹⁴

Clinical researchers are not alone in being influenced by industry sponsorship but institutions themselves are influenced as well. The case of two scientists, Nancy Olivieri and David Healey illustrates this point. These researchers issued a warning for two new drugs which were being tested, going against the interest of their institutions, receiving sponsorship by powerful drug companies, Apotex and Eli Lilly. For their warning, the researchers faced sanctions from their places of employment as well as negative consequences. Apotex and Eli Lilly tried to prevent the negative reviews. Olivieri and Healey's institutions failed to protect the researchers who reported findings well within the confines of academic freedom, but despite this they both lost their jobs. Within research, conflicts of interest are pervasive throughout. Influence may be in study design and presentation of results. Bias of reporting favorable findings and not publishing negative findings occurs. Negative findings are purposively not published. Studies must be first registered; when comparing those studies registered and those with publication in peer reviewed journals show that 25-50 percent remain unpublished.⁹⁵ To aid in transparency in sponsored research, the Physician Payment and Sunshine Act became a law.

2.4.6 The Physician Payment and Sunshine Act

In 2010, the Physicians Payment and Sunshine Act was signed into law. The intent of the law is to make transparent industry relationship with physicians. The

Sunshine Law mandates that the financial relationship between physicians and the pharmaceutical industry be disclosed to the public. In 2012, the industry spent approximately 27 billion dollars marketing products to physicians, according to the Pew Prescription Project. These types of payments can create financial conflicts of interest. Pharmaceutical companies must report any payment of at least 10 dollars that includes gifts, charitable contributions or funds for speaking, travel, consulting work, conferences, or research. The law does not limit payments or gifts, merely discloses them publically.⁹⁶

Pew also reported for 2012 that more than 24 billion dollars was spent marketing to physicians and over 3 billion dollars to consumers, with the intention to promote drugs and influence prescribing habits.⁹⁷ In 2014, the first set of data is released on the Open Payments Website, which is the public website for payments physicians received from industry. The data, which were not fully complete, indicates that for a five month period 3.5 billion dollars was received by doctors and hospitals from industry. While some payments may be necessary and beneficial to advance science, those associated with marketing add expenses to healthcare cost and generate conflict of interest.⁹⁸

Medicine is hailed as being evidence based, which requires objective and unbiased information be available to medical professionals. However, the role the industry has in sponsorship and research finding creates doubt. The industry uses seeding trials, which are marketing trials. Their appearance is scientific, however the trials are unknowingly conducted to market. A physician is presented as having an opportunity to be an investigator in the clinical trial with industry intentions to make the physicians comfortable treating with the drug and more loyal to the brand. The true intent is not disclosed to the physician, or for patient participants or to Institutional Review Boards

(IRBs) for that matter. This failure to disclose undermines patients from making a truly informed choice (to consent) to participate in these studies. These studies are less likely to be published as they are designed to be marketing in nature. Lastly, seeding trials are often redundant because they examine questions that the drug company has already investigated. Litigation documents from the Vioxx trial showed that marketing executives stated feedback from drug representatives had been positive for the drug's perception because of the prescriber's participation in the trial.⁹⁹ Brand name drugs are what generate profits, therefore the industry often cites the value of patents.

2.4.7 The value of drug patents

Patent protection is very important in pharmaceutical industry. The industry is described as being patent intensive; within the drug sector patents are enforced and it is reported they place a higher value on patents than do other competitors in other markets. Commonly known as the Hatch-Waxman Act, the Drug Price Competition and Patent Term Restoration Act of 1984, made changes to patents laws that were developed to encourage innovation in the industry while facilitating quicker generic drugs being introduced. Industry blockbuster drugs lost up to 90 percent of their revenue within a year of coming off patent.¹⁰⁰ Despite this, prices do not decrease after a drug has a generic equivalent; they continue to increase in an aggressive marketing strategy designed to target the (name) brand loyal consumer. Therefore, the industry has a focus on developing brand loyalty or encourage prescriber to move patients to other drugs still under patent protection.¹⁰¹

The industry often cites patents are important to recover the money that goes into drug research and development, however data from companies, the US National Science Foundation, and government suggest otherwise. The sources indicate just 1.3 percent of revenues are spent on developing new molecules. Most funds for the development of new drugs or vaccines come from public sources. Instead, it is thought that marketing gets in the way of real innovation. The industry has a hidden business model, real innovations are certainly welcome, but the industry does not depend on these drugs' revenue for their survival.¹⁰² Investigating the forces that promote disease mongering is the next topic.

2.5 Mechanisms of disease mongering

Disease mongering takes a variety of forms, but centers on people being treated with drugs unnecessarily. Certainly, a need for drug therapy exists to help those who have sincere illness, but the shift has slowly been targeting those who are otherwise healthy. Disease mongering turns these otherwise healthy individuals into new drug consumers. This is done in a variety of ways. Expanding the boundaries of abnormal health is a way disease mongering occurs. The wider the boundaries are for a condition, the more people there are who can be treated for it.¹⁰³

The promotion of the sense of a future illness, something that “may” occur without early proper treatment, generating anxiety in otherwise healthy people is one form of disease mongering. Another form is to promote aggressive medications used to treat mild symptoms of illness or disease. Inflation of the rate of occurrence of disease is considered a form of disease mongering, too. Promoting new and uncertain conditions which mimic common life problems (such as social anxiety disorder), or promoting drugs

as the first solution to all problems without first considering all non-medical treatments would fall under the umbrella of disease mongering.¹⁰⁴ One of the most fundamental ways disease mongering takes place is that it exploits the deepest of human fear, the fear of dying.¹⁰⁵ Disease mongering encompasses a wide range of examples. Next, the areas which propel disease mongering will be explored in greater detail beginning with the expansion and creation of disease topic.

2.5.1 Expansion of disease and creation of disease criteria

These two areas, expansion of disease and creation of disease criteria, are closely related. The market for treatment gets enlarged in two ways. The first is to narrow the definition of what it means to be healthy so that normal experiences are considered abnormal. The second is to expand upon existing forms of disease. The industry has the potential to introduce new diseases or expand on existing diseases. The expansion of disease takes several forms such as including expanding criteria to include a broader population, including populations with mild symptoms, and off-label drug use which expands a drug's use for different reasons. The industry also is closely involved in defining new diseases.¹⁰⁶ There are competing interests at play when it comes to defining what is called 'disease' or what a cluster of symptoms means. Defining what is a disease, especially those which have vague symptoms, is unclear.¹⁰⁷

Creating disease is as the name suggests. Normally, medications should be produced to meet a demand for a disease but with disease mongering, new products are produced that subsequently create a demand. This mechanism of 'drugs looking for a disease' produces a scenario where otherwise normal parts of life or conditions that arise

from outside circumstance (such as shyness as a result of poor social skills) are reduced to biochemical problems. Addressing the issues by means other than drugs is not considered. Drugs become the solution to problems the industry states are problematic to consumers who have their opinions of illnesses shaped by the pharmaceutical industry.¹⁰⁸ The industry fosters the trend of promoting treatment of exaggerated conditions. Conditions are poorly defined, overlap normal human behavior, and often given three letter abbreviations (for example, TLA) as condition names.¹⁰⁹

These types of conditions then become branded. This process makes the presence better known to consumers, physicians, and insurers. The term condition branding is preferred over disease mongering as it is value neutral. A condition brand has two elements. First, the elements of the brand that make it different than competition. Second, brand associations like thoughts, feelings, and content become linked to the brand. Strong condition brands, a medical marketing journal states, "...enjoys high awareness and strong, favorable associations among patients, physicians, payers and other stakeholders. Associations tend to be favorable when a condition is perceived as having serious consequences, for which individuals are not blamed or stigmatized, and which is caused by factors for which individuals are not responsible and over which they have no control."¹¹⁰

A new disease is developed and then people must be convinced they have the condition. New diseases often have a broad range of non-specific symptoms, from mild to severe. Symptoms span a broad range in severity from nonspecific, to extreme suffering. Reporting about new diseases does more than seek to raise awareness and offer proactive solutions, but to also increase the size of the treatment market. The gap between

health and sickness is narrowed. Mild symptoms or pre- symptomatic conditions are also now a part of disease.¹¹¹ Risk factors are often presented as disease.¹¹² Once created, disease can be further expanded in a variety of ways.

Expanding disease takes many forms. For example, a legitimate illness that is disabling a person is expanded to include its milder forms or less debilitating symptoms. This expansion may now include otherwise healthy individuals. Helping the sick is good, targeting the healthy is not; it merely is expanding disease to a broader market. Prevalence rates are exaggerated, for example diseases are defined broadly based on vague, common symptoms. Restless leg syndrome is presented as a common problem. The distinction between mild or severe disease is clouded. Indications of the prevalence of severe forms of illness are not indicated. More diagnostics are encouraged by emphasizing that physicians fail to recognize illness; more people are encouraged to see themselves as ill by illustrating stories of those who never knew they had the condition until they self-diagnosed (this often involves the use of a symptom checklist). Disease awareness is another format that encourages more diagnostics, done by exposing disease but not the industry sponsorship. The suggestion that all disease should be treated falls under the disease expansion mechanism of disease mongering. Drug benefits are overstated by only highlighting dramatic successes with the use of medication. There is also the implication that there are no possible harms from the drugs as well as inference that long term use of the drug is safe and effective.¹¹³

After drugs have been approved by the FDA to treat one condition, there can be expansion of the drug's indications. At a later date, pharmaceutical companies may apply for extending the drug's use. This process is done by submitting new analyses or studies

from existing data for the medication's indication, therefore extending the drug to either a new population or use, or new indications. New indications with SSRI medication, for example, were successful. SSRI drugs were originally approved in the treatment of depression, but their new indications include the treatment of obsessive compulsive disorder, post-traumatic stress disorder, and many forms of anxiety disorders.¹¹⁴ Conditions are also treated for uses for which they are not approved, off-label use and disease mongering is next examined.

2.5.2 Off-label drug use

Off-label drug use is another form of expansion. Drugs are approved and labeled to treat certain conditions. The demonstrated benefits define the limits of acceptable risk for prescription drug use. For example, liver toxicity may be accepted in an approved cancer drug, but not to treat a condition like acne. Before a drug is "labeled" for use in an approved market it must meet safety and efficacy claims to appropriate government bodies and have human and animal data to confirm these findings. A drug may be approved for only one condition however; it is usually legal and often unavoidable for physicians to prescribe medications for another reason. Off-label use is justified because often drugs cannot be tested in certain populations excluded from drug studies, such pregnant women, or children who have only recently been included in clinical trials. Some off-label use is certainly beneficial, yet likewise can be harmful. The industry cannot legally promote drugs for off-label use, however, "word of mouth" or "buzz" marketing occurs by "key opinion leaders", who are not employed, but are paid by drug

companies to legally promote off-label use. As a business procedure, off-label use expands the market to greater populations and generates more revenue.¹¹⁵

Articles appearing in medical journals, newsletters, and magazines are not regarded as promotional, therefore as protected commercial speech they are not subjected to FDA regulations. These articles are often used to promote off-label drug use, boosting unproven benefits of the drug, and downplaying their harm.¹¹⁶ Physicians may be receptive to suggestions of pharmaceutical company peers because off-label drug use is engrained into medicine beginning in medical school and continuing until practice, it has become a part of medicine to listen to drug detailing.¹¹⁷ Criteria to determine disease is the next area in which disease mongering occurs.

2.5.3 Diagnostic criteria manipulation

Diagnostic criteria can be manipulated. Cholesterol often comes under fire in regard to criteria being lowered despite lack of evidence of drug therapy as primary method of prevention.¹¹⁸ New cholesterol guidelines and an online risk calculator are an example. The risk calculator over-predicted risk by 75 to 100 percent and treatment is warranted for anyone with at least a 7.5 percent risk and is considered for those with a 5 percent risk, which could lead to over-prescription of statin drugs.¹¹⁹ Tens of millions of people could be prescribed drugs they do not need. And there are some doctors who feel cholesterol target numbers are too much of a focus in regards to heart health. It is unclear how the ability of statin drugs to lower cholesterol contributes to their effectiveness.¹²⁰ Selling such risk factors as a disease often falls under disease mongering, too because

treatment does not always serve the best interest of the patient.¹²¹ Even once normal conditions can be thought of as disease.

2.5.4 Normal conditions branded as disease

Normal conditions are repackaged as disease. Baldness, for example becomes male pattern baldness. This condition was linked with undesirable emotional consequences when a new medication was licensed for treating male pattern baldness. This is another form of expanding an illness.¹²² Baldness is a classic example, however there are many conditions that were once thought of to be inconveniences, normal parts of aging, or were social issues. These include mild forms of anxiety or depression, ADHD, social anxiety, irritable bowel syndrome (IBS), restless leg syndrome (RLS), low bone density, high cholesterol, erectile dysfunction (ED) and other sexual dysfunctions, and “pre” conditions to diabetes and hypertension. The validity of whether or not the illnesses exist isn’t necessarily in question, however the extent to what constitutes treatment is a bigger concern. Each of these conditions represents how the threshold of diseases has been widened, making the way for more and more treatment using drugs for problems that are mild or may not be medical in nature to begin. Unwarranted concern can develop when normal or mild conditions are expanded to be redefined as disease.¹²³ The term pharmaceuticalization is where the industry transforms human conditions into opportunities for drug intervention.¹²⁴ After the designation of a new disease or the expansion of existing diseases, word must get out about the diseases and this is often done through the practice of ghostwriting.

2.5.5 Ghostwriting

Ghostwriting is another mechanism of disease mongering. Ghostwriting is failing to identify a person who has significantly contributed to research writing of an article as an author.¹²⁵ Ghostwriting is an attempt to have control over the scientific aspect of the drug industry. Industry researchers conduct the research and then seek medical researchers to put their names on this work so that they may increase their publications. The ghostwritten papers essentially seek promoting new drugs to doctors.¹²⁶

It is a practice that encroaches on academic standards and it is argued at times to border on fraud. It is a process that typically involves authors who are paid by the pharmaceutical industry to write the praises of the company's product or to generate negative articles about the competition. Eventually, the authorship credit goes to authors who are academic researchers, but who had little, if any, contribution to the article. The process distorts the industry's involvement and adds to misrepresentation of drug profiles. Some editors are well aware that ghostwritten articles are submitted to their journal but little is done to regulate content.¹²⁷

Ghostwriters can contribute significantly to a publication without being named as authors. Until lately this was thought to be a marginal problem, but there is growing evidence that ghostwriting is becoming a significant problem in publishing. This is misleading to readers because it is understood that to be named an author means one has written the article. The International Committee of Medical Journal Editors has set forth statements regarding authorship credit.¹²⁸ First, authorship should be based on substantial contributions to conception and design, acquiring data, or to the analysis or interpretation of data. Second, authorship should be based on drafting or revising an

article critically for content. Last, authorship credit should be built on final approval of the version to be published. Authors should meet all three of these conditions. Not all journals require authors to meet the conditions, but the conditions are set in place to remind those what is required of authorship.¹²⁹

Ghostwriting often takes place under the broader category of publication planning. Publication planning is the practice of pharmaceutical companies producing articles in medical journals or posters at conferences that establish marketing messages.¹³⁰ Publication planning organizes and shapes the industry data and generates data for publication. The objective is to derive the highest commercial value from the research and to target high profile journals first and in lower profile journals publishing numerous market focused papers.¹³¹ This planning involves the use of a professional medical writer to draft opinion pieces which are included in medical journals. Medical writers are often scientists. They have a vital role in publication planning by ensuring that articles are scientifically valid, persuasive, and well-organized. The writers may work independently as freelance writers who are employed by the drug companies or by medical education and communications companies. These companies receive most of their business from the pharmaceutical industry. A drug may never be mentioned however if there is only one drug to treat a disease, a detailed analysis of the prevalence of the disease, severity, or complications, is used to prepare the market of physician readers by raising awareness. Competing therapies can be framed as inconvenient or their risks are highlighted in order to present the new product more favorably. Publication planning can weaken medical literature. Industry control over studies and authorship of studies and opinion articles misrepresents medical dialog.¹³²

In addition to the medical literature, publication planning also shapes key messaging, which is the message the article conveys. Along with marketing departments, medical education and communication companies identify themes that help to promote sales. The next step is to plan publications around these themes. Articles produced will peak when a new drug goes to market so that the medical community is familiar at the same time the drug can be sold.¹³³

Ghostwriting allows the industry to place marketing messages into articles that are published in medical journals. An example of ghostwriting going against definitive data is the case with hormone replacement therapy. Litigation against pharmaceutical company Wyeth revealed extensive use of ghostwriting hailing the benefits of hormone replacement for asymptomatic women, while it was dangerously causing increased risk of cancers and dementia. Despite this, many OB-GYNs still believe the drug is beneficial which may be a result of the subtle corporate influence in medical journals. Premarin was first used in the 1940s with FDA approval to treat hot flashes. By 1975, estrogen use was linked to endometrial cancer which saw an eight fold increase, thus sales decreased. By the 1980s a progesterone pill was added to counteract the estrogen induced endometrial cancer and hormone replacement therapy (HRT) or hormone therapy (HT) became popular. Into the 1990s, HT was praised for preventing heart disease, colon cancer, tooth loss, and even macular degeneration. However, in the late 90s views of the benefits of HT changed. Research findings indicated HT did not prevent cardiovascular events but instead increased risk for breast cancer and stroke. Later findings indicated increased risk for developing dementia and incontinence. Yet, today many gynecologists believe the benefits of HT outweigh the risks, which is a perception that is not evidence based.

Rather, it could likely be the result of years of influence of pharmaceutical marketing in medical literature.¹³⁴ Another means by which disease mongering occurs is that the definition of disease remains unclear.

2.5.6 Lax definition of disease

Disease mongering has broadened the definition of disease. What was an inconvenient problem in the past could now be considered an illness.¹³⁵ This is because there is not a very precise definition of “disease”. Merriam-Webster defines disease as an illness that affects a person or prevents the body from working normally.¹³⁶

There is great difficulty in detecting and interpreting symptoms in determining illness. The focus on testing is more critical in medicine at present, than are manifestations of symptoms in the determination of illness. Diagnosis lies within the social power of naming, defining, and codifying what is normal and what is abnormal; thus delineating disease. Diagnosis is a cultural event in which illness is identified and categorized within cultural beliefs and meanings about normal and deviant as well as health and illness. The industry’s marketing influence has removed the power to diagnose from the physician onto the patient by self-diagnostic instruments.¹³⁷

Often, there is not a definitive diagnosis but rather descriptive symptoms. For example, a sore leg may be diagnosed as myalgia. Myalgia is simply Greek for muscle pain, but often patients desire to have a diagnosis for their problem. Labeling a symptom is not the same as having a disease. A disease is not a tangible, doctors define them rather than discover them. Examples include having to meet certain criteria for having a disease and if criteria are not met, there is no presence of disease. Disease is a term used

generally with no formal definition. Historically and across cultures disease has been defined by what society chooses to be a disease. There are normally two elements: implying an impairment and something to be treated by a physician.¹³⁸

Illness was once more socially constructed but now defining illness is a pharmaceutical construction.¹³⁹ Diseases were biological conditions and illness was the social meaning of conditions. In time, the shift has gone from a focus on the overall problem to a more individual approach. For example, obesity when labeled a disease put emphasis on treating the individual with surgery rather than examining overall factors that contribute to obesity overall, such as food choices. This process has led to medicalization of many conditions.¹⁴⁰ To examine how disease was constructed in the past and how it is currently constructed is the next focus.

2.5.7 Construction of disease

Medicalization is the term sociologists use to describe the process in which human or life problems that are non-medical are now treated as medical problems. Non-medical, but rather human or life problems exist. For example, shortness may bring about unpleasant feelings in people of small stature. Sadness is a problem humans may face after the death of a loved one. Shyness is an uncomfortable feeling one may experience when meeting new people. None of these are medical problems, they are simply human experiences. While they may certainly be unpleasant, to suggest they are symptoms of disease is a category mistake and would be disease mongering. Living well can mean accepting there are some variations in life; moods, behavior, and appearance can be affirmed rather than being erased. Also, medicalization has other bad consequences

which are much clearer, such as cost. By ever expanding the realm of conditions that require medical treatment also expands the costs of medical treatment, and it is the producer of these new treatments, the pharmaceutical industry for example, who most benefits. Another bad outcome of medicalization is that medicalization reduces human beings to objects and undermines subjectivity. For example, the argument exists that certain criminal behavior should not be medicalized, such as badness as a symptom of a psychiatric disorder.¹⁴¹

This argument suggests that this is because humans can make choices, human beings are not objects at the mercy of outside forces. Humans can choose to do otherwise, to not take part in deviant acts. Arguments against simply using drugs to treat sadness add to the case that humans are not objects that can be fixed but subjects who can be influenced by reasons. While we may benefit from both means of understanding the human condition, it is the medical way that crowds out all others. Lastly, there are social implications to medicalization. Medicalization has a narrow focus on the individual and reducing the suffering of the individual. This leaves out any social structures which may be contributing to the suffering. By changing social structures to fit the individual, rather than targeting the individual to fit the mold of society could eliminate any norm changing variations. Medicalization is shown through category mistakes, expanding treatable disease categories burdening the health care system, undermining the subjectivity of humans, or ignoring foundations of suffering, all of which overstep the boundaries of medicine.¹⁴²

Since the end of World War II, more aspects of life are understood through the disease model framework which leaves conditions suitable for therapeutic interventions.

It was during that time that medical science and the pursuit of corporate profits become intertwined. Medicine has extended beyond the treatment of acute conditions. Now, it includes daily management of chronic disease. Once only visible symptoms were treated, and now risk is treated. The pharmaceutical industry has played a vital role in this transformation to deem more conditions suitable for treatment and in defining health and illness. Medicalization is intended to be a neutral term, not indicating whether the trend is positive or negative.¹⁴³ In the context of this work, the term medicalization implies over-medicalization, which is viewed as problematic in nature.

Traditionally, as stated by Ivan Illich, medicalization was a process which was fueled by the medical profession and physicians, whose authority over health and society led to “medical imperialism”. Among the current drivers of medicalization today in the United States and Europe is the pharmaceutical industry.¹⁴⁴ Medicalization occurs when problems are treated that were not before treated medically, such as illness or disorder, which previously were never viewed as such. Medicalization transforms an abnormal behavior (such as shyness) or a naturally occurring event (such as birth) into a medical issue. This growth of medical authority over a wide range of life domains in the West is a powerful transformation in the last half of the twentieth century. Medicalization has advantages and disadvantages. Advantages include recognizing some people with deviant behaviors as being ill; reducing personal responsibility, blame, and stigma; high quality treatment; and for some conditions a better social control vs. being criminalized for behavior. Disadvantages include making all social problems individualized; the displacement of responsibility to social problems; assuming medicine is morally neutral; experts controlling public debate over the layperson; and medical professionals having

greater social control. In particular, these concerns are applicable to mental illness. The driving force behind medicalization today is the pharmaceutical industry.¹⁴⁵

In the past it was social movement that defined disease but over the past few decades it is biotechnology, specifically the pharmaceutical industry.¹⁴⁶ An example is fibromyalgia, which still generates debate among rheumatologists whether or not it exists. Physicians noted clusters of similar symptoms in the 1980s, its exact pathology unknown in the late 2000s, medications were approved to treat the symptoms. Fibromyalgia is thought to have been an example of medicalization.¹⁴⁷ The pharmaceutical industry employs strategies to generate demand for their product.¹⁴⁸ The power of the industry is not only affecting the individual patients but medical providers and the healthcare industry overall in defining disease.¹⁴⁹ Aside from the personal cost to individuals of risk to their health, it is thought that the process of medicalization is impacting health insurance; one estimate of expenses of medicalized conditions in 2005 was at approximately 77 billion dollars.¹⁵⁰

In 2010, a study by Conrad, Mackie, and Mehrotra was done to identify medicalized conditions and their associated costs.¹⁵¹ Two criteria were used in this determination: 1. The condition was identified in a published study since 1950 as an example of medicalization and, 2. The availability of reasonably valid and current data (in the US) on the medical spending for the condition. Twelve conditions were considered to be medicalized, these are as follows: 1) Anxiety disorders (includes social phobia, anxiety states, dissociative, conversion and factitious disorders, obsessive compulsive disorder, and depersonalization disorder; 2) Behavior disorders (ADHD, conduct disorder, and oppositional defiant disorder; 3) Body image which includes

cosmetic surgeries; 4) Erectile dysfunction; 5) Infertility (primary and secondary female infertility and primary male infertility); 6) Male pattern baldness; 7) Menopause; 8) Normal pregnancy and/or delivery; 9) Normal sadness; 10) Obesity; 11) Sleep disorders; 12) Substance related disorders. These conditions resulted in an estimated \$77.1 billion in annual healthcare spending. One of the policy implications of these results may be the role in which the pharmaceutical industry is a major driver of medicalization to expand markets and the need for more research to be done on the social, economic, and political consequences that are the result of medicalization.¹⁵² Medicalization has had effects on what is considered disease.

2.5.7.1 Effects of medicalization

Perhaps the biggest problem that has resulted from medicalization is that problems have become too individualized. The diseased individual became the focus and what is overlooked are the cultural or social issues that may be a contribution. Factors which could be involved are overlooked, for example socio economic inequality, occupational stress, unnoticed cultural or family events, all of which may have a role in the process. Once a problem becomes dubbed a medical problem, all other alternative root causes are often disregarded. Consequences of a problem, such as unwanted psychological symptoms, are the focus of treatment and not other potential underlying causes which does the greatest disservice when drug therapy would only be partially beneficial in the treatment of the problem. Since medicalization promotes the use of drugs and primary treatment is overlooking other options, this leaves patients susceptible to iatrogenic harm. Mass screenings often produce a false positive result, thus a patient is

put through more invasive testing, all of which causes undue stress and possible injury. Mammograms are an example. It is argued that through increasing medicalization the number of false positives are also rising, thus generating more cases of iatrogenic harm.¹⁵³ Hundreds of thousands of adverse drug reactions are reported to the FDA each year and the number of deaths from adverse drug reactions is also thought to be increasing.¹⁵⁴

Another impact of medicalization is the costs associated with health care. Medicalization is thought to lead to the increase of use of health services and medical treatments, increasing health care spending, and in publically funded health care puts a strain on governments. Certain conditions such as erectile dysfunction, anxiety disorders, or obesity may encourage unnecessary use of medication so that scarce resources are spent on these conditions at the expense of serious disease. Even for serious problems, medicalization contributed to some unnecessary interventions in the cases of individuals who had mild severity of serious disease. Drug companies face accusations that they promote the benefit of preventative treatments but do not address the wasted expense and suffering the drugs can cause to those who would have never become ill.¹⁵⁵ The most powerful force driving disease mongering is the marketing of illness and the drugs used to treat them.

2.5.8 Business marketing procedures

Companies use a variety of means to generate demand for their product; marketing is the most obvious method. Marketing promotes the branded drugs and the companies want the drug names well-publicized. Drugs with a patent, or a brand name

drug (especially blockbuster drugs) are promoted because patented drugs increase profits by giving the company a stronghold on the market for many years.¹⁵⁶ The marketing persuasion of prescription drugs is evident throughout medicine. Research funding, journal publications, FDA approval, therapy guidelines, product labels, medical conference programs, medical education in medical schools and clinically, are all areas that have industry influence. Most people would reasonably believe that physicians are informed about drugs through scientific findings and not advertisements but often this is not the case. Psychiatry in particular may be more vulnerable than other areas of medicine when it comes to the marketing of prescription drugs.¹⁵⁷

Drug companies are pervasive and growing throughout psychiatry. The pharmaceutical industry provides support to mental health advocacy groups. These groups include the National Alliance for the Mentally Ill, National Mental Health Association, National Alliance for Research on Schizophrenia and Affective Disorders, National Depressive Disorder Screening Day, and the Anxiety Disorders Association. Only genuine consumer advocacy groups do not receive support from the pharmaceutical industry. The industry supports clinical trials research at universities so much so that departments may not be in existence without this financial support.¹⁵⁸ The DSM-5 establishes diagnoses based on collections of symptoms or signs to determine if diagnostic criteria are met. This diagnostic process relies heavily on observer report. Nothing about the underlying cause of an illness is given.¹⁵⁹

Targeting both physicians and consumers for marketing purposes is an ethical problem in the context of disease mongering. There have been drug discoveries that have great impacts on treating illness. But, drug marketing is more in alignment with the

marketing of other consumer goods rather than in alignment with the field of medicine.¹⁶⁰

The first example is the well-known area of direct to consumer marketing of prescription drugs.

2.5.8.1 Direct to consumer marketing

Perhaps the most prolific way that drugs are introduced to the public is through direct to consumer marketing. To increase the demand for a product, the industry envisioned a model in which patients could be viewed as consumers with the rights to be informed about pharmaceutical products, as they are with any other consumer goods and services. For years, medical associations and even the industry argued that direct to consumer marketing was a bad idea. In the 1980s, the sway of consumer organizations created ways to “empower patients” so that they were not under the control of their prescribers, patients as consumers could make their own rational decisions. It was with this argument that marketing innovators in the industry convinced those within the industry that direct to consumer advertising was a form of patient empowerment and awareness could be drawn to diseases silently affecting vast numbers of people, people who could be made aware through direct to consumer advertising.¹⁶¹ In the US, the medical establishment is highly consumerist as Americans spend the highest gross domestic product on healthcare compared to any other countries. The US is also the largest consumer market for pharmaceuticals and the highest cost of drugs in the US.¹⁶²

Viagra was initially developed for cardiovascular indications but was not sufficiently effective. However, a product safety specialist at Pfizer noted a significant number of males enrolled in the clinical trial reported erections as a side effect, which led

to the development of the drug for the treatment of erectile dysfunction (ED).¹⁶³ Viagra had a successful marketing campaign in raising awareness to this little known condition. Commercials included well-known public figures. Viagra was FDA approved to treat erectile dysfunction in 1998. It was intended to be used for older men, or those who had other medical problems such as prostate cancer or diabetes, and who consequently had ED as a result of these conditions. Sexual problems were shaped to be viewed as a medical problem with a drug solution. The first famous face to promote Viagra was politician Bob Dole, to target an audience of older men. But, this quickly expanded to target more than only older males. Baseball players and NASCAR drivers both promoted Viagra, expanding the audience so that any man could consider himself to have a form of sexual dysfunction. In its first year on the market, over three million men were treated with Viagra, in sales figures this amounted to \$1.5 billion. Competition arrived in 2003 with the drugs Levitra and Cialis, hailed as improvements to Viagra. Estimates in 2004 suggest more than 30 million men in the US take a form of these drugs. The industry has also subtly promoted the drugs as enhancements to sexual pleasure and relationships.¹⁶⁴ Viagra is the perfect example of a successful marketing campaign.

Since it was permitted in 1997, spending on direct to consumer advertising has nearly quadrupled. The industry's purpose of this advertising is to promote patients to request brand name drugs, even if there is a generic available. Direct to consumer advertising is well-known in the United States. Propelled by the promotion of self-diagnosis through advertising, the industry appeals to an individual's autonomous choice by marketing of prescription drugs to treat many conditions. There are drug ads on TV, radio, and in print. The FDA permitted ads to be aired on television in the US in 1997,

which has strongly influenced the medicalization of many conditions.¹⁶⁵ These advertisements have impacts, they work to change perceptions of illness, conditions, and experiences and often overstate claims of occurrence. This works toward trying to convince healthy people they are sick through drug promotion.¹⁶⁶ Direct to consumer advertising has an interesting history.

In 1962, the Kefauver-Harris Drug amendment gave legislative authority to the FDA to regulate the advertisements of prescription drugs. The FDA had requirements that side effects be included, contraindications and effectiveness of the drug disclosed, and the information be “fair and balanced”. Those requirements did limit what could be advertised via media however spending on advertising increased nonetheless.¹⁶⁷

Before the FDA permitted prescription drugs to be directly marketed to patients there was concern regarding how this may impact self-diagnosis. In fact, in 1984, before direct to consumer advertising of drugs as we know it today occurred, the US House and Senate Subcommittee on Oversight and Investigation requested feedback from 37 drug companies regarding direct to consumer advertising. The majority of the companies were against the idea. The reason was that promoting self-diagnosis would jeopardize the doctor-patient relationship and encroach upon the authority of medical providers.¹⁶⁸

In 1985, the FDA removed the moratorium on direct to consumer advertising so that products could be marketed directly to consumers. Advertising on broadcast media in 1997 opened immense opportunities, particularly television commercials, such that now billions of dollars are spent on direct to consumer advertising.¹⁶⁹ Spending increased from 791 million dollars in 1999 to 4.5 billion dollars by 2004, with increases in spending accounting for increased sales. The drug, Lipitor, for example, grossed over one

billion dollars worldwide in its first year of sales. Direct to consumer advertising has grown significantly and profits soar because of this.¹⁷⁰

It is not legal to do direct to consumer advertising in other countries besides the US and New Zealand. However, different forms of marketing are designed to influence the public perception of drugs, such as disease awareness campaigns in Europe and Australia. Marketing of drugs in a variety of forms is therefore a global phenomenon. However, the US remains the heart of drug innovation and marketing.¹⁷¹ It is stated that drug companies spend more money on marketing than research and drug development.¹⁷² The pharmaceutical industry states that advertising is what consumers want; the industry feels it is not a problem as the competition brought forth through advertising keeps drug cost low for consumers.¹⁷³

Advocates argue that direct to consumer advertising increases the access of information to patients as consumers. By advertising drugs, awareness is made of medical conditions, new therapies for these conditions, and encouragement to seek medical care for such. Particularly with mental illness, advocates state that advertising drugs allows underserved populations to be served and helps to reduce associated stigma. The argument is based on two platforms. First, direct to consumer advertising improves the state of patient knowledge via information that helps them make better choices. Second, ads increase patient agency by giving information that allows them to be more informed consumers of healthcare. In regards to medical decision making, patient autonomy and informed consent would be impossible without such fundamental components. Advocates for direct to consumer advertising pull support from this increase of patient autonomy and patient education. Opponents argue that these claims are problematic. First,

significant amounts of information are missing from ads (alone this would violate patient autonomy) and the framing of ads may be misleading with drug indications, use and efficacy. Second, direct to consumer advertising may erode the doctor-patient relationship by causing frustration and distrust as well as increased pressure on physicians to over-diagnose and over-prescribe advertised medications. In addition, the time physicians spend explaining advertised drugs to their patients may cut into an appointment and have possible adverse impacts.¹⁷⁴ Advertising may also encourage the overuse of medication and lead to an increase in the consumption of newer drugs which are more expensive in contrast to the comparable older versions which are cheaper and safer.¹⁷⁵

Research tends to support that the majority of most physicians view direct to consumer advertising negatively. Reasons cited include a preference by patients to request brand name medications when a generic is adequate as well as asking and receiving unnecessary prescriptions. Despite these reasons, most physicians prescribe the medications their patients request even when they believe it to not be the most effective therapy. The majority of physicians report receiving requests for specific drugs.¹⁷⁶ Ads state to ask your doctor, and research suggests the direct to consumer advertising provides motivation for patients to request certain drugs and those with more exposure to more ads, request more medications. The instance of drug therapy significantly increases.¹⁷⁷ Concerns are impacts on the doctor-patient relationship, cost, and demand for drugs and how advertisements may impact the elderly, low income, and other vulnerable populations. Healthcare costs have annually increased 9.6 percent between the

years 2000-2004 mainly due to the increased cost of pharmaceutical drugs while the industry manufactures see astounding profit at the expense of the consumer.¹⁷⁸

Even in countries that do not allow direct to consumer marketing, there is industry influence. Publically funded healthcare is also susceptible to disease mongering. In the UK, it is general knowledge that a publically-funded healthcare system is not able to pay for every new treatment available but rather has objectives to promote clinical superiority by making cost-effective medical treatments using care that is available. This is the role of The National Institute for Health and Clinical Excellence (NICE), part of the UK National Health Service, to ensure cost effectiveness, which means a combination of therapeutic effectiveness and monetary value. Quality adjusted life years measurement (QALY) is used to compare different drugs with their cost effectiveness, as British pound per QALY. Mass media and the pharmaceutical industry can have an influence on this measure as well. The industry clashes with NICE indirectly, but in particular, when it comes to patient special interest groups. Groups of people are often presented by media as being deprived of life saving treatments by NICE. Industry influence plays a role in skewing the regulatory process.¹⁷⁹

Also, while they cannot do direct to consumer marketing in England the pharmaceutical industry is creative with alternative publicity. Press releases are used to make brands known, Viagra was a successful example. Television commercials are used that do not mention the drug, however conditions are spoken of and the suggestion that viewers speak to their doctors about the problem. The name of the company funding the commercial is given. It is very similar to direct to consumer advertising with the same intent of to increase demand for a product, and the practice is influential.¹⁸⁰

Direct to consumer ads on television have been increasing since they gained FDA approval. The rise in dollars spent in advertising has been significant. Direct to consumer advertising has an impact on the consumption habits of patients and prescribing habits of medical providers.¹⁸¹ Marketing to physicians is the next area to be examined.

2.5.8.2 Direct to physician marketing

Selling is not only done to patients but is also, on a higher level, geared toward physicians. Most marketing is therefore focused on prescribers in the form of detailing, visits from drug representatives, promotional educational activities, and samples. These procedures account for the majority of the promotional budget of pharmaceutical companies.¹⁸² Doctors do not have the means to analyze each and drug study research and to investigate claims of key opinion leaders (prominent academic physicians hired by drug companies). The industry exploits these circumstances to its benefit.¹⁸³ The relationship between a profit driven pharmaceutical industry and a physician caring for patients is necessary to advance science, but with caution. A physician's judgment can become subconsciously compromised with close ties to industry representatives.¹⁸⁴ Drug representatives play a significant role in the marketing process.

2.5.8.2.1 The role of drug representatives

Sales representatives visit physician offices to distribute promotional material and drug samples in a practice known as carpet bombing. Drug companies focus efforts on primary care physicians and their receptiveness to prescribe these new medications. Physicians are the gatekeepers to prescription drugs.¹⁸⁵

Drug representatives (often called drug reps) are trained to be observant, friendly, and helpful to physicians as well as assess a doctor's personality and practice style. Personal information about a physician is valuable to a drug rep; they try to engage in personal conversation about hobbies or interests the doctor may have all to establish a personal connection with a physician. Reps are also trained to recruit "thought leaders" - the physicians who take active roles such as speaking engagements on behalf of the benefits of a product. The return on investment of drug marketing is tracked by pharmaceutical companies and health information organizations. These organizations buy the prescription records from pharmacies. IMS Health is the leading organization. Patient names are not included and only numeric identifiers are used for a physician (their license number, DEA number, or pharmacy specifier). The American Medical Association has the master file of corresponding names and identification numbers of all physicians, contained in its Physician Masterfile. This file has all demographic information for all US physicians, living or dead, member or non-member, and those with or without a license. In 2005, database product sales were more than 44 million dollars for the AMA, which included licensing Masterfile information. Drug companies are the biggest purchasers for prescribing data, used to track those who most prescribe and to examine the effects of promotion. High prescribers are given gifts such as educational grants. Drug companies can see how many specific patients receive a specific drug, how many drugs are written for the competing brand, and how a doctor's prescribing habit changes.¹⁸⁶ Drugs are introduced to physicians by means of detailing and sampling.

2.5.8.2.2 Detailing and Sampling

Drug detailing is the term used by drug representatives informing physicians on medications. The Pew Prescription Project reports as of 2012, approximately 72,000 drug representatives were employed in the US. Detailing gives information and detailing also includes meal, or gifts such as textbooks. The pharmaceutical spends billions of dollars each year on drug detailing. The accuracy and balance of the information that physicians receive in detailing is questionable. Information may be factually incorrect; the benefits are hailed while the risks are downplayed. Evidence suggests detailing impact prescribing habits, for example prescribing cost, non-rational prescribing, drug preference, and prescribing new drugs. Connected to detailing is the practice of sampling. This is giving away free drug samples to physicians, which is a large part of a drug company's marketing budget. Sampling may have influence on prescribing preference. The acceptance of accepting samples has ties with increased awareness, preference, and the rapid prescription of new drugs.¹⁸⁷

The distribution of free samples of drugs among physicians has been shown to increase new prescriptions of these medications. The companies state the drugs are intended to be given to patients who otherwise cannot afford their medication, however, research indicates most people given samples have health insurance. Those given samples tend to have higher prescription cost because the name brand drugs prescribed are more expensive than the generic alternatives.¹⁸⁸ Drugs samples are used as a means of access to the physician and to get them familiar with the target drug. Physicians appreciate the drugs in respect to benefiting their patients and patients like to get the samples, too. Samples are provided only for the most promoted drug, normally one that is the most

costly. Patients who receive these name brand samples almost always continue on with them when a prescription is required for treatment.¹⁸⁹ Incentives are also provided to physicians.

2.5.8.2.3 Incentives to physicians

Physicians are among the biggest target of lobby groups in the field, such as the pharmaceutical industry. Means of influence include small tokens bearing the logo of pharmaceutical product such as mugs, diner invites, grants for research or lecture, invites to conferences and even payments that are not legal. The industry depends on physicians' cooperation. The industry needs their expertise. The joint venture can result in conflicts of interest. Financing conference attendance has an impact of the prescription of drugs. Conference trips paid by industry often result in the industry's drug being included in a hospital dispensary.¹⁹⁰ Research supports claims that industry has an impact on physician's decision making.

Research lies in the hands of physicians so they have a critical role in the launch of products. The ethical problems that arise from this include a sense of entitlement from this powerful role, bias in decision making which may put patients at risk, influence of financial incentive on academic and research interest, and possible restriction of free resource allocation.¹⁹¹ Less obvious forms of marketing occur as well, this is known as indirect marketing and it applies to physicians.

2.5.8.3 Indirect to physician marketing

Indirect marketing is another form of marketing. In 2011 in the US, pharmaceutical and device makers provided 32 percent of funding for continuing medical education credit courses. Courses are regulated by the Accreditation Council for Continuing Medical Education as to prevent them being disguised as marketing. However, educational grants seem to still increase the market for their products, according to a 2007 report by the Senate Finance Committee. Grants to health advocacy organizations are another form of indirect marketing. Patient advocates are assembled groups on behalf of a specific cause to the benefit of drug companies who manufacture drugs used to treat the disease. Groups receiving grants from pharmaceutical manufacturers often endorsed the company position compared to groups who did not receive funding courses on potential drug side effects.¹⁹² Marketing to physicians also subtly takes place through educational events.

Educational and promotional meetings are sales talks, where doctors are invited to discuss drugs with industry-paid physicians, who are often leaders in their field. Often the events are held at restaurants. Promotional mailings are unsolicited promotional materials which pharmaceutical companies send to physician's offices, typically materials such as brochures. The brochures often hail the benefits of the drug, describe the clinical trials, which are normally industry sponsored. A study found this material to be biased in favor of the company's drug over that of their competition in superior performance.¹⁹³

Drug companies also pay for medical conferences, provide support for continuing medical educational events, and meetings of professional organizations. Physicians receive invites to attend in order to learn of new drugs and treatments as well as their use

at these so-called educational events. However, the fairness of the information presented is questionable. Drug companies may use the continuing medical education events as perfect marketing opportunities. The pharmaceutical companies have roles throughout continuing medical educational events. They help to organize and generate publicity for the events. May aid in the preparation of presentations or curriculum. The pharmaceutical companies generate lists of potential speakers and may even indirectly pay them. When backlash occurred around 2008, of the industry involvement, the Accreditation Council for CME required that industry supporters should not have any input into the content of programs or selection of speakers, and consequently industry support in continuing medical educational events appears to be declining.¹⁹⁴ The marketing of the concept of self-diagnosis is another area to examine.

2.5.8.4 The marketing of self-diagnosis

The current stance regarding direct to consumer marketing has completely changed and pharmaceutical companies portray themselves more in a role as a facilitator through their products; a means encourage discussion of treatment options between patients and physicians. Essentially, the advertisements promote self-diagnosis. Self-diagnosis went from a threat to an ideology of the industry in the form of patient empowerment and self-knowledge. Self-diagnosis exists in a cultural context where diseases are marketable and shaped by the pharmaceutical industry. A diagnosis validates patients' view of their symptoms, by giving symptoms a name but it also makes everyday life experiences, such as mood swings, pathological. Marketing medication is valuable to the pharmaceutical industry, likewise, marketing of self-diagnosis itself is also important.

A vast amount of money is spent to ensure that regulatory bodies, patients, and physicians are aware of new conditions and the medications that are available to treat them. Self-diagnosis undermines the physician's role as an authority on health in favor of industry marketing agendas. Thus, diagnosis via self-diagnosis is a marketing tool.¹⁹⁵ Self-diagnosis goes hand in hand with the industry changing the role of patients who were passive receivers of care, to consumers who are actively able to demand and choose products of their choice.

2.5.8.5 Marketing patients as consumers

The notion of free choice is marketed through presenting patients as medical consumers. Medical systems are changing. Health care has become more of a commodity and is subjected to driving forces of the market so that medical care has become more like other goods and services. Individuals can pick their own health coverage, choose their health plan, and select their own medical facilities. Consumers demand services actively, and this notion of desire for options can help shape the scope or possibly even demand for medical treatment for human problems.¹⁹⁶ Individuals play a key role in their health now. This trend is escalating with the greater use of information technology. Individuals have been transformed into active consumers and also expert patients. Medicine is presented to the public as a way to heal their problems.¹⁹⁷

Individuals in a consumer society view themselves as free agents with consumer choice. Because of this, it is not difficult for the pharmaceutical industry to present patients as being empowered by free choice as medical consumers. Moving from a patient to a consumer chips away at the role of the physician being the expert of health

and gives more power to the individual.¹⁹⁸ The industry's marketing push seeks to persuade patients to self-diagnose to ensure sales. This push reconfigures patients into consumers who seek treatment or diagnosis based on their own self-diagnosis and choosing their medications.¹⁹⁹

The pharmaceutical industry has a role in helping shape the view of what constitutes illness and promoting this view to the consumer public. In the US, autonomous choice and direct to consumer advertising create the perfect environment for illness to be marketed successfully to consumers. Closely related, empowerment of free choice is often promoted by drug companies by turning a patient into a consumer.²⁰⁰ Human beings have many needs to satiate and the free market is a means by which these needs may be met. This relationship is nicely fueled by marketing. In free society, humans consider themselves free agents who can exercise choice. Business marketing practices in pharmaceuticals convinces individuals they are consumers of health and can make their own choices based on their own research of which drugs they feel they should be taking, a role once only held by a physician.²⁰¹ However, this has flaws if information these decisions are made upon is inaccurate.

Misinformation from pharmaceutical companies serves to undermine autonomous choice. If information is inaccurate, efficacy of a treatment is distorted, thus impairing free choice as a consumer. A consumer may be unaware that the information is distorted and biased. Patients must depend upon information given to them by the pharmaceutical company with no objective, independent other source for analysis and because of this, patient judgment is reflective of industry judgment. In return, the industry produces drugs a consumer may want but may not need.²⁰²

Patients as consumers are encouraged to distance themselves from disease awareness campaigns in media as advice is often compromised.²⁰³ However, in conjunction with the saturation of direct to consumer advertising that occurs this is not an easy task. Many patients are unaware of the role this advertising plays in their medical decision making choices. Marketing may have led to social changes in which patients rely on medical interventions rather than lifestyle alterations to change their health status, for example. However the FDA states data is lacking to support such claims that public health is being jeopardized by industry broadcast marketing.²⁰⁴ The role that framing a patient as a consumer of their own health choices must be considered in disease mongering, especially when the information presented is inaccurate and hampers making health decisions, self-diagnosis is promoted, and drug ads are abundant. Lastly, disease mongering is not an isolated problem, it has global impacts.

2.6 A global phenomenon

2.6.1 Neglected disease

Evidence of profit being more of a guiding principle rather than health needs is illustrated by drug companies having little interest in treatments for rare conditions, but more so those that are common in third world countries, which are often called neglected disease. The profit margin will not be great because the people of these countries may not be able to afford patented drugs. Pharmaceutical companies often need to be given inducement to develop medications for these diseases and often it is charitable foundations which support research into these third world diseases.²⁰⁵ Over the last twenty years the realization came to light that the current system of research and

developing new drugs is not meeting the majority of the world population's needs, over eighty percent of whom live in low and middle income countries. The need is most illustrated by neglected diseases.²⁰⁶ In 2007, research indicated that the bulk of research for neglected diseases was funded by public and philanthropic donations, investing \$2.3 billion or 90 percent of total funding. The pharmaceutical industry provided around 9 percent of funding. This ranks them third in global investors behind the NIH and the Bill and Melinda Gates Foundation.²⁰⁷

The pharmaceutical industry has been faulted by ignoring low incidence disease and those that are life threatening in developing countries because they do not reap enough profit.²⁰⁸ Rare diseases affect between 6-8% of the world's population, and are often called orphan diseases because the industry will not develop medicines to treat them. Developing drugs for the market for treating these conditions would hurt profit and shareholder investment.²⁰⁹ An estimated one billion people suffer from neglected tropical disease in the world, mainly in developing countries. The populations are poor. Incentive to invest in such research therefore not financially attractive. The drugs available have problems. These are in relation to cost, safety, stability, and potential to become treatment resistant.²¹⁰ Low and middle income countries have unmet mental health needs as well.²¹¹ In the context of global health, medicalization is a problem that is disadvantageous for how the world responds to poor health. Due in part to the exposure of preventable mortality around the world, the area of global health is growing. How health is defined plays a vital role. When healthcare is dominated by biomedicine, this serves as a detriment. Medicalization can impact global health and medicalization has a tendency to escalate especially in connection with powerful institutions.²¹² The industry's

focus on profit and neglecting the needs of many sets a poor example for the US medical model.

2.6.2 US medical model's global reach

The US medical model influences how medicine is conceptualized and practiced in the rest of the world, especially in developing countries. When patients are turned into consumers they are exposed to medicalization of life via bio-education used through faint mechanisms presented as objective information designed to empower the consumer. Regulatory bodies in developed and developing countries cannot keep up with the corporation's outreach to the public.²¹³ Since the 1990s the pharmaceutical industry has had more influence in committees detailing many aspects of disease. Many specialists in these committees are from official and professional organizations or international institutions like the WHO. Almost always, decisions of such experts, presented as evidence based, become adopted worldwide.²¹⁴ Disease mongering has long reaching effects throughout the world by putting effort into profit which neglects serious disease and setting a standard of medicalization. The gap in new drug innovation is another aspect for consideration. The needs of poorer nations receiving affordable medications are neglected in favor of wealthier nations. Often, a strong factor limiting drugs are expensive patented drugs.

2.6.3 Access to drugs limited by patents

Pharmaceutical companies generate profit by their branded drugs but having a patent means a generic equivalent is not available, which has the most impact in the

poorest nations. The 10/90 gap is a consideration in medical research. Ninety percent of economic resources spent annually is spent to address the health needs of the richest ten percent of the world's population. This also implies that ninety percent of the world's population receives the remaining ten percent to fund health research.²¹⁵ Data is not suggestive that this gap is narrowing. The number of people who are enrolling in clinical trial research in poor or lower income countries has substantially increased. However, during the trials access to the new drugs to the poor and low income populations has not increased. The gap between rich and poor countries concerning who benefits from the fruits of the trials widens. The powerful stakeholders in wealthy nations contribute to allowing this injustice to continue. Take for example intellectual property rights, regulated in the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement which are promoted as being done for cost efficacy and efficiency but are morally problematic. There are four parties who feel the effects of this practice: the pharmaceutical industry and its shareholders, patients/future patient in wealthy parts of the world, generic drug manufactures, and patients/future patients in poor parts of the world. The industry benefits the most. The impacts on patients or future patients in wealthy countries is somewhat ambiguous; they lose the ability for generic drugs but have future innovations always in the pipeline which they may access. The generic drug makers are infringed upon, which impacts those in both rich and poor countries in their access to more affordable drugs. For those in most need, patients and future patients in developing countries the TRIPS regime is most harmful. Millions of deaths from diseases such as AIDS or other treatable or preventable diseases, can be linked to the inability to access to affordable generic drugs. TRIPS has its roots in wealthy nations and is enforced

upon the global community. Large numbers of the poorest people fall outside the realm of access to drugs they can afford.²¹⁶

Patents are the biggest driver of research and development of drugs. Prior to the 1990s there was variation in different countries in the type and length of patents. Industrial countries have longer patents (15-17 years) while developing countries usually have shorter patent terms (5-10 years). But, in 1995, TRIPS required harmonizing these laws to the level of developed countries where the big pharmaceutical companies are located. Only the least developed countries have this extended until at least 2016. A medication can cost the same in the United States as it does in India. This creates barriers to access to new treatments and diseases with global incidence.²¹⁷

An analysis of global drug development showed that 1393 new chemical entities were granted authority to be marketed between the years 1975-1999. The distribution was bias toward high income countries, diseases that affect the poor are not allocated sufficient resources. Only 16 new chemical entities developed in the timeframe were for tropical diseases and tuberculosis (which is a poverty related disease) and they were all developed with public sector investments.²¹⁸ This is in contrast to all of the new drugs which were developed that offer little if any, greater efficacy over existing treatments whereas any treatment for a neglected disease represents an improvement. Patents again have a role, as the life of a patent extended over this time frame and yet new drug innovation did not. The existing patent system, a stimulus for new drug investment, seems detrimental to the progress in treating neglected disease when a market monopoly is not enough incentive to address these needs.²¹⁹ Most of the pharmaceutical giants are located in the US, as is most drug development and discovery of disease, however the

reaches of the products are not limited to the United States. The leading force of profit that drives disease mongering has impacts around the world.

2.7 Conclusion

Disease mongering is a global occurrence that turns too many people into patients needlessly. Taking drugs one does not require for conditions that may not genuinely be problematic places their health in jeopardy. Creating illness, expanding illnesses, off-label drug use, manipulation of disease criteria, medicalizing everyday conditions, and ghostwriting are mechanisms that encourage disease mongering.

Disease mongering is also able to easily occur because of a weak definition of what defines disease and how diseases are created. The most prolific way at which disease mongering is forced onto society is through business marketing procedures. These include direct to consumer advertising which focuses on the general public. Direct to physician marketing and indirect physician marketing target physicians through sales representatives visiting practice to detail new drugs to subtle marketing through education and publications. Marketing to patients is also done through promoting self-diagnosis via ads, which encourage patients to facilitate conversations with their medical providers. Also, the push to market a consumer platform of health choice as other consumer goods are sold is encouraged through marketing.

There is a focus on selling drugs and investing in only profitable medications at the expense of diseases which are deadly, but not as lucrative. This evidence suggests incidences of disease mongering occurring and at many different levels. Therefore, there is a need for a framework to ethically analyze disease mongering. The next chapter

describes the UNESCO model framework to evaluate disease mongering and also the importance of why this model is the best choice.

Chapter 3: An ethical framework for assessing disease mongering: the UNESCO model

Chapter 3 will examine the UNESCO ethical model framework, which will be used to assess occurrences of disease mongering. It is necessary to explore the history of bioethics in order to see why the UNESCO model is the most effective framework. Thus, chapter 3 begins by examining principlism and its elements: principle of respect for autonomy, principle of nonmaleficence, principle of beneficence, and principle of justice. Critique of principlism is addressed as to why this model alone is not enough to examine all ethical dilemmas, such as the case with disease mongering. In looking at how ethics has evolved beyond principlism and expanded to bioethics, the work of Potter is included. Potter is critical in the foundation of the field of bioethics. Potter's vision of bioethics is best embodied in the area of global bioethics, which is also included as well as the justification as to why a global model is needed to analyze disease mongering. The aspects of the UNESCO model is discussed. This includes the history of the Declaration, function, aims, articles, and principles are included in the chapter. Lastly, this builds to the articles which are used in the assessment of the analysis. The Articles included are Articles 3, 4, 5, 6, 8, 10, 11, 14, 15, and 16. Therefore, the chapter will begin with principlism.

3.0 Western bioethics

3.1 Principlism

In the Western world the universal approach to standard for ethics, and thus ethical decision making, is a focus on principlism. This approach is built upon human

rights and individuals as autonomous decision makers. The individual's rights and choice therefore must be respect above all. However this is not a model which is universally accepted around the world. For example, African perspectives in bioethics place a stronger value over community than on the individual. In Japan, it can be argued the human rights discourse in bioethics is primarily a Western approach.²²⁰

In ethics today, principlism has become the primary approach to bioethics and it is well-established in Western countries, however it does receive criticism by academics. Principlism became established as the popular method in medical ethics beginning in the 1960s with endorsements from the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in the Belmont Report, which identified respect for persons, beneficence, and justice, as three base ethical principles. Beauchamp and Childress' *Principles of Biomedical Ethics*, was also published in this same year (1979), which is almost known as an official methodology of medical ethics.²²¹

Beauchamp and Childress' *Principles of Biomedical Ethics*, consists of four principles: autonomy, non-maleficence, beneficence, and justice. Principlism applies a set of principles to ethical problems in order to determine the best outcome. This standard of applying the four principles is often taught to clinicians in conjunction with proper legal frameworks to guide the process of ethical decision making. This model is appealing because it is relatively clear and simple, therefore makes it easier for medical decision making, but principlism is limiting with interactions centered on individual interactions. Principlism is often tied to medical ethics. In the nineteenth century, medical ethics became recognized as an academic discipline. Medical ethics has since become a major part of medical study. Key factors of medical ethics centers on the doctor patient

relationship. The key issues at the forefront of medical ethics therefore are centered on confidentiality of the patient and informed consent.²²²

Principlism has critics which are mainly from in academia, but principlism is still widely used and accepted in the West. Principlism was by design condensed and simplified taking morality and condensing it to its key elements so that individuals from wide ranging backgrounds could better grasp moral standards. Principlism is successful because of this simplicity. It is also much in alignment with traditional codes of conduct in the medical profession which have stood the test of time and applicable in different environments, too.²²³ Next, the elements of principlism will be examined beginning first with the principle of respect for autonomy.

3.1.1 Respect for Autonomy

The principle of respect for autonomy minimally states that an individual is free from interference of others and can practice self-rule. Autonomy does not have a clear-cut definition, however most would agree that autonomy has two essential conditions, liberty and agency. Liberty means to be free from controlling influence and agency is the capacity to have intentional action. The meanings of these two features and of additional conditions are necessary, but in addition create dispute. Beauchamp and Childress analyze autonomous actions in terms of those who: 1. Act intentionally, 2. Act with understanding, and 3. Act without controlling influence from others to arrive determine their action. Acts are either intentional or not; however to which there is understanding or no controlling influence can be a greater or lesser amount. The authors state that to be autonomous, only a substantial amount of understanding and freedom from restriction is

required, not a total understanding or complete lack of any influence. To expect otherwise is not realistic to individuals in a practical world where actions are rarely if ever, completely autonomous.²²⁴

To respect autonomous individuals requires recognizing they have rights to hold views, make choices, and take action based on their own personal values and beliefs. Respect acknowledges the value and decision making rights of individuals and enables them to act autonomously disrespect ignores, or lessen other's rights to autonomous action.²²⁵ Nonmaleficence is the next principle.

3.1.2 Principle of Nonmaleficence

The obligation of nonmaleficence is to not inflict harm on others. Often, the principle of nonmaleficence is combined with the principle of beneficence. However, it is important to make distinctions between the two. Obligations not to harm are distinct from obligations to help. The obligation to not harm a person is often stricter than an obligation to help an individual. Nonmaleficence supports more specific moral rules as well. (Other principles justify these as well.) These rules include do not: 1. Kill, 2. Cause pain or suffering, 3. Incapacitate, 4. Cause offense, 5. Deprive others of the goods of life.²²⁶

Next, is the principle of beneficence.

3.1.3 Principle of Beneficence

A requirement of morality, aside from treating people autonomously and not harming them, is to contribute to their welfare. These beneficial acts fall under the principle of beneficence. These require action from individuals to take positive steps

toward helping individuals. Examples of some general rules of moral obligation of beneficence include the following: 1. Protect and defend the rights of others, 2. Prevent harm from happening to others, 3. Remove conditions that will cause harm, 4. Help people who have disabilities, 5. Rescue people in danger. Rules of beneficence require positive action, do not to necessarily be followed impartially, and do not offer legal punishment. Morally, we are forbidden to harm people therefore must always act with nonmaleficence. However, it is nearly impossible to always work towards helping all people all of the time, so it is not immoral to not be able to help every single person who may need help.²²⁷ Lastly, is the principle of justice.

3.1.4 Principle of Justice

Justice may be explained as fairness or that of which is deserved. Injustice on the other hand is a wrongful act or denial of resources for which one has a right. Distributive justice is a term that involves norms of justice in the form of social cooperation; distributive justice references the distribution of rights and responsibilities within a society. Distributive justice includes policies that allocate benefits and burdens in society, taxation for example. Formal justice states that equals must be treated equally, and unequals treated unequally. No criteria for determining equality amongst individuals is provided with the concept of formal justice. Material principles of justice on the other hand, provide specificity; they identify properties for distribution. Obligations are limited to fundamental needs because to deny these needs would be to cause harm to an individual. The following provide a general material principle of distribute justice, to each person: An equal share, according to need, according to effort, according to

contribution, according to merit, and according to free-market exchanges. Theories of distributive justice include utilitarian, which seeks to maximize public utility, libertarian which stresses fair process rather than outcomes, communitarian which emphasize the tradition and practice of justice in a community, and egalitarian which focuses on equal access to life's goods for every rational person.²²⁸ The four principle often draw criticism for a number of reasons which will next be examined.

3.2 Criticism of principlism

The model of Beauchamp and Childress and the four principles are most known as the principles of bioethics. However, when examined in greater detail argument exists the principles are not useful action guides; they serve to offer considerations but not guidance. The principle of nonmaleficence may be an exception as it offers moral rules and not only moral ideals. Moral rules such as, "do not kill" are clear. It is argued that the principle of justice provides only a checklist of moral concerns. The principle offers much insight into differing theories of justice, but no guidance as to how to apply the principle. Also, there is not a clear distinction of what is morally required and what is morally encouraged. The hallmark is the principle of respect for autonomy. If the principle were interpreted as to not deprive of freedom, there may be little debate. As such, it would provide an action guide. However, the use of autonomous action is what causes it to be questioned. Non-autonomous action is not constrained. Not being able to distinguish between promoting autonomy and respecting autonomy also creates confusion with this principle. There is difficulty as to what an autonomous choice or action is, and also not precisely clear the distinction between a moral rule or a moral

ideal. The principle of beneficence has similar problems to those of autonomy with unclear distinction between moral rules and moral ideals.²²⁹

Critics argue principlism is reductionist in that some information is ignored if it doesn't not properly fit within the principles. Other criticism is that principlism pulls from differing moral theories and leaves it up to the individual to decide which carries most weight, as principlism does not address how the individual principles are weighted. Principlism is also presented in a Western context; individuals are privileged over community and individual rights are the focus rather than underlying issues, or social or political factors.²³⁰

Principlism is not responsive to different cultural, economic, and social context. The principle of autonomy's credibility is questioned by non-Western cultures and even by some Western medical providers who are working in third world countries. In certain parts of the world, countries like Japan, China, the Philippines, Indonesia and some parts of Africa do not practice individual decision making in regards to health care. Rather, the decisions are made based on values of solidarity, egalitarianism, and social responsibility. Families or even communities, also have input in decision making or at times are the ones who make the decision on the behalf of the patient. This illustrates the value of social responsibility and solidarity. Families have a duty to care for the sick in both assistance and decision making. Consensus is important because there is a value on the greater good to the community as well in the decision making process. Therefore, the different values of justice when applied to different cultures make the principle of justice difficult to be relevant globally.²³¹

Western bioethics near exclusively places individualism at the center, which may be described as being too focused on the human, while ignoring plants or animals. This is a concept that is not universally recognized in comparison to other parts of the world, this view differs, for example, the acknowledgment of the interdependent nature of all forms of life in the African bioethics viewpoint. Social values supersede individual values in Japan as well, and the separation between nature and humanity is not distinct.²³²

Health and disease itself are not universal, but these concepts are social and culturally constructed. Yet, Western culture tends to find the root of disease in scientific description which indicates a universal comprehension of health. For example, human dignity and well-being and cultural understanding of health and injury is illustrated by the wounded in the war in Somalia. Western medical knowledge and principles were not accepted as those who were wounded and required amputation to survive refused the option. They did not wish to survive at any cost and preferred to die with their whole body rather than live with a missing limb. This created turmoil for the physicians who felt it was their place to save lives, however for the Somali people, their best interest was to refuse amputation. Applying the principles to the Karamoja region of Uganda in a situation of scarce resources (food) illustrates difficulties as well. Medical aid workers traditionally established food stations which allocated food to those most malnourished, which were children and pregnant women. This is based on vulnerability, but also on the fact children represent the future and are innocent. However this notion was not in accordance with local values and customs. Food was given to community elders in part because their wisdom kept communities alive and locals explained that children were a renewable resource, however the elderly cannot be replaced. Thus, principlism is

criticized for being too individualistic and positivist in its beliefs. While it remains popular, new approaches to ethics can address ethical issues in a global context; the principles can be used as guidelines, but, a broader way and interpreting them as well as their appropriateness should be further considered.²³³

Principlism is the most well-known approach in ethics predominantly associated with medical ethics. However, principlism is not the only option. Therefore, in order to see how ethics itself has evolved beyond principlism to a global approach which can be used to examine more bioethical issues, examining the history of bioethics is important.

3.3 Bioethics

Applying principles to a global context is not the only limitation within medical ethics. Medical ethics has expanded from issues that are only associated with the traditional medical practice but further extended to wider areas of medical and scientific practice to bioethics. Bioethics extends to issues beyond just the realm of medicine to areas which were not traditionally addressed but need to be tackled.²³⁴

Bioethics became distinct from medical ethics in the late 1960s as a response to innovations in science and technology especially in the United States in areas concerning bio-science and bio-technology. This was a movement known as technology assessment.²³⁵ Humanism was likely used as criterion for the assessment of technology during this time. Humanism was used to determine if science and technology should be rejected because it was anti-humanistic. Concepts such as human dignity and the ideas of person were at the nature of humanism. Persons were Kantian in that, persons are free and rational beings regarded as having human rights. During this time of technology

assessment, there was a focus on the protection of human beings from disasters of technology, with an emphasis on the protection of human rights. Bioethics, at this time, sought to protect human rights and dignity from harmful biotechnologies. Paternalism was rejected in this time period in favor of rights and informed consent; thus at this stage of bioethics most of the focus was on protection of human rights. The 1980s brought change in bioethics with genetics which were rapidly advancing, with increases in environmental ethics, and non-European models of bioethics. DNA was able to be altered, which meant ability to artificially render the human body and possibilities were established regarding human cloning. Both of these instances meant the possibility of artificially altering humankind was a reality. On a human rights stance, the altering of genetic patterns was challenged by the Council of Europe in 1982. Environmental ethics also surfaced in the 1980s, first in the sense to protect the environment for humans and future generations and second the protection of the environment for its own sake. Lastly, bioethics extended beyond Europe and America. In a Western perspective, bioethics incidents in Asian countries were as perplexing. Human rights in China, for example, is a weak concept whereas there is greater interest in overcoming problems such as poverty and starvation. Asian countries place a greater value on the welfare of the whole community or group, not on the individual, as well.²³⁶ Van Rensselaer Potter is considered to be critical to the discipline of bioethics.

3.3.1 Van Rensselaer Potter

Van Rensselaer Potter is often attributed to coining the term bioethics. Potter grappled to find an adequate term to express the need of a balance between scientific

knowledge of medicine and human values. He first expressed his ideas in 1971 in the book, *Bioethics, A, Bridge to the Future*. Bridging was a common theme throughout Potter's work and thoughts regarding bioethics. Bioethics was originally conceived to bridge the gap between science and humanities. Potter then felt a need later to link medical ethics with environmental ethics. Potter continued to modify the term bioethics throughout his career.²³⁷ At Georgetown University, medical bioethics began to rapidly expand. However, the bioethics at Georgetown were not what Potter envisioned. The model was a type of extension of medical ethics with a focus on medical issues and technologies. The focus was on the patient; how their lives can be improved or extended with medical technologies. The focus was also only short-term and it had no connections to the social, cultural, and political aspects of life. Potter's notion of environmental ethics held long-term views and concern for the human species and it was not in connection to medicine or health care. Potter acknowledged that medical bioethics was somewhat broader than medical ethics with a focus on new technologies, but it was still too narrow to speak to the current problems that were facing humanity such as war, poverty, and violence, which were problem to the survival of human kind. To address these problems, a much broader approach was needed.²³⁸

Potter stated that survival must extend beyond the science of biology alone and must include elements of social sciences and the humanities with an emphasis on a strict sense of philosophy meaning "a love of wisdom". Simply, a science of survival must include more than science alone. Thus, the term bioethics was born to address these two fundamental elements of biological knowledge and human values.²³⁹

Potter worked as a Professor of Oncology for more than 50 years. Potter viewed oncology as interdisciplinary noting it cannot focus solely on medical and individual perspectives. The explaining of cancer extends beyond the individual and the medical perspectives but also includes lifestyle and environmental factors. Potter expressed that progress treating cancer was made, but eliminating it was a distant goal. There was hope at the individual level in alleviating suffering and better treatments but on the larger population scale there was work to be done, for example with the effects of cigarette smoking. His career for a long time was narrowly focused on cancer, but Potter came to discover larger scale problems and concerns.²⁴⁰

Bioethics is the combination of science and philosophical knowledge.²⁴¹ What Potter defines as an ethic, in that it extends beyond medical or environmental bioethics. Potter states, “An ethic is a set of culturally accepted beliefs and guidelines for decisions affecting the course of human activity, with idealistic goals in mind, usually involving the adjustment of competing claims without resorting to the use of coercion unless mutually agreed upon by members of the culture.”²⁴² Potter’s work in oncology spawned his desire to explore greater problems. These problems included were population, peace, pollution, poverty, politics, and progress and moving to the future he regarded these issues critical to the survival of humanity. Therefore a new discipline of bioethics was necessary to address these topics. As a science, bioethics is the science of survival and it uses scientific methodologies by testing ideas in peer groups and builds upon prior existing knowledge. Bioethics is interdisciplinary and has two features: the combination of various categories of knowledge, and the need to continually test and assess.²⁴³

Potter stated that the test of success of technology in culture had a familiar motto, “if it can be done, and sold at a profit, let’s do it”, that line of thought had great impact in changing the world.²⁴⁴ Potter had a special concern for the future of humanity. Potter viewed a divide between those who knew, the scientists, and those who did, those in technology. The knowledge outpaced the ability of having capabilities of handling it; therefore making knowledge potentially harmful. Decisions of policy tended to focus on the short-term effects and not addressing long-term outcomes, which Potter noted. Potter also noted that decisions of the future of humanity needed to include facts as well as values. In order to address these, Potter suggest the formation of a “Council of the Future” where social problems would be debated and in interdisciplinary style with experts from natural and social sciences and humanities as well as open to the public. Potter felt this fashion could bridge the gaps between those who know and those who do, as well as the gap between values and facts.²⁴⁵ This institution would hold the responsibility of predicting potential consequences that may be an outcome of new knowledge. It would replace old convictions and would use tentative statement of policy rather than fixed law. Potter states that for better or for worse that society is moving in the direction of putting the destiny of humanity in the hands of science and technology. In order to preserve the dignity of the human species and the survival of the world, ideas and techniques for arriving at value judgments must be cultivated in the areas where facts alone are not enough.²⁴⁶

The concept of knowledge being harmful is especially relevant when it comes to analyzing the concept of disease mongering. Potter, as a scientist, knew that some information gained through empirical science, if used incorrectly, had the potential to

lead to unwise actions. Potter referred to some knowledge as toxic knowledge, in that some knowledge can be harmful if it is applied in the wrong way.²⁴⁷ Potter states, “Knowledge can become dangerous in the hands of specialists who lack a sufficiently broad background to envisage all of the implications of their work. Educated leaders should be trained in both sciences and humanities. All the implications cannot be foreseen in any case, and all plans must provide for revision. Medical science provides many examples.”²⁴⁸

Knowledge is a sort of Pandora’s Box in that it cannot be put back in once taken out, but rather efforts must be made to deal with outcomes of knowledge, which will always continue to grow. In and of itself, knowledge is not harmful. When knowledge becomes used it is powerful. It is through this power that dangerous outcomes of knowledge can arise. When it is discovered, knowledge may not necessarily be considered inherently dangerous. For example, in the search to find a fitting chemical compound in cancer treatment, it may be discovered that the chemical is quite an effective weed killer. But, when it is used as an herbicide could have the potential to destroy the food supply of a nation. When nuclear fusion was studied, the intent was not there to develop an atomic bomb. When the drug thalidomide was developed as a sleeping pill, there was no foreseeable indication that woman who took the drug during a critical stage of fetal development would likely give birth to a child without arms. In the quest of science to solve the problems of the world, it also inadvertently created new ones. For example, when diseases such as malaria became better controlled, fewer infants died of the disease. Fewer infant mortalities led to population explosion, which created its own challenges, such as famine and poverty.²⁴⁹

Potter stated the concept of bioethics or humility and responsibility. Responsibility meaning competence and indeed excellence; humility being the opposite of arrogance with implied knowledge that shortcomings should be recognized and that people from other walks of life and disciplines be heard. The combination of humility, responsibility, and competence were critical to individuals who wish to be scientists and ethicists.²⁵⁰

Potter's term of bioethics incorporated the science of medicine combined with the values of humans. Bioethics linked the sciences and humanities in its origin and later Potter felt the need to tie medical ethics with environmental ethics. Potter additionally believed that bioethics should include not only medical and environmental ethics but also religious and social ethics, too. Potter valued the health of the biosphere which included issues beyond only those of American but international aspects as well.²⁵¹ Even in 1971 Potter noted that due to the advances in science such as organ transplantation, mechanical valves, and antibiotics that the medical profession was in need of a new set of principles to share complex decisions with patients and society.²⁵²

With vast domains of human life problems not being captured within traditional medical bioethics, Potter reemphasized the need to protect the future of the human species. In Potter's perspective, medical bioethics needed to be combined with ecological bioethics and other forms of ethics related to human life. Potter felt all of these disciplines should be merged in a new approach called global bioethics.²⁵³

3.4 Global bioethics

Potter began to use the term global bioethics in the latter half of the 1980s, a term which aimed to bring together the varying approaches of bioethics in a broad approach. Potter used the ideas of Pierre Teilhard de Chardin, whose work Potter referenced. Teilhard envisioned in what is now globalization, that humanity develops into a large, global community. Teilhard states that the global community will emerge because humans will realize there is interdependency and common destiny not because they come to consensus on accepting a single truth or desire. Teilhard and Potter shared common ideas about the future of human survival and progress. In order for the best possible future, combining the science of biology and the values of humans is necessary. Potter's vision of global bioethics combines two meanings of the word global. Global is a system of ethics and it is unified and comprehensive.²⁵⁴

Potter felt the need of a better balance between humanity and the natural world and if bioethics' long-term goal was the survival of humanity, it should be broad; social and environmental issues relating to medical ones. Globalization is implicit throughout Potter's work.²⁵⁵ Global bioethics is distinct in that it addresses issues in a perspective that considers many areas and methodologies in the search for solutions. Many ethical issues cannot be addressed in isolation because the outcomes can affect many other nation states. Global bioethics has a focus that is not limited to only individual interactions and rights, but to structural issues that impact health around the globe. The scope of ethical problems that exist today extend beyond the scope of what traditional medical ethics may be able to address. Bioethical decision made in one area affect those in other places, thus policy does take place in isolation because it has far reaching

impacts. The interrelated nature is what leads to the importance of global bioethics. Global bioethics takes many factors into consideration, such as economic, social, religious, cultural and political factors. Global bioethics can address situations in which decision and practice by one nation may affect people outside of that nation. Global bioethics recognizes this global context with issues that have potential for exploitation, addressing vulnerability, and defining justice in terms on community not just individual based rights. The non-individualistic approach to justice is also effective in addressing global pharmaceutical markets as well as new drug research trials and testing. Global bioethics does not seek to override medical ethics or bioethics, but is complementary with a slightly perspective and framework and raising different key issues, the three areas have a great deal of overlap.²⁵⁶ Incorporating other aspects other than disease framing is important, such as local meaning and norms, that also frame issues in mental health is important. A valid mental health diagnosis such as Post-Traumatic Stress Disorder (PTSD) in refugee camps in Somolia allowed for better access for health services, but for some a mental health diagnosis also prohibited them from gaining asylum to other countries. Patients views when not incorporated into a broader context can strengthen individualistic solutions.²⁵⁷ Next, the value of considering a global model of bioethics will be addressed.

3.4.1 Why a global model?

When considering the broad-reaching impact the pharmaceutical industry has on not only the West, but world-wide, a global model is more appropriate. Simply, the rest of the world has different ways of conducting ethics compared to the West, to apply

solely Western values and principles are inadequate in analyzing disease mongering.²⁵⁸ Global bioethics does not focus solely on the individual's rights but overarching issues affecting global health.²⁵⁹

The field of global health is growing as well. It is an abundant area of research in medicine and health sciences. This is in part because of increased visibility of preventable death around the world, especially the disproportionate disease burden that occurs in developing countries. Analyses of medicalization are almost exclusively examined in a Western context as well, with a focus on creating illness and patients, while overlooking the social causes of disease, as well as promoting drugs over social change.²⁶⁰ Similar is the case in mental health, which takes a very individualistic approach and gives more priority to increasing medical treatments over other any other factors. This creates an avenue for profit for the pharmaceutical industry as well. Disease mongering is best illustrated in North America and in particular within the area of mental health. The evidence base for two drugs in particular, antidepressants and psychotropics, for example is incomplete, flawed, debatable, or falsified; side effects are harmful; and those in low and middle income countries not represented well in clinical trials. With mental health becoming globalized, it is no longer just a problem of the high income countries especially is treating psychoses and bipolar disorder, for example, become more advocated in the lower income countries. The pharmaceutical industry supports a medicalized framing of mental health, as the more people who are diagnosed with a disorder will further expand the market for treatments.²⁶¹ In 2014, a marketing firm had an estimated projection that by 2015 the global mental health pharmaceutical market would reach \$88.3 billion dollars.²⁶²

Van Rensselaer Potter valued the inclusion of social ethics be included into bioethics. For instance, in the United States there is a great concern regarding the health problems of the nation, however such a narrow focus ignores the great health problems facing the rest of the world. Why not, Potter suggests, use human health as global health principle, to improve the health of the entire human race and not the health of just one country.²⁶³ A great deal of medical technology comes from the United States, but this broader global approach containing the social component which Potter favored is not as widely regarded in the US.²⁶⁴ This is why it is critical to use a global model when most pharmaceutical industry giants are located in the US, but have impacts ranging from research to markets across the world.

Medical research and the drugs they produce impact more than just the individual and to focus purely on individual decision making is not enough. In the UNESCO model this is found in the principles which apply to humankind as a whole such as solidarity, social responsibility, sharing of benefits.²⁶⁵ Core issues of medical research include the interest and welfare of research study participants. These issues are covered with more force in their application compared to existing ethics Declarations, guidelines and policy documents of international research, in the UNESCO model. Article 8 on human vulnerability and personal integrity, Article 13 on solidarity and cooperation, Article 10 on equality, justice, and equity, and Article 13 on solidarity and cooperation cover areas not often embraced in research ethics. Solbakk states that including these principles into the debate on international research is an important step in a unifying language on international research ethics.²⁶⁶

Bioethics concerns all humans regardless of country. Traditional issues of medical ethics face new challenges as is illustrated with informed consent in international clinical trial research. Organ trade, bioterrorism, and medical tourism are new issues in bioethics as a result of a global market. Issues that may only occur in a small number of countries will have impacts in other countries. Even when the moral values of nations differ, common ground can be found as a world community. Potter's second meaning of the notion of global implies that the bridge between science and humanity is unavoidable because many different professionals must work together in order to address problems that affect many. Diversity is necessary to address complex phenomena, not exclusively a Western or Eastern perspective, for example, but various means should be used in global bioethics. A global approach allows a traditional framework to be reconsidered because it may be too domestic or local in its views and brings forward the challenge to search for moral views that can globally be shared.²⁶⁷

The UNESCO model provides a framework which can be applied to the individual, but can also be applied to countries and people of nations who lack ethical rules or regulations. The UNESCO model allows these same standards which could guide a citizen of the US as could guide a citizen of the least developed nation in ethically assessing disease mongering. The UNESCO model has principles which are common to all citizens of the world. The model had respect for cultural diversity of societies. It extends beyond medical ethics but to broader social perspectives of bioethics.²⁶⁸ Next, the UNESCO model, beginning with the background of UNESCO will be explored.

3.5 The UNESCO model

3.5.1 Background of UNESCO

The United Nations Educational, Scientific and Cultural Organization (UNESCO) is a specialized agency of the United Nations (UN) that is responsible for scientific research, education, culture, and communication. For people around the world, UNESCO promotes scientific collaboration so that international peace and common welfare of humanity can be advanced. Additionally, the advances of science shall take place as is stated in Article 1 of UNESCO's constitution in a framework that has a universal respect for justice, human rights and freedoms.²⁶⁹

The Human Genome Project brought forward issues in healthcare that were unparalleled, as well as new social and ethics problems. In part, to address such issues UNESCO adopted three Declarations, the last of which was the *Universal Declaration on Bioethics and Human Rights*. The Declaration was adopted in 2005. Included in its preamble is the statement of a need for the international community to have international principles to offer a foundation for scientific and technological dilemmas amongst humanity and the environment.²⁷⁰

A common framework of ethical principles was the specific request of developing countries. The fear in these nations was that the benefits of new science and technologies would not be reached, but they may instead absorb too much of the burden of risk. International medical research is an example, in the past double standards have in fact taken place in developing nations. Those who took part in research did not receive the same standard of care that they would have in a developed country for taking part in the same research trial. The call for a normative framework from developing countries

provides evidence that richer and more powerful nations are imposing their views onto less powerful and wealthy countries. Rather, it was the less powerful nations who requested a framework be developed.²⁷¹

In ethics, a major objective of the work of UNESCO was to create international normative standards. Standard setting infers a search for universal agreement. There is a sensitive balance to develop universal principles and norms based on shared values as well as the promotion of pluralism through recognizing and improving diversity. Bioethics is a comparatively new field where controversial topics arise which makes this important. Bioethics is also multidisciplinary. Bioethics can also be involved in policy making and legislation. All of these areas combined standard-setting requires the work of many including scientists, lawyers, citizens, and policy-makers. Therefore in developing the Declaration, many different bodies were involved. The International Bioethics Committee (IBC) is a global ethics committee consisting of 36 experts from a variety of backgrounds including, genetics, medicine, law, philosophy, ethics, social science, and history. Experts are from different professional, cultural, and moral backgrounds and come from different regions. They do not represent their member state and only serve on the committee because of their expertise in their respective fields. The Intergovernmental Bioethics Committee (IGBC) consists of 36 Member States, elected by the General Conference. The States are represented by a variety of different people such as a scientist or even officials from an embassy; the State determines who will represent it. Governmental expert meetings are held when important documents need to be reviewed. The Executive Board is a 58 member elected panel which is purported to govern UNESCO. The function and responsibility come from UNESCO's Constitution and rules

created by the General Conference. Lastly, the General Conference consists of representatives of Member States. Each country, regardless of size, has one vote. The matter of whether or not to develop a normative instrument is taken by the General Conference. Standard-setting is important because many areas are limited in their infrastructure in bioethics. There may be a lack of experts, educational programs, ethics committees, legal framework, and public debate. Bioethics affects all people, not just lawyers and scientists as well as highly and less developed countries all the same. Globalization has spread dilemmas around the world. This is why UNESCO aims at promoting a global approach. All value systems are considered and standards to not impose one particular belief or ethical approach to its members.²⁷²

Science and technology have become more and more international. Medical research has become global as are healthcare practices, but guidelines vary or are lacking in different countries, which can lead to unethical practices. For example, the burdens and benefits of scientific advancement is unevenly distributed in poorer countries who are less likely to see the beneficial results of scientific advances in medicine. Science and technology have become global, therefore the need for a global approach to bioethics is critical. Many countries lack experts in bioethics, legal frameworks, educational programs, and ethics committees. Member states direct UNESCO to set universal standards for covering issues which may arise in bioethics and to identify principles and shared values in science, technology, and health care. Having an intergovernmental involvement in ethics generates some controversy despite the need of scientists and practitioners expressing concern, those against this involvement argue that ethics should be left up society, professional organizations and to public debate. Yet, is it common for

countries to have governmental ethical standard setting in countries such as North America, Latin America, and Europe in particular with issues pertaining to medical research and reproductive medicine. To these nations a global framework may be viewed as threatening, as it may challenge their existing standards. However, of the 192 members states the need of an international framework is key because the majority the members lack proper ethical regulation. This is most echoed by developing countries that want to ensure that the same ethical standards are being used everywhere and need a normative framework as guidance. Given this background, UNESCO set forth to put forward a Declaration of fundamental ethical principles. In 2003 and two years later in 2005, the Universal Declaration on Bioethics and Human Rights was released sustaining an international community's commitment to respect set universal principles in developing and applying biomedical science and technology.²⁷³ At the heart of the UNESCO model is the Declaration. The history of the Declaration is the next topic.

3.5.2 The Declaration

3.5.2.1 History of Declaration

One hundred and ninety two member states took two years to reach consensus for the Declaration text with activities taking place in many countries. Expert and regional conferences were held in many countries. Experts from many countries completed questionnaires or wrote suggestion and commentary. Some issues were disputed, abortion, euthanasia, and stem cell research, for example, and consensus was not able to be reached. This was solved using a two tiered approach. This approach entails that at one level is a human rights dialog defining minimum standards which all can agree.

Second, includes local ethical traditions, which go above what human rights may require. For global bioethics minimum standards can be developed which cultures can agree upon. This is expressed in international human rights language and is elaborated by bioethical principles. Conversely, efforts are made to incorporate bioethical standards into cultural and religious traditions. Members of these traditions have their views included in the discourse. This combines the global and local perspective in helping to build and produce global bioethics. At last, 15 principles of global bioethics were agreed upon. Those involved were representatives of states, cultures, and different traditions. The Declaration includes the traditional Principles of Beauchamp and Childress, but also includes those which are more relevant in non-Western countries, such as solidarity, social responsibility, and benefit sharing.²⁷⁴ The purpose of the Declaration is next.

3.5.2.2 Function of the Declaration

The Declaration is a normative and non-binding instrument in international human rights law. It addresses ethical impacts on science medicine and technology primarily on humans but also in a lesser degree on the ethics of environment and animals. The Declaration's purpose is to provide a framework for states to use in the formulation of bioethical legislation and policy. Well-known ethical issues such as informed consent, risk-benefit ration, autonomy, and confidentiality are addressed within the framework. But other principles such as respect for cultural diversity, solidarity, social responsibility and benefit sharing are also included as principles.²⁷⁵ The Declaration addresses issues of medicine, life science, and the associated technologies applied to humans. Additionally, social, legal, and environmental aspects are considered. The Declaration does not claim

to have the capability to address every single ethical issue, rather the aim is to establish a frame of reference for state that guides legislation or policy in bioethics. The Declaration also seeks to promote conversation within societies on the effects of bioethics and the sharing of knowledge of science and technology. The Declaration extends beyond the bioethics principles which have been well-recognized such as the principle of autonomy and individual responsibility, privacy and confidentiality. The Declaration addresses subjects such as access to health care and medicines, proper nutrition and access to clean water, improvement of living conditions, reducing poverty, and the environment. These are topics that go beyond traditional medical ethics and restate the need of bioethics to extend to the political and social world as well.²⁷⁶ The first Article of the Declaration provides the scope.

3.5.2.3 Scope of the Declaration

Article 1 of the Declaration provides the scope. Article 1 states two features of the Declaration: 1. “This Declaration addresses ethical issues related to medicine, life sciences and associated technologies as applied to human beings, taking into account their social, legal, and environmental dimensions. 2. This Declaration is addressed to States. As appropriate and relevant, it also provides guidance to decision or practices of individuals, groups, communities, institutions and corporations, public and private.”²⁷⁷

There are several aims of the Declaration. UNESCO has strived to develop international, normative standards in ethics to guide States to formulate policy or procedure for states in the field of bioethics. In this regard the Declaration is aimed at States. However, it also is relevant to every individual who is concerned regarding

bioethical matters. So, the Declaration also is aimed to help guide individuals, communities, and institutions as well. The Declaration is not a treaty nor is it part of international law. Member States are not legally bound to conform to the Declaration. There are articles which are denoted by the verb “should” that encourage Member States to participate in bioethics education, training, and information sharing, for example. The nature of the Declaration seeks to encourage, be aspirational and educational rather than legally normative. However, it may be assumed that interpretation is analogous to treaties international law.²⁷⁸ Following the scope of the Declaration are the aims.

3.5.2.3 Aims of the Declaration

The aims of the Declaration, which are Article 2, are as follows:

“A. To provide a universal framework of principles and procedures to guide States in the formulation of their legislation, policies or other instruments in the field of bioethics; b. to guide the actions of individuals, groups, communities, institutions and corporations, public and private; c. to promote respect for human dignity and protect human rights by ensuring respect for the life of human beings, and fundamental freedoms, consistent with international human rights laws; d. to recognize the importance of freedom of scientific research and benefits derived from scientific and technological developments, while stressing the need for such research and developments to occur within a framework of ethical principles set out in this Declaration and to respect human dignity, human rights, and fundamental freedoms; e. to foster multi-disciplinary and pluralistic dialogue about bioethical issues between all stakeholders and within society as a whole; f. to promote equitable access to medical, scientific and technological developments as well as the greatest possible flow and rapid sharing of knowledge concerning those developments and the sharing of benefits, with particular attention to the needs of developing countries; g. to safeguard and promote the interests of the present and future generations; h. to underline the importance of biodiversity and its conservation as a common concern of human kind.”²⁷⁹

The Declaration is written in general language and in places ambiguous. The aims of the Declaration are therefore beneficial, as they provide guidance of the purpose of the Declaration. The aims clarify the purpose of States having a universal framework of

ethics for use. The aims offer support to the principles which shall follow and emphasize some features. The aims help to guide in cases where the principles may be unclear in that readers may consider the statement of aims in conjunction with the principle(s).²⁸⁰

The first two articles provide the scope and aims of the Declaration. Articles 3-17 are the core principles of the UNESCO model of ethical assessment. An overview of all of articles will next be examined. However, in the analysis of disease mongering, now all of the articles will be used.

3.5.3 The articles

The UNESCO Declaration uses 15 principles, Articles 3-17, which are arranged from a widening from the moral subjects with the individual (includes human dignity, benefit and harm, and autonomy) followed by other human beings (consent, privacy, equality), human communities (respect for cultural diversity) humankind as a whole (solidarity, social responsibility, sharing of benefits) and finally all living beings and their environment (protecting future generations, protecting the environment, the biosphere and biodiversity). Some principles are well-accepted, such as autonomy and issues surrounding informed consent. Others have been touched upon in prior Declarations, such as sharing of benefits. What makes the principles unique is a balance between the individual and communitarian approach, for example autonomy is recognized as well as solidarity. Social responsibility is an important feature as well. The principles are engrained in rules that govern human dignity, human rights and fundamental freedoms, as well. Articles 18 to 21 express how the principles should be applied: professionalism; honesty, integrity and transparency in the decision making process; setting of ethics

committees, appropriately assessing and managing risk and transnational practice that help avoid exploitation of countries lacking forms of ethical infrastructure.²⁸¹

The UNESCO principles are general and do not provide precise definitions by design. The general nature of the principles are justified because there is a need to have universal norms in bioethics and to respect cultural diversity. The principles are also not solely a product of academic, but also a combination of theory and practicality that may be achieved by the politics of governments. The framework is non-binding; member states are not obligated but encouraged to enact rules. The framework is considered to be soft law, which while it is not law per se, in the long term it is conceived to be. For example a treaty is legally binding, but a soft law are potentially binding. This also is the beginning of a process in which soft law may one day become binding rules. This also allows countries to become more familiar with the framework before they may become law. It is a gradual process and leaves room for discussion, change and reaching consensus on certain issues.²⁸²

In the analysis of disease mongering the following articles will be used: Article 5 on Autonomy and Individual Responsibility, Article 8 on Respect for Human Vulnerability and Personal Integrity, Article 10 on Equality, Justice and Equity, Article 11 on Non-Discrimination and Non-Stigmatization, Article 14 on Social Responsibility and Health, Article 15 on Sharing of Benefits and Article 16 on Protecting Future Generations. The Articles of the Declaration often have overlap, for example informed consent is a document that requires autonomy, consent and autonomy are two distinct Articles. Many of the Articles intertwine in this way. Thus, Articles 3 on Human Rights and Human Dignity, Article 4 on Benefits and Harms, and Article 6 on Informed Consent

are included in detail as they closely connect to the articles used in the analysis. Next, the specific principles will be examined beginning with Article 3.

3.5.4 The Principles

3.5.4.1 Article 3: The principle of respect for human dignity

Article 3 includes human dignity and human rights. Article three states the following, “1. Human dignity, human rights and fundamental freedoms are to be fully respected. 2. The interests and welfare of the individual should have priority over the sole interest of science or society.”²⁸³

Protecting human rights and human dignity has always been the fundamental component of human dignity and human rights, and there are international laws that hold this principle in prominent position. Respect for human dignity forms part of the aims of the Declaration. Likewise, a respect for human dignity is explicit throughout many of the Articles contained in the Declaration such as arguing against discrimination in Article 11, in the framework of respecting cultural diversity in Article 12 and as interpretative criterion of all requirements of the Declaration in Article 28. Human dignity is so critical throughout bioethics because biomedical practices are closely related to basic privilege of every human. This includes a right to life and physical and mental integrity. Human rights are based upon human dignity and therefore rationalized by legal frameworks regarding the control of biomedical activity. Also, respect for human dignity is becoming established as the last obstruction when it comes to some practices, such as reproductive cloning and germline intervention that alter human characteristics. An appeal to human rights is not enough to address these types of issues, as that pertains only to those existing

individuals, not to humanity itself. However, the Declaration appeals to protecting future generations as well and practices that extends beyond only harm to the individual. Under the Declaration would reject such practices under the notion of human dignity.²⁸⁴

Human dignity is a term often used, but it not clearly defined, as is often the case with most moral concepts. Human dignity aims to ensure inherent value to all humans and humanity. Human dignity is a greater term than autonomy alone; because human dignity includes those not yet, such as infants, or no longer such as people with dementia, autonomous. Human dignity aims at the intrinsic value that is equal for all humans; human dignity calls that all human beings deserve respect despite age, health, sex, national origin, political persuasion, or religion. There is an individual notion of human dignity. This is the foundation of all human rights documents where protecting people from harm and promoting self-determination forms the foundation. More recently, a category that is more collective and goes beyond the individual is developing that refers to humanity as a whole. This notion includes future generations. The rationale is that all humans have inherent value and belong to a group (humanity) as a whole, therefore this larger group possess value. This can be applied to technological advances that may affect the integrity of humankind and aims to protect the integrity of what it is to be human. The two views should be seen as complementary, not as competing interests. In its application, the concept of human dignity alone cannot be used to solve every problem but it requires concrete concepts such as informed consent or non-discrimination, which are normally built into the term “rights”. Therefore, the Declaration includes the addition of human rights and fundamental liberties in reference to human dignity, as the Declaration acts as an extension of international human rights laws in the area of

biomedicine. The Declaration seeks to unite two areas of bioethical norms. The first is from Hippocrates, and rose from contemplations of the field of medicine and the other drawn from developing human rights laws; the Declaration seeks to bring these two notions together. Using a human right's framework aids in developing universal standards because human rights laws are based on assumptions that basic rights exist that exceed cultural diversity. Additionally, a human rights framework has a rich history and many international instruments exist to ensure human beings are unconditionally respected. In bioethics, it is a logical choice to draw from this context.²⁸⁵ Next, is Article 4 on benefit and harm.

3.5.4.2 Article 4: Benefit and Harm

Articles 4 states, "In applying and advancing scientific knowledge, medical practice and associated technologies, direct and indirect benefits to patients, research participants and other affected individuals should be maximized and any possible harm to such individuals should be minimized."²⁸⁶ The Declaration is an extension of the 1948 Universal Declaration of Human Rights and is extended into the field of bioethics. Human dignity is the core of both documents as well as the footing of moral and legal obligations that ensue. Article 4 applies the ethical principle of beneficence and non-maleficence. Human dignity is treated as a fundamental property of being a human being, therefore independent of qualities that one may view as undignified, such as appearance or behavior. These are external estimates of worth assigned to humans by other humans, but these assessments of dignity are more of an assessment of social acceptance which occurs in human relationships. This has no bearing on dignity which is the worth of a

human being in the capacity of being a human being, even if one appears to be an undignified person. Every human is equal because they are a human. Inherent dignity therefore generates the moral obligation to do good and to not do harm to other humans. This obligation is achieved based upon the principles of beneficence and non-maleficence. At the lowest level, beneficence requires to do no harm (non-maleficence), a step above this is to remove harm, at the next level would be to prevent harm or evil and lastly at its highest level is the promotion of goodness. While beneficence is not limited to the medical practice, it is the area where it is most applicable through the Declaration. In that regard, the level of a patient (or research study participant's) vulnerability, the risk, and the associated need of the patient must all be factored into consideration. The role of a physician or study investigator requires the higher levels of beneficence. Beneficence has always been the first moral principle of ethics, putting the care of the patient above all.²⁸⁷

Article 4 also includes that all humans should be free from intentional harm. Unintended harm, however, is possible in medicine and in research. Without risk associated with new treatments there could be no medical advances. The moral authorization for tolerating such risk is that there is benefit following treatment; illness or disease may be prevented or improved upon. Harm is acceptable only if maximizing the benefit and minimizing the harm is obligatory. It is necessary for those who work in healthcare to assure that the harms are minimized while the benefits are maximized for those who are exposed to such risk. In the case of research, the role of the physician-investigator requires a patient's vulnerability stemming from eagerness to benefit from an experimental treatment, is not put at risk. There are means in place to weight the risk and

benefits. Benefits to be weighed include the advancement of the interest of patients or society, generating new information which may benefit future generations, or developing policy that helps the common good. The risks which must be factored include the probability or possibility of harming an individual or society. The evaluation of risk is normally done qualitatively and are informal value judgments made by patients, participants, and health professional. Quantifying harms in measures or assessments is not as common and has somewhat limited success. It is important to note that the Declaration gives precedence to the individual over social good.²⁸⁸

Implementing beneficence in a clinical setting puts at odds autonomy and beneficence. To apply clinically requires the physician to accurately assess the patient's condition and thoroughly conveying this information to the patient so that it is understood. A patient may refuse treatments due to individual autonomy, and a physician may refuse to administer treatment requests that violate the professional or moral integrity of the physician as well, and arrange for another provider of care. The human dignity of patients and physicians being upheld is the ethical challenge of Article 4 as it is unavoidable that the personal character of those parties involved will have a role how the Article is interpreted. In a research setting, implementations are simpler due to the tight regulation on human subject research. On the other hand, with physicians as investigators, there can be greater challenges when therapeutic misconception may become a factor. Caring for patients must take precedence over the physician's role as a scientist and the good of the experiment at all times. In sum, Article 4 serves to protect human dignity and rights and implementing this Article relies on maximizing benefits and minimizing harms and putting the welfare of the individual about the interests of

science or society.²⁸⁹ Article 5 is the principle on autonomy and individual responsibility which next follows.

3.5.4.3 Article 5: Autonomy and individual responsibility

Article 5 states, “the autonomy of persons to make decisions, while taking responsibility for those decisions and respecting the autonomy of others, is to be respected For persons who are not capable of exercising autonomy, special measures are to be taken to protect their rights and interests.”²⁹⁰

Autonomy is defined as the state of being self-governed, therefore to be autonomous means that individuals may live their own lives their own ways.²⁹¹ In American culture individual choice has always been highly regarded as a reflection of the American ethos.²⁹² Autonomy is often regarded as the most predominant ethical principle.²⁹³ Autonomy traces its roots from philosophers Immanuel Kant and John Stuart Mill. Kant’s notion of autonomy expresses respect for the person so that they are an end, not merely a means. Mill’s belief of autonomy focuses on liberty. Mill’s perception is that a person’s choice should not be obstructed unless these choices are impeding the liberty of others. One should be protected by the imposition of another, according to Mill.²⁹⁴ Moral philosophers define autonomy as the moral right to choose and for people to follow their own actions and plans for life.²⁹⁵ There are several theories of autonomy. However, each tends to embody these two conditions, liberty which is independence from control and secondly, agency which is the aptitude for intentional action.²⁹⁶

The concept of autonomy can be viewed with the concepts of rational and irrational choice. At times autonomous choice may be questioned, for example with a

person who was under the influence of medication or was delirious. Patients may have stated throughout their lives that should they ever become ill with a form of terminal cancer they do not wish to receive any treatment. Then these patients develop cancer and this causes a great amount of anxiety, stress and they are also receiving medication. Now these patients state they wish to have treatments that could prolong their lives. This is a sudden change from previous beliefs, the influence of stress and medication which could affect decision making abilities has a role. These considerations could cause a healthcare professional to question whether this new outlook on continuing with treatment was an autonomous choice. However, wanting to continue to receive life sustaining treatment is a rational decision and this should not be overridden.²⁹⁷

Autonomy is likely the principle that is most prominent of ethical values. Autonomy stems from reaction to abuses in clinical research and the notion of human rights which emerged during the latter part of the twentieth century. Informed consent provides the most concrete example of autonomy in medicine and in medical research. In the healthcare setting, models of care are no patient centered versus paternalistic. The patient works with the physician to determine treatment goals rather than being merely the receiver of care as determined by the physician. Patients are able to refuse treatments that could be viewed as beneficial by a physician if a patient so desires. The right to refuse treatment is protected by a patient's autonomy. The cases is similar in research. People who take part in a research study are no longer referred to as subjects because this language is suggestive that research methods are being done to them, but rather the term participant is used to suggest the collaborative role with study investigators. Again, informed consent is at the heart of research protocols and is often rooted in law. Consent

in research came about from past cases of abuse that was conducted in human subjects' research where autonomy was disregarded completely. The Tuskegee Study is an example and initiated the development of Institutional Review Boards.²⁹⁸

The Tuskegee syphilis study is one of the most famous historical examples of unethical medical research which took place in the United States. Between the years 1932-1972 a vulnerable population of 399 poor, African American men with syphilis was enrolled in this study. The aim of the study was to examine the natural progression of the disease if it was left untreated. They were given free meals, medical exams, and burial insurance for their participation. Once the treatment of syphilis was discovered in 1947, it became an unethical treatment study as participants were not offered penicillin, which would have cured their disease. Scientists chose to continue this study despite telling the participants more about the illness or providing participants with the option for penicillin. For these nondisclosures, many of the men and their wives died of syphilis. This was an unjustified offer to participate in the study. Beauchamp and Childress note how the subjects' poverty left them vulnerable to an unjustified form of manipulation.²⁹⁹

Another example of disregard for patient autonomy occurred in New Zealand. In 1988, it was discovered that women were entered into a long-term study that tracked changes in their cervical cell. It is referred to as the Carcinoma-in-situ scandal. Each year women were monitored and these changes were recorded however treatment was never offered even though standard of care at the time would be determined the condition to be a precursor to cancer. Many women would go on to develop and die from invasive cancer. Because of the scandal, independent ethics review committees were set up to review human subjects' medical research proposals.³⁰⁰

To be better understood, the notion of autonomy is discussed in four parts. The limits to which autonomy is subject is the first. Exercising autonomy is subject to rare limits which are usually dictated by law. In rare cases as such, restrictions are done to protect the autonomy of others. For example, people can be arrested, detained and questioned, the mentally ill can be forced to be evaluated if they pose a threat to themselves or others, and those suffering from serious, communicable disease which threatens others can also be quarantined to protect the health of others. The conditions which autonomy can be exercised is also examined. To freely be able to make decisions one must possess the ability to do so. Those who are not are deemed to be incompetent. There have historically been some groups labeled as incompetent. These include those with learning difficulties, people with mental illness, children, people who are in shock, elderly who are confused, and people who are unconscious. There are criteria that are used to determine being incompetent: being able to understand the issues that surround the matter; being able to rationally evaluate these issues; a reasonable outcome of the decision, and lastly evidence that a decision has been made. These appear to be objective criteria however much lies in the perspective of the person who judges the behaviors in what rational choices and decisions should look like. It is important to not place too high of a standard upon the decision maker so that their autonomy is undermined because it is not the same choice the person determining their competence would make. A rule of thumb that is applied is that judgments of competence should not be questioned unless there is evidence undermining the assumed competence of decision makers. It is also critical that consent be truly be informed. Inadequate information prevents this from happening. Thus, informed consent requires adequate information be available and that

the information be understandable in order to preserve autonomy. Respecting the autonomy of individuals when it is compromised by their condition is another notion to discuss. Children, for example, would appear to be, by their nature, not able to be considered competent compared to adults because they cannot think like adults. However, assigning a certain age to determine competence has risk. The United Nations Convention on the Rights of the Child states children should have a say in decisions made by adults when it affects them, children should be able to receive and share information, be able to think and hold their own beliefs, and practice their own religion so long as it does not prevent others from enjoying their rights. This is based upon them possessing certain levels of competence. Children getting older and progression of maturity should be used to determine when children are fully competent and capable to making autonomous decisions. This will vary from child to child, however it is not respectful to their rights to set higher standards of rationality and understanding for children. Those with learning difficulties should not be rendered incompetent by definition either.³⁰¹

Competency has a variety of definitions depending on which context it is being examined. In health care, competent judgments distinguish the autonomous choices of individuals whose wishes should be upheld versus those who may need their decisions checked or possibly even overruled.³⁰² While competency relates more to the legal status of a patient's ability, it is closely related to medical incapacity in practice. The legal system determines competency and patients deemed incompetent may be appointed a surrogate decision maker to act of their behalf.³⁰³ It is the right of mentally competent patients to either consent to or refuse treatment.³⁰⁴ In order to make competent decisions,

patients must understand information regarding their care, calculate the risks and benefits and make an informed choice considering all areas. If one is able to carry out this process the person is deemed to be competent.³⁰⁵

People with intellectual disability or mental illness may not be able to make every decision, but they can make some, depending on how complex and serious the decision may be. For people with mental illness, some illness may wax and wane thus there are some times decision making is better than others. For the mentally ill, confused, or unconscious individuals examining their past decisions and meetings with friends and family can also help to guide decision making on their behalf should they be incompetent. This is substituted judgment, and is put into effect to honor their autonomy.³⁰⁶ The substituted judgment standard has its foundation rooted in the thought that the patients are the only one who can properly make their own treatment decisions by virtue of their autonomy. However, patients are incompetent and are unable to make their own decisions. It is viewed as unjust that people lose their decision making rights because they are no longer competent. The substituted judgment standard requires that the surrogate's desires for the patient are not a part of the decision making process. Rather, surrogates should only consider what the patients would have wanted.³⁰⁷

Lastly, is the relation between communal autonomy and individual autonomy. It creates difficulty in certain settings where communal autonomy may prevail over that of the individual, which is highlighted in the Article. Which should be preferred depends on the type of decision that needs to be made. Individuals should not profit from communal treasures for example or give privileged information to strangers with consent of the group. However, this is not to be used as basis that communal autonomy can override

individual autonomy. For example, a research group wishes to obtain tissues samples from members of a group for analysis and is permitted. Yet, no individual member of the group can be forced to giving their tissue for analysis. This individual refusal would also not prevent the communal decision for the study to take place.³⁰⁸ The expression of autonomy is done through informed consent, which is the following article.

3.5.4.4 Article 6: Consent

Article 6 of the Declaration is Consent:

“1. Any preventative, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information. The consent should, where appropriate, be express and may be withdrawn by the person concerned at any time and for any reason without disadvantage or prejudice. 2. Scientific research should only be carried out with the prior, free, express and informed consent of the person concerned. The information should be adequate, provided in a comprehensible form and should include the modalities for withdrawal of consent. Consent may be withdrawn by the person concerned at any time and for any reason without any disadvantage or prejudice. Exceptions to this principle should be made only in accordance with ethical and legal standards adopted by the States, consist with the principles and provisions set out in this Declaration, in particular Article 27, and international human rights law. 3. In appropriate cases of research carried out on a group of persons of a community, additional agreement of the legal representatives of the group or community concerned may be sought. In no case should a collective community agreement or the consent of a community leader or other authority substitute for an individual’s informed consent.”³⁰⁹

Informed consent essentially states that medical interventions or participation in research studies should only be carried out by people who freely give their consent beforehand based on sufficient information. Those who give consent are also free to revoke it at any time for any reason, with no repercussion. Since medical procedures or scientific intervention can pose a risk to patients or participants there must be protection in place in the form of informed consent. Nearly all legal and ethical medical or scientific

agreements worldwide require informed consent which speaks to the value of this document.³¹⁰

The goals of informed consent are protecting patients and supporting autonomy.³¹¹ The preferences of patients (or research study participants) are exemplified in the process of informed consent; informed consent represents the dialog between patient and physician which leads to an agreement regarding their medical care.³¹² Informed consent can be thought of in two perspectives. The first is a patient authorizing a procedure and the second sense of consent is that forms are valid because they have been subject to rules and requirements from the health care setting where a patient is being treated.³¹³ There are conditions of informed consent. These are that a person is competent to act, is given a thorough disclosure about the medical procedure, understands this disclosed information, acts voluntarily and then consents.³¹⁴ Informed consent is the willing acceptance of a procedure by a patient after discussing risks, benefits, alternatives and the nature of interventions with the physician.³¹⁵ The first of the component of informed consent to be explored is competency.

Competency has a variety of definitions depending on which context it is being examined. In health care, competent judgments distinguish the autonomous choices of individuals whose wishes should be upheld versus those who may need their decisions checked or possibly even overruled.³¹⁶ While competency relates more to the legal status of a patient's ability, it is closely related to medical incapacity in practice.³¹⁷ It is the right of mentally competent patients to either consent to or refuse treatment.³¹⁸ It is also understood that competency plays a vital and necessary role in the consent process. What is vague is the precise meaning of competency as it varies depending on the

circumstances it is being used. In medicine if persons are competent to make medical decisions and have not been coerced then their ability to provide informed consent is valid.³¹⁹ The concept of being competent is also closely associated with concept of autonomy. Patients are competent to make a decision regarding their care if they understand the information as it is presented to them and make a judgment or inform a caregiver of their wishes. In order to make competent patients must understand information regarding their care, calculated the risks and benefits and make an informed choice considering all areas. If one is able to carry out this process the person is deemed to be competent.³²⁰ To be competent, one should be free from factors which may diminish competency.³²¹ To be a competent decision maker, one should not be influenced by drugs, mental confusion, disability, injury or depression. Only then can decisions be made with relevant information without the influence of coercion.³²² Competency also includes a patient being free from openly coercive influence, an understanding in lay terms diagnosis and prognosis and risks and benefits of procedures, as well as alternatives.³²³

The duty of disclosure is satisfied by giving information to the patient. However, disclosure is closely tied to understanding. While a physician must disclose the information to the patient, the patient's understanding is a key element to proper informed consent. If a patient cannot fully understand the facts, regardless of disclosure, it may not be considered proper informed consent.³²⁴ One way to ensure that information is disclosed properly is to ask what a reasonable physician would tell a patient. This was the legal standard in many early informed consent cases which is being replaced by what information reasonable patients need in order to make treatment decisions. Proper

disclosure should include patient's current medical status, interventions which could improve prognosis (along with risk and benefits), a professional opinion, and a clinical recommendation. When this information is conveyed, physicians should avoid using technical terms and try to use every day language.³²⁵ Disclosure has its roots in the legal system, risk for example is often cited in much litigation.³²⁶ Litigation may focus on what a physician has not told a patient, however, in an ethical context disclosure is more focused on patient autonomy.³²⁷

Patients often are told things which they do not understand in conversations with their doctors; while the law may refer more to disclosure rather than understanding of information, it may be a physician's associated duty to aid in patient's understanding.³²⁸ Understanding is an essential part of the process of informed consent. The ability to consent to treatment or refuse treatment requires one to understand the information.³²⁹ It is critical for patients to understand associated risks.³³⁰ Consent emphasizes the giving of information. The amount and type of information provided is often cited in a legal context, however, comprehension by the patient is equally as important as disclosing information. A physician is ethically obligated to put forth reasonable efforts to assure understanding of information to patients.³³¹ An informed decision would be justifiable if it encompasses the ideals of the concept of understanding.

A patient's decision is not legally valid if it has not been given voluntarily.³³² Voluntariness as being free from controlling outside choices in making a decision. There are a variety of forms of influence. Three categories include: coercion, persuasion, and manipulation. Coercion entails the use of harm or force over another person and intends for a threat. Coercion also nullifies autonomy because it supersedes a person's intended

course of action. Persuasion occurs when patients come to accept the beliefs which were induced by another. Manipulation is less precise in that the one who is manipulating uses means other than persuasion or coercion to influence another. In healthcare, this is usually in regards to the way information is presented and how it could then have an effect on the patient.³³³ In legal perspectives, voluntariness focuses of pressures levied by others, pressure by an authority figure is a concern.³³⁴ One might view a physician in this role. Paternalism in healthcare holds the view that the highly trained, intelligent medical professional is in an authoritative role and has the ability to know what is right for the patient. Paternalism may be thought of in terms such as being controlling or in charge, as if the physician knows what is best for the patient. Paternalism, however, does not need to be viewed negatively. Paternalistic actions in conjunction with surrogacy can work towards a common goal: The best interest of the patient. When patients are ill they may lack the capacity to make sound judgments. In such a case, paternalism can help guide a surrogate into making an ethical choice in the best interest standard if the patients' wishes in regards to treatment options are unknown. The guidance of medical staff is valuable in such a case.³³⁵

The meaning of the Article in the Declaration should be weighed and interpreted in relation to other principles and provisions. Within the Declaration, distinctions can be made between three kinds of principles. First, principles related directly to human dignity; second, principles concerning the relationships between human beings; and third, principles that preside the relationships between humans and other life forms and the biosphere. Consent expresses autonomy and self-determination, simultaneously by being involved in the decision making process and committing to an act, it is a process that the

person expresses and practices autonomy. Thus, this Article is directly related to Article 3 on Human Dignity and Human Rights and on Article 5 on Autonomy and Individual Responsibility. None of these Articles stand by themselves but are all interconnected. Consent expresses the interests of an individual but the needs or interests of others may be impacted by this decision, which should be considered, too. This creates a connection between linking informed consent to social responsibility. While the individual is first and foremost, family, social groups, and humankind also have moral obligations.³³⁶

In medical practice, consent may be viewed less critically than in research because in medicine a patient often needs help and doesn't have much choice in the matter for interventions. Research is different as many kinds of studies exist which can involve direct risk to a patient such as clinical trial research or no physical risk, such as epidemiological research. Addressing these different areas with informed consent can be challenging. In some provisions of public health research or health policy, informed consent may have no worth, for example. Cultural context is important in consent too. Western values are rooted in individualism whereas other cultures express consent socially rather than individually. This is appreciated in the Declaration but also no agreements of group consent will override that of the individual's informed consent. In sum, the interest of society will never trump the interest of the patient.³³⁷

There is one principle that cannot be used to override other principles, which is the respect for cultural diversity, Article 12. This is relevant in the case of informed consent and should be noted. This means that it cannot be used as justification for a practice that is violating human dignity. In some African countries a communitarian approach is important in making decisions and a group may discuss the issue and a

community leader leads in decision making. Likewise, in many Arab countries it is the head of household who makes decisions, such as a husband rather than a wife who makes important decisions. However, on the issue of informed consent, which requires that is the individual at-hand who makes the ultimate decision regardless of the cultural context, the Declaration states that nobody may violate the principle of informed consent on the basis of a respect for cultural diversity. However, local values and norms do play a role. In the US for example, a consent form typically is a document requiring signature of concerned party. But in other countries, one's word is enough and asking for a signature creates a distrust.³³⁸

3.5.4.5 Article 8: Respect for Human Vulnerability and Personal Integrity

Article 8 states, “In applying and advancing scientific knowledge, medical proactive and associated technologies, human vulnerability should be taken into account. Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected.”³³⁹

Vulnerability, as often used today, means prone to being wounded. Individuals and groups can be considered vulnerable. Vulnerability arose from the realm of human experimentation, where certain populations were mistreated. Groups that were not protected such as prisoners, orphans, and later Jews were exploited by the Nazis. Later other groups, such as ethics minorities, women, and socially underprivileged groups were considered to be vulnerable, with implications these groups should be protected from harm. This view is justified by the principle of autonomy in that by its reinforcement by means such as informed consent provides empowerment. The notion of integrity is

suggestive of “keeping intact”; integrity is a right on non-interference from others in the sphere of the self. The Article sums, that human vulnerability is inherent in all humans, an awareness of this must be considered. Secondly, priority is given to groups labeled as vulnerable protection from harm and respect for this integrity is necessary, so that these groups are not reduced to parts or abstractly viewed.³⁴⁰

The principle of vulnerability is perhaps one of the most disputed principles and receives much scrutiny. Vulnerability is included throughout policy and guidelines in medical research, healthcare, and in bioethics. One leaning of the concept of vulnerability includes restrictive categorizing of individuals, groups, or populations that are deemed to be vulnerable and that vulnerability needs to be overcome. Whereas a human-rights based approach takes the stance that vulnerable or those susceptible receive protection be given an extra layer of protection.³⁴¹

Vulnerability may include a reduced ability to protect one’s own interests.³⁴² Vulnerable people are susceptible of having their dignity, autonomy or integrity at risk. There are a wide variety of elements that may make a person vulnerable. Vulnerability often refers to potential vulnerable populations such as prisoners, children or pregnant woman as examples.³⁴³ However, this is not an exhaustive list of potentially vulnerable populations. The Council of International Organization of Medical Sciences (CIOMS) defines the vulnerable as those who may not be able or who are incapable of protecting their own interests. The group also goes on to expand upon their list of vulnerable populations. The list includes those people with diseases; people who are politically powerless, and those who are not familiar with modern medical notions.³⁴⁴ While these are more equity based concepts of vulnerability, the International Conference on

Harmonization's (ICH) Guidelines for Good Clinical Practice include different reasoning. The ICH's reasons for vulnerability are more concerned with whether the participants' agreement to participate was truly a voluntary choice. The ICH cites that a participant may be wrongly influenced to participate in a clinical trial for example, whether it is justified or not, because of the benefits associated with participation.³⁴⁵ In human subjects' research the concept of vulnerability is somewhat restrictive pertaining mostly to those who are unable to give informed consent or those who are likely to be exploited.³⁴⁶ However, in international clinical trials research, two main ethical concerns are the ones which are predominantly cited throughout the literature. These two concerns are a reduced ability to protect one's own interest and compromised ability to give proper informed consent.³⁴⁷

Research participants may be vulnerable because they are not familiar with scientific concepts or they may be poor or powerless which leaves them open to forms of exploitation. People in developing countries, for example, may not have access to healthcare and are very eager to try a treatment without fully understanding the associated risks of experimental procedures thus becoming an informed consent issue.³⁴⁸ This notion of vulnerability being related to an improper understanding of informed consent and exposing research study participants to forms of exploitation and is also the stance of National Bioethics Advisory Committee. The NABC suggests there are six different types of vulnerability-inducing circumstances. These six elements have a common theme of two basic concerns which deal with informed consent and exploitation, too. The NBAC notes difficulties in informed consent are derived from participants who have limitations or difficulties making decisions or because of their situational

circumstances. Secondly, those who are very sick are open to exploitation because of the medical benefits, the poor may be desperate for the payments or access to free healthcare. All of these conditions leave the participants vulnerable to a variety of forms of exploitation.³⁴⁹ Those who do not fully understand the informed consent process, for example children or those who are mentally ill, may be considered vulnerable.³⁵⁰

Beauchamp and Childress also provide an explanation of vulnerability and exploitation of participants in human subject research. The authors focus is specifically on those who are economically disadvantaged who are recruited and enrolled in clinical research. The studies are predominantly pharmaceutical trials. The authors define economically disadvantaged persons as those who lack health care, may be homeless, malnourished but still have the mental faculties to participate in a research trial.

Beauchamp and Childress note that between 50 to 100 percent of all healthy research subject participants motivation for being a part of an experiment was solely for financial need or reward. This sampling of participants was only in North America, the authors state that the scope of the poor in developing countries is largely unknown.³⁵¹

Ruth Macklin takes a quote from The Declaration of Helsinki (October, 2000) and notes the following as it pertains to research participants:

Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves and for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.³⁵²

While this overview provides important information and expressing concern for some research populations it is important not to label all people from one group as being vulnerable. By labeling entire groups there is a risk of stereotyping, overly protecting or

disqualifying some members of the group from soundly participating in research. By using the notion, “vulnerable population” it is suggesting that everyone who belongs to a group is labeled as vulnerable whereas it may be better to consider the circumstances which would allow for certain people within that group to have greater risk to exposure of vulnerabilities.³⁵³ To include all people of a specific group (i.e., all uneducated or all people who are poor) fails to embrace the idea that a vulnerable group consists of individuals. While members of such populations considered vulnerable may in fact be vulnerable, the poor for example, not every single poor person may have specific qualities that render them vulnerable. For example one may have difficulties that diminish his or her ability to make a decision, others may misunderstand the research, and some may be coerced.³⁵⁴

Article 8 of the Declaration seeks to address both viewpoints and offer two moral routines of protection. The human-rights based regime is directed toward persistent or universal vulnerability. The second is aimed toward accidental states and instance of fallen vulnerability, which is a type of vulnerability requiring additional means of protection and identification of those populations in need of protection who are not covered by the human-rights regime.³⁵⁵

Article 8 is applied in human subject research, clinical medicine, and health policies. It is recognized in research that despite obtaining informed consent, individuals are still susceptible to being vulnerable through subtle acts such as coercion to participate with offers of free health care or compensation. Also, vulnerability exists when medical success is exaggerated by the media. Patients and society are presented unrealistic expectations that medicine is the solution to all human problems and other solutions are

ignored. In clinical care, vulnerability serves to reinforce patient rights, it appeals to providers of care to have balanced relationships with patients, and institutions to protect patients. In the area of health policy, at all levels, vulnerability requires that the benefits of some should not come by means of exploiting others, also that the greater well-being of some will make those who did not benefit more vulnerable. This principle requires acknowledgment that a human body is a subject, not an object that is separate from the individual it encompasses. In research, a need to not only protect the safety and health of the actual body of the participant, but to also uphold an individual's personal integrity. The relationship between physicians and patients calls for doctors to focus on the patient and not just the illness and to view the relationship along the lines of a partnership at treatment of illness. In policy, the principle plays a role of not permitting the human body to become commercialized.³⁵⁶ Article 10 next examines equality, justice, and equity.

3.5.4.6 Article 10: Equality, Justice, and Equity

Article 10 states, “the fundamental equality of all human beings in dignity and rights is to be respected so that they are treated fairly and justly.”³⁵⁷ Justice is virtue that also been historically understood as being practice; claims based on justice have rights, and therefore something is due. Justice is a complicated term with different meanings. Aristotle's notion of justice is still relevant today, known as general justice, provides the framework of normative ethics; that is each person is given when it due. This is a formal concept of justice in that what is “due” is not defined. Also, it does not identify terms in which equals ought to be treated equally nor is there criteria for determining whether two individuals are equals. Other concepts of justice include material concepts, which are

more specific. Corrective or communicative justice is described by Aristotle as a form of justice that requires wrongdoers to pay damages to victims accordingly by injuries that were caused. Aristotle described distributed justice as dividing fees or wealth for example, among a population. With corrective justice, victims of wrongdoing are equally compensated, on the other hand, distributive justice calls for a distribution proportional to one's merit. In the modern era, Aristotle's notion of distributive justice changed. Distributive justice in Aristotle's time rewarded worthy people for their merits, now this form of justice must allocate needs regardless of one's merits. Basic needs should be given to all, not as charity but as a justice based right. When scarcity becomes an issue, distributive justice becomes more important. To justify distribution in such a case many forms exist such as liberal, socialist, or utilitarian, but not one is agreed upon universally.³⁵⁸

Rawls' view of justice is from an egalitarian viewpoint. He theorizes that we all begin in the original position as free, rational and equal people. Everyone would be shielded behind what he calls "a veil of ignorance" where we are all blind to race, gender, sex, disability, social status and other such instance which could lead to discrimination. From this perspective, everyone is equal because we do and would not know what social status we would be a part of. A self-interested and rational person would not likely want to be in a disadvantaged group. Thus it would be a fair and equal foundation to all. We may then select principles of justice which would also be fair from this mindset.³⁵⁹

These two principles maintain: Each person is to have an equal right to the most extensive basic liberty compatible with a similar liberty for others (i.e., the right to vote.) This would provide equal liberty to all. The second principle states that social and

economic inequalities are arranged so that they both a. reasonably work to everyone's advantage b. are attached to positions open to all. Therefore, a rational person may have more power or be more advantaged (or another good which could lead to an inequality) if this inequality results in bettering (or maximizing) the outcome for those who are the worse off or least advantaged (the minimum). Lastly, public positions are open and available to all. Rawls states that these principles "govern the assignment of rights and duties and regulate the distribution of social and economic advantages" as applied to the basic structure of society. The result would be a just and fair society.³⁶⁰

Rawl's theory of justice is one of the most valuable calling for each person to have equal rights to the biggest system of basic, equal liberties well-matched with a similar system of liberty for all. All social values should be distributed equality, these include liberties, opportunities, wealth, social bases, and self-respect. Unequal distributions are acceptable when they benefit all members of society or to those most in need. Equity may be more important than justice, which Rawls considers a fundamental requirement of justice, where all members of society define and accept rules, benefits, and charge. Differences must benefit all members of society. Equality is a more recent principle, but in combination with justice and equity is critical. All humans are different in their physical, mental, genetic, or psychological values or principles. However, in terms of justice, rights, opportunity, freedoms, benefits, opportunity, and dignity all humans are considered equals. Article 10 states requires to obtain justice and equity, all humans are treated equally in their dignity and rights.³⁶¹

As technologies have advanced and more resources are available, the ethical problems which accompany them have been on the increase at greater rates than

technology. The technical advances that help to improve upon life, and create new ethical dilemmas. The Declaration is designed to address such issues that arise with technological advances. All human beings must have their dignity, rights, and freedoms maintained when applying new technologies. The direct and indirect benefits of technology must be clearly and scientifically disclosed so that potential harm is reduced. Autonomy, vulnerability, personal integrity, privacy, and confidentiality must be respected. Discrimination must be avoided, and cultural diversity respected. Thus, in order to uphold Article 10 and meet the criteria for equality, equity, and justice, the principles on human dignity and rights, autonomy, beneficence, non-maleficence, integrity, confidentiality, and privacy must first be obtained. The framework acknowledges it cannot solve all ethical problems. There is still work to be done in order to fill the gap between principles and the actual way of dealing with new matters that arise. However, it provides a means of facilitating discussion for important topics.³⁶² Next, Article 11 is examined.

3.5.4.7 Article 11: Non-Discrimination and Non-Stigmatization

Article 11 states, “no individual or group should be discriminated against or stigmatized on any grounds, in violation of human dignity, human rights and fundamental freedoms”.³⁶³ The article was developed to address discrimination and stigmatization, which are violations of human dignity, human rights, and fundamental freedoms. The needs to address these topics were identified in the earliest stages of the Declaration. Article 11 works in conjunction with other articles in the Declaration; all principles are interrelated and complementary and the Declaration is best understood as a whole.

Reading Article 11 alone is a broad statement, but when combined with Article 1 it is important to recall a focus on the ethical issues related to medicine, science, and other technologies as applied to humans as it related to discrimination and stigmatization.³⁶⁴

Discrimination is the first of the two distinct topics covered in Article 11.

Discrimination is a legal term that is well-known in human rights and State law adhering to international human rights law. Article 2 addresses that all humans are born free and equal in dignity and human rights. Article 7 addresses discrimination specifically in that all are equal in the law and entitled to equal protection against discrimination.

Conventions have addressed racial and gender discrimination. The Convention on the Elimination of All Forms of Racial Discrimination commits State Parties to not take part in racial discrimination. This is through not supporting persons or organizations who take part in racial discrimination and to take proactive measures that promote ending racial discrimination. Likewise, for gender, The Convention on the Elimination of All Forms of Discrimination Against Women, takes a similar stance to State obligations. The Convention defines discrimination against women in part as any distinction, exclusion, or restriction made on the basis of sex.³⁶⁵

Article 11 makes no attempt, and there is no need, to duplicate the entirety of international law as it pertains to discrimination; the prohibition against discrimination references this large body of law. The Declaration does not seek to create new human rights or new grounds for discrimination as it is a non-binding document and not a convention. With reference to human rights and discrimination especially, the Declaration seeks to apply this body of law to ethical issues that occur within the context of medicine, science, and such technologies.³⁶⁶

Stigmatization has no foundation in international human rights law, but it appears in the International Declaration on Human Genetic Data. Stigmatization is referenced in regard to human genetic data so that the genetic materials are not used for purposes that lead to individuals, families, or groups or communities being stigmatized. The Declaration holds a stance that stigmatization refers to communication or conduct that characterizes a group or person negatively in the context of medicine, science, and associated technologies and that infringes upon their human dignity, rights, or fundamental freedoms. Stigmatization is the negative labeling of a person or group, however this is done in such a limited or indirect way that it in no way violates the law.³⁶⁷

The possibility of the sciences to contribute intentionally or unintentionally to discrimination or stigmatization of people or groups was an early consideration in the Declaration. The Declaration being rooted in established international human rights laws gives hardy meaning to this simple but fundamental article.³⁶⁸ Next is Article 14 on Social Responsibility and Health.

3.5.4.8 Article 14 on Social Responsibility and Health

Article 14 is on social responsibility and health, it reads:

“1. The promotion of health and social development for their people is a central purpose of governments that all sectors of society share. 2. Taking into account that the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition, progress in science and technology should advance: a. access to quality health care and essential medicines, especially for the health of women and children, because health is essential to life itself and must be considered to be a social and human good; b. access to adequate nutrition and water; c. improvement of living conditions and the environment; d. elimination of the marginalization and exclusion of persons on the basis of any grounds; e. reduction of poverty and illiteracy.”³⁶⁹

The promotion of social responsibility for health was established by the WHO Fourth International Conference on Health Promotion in 1997. The conference promoted the idea that decision makers have a commitment to social responsibility and health should be promoted by policies and practice that: avoid harming individuals health, use sustainable resources and protect the environment, discourage the production and trade of harmful goods such as tobacco, ensure safety of citizens in the market and work place, and use equity-focused health impacts assessment in policy. At the WHO's fifth conference on global health promotion the themes of what constituted social responsibility, its measurement, gender and equity, cultural diversity, and cases studies developed. In Article 14, the divide between developed and lesser developed countries and health is addressed. Technology advancements increase but lesser developed countries continue to fail to see the benefits of this progress. The access to health care and medication is considered as well as social and economic policies, and the benefits that investing in health are considered.³⁷⁰ Next is Article 15 on the sharing of benefits.

3.5.4.9 Article 15: Sharing of Benefits

Sharing of benefits, Article 15, states:

“1. Benefits resulting from any scientific research and its application should be shared with society as a whole and within the international community in particular with developing countries. In giving effect to this principle, benefits may take any of the following forms: a. special and sustainable assistance to, and acknowledgment of, the persons and groups that have taken part in the research; b. access to quality health care; c. provision of new diagnostic therapeutic modalities or products stemming from research; d. support for health services; e. access to scientific and technological knowledge; f. capacity-building facilities for research purposes, and g. other forms of benefit consistent with the principles set out in this Declaration. 2. Benefits should not constitute improper inducements to participate in research.”³⁷¹

The focus of Article 15 is on the benefits of scientific research. In the development of the Article, the awareness that priorities are given to individuals in wealthy countries and families and larger groups in developing countries was realized. When the principles are applied in practice some areas such as mother and child care, health care facilities, and research will have valuable significance. The impact on health care facilities is important as it addresses the pharmaceutical industry. For example, drug patents have very high costs and these drugs take 10 to 12 years to be on the market. The high costs of these drugs make it impossible for those in low-income countries to obtain the medications. Patent laws and the World Trade Organization make the process of low-income countries developing their own medications difficult if not impossible. Slight progress occurred with the production of generics and licensing but not enough. Few, less than 10 percent, of patients with HIV or AIDS in several African countries receive protease inhibitor drugs which is an indication of work that lies ahead. Article 15 seeks in part to protect those who participate in research studies, stating that participants should share in the benefits that may arise from their participation.³⁷² The last article to be included in the analysis of disease mongering is Article 16 on protecting future generations.

3.5.4.10 Article 16: Protecting Future Generations

The final article used in the analysis of disease mongering is Article 16, Protecting future generations. The article states, “The impact of life sciences on future generations, including on their genetic constitution, should be given due regard.”³⁷³

This principle contains Potter's notion of global bioethics in that the need to ensure that future generations are protected is critical. Potter states that the planet does not belong to any one generation but rather each generation inherits it. As a species, humans should not bequeath upon the next generation a damaged planet. Potter states that ethics should extend from the human community to a community that includes ecosystems; soil, water, plants, and animals with which we exist as well. The interdependence and the fragility of the planet a vision that incorporates past, present, and future generations is necessary.³⁷⁴

Ethical responsibilities should not only be applied to the current generation, but also to future generations. This principle protects the future of humanity. It is a beneficial principle with new technologies as they rapidly progress. These technologies should contribute to improving life, and potential undesired outcomes that may affect future generations should be considered. The articles invokes a commitment to not only one's self, but to members of future generations.³⁷⁵

3.6 Conclusion

In the United States, the primary approach of ethics is centered on principlism with a strong focus on the individual and personal autonomy. However, when considering the problem of disease mongering, a broader population is at risk which makes a global framework more beneficial.

A shift to a focus on global health may broaden the issues which affect millions of people. This makes a global model with a broad inclusive focus an attractive analytic fit for examining disease mongering which may impact anyone taking prescription

medications. In order to illustrate the concept of disease mongering, particular conditions will be examined within the UNESCO framework. The first condition, examined in the following chapter, is Attention Deficit Hyperactivity Disorder (ADHD).

Chapter 4: Ethically assessing ADHD in the UNESCO framework

Attention Deficit Hyperactivity Disorder (ADHD) is often used to illustrate the concept of disease mongering therefore making it appropriate to analyze through the UNESCO framework model. There are many reasons why ADHD is implicated in disease mongering; such as concerns it is over-diagnosed, that it medicalizes childhood behavior, or it is an area ripe for expansion to include a bigger population (such as adults with ADHD).

The pharmaceutical industry is evidenced as propelling ADHD forward by a two decade long campaign that publicized ADHD, and promoted medication to parents, teachers, and physicians. An already established children's market has additionally led to a focus on the market of adult ADHD, which is even more profitable. Classic cases of ADHD affect a small proportion of children but the trend is towards treating even the slightest symptom that leads to the diagnosis and medication. ADHD is now narrowly behind asthma as the second most frequent long-term diagnosis of childhood.³⁷⁶

A brief history is provided to illustrate the evolution of the disease. The criteria for ADHD is provided. Examples of associated areas of disease mongering are offered. Lastly, the condition of disease mongering is analyzed through the UNESCO ethical framework model.

ADHD is a good choice for analysis because as a diagnosis it is particularly elastic and through time has been stretched to include more and more people in its diagnostic criteria. There are social advantages of a diagnosis that range from mitigating blame, for example, all the way to disability benefit for individuals with the diagnosis. Medical expansion of conditions like ADHD can be limited by the medical professional

and insurance carriers, however, with active claim-makers, stakeholders who are committed, and receptive possible clients, expansion of disease occurs readily and with minimal opposition. Diagnostic expansion occurs when already established disorders (such as ADHD) move forward with more claims as inclusion criteria such that one legitimized illness begets another. In our society, the flexibility of medical diagnoses allows for expansion and therefore results in an ever increasing medicalization of more health problems.³⁷⁷

The problems with medicalization include that everything becomes pathologized, all human difference becomes a medical problem, medicine defines what is normal, attention is focused on the individual and not the social context, which may be the important source of the problem and people are at risk for the adverse side effects associated with medications. For these reasons, it is important to recognize when medicalization of ADHD occurs.³⁷⁸ First, a historical account of ADHD and its changes throughout time is provided.

4.1 History of ADHD

The field of psychiatry is especially ripe for disease mongering because medication is common treatment for mental illness. Much good has come from psychiatry such as a greater acceptance of mental illness and better treatments. But, there have also been an emergence of lifestyle drugs in psychiatry, as in other areas of medicine, fueled by pharmaceutical marketing. Attention Deficit Hyperactivity Disorder (ADHD) often comes under fire in relation to disease mongering. While ADHD can

certainly be a debilitating condition, the question of disease mongering arises when over diagnosis occurs in case of those who do not have the condition.³⁷⁹

Most physicians who treat the condition, teachers and parents who report it, have little insight into the complex history of the disorder. When the history is examined, a more nuanced picture emerges that reveals the way society, culture, and patient activism play vital roles. The pharmaceutical industry's aggressive marketing and creation of the condition have an impact on the proliferation of the disorder as well.³⁸⁰

References to ADHD existed in Shakespeare's character of King Henry VIII stating that the King displayed problems with inattention, hyperactivity, and poor impulse control. It was not until the 1950s that ADHD became to formally take form. The first DSM, the DSM-I, was published in 1952, however it contained no entries for any type of behavior problems, which didn't occur until the DSM II.³⁸¹

ADHD has a long history. It first emerged as a diagnostic category in the 1950s. A few of the former names for the condition included Minimal Brain Dysfunction (MBD), Hyperactive Syndrome, Hyperkinesis, and Hyperactive Disorder of Childhood. There were slight differences in each category, but the terms were used interchangeably in practice, with Hyperactivity and MBD most often used. The DSM-III, in 1968, recognized minimal brain damage and hyperkinetic reaction as a childhood disorder. This disorder was characterized by over-activity, restlessness, distractibility, and short attention spans, especially present in young children and often lessening by adolescence. The disorder had two distinguishing characteristics: inattention and hyperactivity. Both still exist presenting in different fashion, over the course of 30 years to present day DSM. The diagnosis also had the possibility of lasting outside of childhood and into

adolescence. There is no solid evidence of a biological cause; there was an assumption of an organic pathology. Most children presented symptoms in school and the major treatment for the disorder was stimulant medication, especially Ritalin. ADHD became well-known in the 1960s, in part due to the fact the medication used to treat it caused controversy.³⁸²

In 1968, the DSM-II was published. In this version, the reference of hyperkinetic reaction of childhood was included. This was in reference to attention disorders. In the DSM-II, the disorder was characterized by over-activity, restlessness, being distracted, and a short attention span. This was noted to exist especially in young children, and disappearing by adolescence.³⁸³

By the 1970s it became the most common childhood psychiatric problem. Most children were diagnosed by their pediatrician or family doctor. Epidemiological studies with sound methodologies were lacking in the 1970s, but it is commonly estimated that between 3 and 5 percent (some estimates as high as 10 percent) of elementary school students were hyperactive. It was believed that more boys were affected than girls, at a possible of 8:1 ratio. ADHD was viewed as essentially a disorder of childhood that children were thought to outgrow by adolescence.³⁸⁴

Diagnosis became dramatically changed in the 1980s. Psychiatry became reorganized and transformed to a well-known specialty. In this decade, ADHD would soon become known a well-known acronym.³⁸⁵ Known then as ADD (Attention Deficit Disorder with or without hyperactivity) it first received its name in the 1980s. Rather than just hyperactivity, a stronger focus centered on inattention as well at the time, which also opened the diagnosis to a wider population who could be treated; not just children who

ran around at school, but those also who daydreamed. ADHD, as it stands to be known today, was coined in 1987 in the DSM-III with a focus once again back on hyperactivity. ADHD was recognized for 30 years, but only until it was given a name did it reach near epidemic proportions.³⁸⁶

There are various perspectives of ADHD. A bio-neurological model of ADHD is a medical model. A bio-neurological model is also the dominant model of ADHD and appeals to “hard science” of the condition adhering to the fact that ADHD is due to a neurological dysfunction. There is a strong defensive stance to those who counter this biological perspective. An International Consensus Statement on ADHD was issued in 2002:

We, the undersigned consortium of international scientists, are deeply concerned about the inaccurate portrayal of attention deficit hyperactivity disorder (ADHD) in medical reports. This is a disorder which we are all very familiar and toward which many of us have dedicated scientific studies if not entire careers. We fear that inaccurate stories rendering ADHD as a myth, fraud, or benign condition may cause thousands of sufferers not to seek treatment for their disorder. It also leaves the public with a general sense that this disorder is not valid or real or consists of rather trivial affliction...

The views of a handful of non-expert doctors that ADHD does not exist are contrasted against mainstream scientific views that it does, as if both views had equal merit... In fact, there is no such disagreement-At least no more than there is over whether smoking cause cancer for example, or whether a virus causes HIV/AIDS. The U.S. Surgeon General, the American Medical Association, the American Psychiatric Association, the American Academy of Child and Adolescent Psychiatry, the American Psychological Association, and the American Academy of Pediatrics, among others, all recognize ADHD as a valid disorder.³⁸⁷

There are two schools of thought regarding the etiology of ADHD. There is the neurological perspective that reduces ADHD to dysfunctional neurological structures of the brain. The other side of the debate is the psychodynamic discourse. This defines ADHD in the context of an environmental condition such as troubling family dynamics, conflict at school, or being labeled as deviant by peers and excluded by peer groups. The

neurological stand is that ADHD exists apart from any social influence and is an organic condition. It is stated that the rise of ADHD is not because clinicians are being trained to identify it easily but due to the better understanding of brain-based behaviors and advances in medical technology. The responses to drugs such as Ritalin or Adderall serve as further proof of the organic nature of the disorder. On the other hand, the psychodynamic approach does not completely dismiss that there may be biological roots. However, the psychodynamic approach appeals to clinicians to consider the social contexts of children. It also appeals to cultural specificity. For example, if North America and Europe have similar medical technologies, why are there so few cases of ADHD reported in Europe in comparison to North America, and why is most stimulant medication consumption predominately occurring in North America? Even clinicians themselves are unclear of the diagnosis as they act as confirmers of the disorder rather than autonomous discoverers who independently gather information and produce a diagnosis.³⁸⁸

ADHD remained debatable as to whether it is a reflection of American cultural and societal trends in relation of the beliefs and behaviors of its society. Many other countries use the American model so it is important to bear in mind that the model is formed around American science and ontology. Thus the influence of the DSM is significant.³⁸⁹

ADHD remains a contested disorder as biological and neurochemical explanations create contentious debate. Its presence, whether medical or social, as an illness is undeniable. While medical tests are lacking to diagnose the condition, the DSM serves to provide a power medical reality to the disorder.³⁹⁰

In the context that ADHD was once considered a social problem, it has now become individualized. ADHD is currently been defined as an individual biological abnormality. Rather than examine the behaviors that could contribute to such a condition (such as lack of physical activity) the focus remains on controlling individual behaviors with medication in a disease category. The DSM (Diagnostic and Statistical Manual) generates debate on matters involving individualized solutions.³⁹¹ ADHD has a long history within the DSM as well. Criticisms of (various versions) of the DSM are next explored.

4.2 Critique of DSM criteria

The number of people with ADHD has grown tremendously since its inclusion in the DSM-III-R in 1987, when a simplified and standardized diagnosis was provided. Parallel to the increase was the mass marketing of medications addressing ADHD. Prescriptions for ADHD drugs have also risen exponentially.³⁹²

The American Psychiatric Association's DSM helped to legitimize psychiatric disorders and became the official guidebook for diagnosing in psychiatry. Not all medical diagnoses are contained within the DSM. It is not a scientific document, but rather a collection of social values, political compromise, scientific evidence, and serves to provide guidance to insurance forms. The DSM has undergone numerous revisions over the years. This is reflective of the changes of approaches that were taken by mental health professional in their quest to understand human problems as psychiatric conditions. For example, in the 1950s psychoanalytic theory was dominant within the DSM, a reflection of the current thought of the time. In the 1980s, the psychoanalytic approach was largely

abandoned in favor of a biomedical model and a categorical approach to diagnosis. This was the DSM-III version. In the DSM-III, psychiatric clusters of symptoms were being paired with distinct underlying diseases, for example depression or schizophrenia. This was being hailed as a scientific endeavor, which is further strengthened in the 1990s with the DSM-IV. Its revisions included almost 400 of these distinct medical diagnostic units.³⁹³ The criteria of the DSM are not the only area that draw concern, but the latest version, the DSM-5, does as well.

4.2.1 Criticism of DSM-5

The DSM-5 has come under criticism as being a lightning rod for disease mongering. Disease categories have been broadened again and new conditions have been added that will redefine more people with a mental illness. These people in turn will need pharmaceutical treatment. These decisions were made by individuals who have financial ties to industry. For ADHD in particular this is relevant because 11 percent of US children have had the diagnosis at some point in their lives, which is a 41 percent increase over the last decade.³⁹⁴

The DSM-5 is the most significant revision since 1994 and this revision has also created the greatest debate. This version of the DSM was rushed to publication, leading to copyediting errors that have the potential to have real impact on patients. There is also argument that the American Psychological Association behaved more like a corporate organization seeking profit than a scientific organization. Scholarly criticisms of the DSM-5 were not addressed by the APA, rather they were suppressed. The National Institute of Mental Health (NIMH) refused to provide funding to the DSM-5. The DSM is

accused of being a medicalized dictionary of defining criteria for disorders, but not describing what a mental disorder is.³⁹⁵

The DSM-5 sets the criteria for ADHD, which is believed to cause serious impairment for children. ADHD has no definitive test and experts agree that symptoms are open to interpretation by doctors, parents, and patients. The APA receives significant funding from drug companies, has loosened the criteria for ADHD so that some of the symptoms such as “often has difficulty waiting his or her turn” mimic normal, childhood behavior.³⁹⁶

The DSM is considered the bible of psychiatry. It also receives much attention for the medicalization of mental illness. The conditions included provide definitions and criteria for psychiatric disorders and are often used for diagnostic and medical billing purposes. The DSM is always a potential for medicalization with each new disease entry with its revisions. Critics argue that the pharmaceutical industry has a strong influence as to what is included in the DSM.³⁹⁷ Other problems related to the ever increasing prevalence of ADHD and its changes in the DSM-5.

4.3 DSM-IV version of ADHD criteria comparison

The older version of the DSM, the DSM-IV, classified ADHD as “Disorders First Diagnosed in Infancy, Childhood, or Adolescence”. This was in the same classification category as mental retardation, learning disabilities, communication disorders, pervasive developmental disorders, feeding and eating disorders of infancy and early childhood, elimination disorders, and tic disorders. Two sets of symptoms were indicated: inattention and hyperactivity-impulsivity and included within each were nine behaviors.

There were three subtypes, predominately inattentive, predominately hyperactive-impulsive, and combined type ADHD, each defined by the classification of symptom category. For at least six months more than six of nine symptoms of predominately inattentive or predominately hyperactive-impulsive should have been present. These symptoms must have caused an impairment in two or more settings (such as home or school), and have been present before the age of seven. ADHD was excluded if there was presence of an autistic disorder or developmental disorder. The diagnostic criteria was tested with children and adolescence in field trials; clinical utility was never assessed in adults.³⁹⁸ In the next section, the DSM-5's criteria, as well as other relevant associated features will be reviewed in detail.

4.4 DSM-5: ADHD

4.4.1 Overview of ADHD

The DSM-5 defines ADHD as a persistent pattern of inattention and/or hyperactivity, which also must interfere with development or functioning. It states that in population surveys ADHD is present in 5 percent of children and about 2.5 percent of adults. ADHD has a course of development. Parents tend to notice excessive motor activity when children are toddlers, however the symptoms are difficult to distinguish between those considered normal behaviors for a child of that age. ADHD is most often identified during the elementary school years. In addition, inattention becomes more obvious and impairing. ADHD is reported to remain stable through adolescence however, there are instances of some individuals who have a worse course of the condition due to the development of antisocial behaviors. The motor symptoms associated with ADHD

tend to decrease with adolescence and into adulthood, however restlessness, inattention, poor planning, and impulsivity remain.³⁹⁹ Next, is the criteria to be diagnosed with ADHD beginning with the inattentive subtype.

4.4.2 Criteria for diagnosis

4.4.2.1 Inattention ADHD

Criteria for diagnosis of ADHD include the persistence of inattention and/or hyperactivity-impulsivity interfering with functioning or development. First, the symptoms of inattention are presented. Inattention criteria indicates there must be a significant impact on functioning that is present for at least six months to a degree not consistent with developmental level and that negatively impacts social, school or occupational activities. Older adolescents and adults (17 years and up) require just five symptoms present. Additionally, symptoms should not be the result of oppositional behavior, defiance, hostility, or a failure to understand instructions. These symptoms include: often failing to pay close attention to details or making careless mistakes in school work, at work, or other activities; difficulty sustaining attention in tasks for activities for example, in lecture, conversations, or long readings; often not listening when directly spoken to (mind seems to be elsewhere even with lack of distraction); often not following through on instructions and failure to finish school work, chores, or duties at work (for example, starts tasks but quickly loses focus and is easily sidetracked); often difficulty organizing tasks (for example, sequential tasks, keeping material together, being messy, disorganized work, poor time management skills, failure to meet deadlines); often loses things that are necessary for activities (such as books at school, eyeglasses,

keys or paperwork); often distracted by extraneous stimuli; or is often forgetful of daily activities (such as chores, errands, or for older adolescents or adults, returning calls, paying bills, or keeping appointments.)⁴⁰⁰ Next are the criteria to receive a different from of diagnosis of ADHD, which is the hyperactive or impulsive type.

4.4.2.2 Hyperactivity or impulsivity type ADHD

Hyperactivity or impulsivity type ADHD is categorized by six or more of the following symptoms which have often been present for at least six months. These symptoms must also be inconsistent with developmental level and have a negative impact on functioning. These symptoms of Hyperactivity or impulsivity include: fidgeting, tapping hands or squirming in seat; leaving the seat where remaining seated is expected (such as at school), running around where to do so is inappropriate (in adolescents, this can be displayed as feeling restless); unable to play or do fun activities quietly; being “on the go” like s/he is “driven by a motor” (for example, an inability to be comfortable for long periods of time, like at a restaurant or meeting); talking excessively; blurting out an answer before a question is finished (butting into conversations or not waiting for a turn in a conversation); difficulty waiting for turns (for example, while standing in a line); or interrupting or intruding on others (butting into conversations, games, or activities; using other people’s belongings without their permission, or intrude or take over what another is doing). Also, several symptoms should have appeared before age twelve. Several hyperactivity or impulsive symptoms must have been present in two or more settings (such as home and school). There should be clear evidence that these symptoms impair everyday functioning and symptoms are not occurring during the course of schizophrenia

or psychotic disorder, and are not better explained by another disorder such as a mood or anxiety disorder, dissociative or personality disorder, substance use or withdrawal.⁴⁰¹

It should also be specified if inattention criteria and hyperactivity criteria have been met for the past six months, only inattention is met and hyperactivity-impulsivity is not met in the past six months, and if hyperactivity-impulsivity is met and inattention is not met for the past 6 months. Partial remission should also be noted. This is, when full criteria was previously met, fewer than full criteria had been met for the past 6 months, and the symptoms still result in partial impairment socially, academically, or occupationally. The severity of symptoms must also be specified. Mild is the following: few, if any symptoms in excess of diagnostic criteria are present. Symptoms also result in no more than minor impairments in social or occupational functioning. Moderate are symptoms of a functional impairment that is between mild and severe symptoms. Severe symptoms are those in excess of the ones required to make the diagnosis, or several symptoms that are particularly severe, are present or the symptoms result in a marked impairment socially or occupationally.⁴⁰² The diagnostic features of ADHD are presented in the next section.

4.4.2.3 Diagnostic features

The critical component of ADHD is a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. Inattention is characterized as getting off task, lacking persistence, having a difficult time staying focused, and being disorganized and these are not due to defiance or a lack of understanding. Hyperactivity refers to excessive motor activity that is inappropriate, such

as running around too much. It is also represented by fidgeting, tapping or too much talking. In adults, it presents as extreme restlessness or wearing other people out from activities. Impulsive behaviors present as being socially intrusive, such as often interrupting others and or making serious decisions without considering the long-term consequences, such as accepting a job without having enough information. ADHD is stated as beginning in childhood, thus requires that several symptoms be present before the age of twelve years of age. Adult recall tends to be inaccurate therefore obtaining secondary information is beneficial. The disorder must manifest in more than one setting and confirming the occurrence of behaviors across settings is most accurate with the consultation individuals from these settings (such as a school teacher). Symptoms may be minimal in cases where the individual receives rewards for positive behavior, is closely monitored, in in a novel setting, taking part in an activity that is enjoyable, has external stimulation, or is interacting on a one-on-one basis with another.⁴⁰³ ADHD also has some associated features.

4.4.2.4 Associated features of ADHD

A biologic marker for ADHD is lacking. In comparison to children who do not have ADHD, as a group those with ADHD have some differences. These differences include increased slow wave electroencephalograms, reduced total brain volume on magnetic resonance imaging, and possibly a delay in posterior to anterior cortical maturation. However, these findings are not diagnostic. While not specific to ADHD, mild delays in language, motor, or social development often co-occur. The associated features can include, low frustration tolerance, irritability, or mood lability. School or

work performance is often impaired even in the absence of a learning disability. Those with ADHD may display cognitive problems on tests of attention, executive function, or memory. However, these tests are not sufficient to serve as diagnostic criteria of ADHD. By early adulthood there are other associations with ADHD. These associations include an increased risk of suicide attempt, primarily when the co-morbid disorders of mood, conduct, or substance use are present.⁴⁰⁴ There are some risk factors which may be associated with ADHD, too.

4.4.2.5 Risk factors

There are risk and prognostic factors associated with ADHD. They fall into four categories that are detailed in the DSM. These are temperamental, environmental, genetic and physiological, and course modifiers. First are temperamental factors. The following traits may predispose some children to the disorder but are not specific to ADHD. These traits are reduced behavioral inhibition, effortful control or constraint, negative emotionality, and/or elevated novelty seeking. The second are environmental factors. These factors include a very low birth weight, which can account for a two to three fold risk for ADHD (but most children born with a low birth weight do not develop ADHD). There is a correlation between ADHD and smoking, however some of this association is common genetic risk. For a minority of ADHD cases, diet can be a factor. Child abuse or neglect, being placed in numerous foster homes, the exposure to neurotoxins (such as lead), infections (such as encephalitis), or being exposed to alcohol in utero are also contributing factors to ADHD for some. It is not known if it is causal, but exposure to environmental toxicants has been correlated to ADHD as well. Next is the genetic and

physiological component. ADHD is increased in first-degree biological relatives or those with ADHD making heritability significant. Specific genes are correlated to ADHD. Impairments in hearing or vision, metabolic disorders, sleep disorders, nutritional deficiencies, and epilepsy can be considered possible contributing factors to ADHD symptoms. There are some physical characteristics associated with ADHD. In some cases, there is a slight increase of cases of hypertelorism, highly arched palate, and low-set ears. Neurological soft signs and subtle motor delays may be present. Lastly, are course modifiers of ADHD. The patterns of family interactions are not likely to cause ADHD, however, they can have an influence on the course of the disorder or contribute to the secondary development of conduct problems.⁴⁰⁵ Next, are cultural components of the disorder.

4.4.2.6 Culture related components of ADHD

Differences in ADHD prevalence rates across regions are often attributed to the different diagnostic methods and methodology used. There may be cultural variations in attitudes about or interpretations of childhood behaviors. The clinical identification rates of ADHD may be lower in the United States in Latino and African American populations than for Caucasian populations. Informant symptoms ratings may be influenced by two factors: the cultural group of the child or the informant. This suggests culturally appropriate practice in assessing ADHD.⁴⁰⁶ In the next section, the role of gender is examined.

4.4.2.7 Gender and ADHD

ADHD appears more frequently in males than females in the general population. The ratio in children is 2:1. The ratio in adults is 1.6:1. Compared to males, females with ADHD are more likely to present with inattentive type features of the disorder.⁴⁰⁷ Next, the consequences of an ADHD diagnosis are examined.

4.4.2.8 Consequences of ADHD

ADHD is associated with poor school performance and social rejection in children. In adults, ADHD is associated with poor job performance, as well as attainment and attendance, and a higher likelihood of unemployment. Adults with the diagnosis tend to have more interpersonal conflicts. In contrast to their peers who lack ADHD, children with the diagnosis are more likely to develop conduct disorder in adolescence and antisocial personality disorder into adulthood; this increases the risk of substance abuse and incarceration. Those with ADHD are more likely to receive injuries than those without ADHD. Those with ADHD also have more traffic accidents and violations. ADHD individuals also run a greater risk to be obese. Failure to properly attend to on-task behaviors requiring sustained mental effort results in those with ADHD are being perceived as being lazy, irresponsible, or failing to cooperate. Family relationships are poor and characterized by discord and negative interactions. Peer relationships are impacted by rejection, neglect or teasing for those with ADHD, too. Those with ADHD, on average, obtain less schooling, in contrast to their peers have a reduced intellectual score, poorer vocational achievement, however it must be noted that this is greatly variable. Severe forms of ADHD have significant impacts on social, family, and school

or work functioning. Lastly, deficits in academics, school problems, and peer neglect are more often associated with increased symptoms of inattention, to a lesser extent peer rejection and accidental injury are more associated with marked symptoms of hyperactivity or impulsivity. There are also disorders that should be distinguished from ADHD.

4.4.2.9 Differential diagnosis

There are several other disorders that are similar to ADHD, but are not ADHD. These disorders must be distinguished from ADHD. They include: oppositional defiant disorder, intermittent explosive disorder, neurodevelopmental disorders, learning disorders, intellectual disabilities, autism spectrum disorder, reactive attachment disorder, anxiety disorders, bipolar disorder, disruptive mood dysregulation disorder, substance use disorder, personality disorders, psychotic disorders, medication-induced symptoms of ADHD, or neurocognitive disorders. Many of these disorders have features that are similar to ADHD, and they may be diagnosed as comorbid disorder, but it is important to distinguish them the ADHD.⁴⁰⁸ In the next section, disorders which can occur along side of ADHD are examined.

4.4.2.10 Comorbidity

Comorbid disorders are the ones that occur alongside ADHD. In a clinical population they are frequently present. In the general population, conduct disorder is the most frequent comorbid disorder with ADHD. Conduct disorder is present in approximately half of children who have the combined type ADHD and about a quarter

of children who have predominately inattentive type ADHD. The majority of children who have symptoms of disruptive mood dysregulation disorder meet criteria for ADHD, however the inverse is not the case. Learning disorders occur frequently amongst those with ADHD. Anxiety disorders and major depressive disorders occur at a lesser rate in individuals with ADHD, but at a higher rate than in the general population. The same is true for intermittent explosive disorder. In the general population, adults with ADHD have higher instance of substance abuse compared to (clinical population of) adults with ADHD. Also in adults, the following conditions can co-occur: antisocial and other personality disorders, obsessive-compulsive disorder, tic disorders, and autism spectrum disorders.⁴⁰⁹ This concludes the examination of DSM criteria for the diagnosis of ADHD and its associated disease factors. There is a broad range of other factors that are associated with ADHD as well, such as risk factors, cultural components, the role gender may play, consequences of ADHD, and similar diagnoses and comorbidity. Next, the factors involved in diagnosing ADHD will be analyzed.

4.5 Factors involved in diagnosing ADHD

4.5.1 Clinical Judgment

Psychiatric conditions involve a judgment, first at the level of the experts who formulate the criteria for the diagnosis and secondly, at the level of the clinician who is diagnosing it. The difference between what is normal behavior and what is abnormal is not something that is written in nature. These characteristics of a condition being present may be most visible at extreme ends of the spectrum, but diagnosing when it is unclear creates disagreement.⁴¹⁰

ADHD is diagnosed based upon the cluster of symptoms and a level of impairment that is presented in the DSM. The DSM categories were created by experts drawing upon clinical experience and research. The symptoms are not based on pathophysiology of symptoms and diagnosis is not based on physiological testing. Thus, a diagnosis of any psychiatric condition is based on clinical judgment, on interpreting diagnostic criteria, clinician training and experience, clinician's observation of the child during an appointment, parent and teacher reports of child behaviors, and most times the results of a diagnostic instrument, such as a checklist⁴¹¹ This flexibility in diagnosis contributes to psychiatric conditions being ripe for disease mongering. There are other considerations to be taken into account for a valid diagnosis which are next considered.

4.5.2 Components of a psychiatric diagnosis

Robin and Gruze's criteria for psychiatric diagnosis requires that a valid psychiatric diagnosis has the following characteristics: clear clinical descriptions, be distinguished from other disorders, have a predictable clinical trajectory, aggregate in families, and be identifiable in laboratory studies.⁴¹² A biological test for ADHD and other conditions is currently lacking. This is because the area is incredibly complex as noted by geneticists and neurobiologists. It is generally accepted that for a biological diagnosis to work, more needs to be known, such as a greater understanding about how myriad genes, multiple neural circuits, and myriad environmental variables all interact over time and in a developing organism.⁴¹³

There are six issues in which the current diagnostic system can result in disagreements about whether a psychiatric disorder is present, and if there is one, which

one. The first is heterogeneity within diagnostic categories. Children with different symptoms can receive the same diagnosis. For example, in the DSM-IV, for children to receive the ADHD diagnosis, they must have exhibited at least six of the eighteen symptoms listed. The symptoms were divided into one of two groups: inattention and impulsivity-hyperactivity. The nine symptoms of inattention included: often making careless mistakes, often having difficulty sustaining attention, and often not seeming to listen when spoken to directly, for example. A child exhibits some of the nine symptoms of hyperactivity-impulsivity type ADHD if the child often fidgets, often cannot stay seated, blurts out, and has difficulty awaiting a turn. However, different children can display a different cluster of these eighteen behaviors, and receive the same diagnosis of ADHD based on different symptomology. Second, is overlap between diagnostic categories. Children with some of the same symptoms receive a different diagnosis. The DSM- IV's criteria for bipolar disorder required a period of elevated, expansive, or irritable mood for at least one week. During that time of elevated mood, at least three of the following symptoms must have been present: (1) feelings of grandiosity, (2) decreased need for sleep, (3) pressure to keep talking, (4) racing thoughts or ideas, (5) distractibility, (6) increased goal-directed activity and psychomotor agitation, or (7) excessive involvement in pleasurable activities that have a high likelihood for poor consequences. Those presenting with irritability must exhibit at least four symptoms. Several are similar to criteria used in diagnosing ADHD: a pressure to keep talking, psychomotor agitation, and distractibility. Combining symptoms of oppositional defiant disorder (ODD), often characterized by an irritable mood, it may be difficult to determine which diagnosis; bipolar disorder, ADHD, or ODD is best. Clinically, children presenting

with a mix of symptoms often receive more than one diagnosis and more than one medication is involved in treatment.⁴¹⁴

Third, is that symptoms of the same disorder can look different in children and adults. DSM-IV contains a special section of disorders normally first diagnosed in infancy, childhood, or adolescence. This includes ADHD. In the 1970s, for example, children were not diagnosed with depression, however in the 1980s, researchers argued that symptoms of depression can be different in adults and children. Today, it is uncontroversial within psychiatry that children can be depressed, even if it is debated on how best to treat.⁴¹⁵ The same is true for ADHD; what was once exclusively a disorder of childhood is now diagnosed in adults. Adult ADHD is also viewed as an accepted diagnosis.

Fourth, a careful diagnosis requires identification of symptoms and evaluation of impairment. DSM-IV clearly stated that the presence of symptoms alone does not warrant a diagnosis a diagnosis is warranted only when symptoms are causing a significant impairment. It could be inferred that making an appointment for a clinician for an evaluation is representative of an underlying impairment. Assessments are not always done in a diagnostic workup, in cases where they are done, the rates of diagnosis is lower. Reimbursement systems may require a DSM diagnosis and this may encourage a clinician to record a diagnosis even when the severity criteria are not fully met. This is done in order to justify the requirement.⁴¹⁶

Fifth, the diagnostic system does not encourage assessment of the child's context. That is that the context of symptoms is not considered within the DSM. The DSM allows for sadness due to the loss of a loved one for example, but other normal human problems

that may trigger intense sadness are not included. For example, a lack of meaningful attachments to job loss (in adults) and for children being bullied or neglected. Sadness due to life circumstances can be too quickly labeled as depression. This is important because failing to discuss contextual explanations for problematic behaviors can suggest that context is irrelevant to diagnosis and treatment decisions. If a child's moods and behaviors are adaptive or appropriate responses to adverse, traumatic, or other difficult contexts, it would be a serious mistake to treat the child but make no changes to the child's environment. A contextual explanation does not alone indicate that the child is not suffering from a disorder either. Just as a child whose fever results from consuming unclean water needs both a medication for the fever and an improved water supply, so would an abused child suffering a disorder. The child may be helped both by drug treatment but also to environmental changes.⁴¹⁷

Lastly, is number six: Symptoms and impairment are dimensional and children are developing organisms. The significance of context and impairment is important. Yet, there is a second deep troublesome area in the diagnostic manual. The body of the text of the DSM uses categories to name symptoms yet states it is dimensional. It is referenced in the DSM-IV that symptoms appear on a continuum of intensity and that disorders can, too. Symptoms such as sadness, for example, can be exhibited to a different degree. A cluster of symptoms present can produce a different degree of impairment. Labeling children is a challenge because they are still developing and their moods and behaviors are different than adults and can vary depending on the child's age. For example, a four-year-old child talking with an imaginary friend is normal, but not for a fourteen year old

child or an adult.⁴¹⁸ Often, there is speculation that ADHD has an organic nature such as other illnesses.

4.5.3 Organic nature of ADHD

ADHD critics argue that there is no proof that ADHD is a symptom of an organic brain disease and that the ADHD explosion is medicalization. Supporters in turn argue that ADHD is not a physical disease but is defined as a mental disorder. It does not help the case of ADHD as a serious condition in that many of the behaviors are typical of children. Neuroimaging studies which intend to uncover the pathophysiology of ADHD receive criticism for having incoherencies and methodological flaws. Critics state that ADHD is the manifestation of adults' annoyance by certain normal childhood behaviors, their own efforts to eliminate these behaviors for their own distress the behaviors cause, and a willing medical profession ready to diagnose childhood behaviors that are deemed disturbing. At the risk of being stigmatized and going against the mental health establishment, a British child and adolescent psychiatrist, Sami Timimi and 33 co-endorsers maintained the stance that there is no compelling evidence that shows that ADHD is a strongly heritable, biochemical brain disorder.⁴¹⁹ Next, are the specific instances of disease mongering that are attributed to ADHD.

4.6 ADHD and disease mongering associated with diagnosis

When ADHD was first diagnosed and treated, it was viewed as a disorder for children, mostly boys. But as the focus of the definition shifted away from hyperactivity and on to attention an increasing number of girls were diagnosed. Soon, adolescents were

diagnosed with ADHD. And during the past two decades there has been a rise of adult ADHD. The thresholds for ADHD, both in terms of age and behavior, have also shifted. A once childhood only disorder can now be considered a lifetime disorder consequently affecting a far greater number of people. The engines fueling medicalization of ADHD have shifted as well. In the 1970s, physicians held a critical role, but currently it is in large part propelled by the pharmaceutical industry.⁴²⁰

Life in the twenty-first century is becoming increasingly medicalized and more and more people are likely to be labeled as having a disease. The inability to sit still or pay attention is quickly labeled as ADHD. While some people do suffer from the condition, it is the increasing amount of people being given a disease label who may not have ADHD that is concerning. They are subjected to disease management with prescription drugs that may offer little long term benefits, while the harm may be significant.⁴²¹

ADHD is often considered a classic example of medicalization. For the past 40 years, ADHD has been a common diagnosis occurring in childhood. With the expansion to adult ADHD, it is now viewed as a lifetime condition. ADHD was once also just a condition of North America and a few other countries, but there is new evidence that suggests that now ADHD has expanded around the globe.⁴²² Over-diagnosis is the first element of disease mongering in ADHD to be examined.

4.6.1 Over-diagnosis of ADHD

The Centers for Disease Control and Prevention report that 15 percent of high school age children are diagnosed with ADHD. In 1990, 600,000 children were

diagnosed with ADHD; today 3.5 million children have received the diagnosis, numbers which are suggestive of an ADHD epidemic.⁴²³ A 2014 New York Times article cites a CDC report stating that more than 10,000 toddlers in the US (ages 2 or 3) are being medicated for ADHD, which is outside of practice guidelines.⁴²⁴ Over three decades the number of children treated with stimulant medications has had a marked increase. In the 1990s, the surge of medication used to treat ADHD became apparent.⁴²⁵ Another factor involved is that childhood and associated behaviors are becoming too medicalized.

4.6.2 Medicalizing childhood behavior

Articulating what a disease consist of is not an easy task, but there is a general sense that “we should know it when we see it”. Unfortunately, this is not often the case. Whether or not people consider themselves to be ill varies from class, gender, ethnic group, and other less obvious factors. What is considered a disease also changes over time. It is important to distinguish diseases because medicine has the ability to treat conditions with powerful interventions. A difficulty with ADHD is distinguishing normal behaviors of children or ones that are disturbing. With a soft definition of what is disease, this can be difficult leaving interpretation open to disease mongering. With increasing rates of diagnosis, disease mongering starts to become suspect. Critics of the growing trend of ADHD cases argue the real issue is a school system or parents who are not properly controlling their children. Proponents state that these children have poor behavior due to the fact they have a medical condition that requires treatment. This leads to the question if disease opportunity is being created by the pharmaceutical industry.⁴²⁶

There tends to be three arguments that center on whether or not ADHD is a medicalized disorder. The first is that ADHD is a socially constructed illness. This creates confusion because many diseases can be considered socially constructed. A second argument focuses on the etiology of ADHD. There is debate if ADHD is a social and environmental condition or if it has a biological basis and to what extent either is more powerful. Third is the stance that ADHD is a recognized condition with a combination of social factors and biological roots. However, the ethical concern here is that the condition is being over-diagnosed and stimulant drug treatment is being overused.⁴²⁷ Conrad noted in 1975 that ADHD is socially constructed by three forces, the revolution of pharmaceuticals, government intervention and trends in medical practice. These are arguments that are still valid today. The pharmaceutical industry promotes ADHD through “disease awareness” campaigns, clinicians diagnose and treat the condition, and the American with Disabilities Act recognizes ADHD as a disability that warrants special accommodation.⁴²⁸

Rather than a focus on outside conditions that may lead to restlessness such as a lack of physical activity, individuals’ behaviors are the focus because individual behavior can be controlled through pharmaceutical intervention.⁴²⁹ Character flaws that children may exhibit or those that are the result of poor parenting, such as misbehaving in schools, fighting, or stealing are understood today in a medical context. Within that context requires a medical (drug) intervention. Medical language exonerates children from deviance. The explosion of the medical diagnosis of ADHD lends merit to claims that it is being over-diagnosed and over-medicated. What is now being treated medically was defined as normal childhood struggles in the past. This illustrates a cultural shift in that

there is a new view of what childhood should look like; there are distorted expectations of children, different expectations of what they should tolerate, how they should respond in social situations, and how they should navigate social institutions. This cultural shift is fueled by mutually reinforced dialog between medicine, educational psychology, and parenting psychology.⁴³⁰

There is difficulty distinguishing between behavior that is debilitating and that which is a part of life. A mental health diagnosis is also subjective. This makes mental health problems vulnerable to over-diagnosis. There is difficulty determining when criteria such as being inattentive or disorganized warrant formal diagnosis. Rather than narrowing the focus, the DSM is expanding upon ADHD criteria. Rates of ADHD are expected to rise with the DSM-5 and 78 percent of those advising for ADHD for the new version have industry ties and potential financial conflicts of interest. Severe cases of ADHD are obvious but the bulk of the subjectivity lies in the subtle cases and that is where opinion differs. Objective data is lacking to support the validity of diagnoses. This results in those facing the diagnosis to potentially be subjected needless to overtreatment.⁴³¹ ADHD is not limited to only children and adolescents. Adult ADHD has created another market.

4.6.3 Adult ADHD

The popular ADHD drug Adderall sums the wide net which is cast for the treatment of the disorder. In coming up with the name for an “ADD” drug, the words “ADD” and “for all” were combined to form the name “Adderall”. The fastest growing market for ADHD is for adults who were never diagnosed.⁴³²

ADHD was considered a primary disorder of childhood. Starting in the 1970s, studies that followed children from childhood into adulthood were published. These studies estimated that for some children, the hyperactivity of childhood persisted into adulthood and they did not outgrow their symptoms. Their symptoms still caused some problems as adults. The most notable symptoms were restlessness and poor concentration. Further research was conducted in the 1980s to identify any comorbidity, for example, that may compound the diagnosis. Reflective of the thinking of the 1980s was that they were children who had ADD (known at the time) and it was not a disorder that was overlooked as they grew up but rather they were hyperactive children who had grown up. The DSM-III of the 1980s began to show an interest of ADHD beyond childhood. First, this version has a trend to define disorders by symptoms versus etiology; the version classified ADHD by its main symptoms: hyperactivity or inattention. Attention deficits had two subtypes, with and without hyperactivity, and were mainly focused on behaviors exhibited before the age of seven. Second, the range of behaviors included became more comprehensive. Thus, those who may not have qualified in an earlier version of the DSM could now by this new standard. The possibility for these symptoms to last beyond childhood with the possibility into adulthood became accepted.⁴³³

The DSM-III was revised in 1987 to the DSM-III-R. ADD was renamed to its current designation as ADHD. Children could now meet criteria for ADHD who were hyperactive and impulsive not inattentive. This resulted in 50 percent more children receiving the diagnosis.⁴³⁴ This was to reassert the condition of hyperactivity as one condition of the disorder. During this time, there were also subtle shifts. The new criteria

did not refer to ADHD in adulthood. However, it did leave the door open for an expanded definition beyond adult hyperactives (ones who maintained ADHD from childhood into adulthood) to ADHD adults (who had no childhood diagnosis.) ADHD symptoms now were expanded to the workplace with less emphasis on specific classroom behaviors. Adult ADHD was possible, but not specifically emphasized yet. In the same year the DSM-III-R was published a book came out aimed at the general public speaking of a “new” type of ADHD adults, those who were never diagnosed as children but suffered as adults with the symptoms of the disorder. Highly visible accounts of ADHD (by successful authors) were now in the public and the psychiatric profession noticed. Clinics for adults with ADHD emerged in the late 1980s. A widely cited study, by Alan Zametkin of the NIHM in 1990 produced an unintended outcome. Zametkin conducted PET scans with adults who endorsed having symptoms present as children, and who had children with the diagnosis themselves hoping to identify any biological markers. The unintended outcome was that the researcher’s work was cited as evidence that adults can have ADHD. Follow-up studies that did not confirm the original study’s findings did not receive as much publicity.⁴³⁵

In 2002, Strattera became the first drug approved specifically for adult ADHD. A television ad campaign was launched by the manufacturer, Eli Lilly, to make the public more aware of the condition. The ads included adults forgetting items, arriving late for appointments, and completing work assignments late. All of the implications were that it was the result of adult ADHD. By the end of 2004, more than 2 million people (not all adults) were using the drug as other drugs like Adderall XR and Focalin were granted

FDA approval to treat adult ADHD which resulted in nearly doubling the pharmaceutical industry's pediatric market for the drugs.⁴³⁶

Adult ADHD is self-initiated and self-diagnosed and creates a shift away from personal responsibility and individualizes life problems. Now, with a medical excuse the blame is moved from the person to the body being at fault and this has consequences. For adults, ADHD is centered on performance more than behavior. This is manifested in how tasks are accomplished, difficulty adapting, or on levels of success that is achieved. Those individuals may feel that they should or could be doing better, so they seek help for their performance. A diagnosis of adult-ADHD provides a rationale for their poor performance and lets them re-evaluate their past behaviors. This reduces self-blame. Rather than think, "I always thought I was stupid", the factors that always resulted in chaos can now be labeled ADHD. Additionally, the diagnosis results in being labeled as having a disability, which can serve as a means to the possibility of benefits and accommodation. Adults with ADHD have filed civil suits under the Americans with Disabilities Act to receive special accommodation in the workplace and for education. Before the diagnosis of ADHD, these people may not have seen themselves as "disabled". Now they may be entitled to untimed tests, oral vs. written administration of exams, additional time to complete tests, work assignments with written instructions, extra clerical support, increased frequency of performance appraisals, checklists for tasks, diminished-capacity arguments in criminal suits, and protection from discrimination. In the workforce, this may mean special office equipment such as furniture, tape recorders, or laptops, organizational schemes (like color coding, alarm clocks or a buddy system) to serve as reminders and keep employees on track.⁴³⁷

Adult ADHD provides a good example of disease mongering by expanding a category to include a wider range in its definition. The age criteria were extended to include adults and inattention was given a strong focus. These two elements allowed for an entire population to be included and erased the view that it is only a condition exemplified by hyperactive children. Thirty years ago the notion of adult ADHD would have been considered an oxymoron, but today it is recognized as a legitimate disease that can be claimed, diagnosed, and treated.⁴³⁸

ADHD in adults became an increasingly known phenomenon in the public sphere and it grew in literature as well. In the mid-1980s, articles were few but did include those who were diagnosed with childhood ADHD which followed them into adulthood. It was not until the 1990s that exclusive adult ADHD became to appear in popular media. Articles in a modest amount did contribute to spreading word of the condition.⁴³⁹

Popular book titles of the time include, “You Mean I’m Not Lazy, Crazy, or Stupid?” which showed the shift a diagnosis of adult ADHD can bring to an individual, and is now hailed as a “classic self-help book”.⁴⁴⁰ News media contributed as well. Major news outlets had programs with experts describing adult ADHD and explaining how the condition went misdiagnosed in childhood, allowing for adults to reinterpret their current and childhood behavioral problems into a medical diagnosis of ADHD. Magazines began to run stories on the topic as well, detailing accounts of individuals whose lives had been changed for the better upon the diagnosis, noting there was now a “medical” reason for all of their problems. Advocacy groups also began to form, with CHADD (Children and Adults with Attention Deficit Disorder) as the largest support group. CHADD lobbied to have ADHD in adults included as a psychiatric or behavioral disorder to legitimize

disability claims to entitlements. Ciba-Geigy, a pharmaceutical company that manufactured Ritalin, is another stakeholder. In the 1970s Ritalin provided as much as 15 percent of their gross profit. Ciba worked with CHADD providing financial assistance, which caused public outcry speculating neutrality of the group. The company has a long history promoting hyperactivity and then it began to promote ADHD as a medical disorder. The patent for Ritalin has expired a long time ago, however, the amount of the generic form of methylphenidate, increased. The redefinition of ADHD as a lifetime disorder means that those diagnosed will require a lifetime of medication.⁴⁴¹

CHADD was considered a lay-professional alliance group and promoted the expansion of ADHD to adults. Those who receive the diagnosis embrace and promote the condition, which is not the case for all psychiatric conditions. Adult ADHD became popular through television, popular literature, the Internet which quickly spread word of treatments. This created a new market by individuals who previously were “undiagnosed for years” knowing a treatment was available. A feedback loop among professionals, claim makers, media and the public was created that led to creation, expansion, and application of this illness into a medical category. Essentially, adult ADHD is now just taken for granted as a naturally occurring phenomenon, penetrating the consciousness of the public. It is merely accepted, its history not examined, and is assumed as universally significant regardless of cultural context. Due to the climate of more and more individuals being more medically aware, symptoms must be matched to a corresponding “disease”.⁴⁴²

The disease among adults is largely one of self-diagnosis. Adults see or read something they feel describes themselves. Online quizzes are available sponsored by drug

companies that encourage to seek treatment. These quizzes, such as one presented by Shire pharmaceuticals, present users a few questions, for example, “difficulty remembering appointments”. If a user answers three of the six questions split with “rarely” and “sometimes”, ADHD is “possible”; five questions as “sometimes”, ADHD is “likely”. Medical education videos are also available online. They show just how quickly (in six minutes) a doctor is able to diagnose an adult with ADHD, than offer medication as treatment.⁴⁴³ The environment within which children spend most of their time is also a consideration for disease mongering in ADHD. Schools and teachers especially have critical roles in the process.

4.6.4 The role of teachers and schools

Primarily, school is where ADHD is initially suspected. Educators also have a critical role in the diagnosis of ADHD. Both children and childhood became objects of scientific research. Two mutually-reinforcing ideas were critical in regards to ADHD. First, the behaviors that a normal child may have were identified, such as temper tantrums or mood swings. Second, the development appropriate of such behavior of a child, for example a two year old throwing a temper tantrum in public is more acceptable than a twelve year old doing so. Together, they add up to why some behaviors are age inappropriate and are therefore concerning medically.⁴⁴⁴

Teachers play a significant role in the diagnosis of ADHD and as a group often serve as the impetus for parent’s to seek treatment for their child. Teachers function as disease-spotters. They are “educated” in spotting ADHD in children and often a major source of information on the diagnosis and management of ADHD comes from

pharmaceutical company websites.⁴⁴⁵ ADHD has impacts on educational performance which means teachers have a key role in advocating for the illness. The pharmaceutical industry has strategies to frame educators' responses to ADHD. The role of the teacher extends beyond educating the parent about the condition, but also a teacher has an active role in the diagnosis. The DSM includes teachers and there are measures such as the Conners Teacher's Rating Scale which are given to teacher to complete in regard to a child's classroom behaviors. The Internet is a popular means for drug companies to attract teachers. They do so in the same way as they target physicians, familiarizing them to drug therapies. Major drug companies have independent websites that are targeted for teachers designed to "educate" them and to approach parents regarding ADHD treatment options. Links to the drug manufacture's website are often included. Free hotlines to ask experts and links to government websites such as US Individuals with Disabilities Education Act are included. School nurses are also a popular group of the pharmaceutical industry. ADHD resource kits are provided to school nurses. Teachers are often recruited by advocacy groups, too. The pharmaceutical industry's penetration of school systems is a new phenomenon.⁴⁴⁶

The school itself is the context in which ADHD is specifically diagnosed. England, which has a lower occurrence rate of ADHD, has a traditional authoritarianism responding to unwelcome behaviors by the use of discipline. American schools by contrast, have a medical authoritarianism which frame poor behaviors as medical rather than disciplinary matters. Because of the development of a medical model to treat inappropriate behaviors, the suggestion to use traditional forms of punishment is viewed as being a throwback to a bygone era. Those who advocate the medical approach present

what is viewed as a more scientific and sophisticated way to address problem behaviors. Take for example normal behaviors of childhood that are nonetheless unwelcome. If they are brief, a medical model labels them as acute. If they last longer; they are viewed as a chronic problem.⁴⁴⁷

In addition, the consideration of school environment, a non-pathological factor, is not often taken into consideration. ADHD is stated to be in conjunction with activities that require sustained mental effort. This would be typical for many subjects in school. ADHD is said to worsen when sustained attention or mental effort is also necessary. It is not considered how these symptoms are lacking when it is an enjoyable activity or when the student is involved in one-on-one interactions. In other words, the impact that a boring presentation of subject matter or a tedious instructor is overlooked in regards to holding the attention of a student. In part inattentive or hyperactive behaviors could be in response to dull assignments, monotonous conversations, working on repetitive tasks, by not being strictly controlled, and similar circumstances.⁴⁴⁸ The biggest occurrence of disease mongering of pharmaceutical companies is directed to physicians to encourage the diagnosis and prescription of medications to treat ADHD.

4.6.5 Marketing to physicians

Patients can only take medication which has been prescribed for them by physicians. Drug companies strive to educate physicians that ADHD is a lifelong condition. However, this is not proven nor are the risks or efficacy of long-term use of medication used to treat the condition known. Drugs are portrayed as relatively harmless and symptoms (which could be caused by numerous other issues) should be treated with

drugs. The drugs are portrayed in ads which appear in medical journals as having the ability to improve academic performance or allow patients to experience life's successes.⁴⁴⁹ ADHD extends to a global scale as well.

4.7 Global impact of ADHD

The Western notion of mental illness is becoming more widespread around the globe. This has been done in the name of science with the belief that mental illness has a biologic basis of psychic suffering, to reduce stigma, and dispel non-scientific myths. However this process of teaching others to “think like us” has also exported Western symptoms. The DSM has become a worldwide standard for diagnosis. Western psychiatrists and journals are viewed as the premier standard. Intentions may be the best, but as Western disease categories gain dominance, micro-cultures that shape the illness experience are being ignored.⁴⁵⁰ The US medical standard also makes way for the global rise in ADHD diagnosis and treatment.

4.7.1 Global rates

The core symptoms of ADHD are also the typical behaviors of childhood, being hyperactive and impulsive. There is not a clean line that distinguishes normal from abnormal developmental behavior. This is a concern as to why it is being over-diagnosed. The concern regarding over-diagnosis had historically been focused on the United States, where the proliferation of the disorder made national headlines when the large number of cases of children diagnosed was reported. Recently, the global impact of ADHD has been given more attention. There is growing evidence that the US is not alone in this growing

epidemic and that ADHD and the use of medications to treat it have been increasing in many parts of the world. For example, the prevalence of South American countries such as Columbia, stand at over twenty percent, Europe where Spain's rate is between three and nearly seven percent, and in the United Kingdom between two and five percent of the population. Australia varies between two and almost ten percent. And the same applies to the rate of medication expenses over the past decade. In some countries outside of the US such as The Netherlands, Norway, and Sweden, the use of stimulants is declining. The US is still, however, the largest consumer of methylphenidate, at sixty six percent of the global use.⁴⁵¹

In the US, more than 10,000 toddlers (age 2 or 3) are also now being medicated for ADHD outside of pediatric guidelines, according to the CDC. Standard practice guidelines do not address the diagnosis in children 3 years and younger and use of medication in that age group largely remains untested. Experts feel that diagnosing ADHD at that age is inappropriate because hyperactivity and impulsivity are developmentally appropriate behaviors for children that age.⁴⁵² This is concerning if this non-accepted practice could begin to spread.

ADHD and its treatments have migrated from the US to the global arena. Prior to the 1990s, there was little information about ADHD being diagnosed in other countries, which was at the time speculated to be culture bound, thus limited to English-speaking countries. Global data remains sparse, but the indications are there is a global prevalence and there is an increase in consumption of ADHD medication worldwide.⁴⁵³ This leads to ethical problems.

4.7.2 Ethical problems with global expansion

There is a significant ethical problem with the expansion of ADHD being diagnosed in developing nations because this imposes a distinct American set of norms on local populations in the name of science. The concern is that by globalizing the DSM norms creates another market for pharmaceutical companies to sell drugs and opens it up to a huge market to do so. Debate also exists that there is an effort to make universal Western psychiatric categories. This is ethically troubling in that structural violence, for example, is ignored in favor of an individual approach essentially ignoring conditions that may impact mental (and physical) well-being. Debate also exists between a relativistic versus a universalistic view of ADHD. In a relativistic view, culture shapes development; a disorder should not be considered universal or naturally occurring. Only if diagnosis embraces cultural sensitivities and makes clear distinctions between internal and external problems may it be used in treatment. The universalistic perspective on the other hand, states that psychiatric disorders are universal. However, how the symptoms manifest may be shaped by culture. Defining culture creates some problems as well, in both cases.⁴⁵⁴ The way that ADHD is diagnosed in different countries also varies. In the next section, the instrument most widely used outside of the United States, the International Classification of Disease (ICD), is examined.

4.7.3 Global diagnostic criteria

4.7.3.1 International Classification of Disease (ICD)

Methods used to diagnosis ADHD is an important consideration. To examine the differences between the US and Europe, the ICD must be examined. The ICD-10 requires

that a child must exhibit all three dimensions of inattention, hyperactivity, and impulsivity. These also must be present both at home and at school. By contrast, the DSM model is much more relaxed requiring just one dimension and symptoms present either at home or at school.⁴⁵⁵

ADHD varies across countries. In the UK, the rate of reported cases of ADHD tends to be lower than in the US. . In the US the DSM is used to diagnose mental illness while Europeans are using the International Classification of Disease (ICD). The ICD is much stricter for diagnosing illness, but the DSM has become the more widely used instrument.⁴⁵⁶

Diagnostic criteria are the biggest factor in the UK's diagnosis of ADHD. The ICD refers to what is known as hyperkinetic disorder (HKD), which is what in the US ADHD is. The ICD offers a higher threshold in contrast to the DSM to meet criteria, therefore only extreme cases are included under these standards. In Germany, the prevalence rates for ADHD began to rise in the 1990s, likewise drug prescriptions. Prior to the 1990s, amphetamines (used to treat ADHD) had no role in the country and were not approved to treat children. However, with approval and marketing, the treatment numbers began to climb. ADHD prevalence rates also increased because of professional exchanges of ideas with US health experts and drug marketing. For ADHD, the DSM criteria are permitted to be used rather than the ICD in Germany. France reports a small population of children with an ADHD diagnosis and it is most attributed for the preference of using restrictive diagnostic tools. These include the French Classification of Child and Adolescent Mental Disorders (CFTMEA) or the ICD. Outside of research purposes, few French psychiatrists use the DSM. French physicians view ADHD as a

psycho-affective disorder and favor psycho-social interventions. Stimulant medication is used as part of a multi-modal treatment plan only when other approaches such as education or psychosocial interventions are not enough. Stimulant drugs were initially strictly controlled in France and only specialists could prescribe these drugs from three hospital pharmacies and only a week's supply was given. Currently, general practitioners may prescribe the drugs for 28 day prescriptions that may last one year. French psychiatry is grounded in psycho-pathological and psychoanalytic treatment. Most clinicians prefer the stricter diagnostic tools and non-drug treatments as a first-line in the treatment of ADHD.⁴⁵⁷

In Italy, ADHD may be viewed more as a learning or personality disorder whereas it is considered a behavioral disorder in the US. Until recently, most Italian clinicians had limited knowledge of the condition as defined in the DSM or ICD, rather referred to cases as “problem children”. In 2001, most pediatricians had heard of ADHD, but did not know how to diagnose it. Ritalin was hard to obtain in Italy as its use was very restricted in 1989. It then became illegal for over a decade due to abuse by college students. After lobbying by a variety of groups, Ritalin was brought back to the Italian market with less restrictions in 2007. However, drug treatment for mental health problems is low in Italy, as medications to treat them are not the norm. In Brazil, the acceptance of ADHD as a medical condition was a slow process due to a preference for psychoanalysis in school and not favoring a medical approach. As in other developing countries, data of DSM rates in regards to ADHD is scarce. However, there is a trend in Brazil to recognize ADHD more often and the treatment is drug therapy, yet resistance

amongst professional still remains.⁴⁵⁸ Another result of the spread of ADHD is the rise in the globalization of prescription drug use to treat it.

4.7.3.2 Global drug consumption

As ADHD became more and more medicalized, the primary treatment for it became drug therapy. Methylphenidate is the drug of choice, in the US which is a controlled substance and is globally tracked as well. The increase in global consumption of methylphenidate. Methylphenidate global consumptions more than doubled in 2007 from 25 tons to 52 tons in 2008, US drug advertisement being one of the factors influencing such a rise. This also illustrates how accepted drug treatment is for treating ADHD and other countries use this medical model in treating ADHD from far corners of the globe.⁴⁵⁹ The different cultures in which children are raised throughout the world is next considered.

4.7.4 Social-Cultural impacts

Anthropologists speculate that the contextual factors that may be contributing to ADHD in the United States. US parents tend to place a high value on stimulating cognitive development in children by arousal and activity. In contrast, in the Netherlands rest and regularity are promoted in the young. This leads to speculation that in the US, the drive to have children who are stimulated inadvertently cultivates behaviors that are not desired, such as hyperarousal or inattention. Implications as such could contribute to the higher than average rates of ADHD in the US, as well. Likewise, mothers across various countries around the world may report that their children are displaying the same

behaviors. However, whether or not these behaviors are interpreted as a problem (ADHD) is debatable. Thus, behaviors that are appropriate and acceptable in one cultural context may not be appropriate in another.⁴⁶⁰

4.7.5 Contributing factors

Five key elements contribute to the globalization of ADHD: 1. Trans-national pharmaceutical industry, 2. the increasing use of the US model of psychiatry as a standard, 3. DSM criteria adoption in diagnosing ADHD, 4. Internet websites that include screening tools, 5. ADHD advocacy groups. ADHD drug marketing has become a great potential for the pharmaceutical industry. More markets become appealing when restrictions are lifted in certain countries (such as Italy and France). The “lack of awareness” by drug companies is also noted in countries like Japan, the UK, and Germany. The pharmaceutical companies call for marketing and awareness campaigns to “educate” those on the diagnosis and treatment of ADHD. There has also been a push to reach teachers who can be viewed as “disease spotters” as diagnostic assessments for ADHD often involve teachers. Online resources also are there to implicitly educate the public about the condition. The US may have reached a saturation in the market for ADHD, but the global market has not, therefore making it an attractive consumer base for pharmaceutical companies.⁴⁶¹

The influence of Western psychiatry is noted in regard to the global increase of ADHD. The US is a biological model, which treats ADHD with the use of psychoactive medications. This medical model is extending beyond the US. This could be for several reasons. Physician training is becoming more similar and there are limited training

programs available in child psychiatry therefore, students are often sent to other countries for training. International medical graduate students represent a third of US medical schools, the number of these physicians who return to their countries is unknown, and however it could explain how US models migrate. The global shift from the ICD to the DSM model in diagnosing ADHD is another factor. More and more research literature is using the DSM in analyses. The DSM casts a much wider net in the diagnosis of ADHD than the ICD. Another factor is the wide availability of medical information found on the Internet. This includes self-diagnostic tools, support groups, chat rooms, list serves, and more. This can contribute to knowledge and growth of the condition in other countries around the world. Problems arise when the groups have pharmaceutical industry sponsorship that essentially promote their products. This promotional nature of the message can be lost in translation in non-English speaking nations. Internet symptom checklists often originate in the US and migrate to other countries in their native languages. The problem with checklists is they do not indicate a diagnosis per se; they appear to be self-diagnostic “do it yourself” ADHD diagnostic tools and originate in the US, but only a medical professional can diagnose ADHD. Lastly, patient advocacy groups have a role in the globalization of ADHD. These types of groups offer a variety of information and help shape policy of ADHD. Some of these groups are funded by drug companies or are connected to US based groups, such as CHADD (which receives industry funding). The groups’ conferences bring a global audience together.⁴⁶²

Since 2000, the FDA has cited every major drug company, some more than once, who manufacture drugs such as Adderall, Concerta, Focalin, Vyvanse, and non-stimulants like Intuniv and Strattera for false and misleading advertising.⁴⁶³ The drugs are

viewed as harmless, like taking aspirin despite the fact they are in the same drug class as morphine or oxycodone because of potential of abuse and addiction. Because of this, it is important to examine the drugs used in the treatment of ADHD.

4.8 Drugs used to treat ADHD

4.8.1 Access to alternatives

Despite the data supporting the safety and effectiveness of some psychosocial treatments for behavioral disorders, drug treatments are most readily accessible to most patients. One reason for this heightened availability is that drug treatments are more aggressively marketed to practitioners and patients than psychosocial treatment. Payment of services through private insurance is another issue; coverage for psychosocial treatments is often more limited than treatment with medication. In standard clinical practice, children are frequently given medications and then not seen again for weeks. Drugs are started and stopped with a minimum of information and medication doses are haphazard. In the past two decades, managed care has essentially limited access to and utilization of psychosocial interventions for treating mental health disorders. It is easier for patients to obtain referrals for medication management and drugs than therapy, thus, making one choice, drugs, much more or an attractive option. Claims for psychosocial interventions may carry higher copays and deductibles than do visits for medication management. Psychosocial interventions may be subject to annual limitations on visits.⁴⁶⁴

The drugs used to treat ADHD also have the potential for side effects.

4.8.2 Side effects of drugs

Side effects of the medications are one of the biggest risks to those who may not need to take the medications. They range from mild to severe. Consideration of impacts of side effects is an important component of disease mongering because there is exposure to drugs which may not be beneficial, but instead expose the users to harm.

There are a wide variety of prescription drugs available on the market which are used to treat ADHD. The medication of choice is a form of stimulant drug: Methylphenidate (or Ritalin) and Adderall. Both drugs are stimulant medications with slightly differing biochemical reactions in the effects they pose on neurotransmitters, but the drugs both aim for the same result. These medications lead to an increase of arousal, energy level, and attention.⁴⁶⁵

Ritalin is effective and its common side effects generally are difficulty of sleeping and decreased appetite. However, severe side effects include cardiac events in those who are not aware of an underlying heart condition.⁴⁶⁶ Another popular stimulant medication is Adderall. Adderall XR (extended release) is becoming increasingly popular; it is the most prescribed brand name medication for the treatment of ADHD in the United States. There is a possibility that this increase in prescribing the medication could lead to an increase in its illicit use as well.⁴⁶⁷ The US Food and Drug Administration has created a website to divulge the associated risks associated with Adderall and Adderall XR. This website is in response to attention of the risks associated with prescription stimulants and possibility of adverse effects.⁴⁶⁸ More troubling than side effects may be the potential for abuse and dependency these drugs pose.

4.8.3 Potential for abuse

There is also a potential for dependency or abuse of these medications. Stimulants are schedule II controlled substances.⁴⁶⁹ Ritalin and Adderall both have a high potential for abuse and addiction in relation to the part of the brain involving motivation.⁴⁷⁰ Stimulants can prove dangerous if not taken as prescribed. For instance they are to be taken orally only; however it is becoming more common for pills to be crushed and snorted, taken intranasal. Even for those who do not intend on this, this possibility of leading to a serious addiction is not an uncommon occurrence.⁴⁷¹

For those who take the medications to treat ADHD at a regular dose, side effects are generally mild.⁴⁷² For those with ADHD, the therapeutic effects of stimulant medication work by increasing levels of catecholamine in the prefrontal cortex and the cortical and subcortical regions of the brain. This is the mechanism responsible for improved cognition and behavior for individuals who have ADHD.⁴⁷³ However, because of their effects, these drugs are appealing for other reasons.

Medications for the treatment of ADHD are amongst the most highly sought medications by students. The primary method to obtain the drug is to purchase from someone who has a prescription for stimulant medication in the treatment of the disorder. The safety concerns for taking medication without medical monitoring include possible dangers from other medication and alcohol interactions, abuse potential, and adverse physical or psychological events. The greatest risks of stimulant medication are the most dangerous side effects of these drugs such as stroke, cardiac events and hypertension.⁴⁷⁴ How ADHD medications affect the human brain is also an important consideration.

4.8.4 Drugs and development

These medications are directly involved with the most complex organ in the human body, the brain. Therefore the risk of unintended side effects is critical to bear in mind as they could be very consequential. This is especially the case as these are otherwise healthy individuals where the risks may outweigh the benefits for some. Medications taken by young people with parts of the brain still in stages of development could have the possibility for unknown long term effects.⁴⁷⁵

In animal research there are conflicting points about the use of stimulant medications and how these may apply to humans. Chronic administration of stimulant medication in young animals can have an effect into the animal's adulthood. Some studies suggest a positive effect, such as modifications in the reward-related circuits which into adulthood could mean a better self-control. Conversely, some research indicates reward related areas of the brain have biochemical changes in adult mice akin to those which are associated with cocaine use. These were findings that led the U.S. National Institute for Drugs Abuse to express concern that using stimulant medication for nonmedical reasons could lead to addiction.⁴⁷⁶

Medicine's and child/adolescent psychiatry's dependence upon the pharmaceutical industry runs deep. Its influence through marketing and other financial means is powerful. Even the American Psychiatric Association rejected stiffer financial conflict-of-interest rules in the past, which makes it clear that it is unlikely that the industry's influence will diminish anytime soon.⁴⁷⁷ The research, development, and marketing of medications would be less concerning were it clear that these treatments are safer and more effective than psychosocial alternatives. Medications are FDA approved, thus

sufficient data shows they are safe and effective, psychosocial treatments have no such approval equivalent. Nevertheless, there are ongoing concerns about the drug approval process and as a result about drug safety and effectiveness. These concerns are not exclusively limited to drugs used to treat children diagnosed. They also concern the impact of medication on the developing brains and bodies of children. They thus expand the ethical obligations that physicians and parents have to minors for whom they are making treatment decisions.⁴⁷⁸

The DSM-5 has been changed and expanded to include a broader population who can now be diagnosed with ADHD. The DSM also favors a medical (drug) model of treatment. A biological test of ADHD is lacking as well as biological markers for the disorder. The diagnosis of ADHD heavily relies on clinical judgment. There is also ambiguity whether ADHD is considered a physical disorder of the brain or a mental disorder. All of these unclear factors can create the condition to be more open to disease mongering. ADHD is thought to be over-diagnosed, medicalizing normal childhood behaviors into psychiatric conditions, and for the first time now includes adults in the pool who can be diagnosed. This ever broadening condition means more and more children and adults are being diagnosed with ADHD. This trend has extended beyond the United States as other nations look to the DSM as the standard of treatment of ADHD. The global consumption of drugs used to treat ADHD is on the rise. These are powerful drugs that have the potential for serious side effects or even abuse. The culmination of all of these areas raise ethically challenging questions, in particular –is ADHD a condition in which disease mongering occurs? Therefore, given the increasing rates of diagnosis and ever growing population meeting criteria for ADHD it is suspect that disease mongering

is taking place. Therefore, it is necessary to assess through an ethical framework. The UNESCO framework will be put into place to examine disease mongering with ADHD.

4.9 Analyzing disease mongering in ADHD using the UNESCO framework

The pharmaceutical industry may promote itself as being humanitarian in its effort at combating disease, but mounting evidence is more suggestive of the commercial interests of the industry. The industry appeals to the individual through advertising but this hides the real motive of simply creating more drug consumers. The impact is not just the individual, but society as a whole. Within the UNESCO framework the relevant principles in respect to analyzing disease mongering include several articles with a focus on the individual, society, global and future generations. These include the following: Article 5 is a focus on autonomy and individual responsibility. Article 8 is respect for human vulnerability and personal integrity. Article 10 is equality, justice and equity. Article 14 is social responsibility and health. Article 15 is sharing of benefits. Article 16 is protecting future generations.⁴⁷⁹

4.9.1 Article 5 Autonomy and individual responsibility

Article 5 has a focus on autonomy and individual responsibility. Article 5 states, “the autonomy of persons to make decisions, while taking responsibility for those decisions and respecting the autonomy of others, is to be respected. For persons who are not capable of exercising autonomy, special measures are to be taken to protect their rights and interests.”⁴⁸⁰

Ultimately people of sound mind and uncompromised by their condition are free to choose as they will medically, which the article would support. But, in the case of disease mongering in ADHD, the pharmaceutical industry is at times promoting disease and medications that are can be unhelpful, unnecessary and/or may create unnecessary harm. This puts autonomy in jeopardy.

ADHD is suspect to disease mongering by its explosive rate of diagnosis, expansion into adults, and broadening of DSM-5 criteria to include younger children. Allen Frances, DSM-IV chair, stated in 2014, “Drug companies were given the means, the motive, and the message to disease monger. They succeeded beyond all expectations in achieving a triumph of clear advertising over common sense”. Universal acknowledgment exists that ADHD is being diagnosed in too many children and both ends of the spectrum –preschoolers to adults- are now included. The greatest success is marketing the condition of ADHD and not great science by drug companies.⁴⁸¹

The goals of informed consent are protecting patients and supporting autonomy.⁴⁸² Thus, autonomous decisions are based on the notions of informed consent: competency to act, disclosure, understanding this disclosed information, and acting voluntarily.⁴⁸³ Autonomy of the individual to freely take the drug exists, but it is based on industry facts which may be inaccurate or misleading. This alone compromises the autonomous choice on an individual.

The industry also essentially uses autonomy as a selling point in its advertising. Ads encourage patients, who are framed as consumers, to “talk to their doctor”. Over the last decade, evidence-based approaches to the management of psychiatric illnesses have incorporated the concept of shared decision making between clinicians and patients, a

shift from a paternalistic model where a physician makes decisions for patients. However, this collaborative model only can work if there is transparency and informed consent. Risks and benefits must be disclosed. Any alternatives to the proposed treatment discussed. Disclosure of important information is critical, too.⁴⁸⁴ In the case of ADHD, school teachers are promoted to encourage discussions with parents in order for them to seek possible treatment for their child. The disease mongering which takes place in the case of ADHD compromises autonomy in that it exploits its notion to encourage more people to seek drug treatment and undermines the ethical concept by not providing accurate information about conditions.

It is also critical to uphold the article of autonomy to make informed decisions and uphold the autonomy of those who are unable to make their own decisions. Children fall into this category as a vulnerable population who have the ability to have their autonomy compromised. The misleading ads to parents and teachers and the push by the industry to physicians to medicate more and more children make the disease mongering especially concerning which leads to Article 8.

4.9.2 Article 8: Respect for Human Vulnerability and Personal Integrity

Article 8 states, “In applying and advancing scientific knowledge, medical proactive and associated technologies, human vulnerability should be taken into account. Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected.”⁴⁸⁵ Often, vulnerability is defined as being at an increased risk of harm, and/or as having decreased capacity to protect oneself from harm. In bioethics, this is people's risk of harm to health, to well-being or to autonomy.⁴⁸⁶

Children in particular are a vulnerable population who are unable to fully protect their own interests. Children rely on adults and medical professionals to ensure their health and well-being. However, disease mongering associated with ADHD instead leaves children open to more exploitation. Drug company marketing can exploit parental fears that their child has a problem that needs medical treatment or parents may feel coerced by a school system (which has been influenced by the pharmaceutical industry as well) to medicate their child. There are other treatments for ADHD, such as psychosocial treatments like therapy or behavior modification techniques that can be implemented in the home or school. However, presenting this as a viable treatment plan is made less attractive or as beneficial as drug treatment. This too exploits fear of that parents are not providing their child the best possible treatment by considering anything other than medication treatment.

Children can be a big pool for the drug industry. The ambiguity of distinguishing the characteristics of childhood from abnormal ones associated with ADHD is unclear which increase vulnerability to unnecessary drug treatment. ADHD makes childhood behaviors more vulnerable to being labeled as a medical condition that is best treated with a drug treatment.

Evidence of disease mongering through misleading claims and ever widening treatment boundaries of ADHD violates this principle by exploiting children. Otherwise normal developmental behavior patterns are reframed as disease, which compromises children's integrity. The trend of the US being the country with an overwhelming number of children with ADHD compared to the rest of the world is also suspect of childhood behaviors becoming medicalized. The drugs are made to look very attractive to

conditions in which treatment boundaries are expanding, making medication the only obvious option. Other factors which may be contributing to the symptoms, such as family conditions, t are largely ignored (unless other symptoms can be used to include a comorbid diagnosis and subsequent treatment.) The sheer volume of children being diagnosed leaves them open to exploitation by the drug industry in the quest to sell more products to parents and teachers who are led to believe these behaviors are abnormal.

Fears of failure at home (for children) and at work (for adults) are exploited through advertising that gives the impression that if children take medication for their symptoms they will be more successful at school. There is an implication that those with (untreated) ADHD are at higher risk for dropping out of school, failing, or even developing substance use problems. Other comorbid mental health issues are also cited in conjunction with and ADHD diagnosis. Oppositional Defiant Disorder, Conduct Disorder, Depression and Anxiety are among notable diagnoses. This exploits fear. Article 10 examines how disease mongering in ADHD impacts, equality, justice, and equity.

4.9.3 Article 10: Equality, Justice, and Equity

Article 10 states, “the fundamental equality of all human beings in dignity and rights is to be respected so that they are treated fairly and justly.”⁴⁸⁷

As technologies have advanced and more resources are available, associated ethical problems increase too. All human beings must have their dignity, rights, and freedoms maintained when applying new technologies. Autonomy, vulnerability, and personal integrity must be respected. In order to uphold Article 10 and meet the criteria

for equality, equity, and justice, the principles on human dignity and rights, autonomy, beneficence, non-maleficence, integrity, confidentiality, and privacy must first be obtained.⁴⁸⁸

As evidenced in Article 5, the disease mongering associated with ADHD already violates autonomy, therefore Article 10 is violated as autonomy is an element associated with human dignity. Children who are overactive in schools are also automatically assumed to possess a deficit which accounts for this behavior. Behavior or classroom modifications are rarely implemented, however drug therapy is a common first solution. The fairness to going immediately to medication as a first line of treatment is suspect in justice and fairness for children.

From the perspective of justice, in the US the primary goal of treating ADHD is aimed at the individual level and treating the child. This perspective largely ignore any contextual areas surrounding ADHD such as poor school systems or method of instruction. Parents are not supported in helping their children with other techniques that aid in on-task, appropriate behavior and structural issues of schools, such as limited recess or physical activity, are also largely not considered as contributing factors to ADHD. It could be argued that ADHD medications target only the symptoms but ignore the broader social factors that may be contributing to problem behaviors. Research by Kuo and Taylor found that “green” or outdoor activities reduced ADHD symptoms in children significantly more than any other setting and the findings were consistent across age, gender, and income groups.⁴⁸⁹ To ignore other contributing factors and treatment options is an injustice. On a global level, justice is disregarded as illustrated by the increase of consumption of ADHD medication with a focus on selling more medication

for a disease that is not life threatening when drug development for illnesses such as malaria or tuberculosis are given little consideration.

4.9.4 Article 14 on Social Responsibility and Health

Article 14 is on social responsibility and health, it reads:

“1. The promotion of health and social development for their people is a central purpose of governments that all sectors of society share. 2. Taking into account that the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition, progress in science and technology should advance: a. access to quality health care and essential medicines, especially for the health of women and children, because health is essential to life itself and must be considered to be a social and human good; b. access to adequate nutrition and water; c. improvement of living conditions and the environment; d. elimination of the marginalization and exclusion of persons on the basis of any grounds; e. reduction of poverty and illiteracy.”⁴⁹⁰

With the majority of pharmaceutical industries being in the US and ADHD being one of the leading diagnoses in children, this is setting a global standard that is making pathological many childhood behavior patterns. Health is not being promoted, but disease awareness in the form of advertising is what saturates the US market, which is not intended to promote good health but to sell a product. This process drives medicalization. The US model of medicine in the DSM is also contributing to the global trend of ADHD, which is spreading. The US model is a biological/medical model for the treatment of ADHD which uses drugs as the primary means of treating ADHD in children and adults. The ICD is no longer the standard for diagnosis in other countries where it had been in the past. The ICD is much stricter than the DSM. Implementing the DSM model rather than the ICD means that more drugs will be used to treat ADHD globally.

This is also a socially irresponsible because funneling money into disease promotion is not saving lives. Reaching the highest possible health standard is at odds

when those who are taking medication, with possible side effects and other risk, may not need them. (These risks, if requiring treatment, further burden the health care system, too.) This is compromising health, not striving to improve it. The fact that health insurance, a pooled system, is being burdening with prescriptions that may be unnecessary hurts those who have drugs essential to their well-being, too. In regard to technology, this too may be a problem. One of the biggest tools in the process of disease mongering is the Internet, which is problematic because it promotes self-diagnosis. This allows anyone, students, teachers, and parents, to complete symptom checklists to determine if ADHD may be present, then seek medical treatment to validate these suspicions. These websites are sponsored by pharmaceutical companies and appear to be more of another form of direct to consumer advertising in their nature than aiding in the diagnosis of a serious brain condition. As Article 14 states, this is especially important for children. Children are the biggest target population involved in disease mongering with ADHD. Next, the violations present in Article 15 are examined.

4.9.5 Article 15: Sharing of Benefits

Sharing of benefits, Article 14, states:

“1. Benefits resulting from any scientific research and its application should be shared with society as a whole and within the international community in particular with developing countries. In giving effect to this principle, benefits may take any of the following forms: a. special and sustainable assistance to, and acknowledgment of, the persons and groups that have taken part in the research; b. access to quality health care; c. provision of new diagnostic therapeutic modalities or products stemming from research; d. support for health services; e. access to scientific and technological knowledge; f. capacity-building facilities for research purposes, and g. other forms of benefit consistent with the principles set out in this Declaration. 2. Benefits should not constitute improper inducements to participate in research.”⁴⁹¹

The standard of mental health treatment in the US has spread globally via diagnosis standard in the DSM model. The DSM model has a strong focus on treating mental illness with drugs with a focus on biology. Many countries also have physicians who are trained in the US on this medical model. These factors both contribute to the trend of more ADHD cases being diagnosed and treated in other countries. Thus, medicalized US standards are being exported. This may be a harmful trend, in particular in countries that are resource poor where funds are allocated to the treatment of behavior problems and overlooking greater structural factors that could be contributing to undesirable behaviors.

Growing evidence supports that ADHD is an over treated condition in the US thus neglecting other more serious disease domestically and globally is another factor. Devoting great resources to a disease that is being constantly expanded to generate better profit is in violation of this principle. The new science coming from the US is spreading disease mongering more so than treating life threatening illnesses and the diagnostic interventions may be nothing more than a mode of disease mongering with the case of ADHD. How all of this impacts future generations is included in the following, Article 16.

4.9.6 Article 16 Protecting Future Generations

The articles states, “The impact of life sciences on future generations, including on their genetic constitution, should be given due regard.”⁴⁹²

ADHD is ever growing and the target populations are children, the future generation. Giving powerful stimulant medications, often times without merit, may have

unforeseen outcomes on children throughout their lives. Unnecessary drugs given to children who may not need them violates the principle. In addition, the new DSM-5 criteria include more children than any other previous version as the age of onset required to meet criteria rose from age 7 to age 12. It is also being reported that toddlers are now taking powerful stimulant medications. The long term impact of these medications is not known. It remains unknown at this time, with a wider boundary for diagnosis, how this will impact an even greater number of children in the future.

4.10 Conclusion

ADHD has a long history. It began as a childhood disorder that first emerged as a diagnostic category in the 1950s. ADHD has evolved over time. Today, it is one of the most common conditions of childhood and in the latest version of the DSM-5, ADHD criteria is included for the first time as a diagnosis for adults. Along with that history there is concern that the condition is either being over-diagnosed or is turning otherwise normal childhood behaviors into medical problems which require a drug solution. There is no definitive test for ADHD or any biological markers. Rather, the diagnosis relies on the judgment of the clinician and reports from parents, teachers and self-reports for adults. It is also unclear whether ADHD is a physical disorder of the brain or a mental disorder. The DSM-5 provides an extensive overview of inattention/hyperactivity and impulsivity along with its many other features such as cultural components, the role of gender in ADHD, consequences of the condition, risk factors that contribute to ADHD, and similar and comorbid diagnoses. The new criteria has lowered the age of onset and included an adult population as well.

The disease mongering associated with ADHD includes the vast rate at which it is diagnosed, the medicalization of childhood, and the expansion into adult ADHD. Teachers, parents, and physicians all have a role and are all influenced by pharmaceutical companies in their marketing approaches which are propelled as symptom recognition of a disease that needs to be treated. The impact of this medical model within the U.S. is now disseminated in the rest of the globe, influencing the diagnosis and treatment of ADHD. The same applies to drugs, as the prescription and consumption is also globally on the rise, in part due to US influence of the medical model and drug companies' promotional push. The drugs used to treat ADHD are powerful and have potential for abuse, for those who lack the condition this is concerning. The ethical concerns regarding occurrence of disease mongering associated with ADHD are explored in the UNESCO model framework.

In summary, the articles 5, 8, 10, 14, 15, and 16 are violated when ADHD is examined in the UNESCO model. Autonomy and an individual's right to make the decision is undermined by deceptive or misleading pharmaceutical company promotional materials intended to sell drugs more so than educate the public about a condition. Autonomy is promoted by the drug industry to consumers in ads and suggestions to ask their physician about treatment options. The treatment option is almost always a drug. It is especially concerning that these choices to medicate behaviors are most often not being made by the individual but rather by parents.

Children are a vulnerable groups who are unable to protect their interests. The pharmaceutical industry targets parents, teachers and physicians to notice symptoms of ADHD and treat them medically and there is implied fear of negative outcomes by letting

the disease go unnoticed such as bad grades in school or even a path toward future deviant behaviors. Other alternatives are not suggested nor are broader social contexts that may contribute to negative behaviors associated with ADHD.

Ignoring alternative options to address problem behaviors also violates justice for those with ADHD as medication doesn't solve the broader problems that may also contribute to inattentive or hyperactive symptoms. By strongly promoting ADHD globally, more serious health conditions that threaten lives are overlooked. The strong influence of the US medical model for treatment is also contributing to the global expansion of ADHD and drugs used to treat it. The US model of the DSM is becoming the gold standard in psychiatry replacing instruments used in other countries such as the ICD which were stricter in diagnostic criteria. The influence that the drug industry has with the authors of the DSM generates concern as well.

Lastly, the target population of ADHD is children which creates concern for future generations and powerful stimulant medications. With explosive rates of diagnosis, many children being medicated and even toddlers being given these drugs, it creates a concern on how this will impact them. The new diagnostic guidelines also create concern because more children and now adults will be included to further expand drug treatment. The effects of expansion of criteria to include more children will only be known in time.

Chapter 5: Ethically assessing PMDD in the UNESCO framework

Premenstrual dysphoric disorder (PMDD), is another condition that is often used to illustrate the concept of disease mongering making it also appropriate to analyze through the UNESCO framework model. PMDD is implicated in disease mongering because it is a newly minted disease, it has never before appeared in the DSM as a diagnosis. There is criticism that PMDD does not even exist, but rather it medicalizes the naturally occurring process of menstruation.

What is now recognized as PMDD first became known as premenstrual tension in 1931, later in 1953 it was renamed premenstrual syndrome (PMS). The psychiatric symptoms of PMDD include irritability, mood swings, depression, and anxiety. Symptoms begin shortly before the menstrual period and subside at the onset of menses. The condition of PMS gained notoriety in the 1980s when used as a defense in helping a woman suffering from severe PMS be acquitted of murder.⁴⁹³

In most of the non-Western world, women report experiencing physical symptoms surrounding the time of the menstrual cycle. However, they do not believe that their emotional state at that time is abnormal or signifies a problem. It is only in the West that women hold the belief that their emotional state surrounding menstruation is abnormal and may even require professional intervention. This leads to the notion that even PMS may be a culture-bound syndrome; that is a dysfunction limited to one society but not found in others.⁴⁹⁴ PMS tends to be treated as a joke in popular culture, but, PMDD is different. PMDD is a medical diagnosis. Concerns surrounding receiving the diagnosis include being an unfit mother in a custody case or not being fit to serve political office, for example.⁴⁹⁵

PMDD is a disorder that doesn't exist in half of the world and in the past its symptoms were considered a normal part of the menstrual cycle. The ICD 10 does not recognize PMDD as a disease. Drugs used in the treatment of PMDD were approved by the FDA before its official label as a condition. The origins of PMDD are traced to the loss of patent for the drug fluoxetine (brand name of Prozac). Manufactures of the drug enrolled a group of experts, FDA officials, and PMDD was officially born. As a result, fluoxetine was relabeled and repackaged and approved for the treatment of a PMDD. The biggest setbacks for promoting PMDD came when the European Medicines Evaluation Agency refused to support the condition as it could lead to too many women diagnosed and treated for a condition which they may not have. Lilly, the drug company, stopped marketing campaigns in Europe.⁴⁹⁶

A brief history is provided to illustrate the evolution of PMDD. The DSM criteria and aspects for PMDD are also provided. Examples of associated areas of disease mongering are presented. Lastly, the condition of disease mongering in PMDD is analyzed through the UNESCO ethical framework model.

PMDD is a good choice for analysis because as a diagnosis it is particularly controversial, has heavy ties with industry, and is a new diagnosis in the DSM. An overview of the menstrual cycle is first provided to better understand how PMDD factors into the process because it is a diagnosis that includes critical time elements of the onset and offset of symptoms in relation to phases of the menstrual cycle. It also is a condition that has a medical focus.

5.1 The menstrual cycle

5.1.1 Evolution of menstruation

Despite the fact that PMDD is an illness that surrounds the menstrual cycle, menstruation as a topic is still an area that is somewhat taboo. The menstrual cycle is a biological, psychological, socially, and culturally relevant occurrence. The first menstrual cycle research conference was held in 1977 and a well-known biologist and founding member of The Association for Women in Science refused to present a keynote address because she felt that focusing on menstruation points out that women are different than men, which would be used against women.⁴⁹⁷ Menstruation was a topic which was not spoken of with comfort. At the time, ibuprofen, which was not yet an over-the-counter drug, was approved for treating abdominal cramps that occur with menstruation. In addition, it was inappropriate to address menstruation on television or radio commercials, and surely menstrual products as well. Today, menstruation is a topic which is socially more acceptable to discuss, however it is still often referenced in vague, indirect terms.⁴⁹⁸

Menstruation is often associated with shame as well. The products advertised for menstrual products are “hygiene products” suggesting that the process is unclean and to be overcome. Girls are taught the process of menstruation as a medical event and it is only normally a topic of conversation once the process has begun. There is fear and intolerance associated with menstruation, as menstrual products often promote secrecy or discreteness stating that “nobody ever has to know you’re having your period” as if it is a shameful or mortifying event. The name of a menstrual period is even given codes such as “visitor” to serve as a reminder that it is unspeakable.⁴⁹⁹

It has also taken quite some time for issues that surround women's health to be given proper attention. Hormone therapy is an example. This was heralded as a beneficial treatment for women in menopause presented by drug ads as a fountain of youth.⁵⁰⁰ The drug Prempro is one such example, the drug was a combination of estrogen and progestin. Studies emerged that the drug did not help women with positive effects but rather research indicated that it exposed them to unanticipated negative side effects. It took from 1997 to approximately 2002 for this evaluation to solidify. In addition, this kind of outcome took all of the major feminist health groups raising questions in regards to the effects of long-term hormone therapy; women in health care, universities, and the community to be population for women's health, and women in Congress to demand attention for women's health issues.⁵⁰¹

In 1993, there was a Premenstrual Symptoms symposium held by the American Psychological Association (APA). At this conference, the new condition of PMDD was emerging and was discussed. PMDD was differentiated from Premenstrual Syndrome (PMS) and by PMS contributing to the worsening of symptoms of an already existing depression. At the conference it was presented that PMDD was rare and affected few women, and further elaboration was presented on the concerns of potential over-diagnosis for PMDD. Concerns from feminist thinkers felt that a patriarchal context of PMDD would occur, which disregards the woman's knowledge of menstruation since men "see" it in their practices. Some feminists sought to instead validate women's experiences and refuse to over-medicalize women's bodies. These researchers viewed the symptoms of PMDD in a holistic perspective and not a disease manifestation. There is an understanding of many issues in a woman's life that have impacts rather than simply just

the effects of hormonal changes that occur with the menstrual cycle.⁵⁰² However, as is the case in present day, PMDD is now presented as a mental health diagnosis. It is helpful to understand the physiology of the menstrual cycle as it is critical in the diagnosis of PMDD. This is next investigated.

5.1.2 Biological process

Females experience menstrual periods that occur during a monthly menstrual cycle. This natural occurrence provides hormones that aid in health and also prepare a body for the possibility of pregnancy. A cycle begins on the first day of a menstrual period and continues until the first day of the next period, which on average is 28 days. The fluctuation of hormones each month control the menstrual cycle. In the first phase of the menstrual cycle, estrogen rises. Estrogen is responsible for the uterus to thicken and grow, which is where an embryo is nourished should pregnancy occur. Concurrent with the uterus is growing, an egg or ovum in one of the ovaries begins to mature. At around day 14 of the cycle, sometimes called the follicular phase, the egg leaves the ovary during a process called ovulation. At this time, or luteal phase, the egg travels via the fallopian tube to the uterus. Hormones increase to prepare the uterine lining for pregnancy, which is most likely to occur during the 3 days before or on the day of ovulation. If an egg is fertilized by a sperm cell, it attaches to the uterine wall. If it is not fertilized, the egg will break apart. Hormone levels drop and the thickened uterus lining is shed during the menstrual period.⁵⁰³ A brief overview of the condition known as PMDD is next provided.

5.2. PMDD defined

Premenstrual dysphoric disorder (PMDD) is a severe form of premenstrual syndrome. It is characterized by depression, anxiety and other physical symptoms that impair function and impact quality of life. Those with PMDD are reported to have comorbid mood and anxiety disorder and are at an increased risk of suicide. The age of onset is early adulthood, however, proper diagnosis and treatment often does not begin until after 30 years of age. The etiology is still debated. In the luteal phase, abnormal estrogen signaling and an altered expression of the genes involved in neurotransmitter pathways have been described.⁵⁰⁴

The twelve month prevalence of PMDD is between 1.8% and 5.8% of menstruating women. Retrospective ratings tend to be dramatically inflated in comparison to the completion of daily ratings. The estimated prevalence, however, based on daily record of symptoms for 1-2 months may be less representative, as those with most severe symptoms may be unable to tolerate the rating process. The most exact estimate of PMDD is 1.8% of women whose symptoms meet full criteria without a functional impairment and 1.3% for those meeting criteria with functional impairment and without co-occurring symptoms from another disorder.⁵⁰⁵ The symptoms of PMDD are physical and psychological in nature.

5.3 Symptoms of PMDD

PMDD, like premenstrual syndrome, has a pattern of symptoms linked to the menstrual cycle. The most pronounced symptoms occur in the late luteal phase and

decrease during the menstrual period. Women are symptom free during the follicular phase of the menstrual cycle.⁵⁰⁶

PMDD has essential features. These features are mood swings, irritability, dysphoria, and symptoms of anxiety that reoccur at the premenstrual phase and remit at onset or shortly after menses. In addition, behavioral and physical symptoms are present. The symptoms must have been present for most cycles during the past year and interfered with everyday functioning. The intensity or expression of symptoms may be tied to social or cultural background of the affected woman, family perspectives, as well as more specific factors such as religious beliefs, social tolerance, or female gender role issues. Symptoms of PMDD tend to peak around the time of the onset of menses, it is not atypical for them to remain for several days after the onset of menses. The follicular phase of the menstrual cycle must be symptom free. The core symptoms of PMDD are mood and anxiety, however physical symptoms are also common. However, physical symptoms alone in the absence of mood and/or anxiety symptoms are not enough to meet criteria for diagnosis. Symptoms of PMDD are comparable to another disorder, such as depression, in their severity, however not in their length of time. A provisional diagnosis of PMDD requires at least two symptomatic cycles.⁵⁰⁷

The symptoms of PMDD should be recorded. This involves the use of daily ratings scales, for at least two menstrual cycles where a woman is symptomatic. However, if ratings are not collected as such, a provisional diagnosis can be made. This should be noted as “PMDD provisional”.⁵⁰⁸ The DSM-5 diagnostic criteria must be used in order to make the diagnosis of PMDD.

5.4 DSM-5 criteria for PMDD

5.4.1 Diagnostic Criteria A

PMDD has a complex and lengthy set of criteria and it is divided into Criteria A, Criteria B and Criteria C. The criteria for A include the following, for the majority of menstrual cycles, at least 5 symptoms must be present before menses onset. The symptoms must begin to improve shortly after the start of menses. The symptoms must be absent in the week after menses.⁵⁰⁹ The DSM requirements of Criteria B is the next segment.

5.4.2 Diagnostic Criteria B

Criteria B for PMDD also includes its own subsections, 1-4. One or more of the following symptoms must be present. 1. Marked affective lability (for example, mood swings, feeling fearful all of the sudden, or a heightened sensitivity to rejection), 2. Increase in personal conflicts or marked irritability or anger, 3. Noticeable depressed mood, feelings of hopelessness, or self-deprecating thoughts, or 4. Clear anxiety, tension, and/or feelings of being on edge or keyed up.⁵¹⁰ After that, is the DSM diagnostic criteria for section C.

5.4.3 Diagnostic Criteria C

Criteria C includes 7 subsections. For these, one or more must additionally be present to reach a total of 5 symptoms when combined with those of Criteria B. These symptoms include: 1. Decrease in the interest of usual activities (school, work, hobbies, or friends), 2. Subjective difficulty concentrating, 3. Lethargy, being fatigued easily, or a

clear loss of energy, 4. Marked change in appetite such as eating too much or lack of appetite, 5. Insomnia or hypersomnia, 6. A feeling of being overwhelmed or out of control, or 7. Physical symptoms that include breast pain or swelling, joint or muscle pain, being bloated or the feeling of weight gain. An important note is that the symptoms of Criteria A-C must be present for most menstrual cycles that occurred in the preceding year.⁵¹¹ Lastly, are the diagnostic criteria for sections D-G.

5.4.4 Diagnostic Criteria D-G.

Additional criteria also exist. These are Criteria D-G. Criteria D states: the symptoms should cause a significant distress or interference with daily life. This includes work, school, activities, or relationships with others (for example, avoiding social activities, not being as productive or efficient at work, school, or home). Criteria E states that this disturbance is not due to an aggravation of an already existing disorder such as depression, panic disorder, dysthymia, or a personality disorder. Symptoms can, however, co-occur with any of these disorder(s). Criteria F references Criterion A stating that Criteria A should be confirmed by the use of daily ratings during at least two symptomatic cycles. However, diagnosis may be confirmed conditionally prior to these ratings. Lastly is Criteria G, stating that symptoms should not be as a result of the effects of substance use such as drug abuse, another medical treatment, or medication; also as the result of another medical condition, such as hyperthyroidism.⁵¹² PMDD is mainly treated with SSRI drugs.

5.5 Treatment

Selective serotonin reuptake inhibitors (SSRI) drugs are most common in North America and the UK follow the US guidelines for treating PMDD with these drugs. In addition, hormones and analgesics are also used in treatment in North America and the UK. Germany and France, for instance, use hormonal treatment and a plant extract, Vitex agnus-castus, which is considered alternative treatment in much of the rest of the English-speaking world to treat PMDD.⁵¹³ To distinguish from PMDD, PMS is presented.

5.6 PMS

5.6.1 Symptoms

PMS differs from PMDD in the following ways. First, a minimum of five symptoms is not required. Second, there is no requirement of affective symptoms for women who have PMS. PMS may be more common than PMDD, however prevalence varies. PMS shares the same symptoms during the premenstrual phase of the menstrual cycle, however it is considered to be less severe. The presence of physical or behavioral symptoms in the premenstrual phase, without required affective symptoms, likely meets criteria for PMS and not PMDD.⁵¹⁴

Premenstrual Syndrome includes symptoms that occur days prior to the onset of menses. The most common symptoms include fluid retention, most often in the breasts and abdomen, acne, food cravings, muscle or joint pain, fatigue, sudden bursts of energy, irritability, anxiety, tension, sadness, moodiness, changes in bowel habit, insomnia, an altered sex drive, and a feeling of a loss of control. There are many more changes that have been reported in conjunction with the onset of menses, this is not an exhaustive

list.⁵¹⁵ Existing medical conditions can also be exacerbated in the premenstrual phase, but do not cause them; allergies, asthma, sinus problems, and migraine headaches are a few examples. Many women also label symptoms as being associated with PMS. For example, some women who report as suffering from PMS have a stressful job, financial strain, an unsatisfying marriage, family conflicts, or an overly busy schedule. There is no single organic cause associated with PMS, it is vaguely and variously defined, and may safely be stated PMS is beyond diagnostic capacities of current medicine.⁵¹⁶ Because PMS is so vague, it contributes to every woman having her own experience with it, encourages self-diagnosis, and this validates the construct that women are akin to having a “Dr. Jekyll’s elixir” effect. That is, women’s hormones are compared to this potion that can turn them from being placid to enraged, such as Dr. Jekyll and Mr. Hyde.⁵¹⁷

Premenstrual Syndrome is a condition for which there is no diagnostic basis, but more so, it relies on subjective symptom reports. PMS can affect women from all areas of the world with a general consensus that it is a common condition. There are a multitude of definitions, diagnostic rubrics, and methods for PMS. Most women know when they experience it, and others may be able to identify women who are experiencing it. PMS is poorly understood, even within research as results often prove treatment is no better than placebo. There are over 65 different rating scales for PMS and over 150 symptoms can be included.⁵¹⁸ Essentially, two women with completely different symptoms can both be diagnosed with PMS. Few women also seek clinical help for dealing with PMS. PMS may not be considered a dysfunction but an uncomfortable and inconvenient phenomenon which drags around the menstrual cycle as a result of phase shifts. This could be different for each woman. Thus, diagnostic criteria are not every useful and

instead the locus of control in treating symptom and obtaining relief should rest with the individual woman.⁵¹⁹ Next, the problems that have historically surrounded the menstrual cycle are presented which have led to PMDD being recognized as a distinct mental health diagnosis today.

5.7 Menstrual Problems

5.7.1 History

Cultural beliefs that women are unpredictable, unstable, or emotionally capable for certain social situations date back to ancient Greece. Menstruation, an obvious difference between the sexes, came to be considered the “proof” of this divide. PMS is also considered a social construct that began around the time of the Great Depression when Robert Frank, a gynecologist from the US, published an article on “Premenstrual tension.” Frank wrote how his female patients complained they felt tense or irritable, or cried easier than usual. He also noted that their behavior was “foolish and ill considered” in its action. Frank’s article contributed to Victorian era notions that intellectual exertion may be affected by menstruation thus contributed to the notion women should not be in the workforce and jobs are better left to men.⁵²⁰

Premenstrual syndrome first appeared in two medical papers in 1931, one paper by German psychoanalyst Karen Hornay and Frank, both of which were very influential.⁵²¹ The disorder was first categorized in 1931 known as premenstrual tension. In 1953, it became known as premenstrual syndrome. Kathrinia Dalton, a British endocrinologist coined the term PMS in 1964. Dalton’s work greatly expanded on the symptoms of PMS as well. Coining a term also contributed greatly to the functioning of a

woman's body becoming a medicalized condition, articulating specifically that a menstrual cycle was a problem that needed to be solved. PMS also become more well-known and gathered more attention in the 1970s as a result of the Women's Liberation Movement. Medical and behavioral science took note.⁵²²

There were three well-known court trials in the UK in the 1980s. In 1980 and 1981, defendants pleaded that they had diminished responsibility with success for crimes of manslaughter, arson, and assault. This was widely publicized.⁵²³ The details of the crime, by today standards would not have likely been accepted in the courts. One woman had a history of mental illness and criminal activity including violent acts. She stabbed a co-worker to death during an argument. The other case by today's standards would likely be classified as traumatic stress. A battered woman killed her boyfriend by running him over with a vehicle. This occurred after a violent argument and drinking alcohol heavily. The substantial coverage of the trials introduced many people around the world to the concept of PMS.⁵²⁴ Shortly after this time, PMDD was noticed in the mental health community. This is how the connection between a biological process of women of childbearing age and the connection to mental illness first began.

5.7.2 In connection with mental health

Difficulties surrounding the menstrual cycle and a mental health connection began in the 1990s and were aided by a US psychiatrist, Robert Spitzer, who engineered the DSM-III upheaval. Spitzer was invited to several conferences on PMS. At the time, Spitzer knew little information on the topic of PMS, but he noted the interest PMS gathered in the mental health community. Spitzer was the chair of the DSM-III work

group revision and felt it was his obligation to include the concerns of mental health professionals in regard to PMS. Therefore, a PMS advisory committee was established. The possible re-classification of a menstrual cycle related problem into a mental disorder created a great deal of concern within the psychiatry community. There was distress that doing so would stigmatize a normal function of a woman's body.⁵²⁵

The possible inclusion of LLPDD, late luteal phase dysphoric disorder,(which is now PMDD) in the DSM created great controversy and massive protests at the APA conferences in 1986 by the Association for Women in Psychology. Letters and petitions against LLPDD's inclusion represented over six million people. Spitzer put forward a compromise, LLPDD would go into its own special category, and appendix, which was an area designed for topics needing further study.⁵²⁶ Despite the concerns, the condition was recommended by the PMS advisory committee to be included within the manual.⁵²⁷ The process began with an inclusion of the disorder in the DSM-III-R.

5.8 DSM-III-R and PMDD

When published in 1987, a severe form of premenstrual syndrome called late luteal phase dysphoric disorder (LLPDD) and diagnostic criteria was included in the DSM-III-R in appendix A. It was not an official disorder. Mentioned earlier, the appendix was a section for criterion sets and axes provided for further study. Moreover, the DSM appendix was principally created in order to contain the new syndrome of LLPDD.⁵²⁸

At first, it was considered a small victory that it would only be included in the appendix. However, when the manual was published there was concern. LLPDD had a diagnostic code, a title and symptom list, and a cutoff point (number of criteria that must

be met).⁵²⁹ LLPDD placed emphasis on timing and severity of symptoms. There was a precise beginning of symptoms and endpoints of symptoms in accordance with phases of the menstrual cycle.⁵³⁰ It looked like any other category in the main body text. In addition, the appendix did not state that this label should not be applied to patients. Lastly, the category was ultimately listed under the Mood Disorders section in spite of the author's assertions that it was not.⁵³¹ Work would begin for another revision of the DSM with the DSM-IV, and more changes for LLPDD.

5.9 DSM-IV and PMDD

DSM-IV work began soon after the publication of DSM-III-R. The LLPDD workgroup was formed and recommendations were made to have the diagnosis included in the DSM-IV. There were differing opinions on the topic. Some argued it should be left in the appendix, others felt diagnosis should be moved into the main manual, and some felt it should be eliminated completely.⁵³²

Early 1990s research by the LLPDD subcommittee began work on LLPDD. Through a widespread literature review, they found that very little research supported such an entity as premenstrual illness and the relevant research was preliminary and methodologically flawed. The committee failed to mention that carefully done research found that the disorder of LLPDD did not exist.⁵³³

Senior psychiatrists reviewed and then suggested LLPDD remain and be kept in the appendix. Earlier, in 1988, as DSM-IV was underway, a psychologist, Paula Caplan was asked to be a part of the work group on LLPDD as an advisor. Caplan soon severed ties as she felt her scientific input was not wanted. But later, she became aware of the

decision to retain LLPDD in the appendix and argued that menstrual related distress should not be classified as a mental illness and began a campaign against its inclusion, which proved unsuccessful. LLPDD was renamed to PMDD and kept in the DSM.⁵³⁴

Methods to measure the disorder were needed. The DSM-IV workgroup on late luteal phase dysphoric disorder suggested that ratings instruments be implemented to determine the real prevalence of the disorder in the general population of women. This was because previous work had wide ranges from 7% to 54% of women depending on study methods and diagnostic algorithms.⁵³⁵

The workgroup suggested the use of daily ratings to improve accuracy of diagnosis by confirmation of the timing of symptom onset and offset. For the DSM-IV, late luteal phase dysphoric disorder was renamed “premenstrual dysphoric disorder” and the diagnostic criteria were only slightly modified. Newly named PMDD was included in the appendix of the manual. The workgroup felt more work was still needed for PMDD to be its own distinct category included in the DSM manual, specifically data on prevalence, and specific criteria were necessary. All categories and diagnoses were reviewed for the process of creating the DSM-5.⁵³⁶ The detailed process of inclusion as a distinct entity in the DSM is discussed below.

5.10 DSM-5 inclusion process of PMDD as a distinct category

Approximately every 12-18 years the DSM is revised and advancements in knowledge are implemented into an updated version. The DSM-5’s revision began in 2006. A Mood Disorders workgroup considered the changes to this category in the DSM. The mood disorders group was broken down into subgroups, one of which was the

PMDD sub-workgroup. Each workgroup was permitted to consult with outside “advisors” but chairs were to forgo any industry honoraria. The PMDD group was headed by Kimberly Yonkers and included experts in the field of PMDD.⁵³⁷ There were eight individuals from different countries including United States, Canada, Sweden, and United Kingdom, six of whom were experts in PMDD or reproductive mood disorders. This group examined criteria and previous evidence that was emerging regarding the prevalence of PMDD, impairment and course of the disorder, and treatment response differences from other mood disorders in the DSM. After a literature review, the group concluded that PMDD should be moved from the appendix of the DSM and be included as a diagnosis in the Mood Disorders section.⁵³⁸ To be included as an independent category in the DSM manual, there are requirements for a diagnostic category.

5.11 Inclusion into the DSM

To be included in the DSM-5, a category must have sufficient empirical support. This includes that it be distinct from other disorders, has antecedent validators (such as familial aggregation), concurrent validators (such as biological markers), and predictive validity (with respect to diagnostic stability, ability to predict the course of the illness, and response to treatment).⁵³⁹ These specific areas will be examined in detail.

5.11.1 PMDD as a distinct diagnosis

Clinical and epidemiology studies show that some women consistently have distressing symptoms surrounding their menstrual cycles. The prevalence varies among populations assessed and research methods, however the pattern of symptoms makes

PMDD distinct from other disorders –onset occurs in the premenstrual phase and had a pattern of onset and offset that recurs predictably. Symptoms for PMDD may overlap with those of other mood disorders but are different than other mood disorders. For example, rather than depressed mood or no interest in pleasurable activities, with PMDD there is irritability and mood swings. Irritability and mood swings may be common with bipolar depression, however what makes the symptoms distinct with PMDD is that they are in conjunction with phases of the menstrual cycle. Physical symptoms such as bloating and breast soreness are unique and are the most reported symptoms of women who have PMDD. The treatment of PMDD is similar, and different, to other mood disorders. Treatment with SSRI drugs is similar to depression and anxiety, however for treating PMDD, SSRI drugs prove to be more effective than noradrenergic agents indicating a shorter onset of action. Oral contraceptives are also effective in treating PMDD and there is no indication they would be effective in treating other mood disorders.⁵⁴⁰ Next, another distinction, antecedent validators, is examined.

5.11.2 Antecedent Validators

Family grouping of premenstrual symptoms is due in large part to genetic factors and has small, if any, environmental roots. PMDD has been found in the US, Canada, Europe, India and Japan, thus it is not bound by culture. PMDD rates between Caucasians and African Americans are comparable and remain stable over time. As is the case with other psychiatric disorders, other variables such as the physical and mental responses to stress have been examined with PMDD. Further research is needed to confirm, however there is some suggestion that personal trauma and change of seasons may have impacts

on PMDD. A major depression is the most frequently reported past psychosocial disorder in women who report to have PMDD. Some women with PMDD may have been reported to have had depression in the past rather than PMDD, which is an important consideration. Next, are concurrent validators.

5.11.3 Concurrent validators

There is no biomarker that is associated with PMDD, however due to onset and offset of symptoms the role of hormones has been examined. However, there is no positive findings in relation to hormones of women with PMDD and those without it. Some studies suggest a correlation between symptom severity and levels of estradiol, progesterone, or neurosteroids. Research by Schmidt, which offered strong evidence, suggests that some women with PMDD are more sensitive to estradiol and progesterone than control subjects; women who received Gonadotropin-releasing hormone agonist treatment experienced improvement in mood and physical symptoms and when discontinued negative symptoms returned.⁵⁴¹ Gonadotropin-releasing hormone agonist is started and when normal hormones –estradiol and progesterone- are added back this triggers negative affect in women with PMDD but not in healthy women. The suggestion is that women with PMDD are more sensitive to normal hormonal fluctuations.⁵⁴²

Neuroimaging studies are in early stages with regard to PMDD. There is some evidence to suggest differences in neural network activation, glucose metabolism, and neurotransmitter concentration potentially with women who have PMDD and healthy controls. There is also some evidence of differences in cortical activity or physiological arousal in women with PMDD in contrast to comparison subjects. In addition, concurrent

validity also includes aspects between a specific disorder, in this case PMDD, and other psychiatric disorders. The disorder must be distinct, even if similar. PMDD requires symptoms be limited to the luteal phase of the menstrual cycle, however those with a primary depression for example, report worsening of their depression symptoms during this time and women treated with tricyclic antidepressants improved in respect to symptoms of depression, but not PMDD.⁵⁴³ The next requirement to be included in the DSM as a distinct diagnosis are predictive validators.

5.11.4 Predictive validators

PMDD criteria have shown to have diagnostic stability. First, to meet PMDD criteria, women must have the required pattern of symptoms in at least half of their menstrual cycles in the previous year. Charting of symptoms is not required. However, in studies that required daily monitoring of symptoms, appropriate symptom patterns have been documented across 2 to 3 months; the types of symptoms were consistent as well. Data on symptoms of PMDD from the DSM-IV workgroup was confirmed by analysis of data on daily symptom ratings and confirmed those listed in the DSM-IV. The DSM-5 workgroup also analyzed epidemiological and clinical cohorts of women who completed daily ratings which confirmed symptom clusters of the DSM-IV. In predicting the course of PMDD, the peak of severity for the most severe symptoms occurred either the day before or the day of onset of menses and continued through the first two to three days of menstruation. The onset and course of illnesses should be predictable over time. After treatment is ceased, symptoms of PMDD return, which suggests PMDD is predictable. As long as women are premenopausal and PMDD is already established, symptoms are

likely to return if they are not treated. It is not until either menopause or hysterectomy that the symptoms of PMDD cease.⁵⁴⁴

Lastly, one of the strongest predictive validators of PMDD as a distinct disorder from mood disorders is the response to SSRI treatment. A meta-analysis of SSRI use in treating PMDD demonstrated consistent response quickly unlike other psychiatric conditions. The use of oral contraceptives was also beneficial.⁵⁴⁵ SSRI drugs are effective as a first line drug therapy in treating PMDD. Fluoxetine was the most effective. Treatment can be effective in a few days to within one menstrual cycle.⁵⁴⁶

The combination of PMDD being a distinct category in the DSM was confirmed by antecedent validators, concurrent validators, and predictive validators. Therefore, it is deemed as a distinct illness from all others in the DSM. The importance of this is next explored.

5.12 Benefits of PMDD being including in DSM-5

The aforementioned areas are the validators of including the diagnosis of PMDD as a new, distinct diagnosis in the DSM. Benefits are that now research for the condition can have more stringent criteria for clinical trials as well as studies on the pathology of PMDD. Also, now that it is in the DSM, the FDA is able to approve drugs to be used in the treatment of PMDD. Women with PMDD can also represent a new group not represented well by other diagnostic categories. With clear boundaries, women's complaints regarding associated symptoms cannot be dismissed by medical providers. Another benefit is that accurate data on treatments and services of treating PMDD can be obtained. Having its own code is beneficial rather than being coded as depression not

otherwise specified (NOS). PMDD as a distinct disorder paves the way and encourages new treatments for the disorder as well. The DSM-5 workgroup felt PMDD as an illness had matured to the point of including in the DSM, a move that in itself further legitimizes the condition as well. The DSM-5 workgroup recognizes the concern of PMDD being included, citing claims that it medicalizes menstruation and since it only involves women could suggest that women are unable to perform activities during the premenstrual phase of the menstrual cycle. One group addressed concerns and stated that PMDD only impacts a small group of women and it is inappropriate to generalize the condition to all women.⁵⁴⁷ The group also points out that it would be clearly stated in the DSM that only a small number of women are impacted and that the overall health of women with an empirically supported diagnosis would be greater than unfounded stereotypes.⁵⁴⁸

In December of 2012, the American Psychological Association (APA) Board of Trustees approved the DSM-5. This vote approved the move of PMDD to a full diagnostic category with a distinct code, historically classifying premenstrual disorders.⁵⁴⁹ Thus, the birth of PMDD took place as a mental disorder.

5.13 The value of the DSM

The DSM has a critical role in the drug approval process for new drugs as well as the regulatory process of patent extension of previously approved drugs. The FDA requires an identifiable psychiatric disorder before it considers an application of a new drug. This creates an influential environment that revolves around treatment guidelines and diagnostic criteria for authors of disorders, drug regulators, and manufactures. This explains why there was fear of industry influence on the DSM-5 revision process. With

each new revision, the APA allows more diagnostic categories. (PMDD is an example.) The first DSM included 106 identified disorders, the DSM-IV had an almost triple amount of diagnoses. It is also important to note a shift that occurred when the DSM-III was released in the conceptualization of illness. Earlier versions of the DSM were criticized as being pseudo-science, thus a strong emphasis was desired to have a manual rooted in empirical validity and reliability. This would also be a shift that benefited the pharmaceutical industry. DSM-III chair Spitzer sought a nosology that was valid and reliable, but also one that was disease oriented, not merely descriptive. Therefore, the DSM implemented the bio-psychological model. Any terms that referenced psychoanalytic theory, such as neurosis, were removed. The replacements included terminology of specific symptoms and threshold criteria in an overt way to increase diagnostic reliability. The emphasis was now on symptoms and a disease model of the DSM was adopted to solidify psychiatry as a medical profession, therefore the DSM and psychiatry became legitimized. However, this also allowed the drug industry to take unintentional roots because conditions were now drug dependent. Over time policies, financial incentives, and norms became more dependent on industry; scientific objectivity became compromised as well and a deviation from the public health nature of psychiatry and instead facts became distorted and normalized.⁵⁵⁰

To illustrate influence, in 1980 (when a disease model was adopted) the APA permitted pharmaceutical companies to sponsor symposia at its annual conference. This meant more industry money went into the APA, and the conference's content became altered, too. Ads in the APA journals, sponsoring symposia, advertising booths at conferences, and educational grants from which industry accounted for \$14 million of the

funds of APA's revenue as it rose from \$10.5 million in 1980 to \$65 million in 2008.

Despite the express link of biology to psychology, the DSM-5 lacks any biologic marker for any diagnosis. This is despite advances in neuroscience, molecular biology, and brain imaging in distinguishing normal from abnormal brain functioning. Therefore, the DSM remains vulnerable to the influence of industry.⁵⁵¹

Including PMDD in the DSM has, however, generated concerns as well. There are a variety of reasons that make PMDD questionable. These areas of concern are next explored in more detail.

5.14 DSM-5 concerns

PMDD created controversy throughout multiple revisions of the DSM and also because decades of research failed to show clear and stable empirical data that PMDD is a separate entity. There have been serious problems with the methodology of research stating that the cause of PMDD is hormonal. There are also no standardized assessments for a diagnosis, which creates criticism regarding the validity of diagnosis. Despite the concerns of validity and reliability of PMDD, the hormonal and neurotransmitter model has been heavily marketed.⁵⁵² There are multiple other concerns regarding PMDD now being a diagnosis, such as the risk of false positive diagnosis.

5.14.1 Risk of false positives

False positives are a concern with PMDD. The DSM-IV sourcebook noted women tend to seek treatment for normal premenstrual issues, label it PMS, but not meet criteria for PMDD. PMDD symptoms may better be explained by underlying preexisting

disorders, such as depression or anxiety. Women may prefer the less stigmatized diagnosis of PMDD over other psychiatric disorder diagnoses. Epidemiologically, there was a high risk of false positives for PMDD. There was also concern women would seek a diagnosis of PMDD even if they did not have the condition, despite tightly written criteria, a diagnosis could be made theoretically minus daily ratings of a woman's functioning.⁵⁵³ The validity of the diagnosis is also questioned.

5.14.2 Diagnostic validity threats

In regard to the diagnostic validity of PMDD, it is notable that the LLPDD workgroup studied PMS and not PMDD. Thus, much of the information of PMDD comes from information taken from PMS. The question was raised that how much of the psychiatric symptoms may be the normal problems of life simply exacerbated by physical pain of menstruation. The findings of differences of women with and without PMDD in regard to levels of neurotransmitters and hormones did not have strict correlations on onset and offset of symptoms. Again, symptoms are self-reported and made on this subjective basis rather than on biological markers.⁵⁵⁴ The role of gender and society was another area of concern.

5.14.3 Gender inequity

The LLPDD work group also recognized cultural implications of sex roles – concerning was the notion that women are not as prone to anger compared to men, but more emotionally receptive. Based on this assumption, women who express anger would be given a lower threshold in contrast to a man, thus considered inappropriate and

pathological. There was also concern that no research was presented on links between male hormones and violence, but easy assumptions were made for female hormones and emotional regulation.⁵⁵⁵

Feminists point out how PMDD sustains the stereotype that women are emotionally unstable, and also undermines the roles that stress, sexual abuse, and violence have in their experiences of emotional distress. The label of PMDD encourages women to view conflicts as an internal problem rather than a social one. Thus, by making PMDD a mood disorder, the role of interpersonal and contextual factors in the women's experience of emotions becomes marginalized.⁵⁵⁶

PMDD is limited to women, those against PMDD's classification as a mental health diagnosis cited that because it is a female condition, that it could be used against women. For example, it could be stated that menstrual cycles make women more emotionally unbalanced and dysfunctional each month. This claim could be supported because PMDD is an official diagnosis by the fact it is included in the DSM. PMDD could also be used as a façade to pacify women's anger for greater problems. For example, how women's reactions to abuse or mistreatment can be mislabeled as a mental problem; something that was internal and not a reaction to outside circumstances.⁵⁵⁷ The role of the pharmaceutical industry in the creation of PMDD has been strong.

5.14.4 Pharmaceutical industry's role

Psychopharmacology is the standard treatment for mood disorders. In 2006, it was reported that 100% of the individuals who served on diagnostic panels had financial drug industry ties including receipt of honoraria, speaker's bureaus, or corporate boards. Fifty

eight percent of the DSM-5 panel members, who are members serving specialized groups that make revisions, had financial relationships with the pharmaceutical industry.⁵⁵⁸

Implicit bias is a concern when it comes to financial conflicts of interest as most humans have implicit bias of which they are unaware. Because psychiatry is a medical subspecialty that does not have biological markers makes it more vulnerable to the influence of industry in regard to criteria for and measurement of diagnosis. Being transparent about industry ties, which the APA does report, still not remedy implicit or unconscious bias.⁵⁵⁹

The role of drugs in the treatment of mental illness is especially concerning for women, as they are prescribed and take psychotropic medication more than men. As is the case with PMDD, antidepressants are being prescribed to treat conditions other than depression. This is problematic when chronic side effects are a potential and this is frequently omitted in favor of touting the benefits of the drugs, creating unbalance.⁵⁶⁰ A critical time point in the formation of PMDD was when the patent of an existing medication was set to expire. Multiple agencies working together pushed forward to make sure PMDD was created so that Sarafem could be used in its treatment.

5.15 The importance of Sarafem

Those both inside and outside the mental health community feared the push to create PMDD as an illness was led by the pharmaceutical industry to create a new, large market for antidepressants.⁵⁶¹ PMDD was not yet a category in the DSM, but in the appendix, when the patent for Prozac was near its expiration in 2000. Eli Lilly, the manufacturer, applied for a patent for a drug called Sarafem during this time. Sarafem,

which was Prozac, but in a newly colored pink (or purple) colored pill, was approved for the treatment of PMDD. In Sarafem's first six months on the market, sales were \$19 million.⁵⁶² In fact, many of the PMDD subcommittee members received their research funding from Lilly, and the relationship Lilly had with the DSM is a conflict of interest. Some of the biggest studies cited supporting the notion of PMDD as a disease are also funded by Lilly.⁵⁶³

The drug was reportedly named Sarafem as a diversion for any concerns that women may have taking a powerful antidepressant. (Prozac was well-known.) It was noted how the name Sarafem is close to the word seraphim, which is an order of angels. It is also a name from the Old Testament, Sarah, who was a good woman and ideal wife, coupled with term "fem", which is shorthand for feminine. The implications of the name of the drug are important. It can be argued there were reasons why in this pharmaceutical drug marketing Prozac was renamed Sarafem, with the subtle use of a model woman and inclusion of an abbreviated form of the word feminine. This can be made clearer if hypothetical drugs such as Abrahamasc or Mosesmasc were invented to help men manage cyclical episodes of tension of angry outbursts.⁵⁶⁴

The television ads also stated that "you might think you have PMS but you really have PMDD" in a voiceover of the first commercial. This commercial featured a frantic woman in a grocery store who was angry because she couldn't remove her shopping cart from the row of carts. Another showed a woman who was scowling at a calm looking man, with a clear message that came across that he did nothing to provoke this anger. The ads did not appear to have the intention to target the small amount of women reportedly affected by PMDD. Similarly, the drug's side effects were somewhat serious with

digestive, sleep, and sexual problems as a result. These may be acceptable for a person with severe depression, but not so much for a “moderate” case of PMDD. The most concerning side effect of Prozac is the risk of suicide, which was known in internal Lilly internal memos, but not reported to the FDA prior to the approval of the drug.⁵⁶⁵

The drug ads on television stated, “PMDD affects millions of women...but the good news is that your doctor can treat PMDD with a new treatment called Sarafem”. Women were not told it was Prozac or that its patent that generated over 2.6 billion dollars in 1999, was expiring at the same time the company was seeking FDA approval for Sarafem. In 2000, Lilly received a warning letter from the FDA regarding use of that advertisement as it did not distinguish between PMDD and PMS and minimized the information of risk. Many women likely received treatment for a condition they did not have because of this ad and were not told that they were taking Prozac. Perhaps the disclosure of the true nature of the drug would have better guided women in making an informed decision regarding their treatment option.⁵⁶⁶

The repackaging of Prozac as Sarafem (the formula is the same) was helped by the financial relationship between the APA, DSM, FDA, and industry; the majority of the PMDD panel experts in the DSM-IV had industry ties. These experts were the ones who reported to the FDA with their expert opinion that PMDD was a legitimate and distinct diagnosis which was critical in the approval of Sarafem. A decade later and multiple critiques by feminists about the validity and reliability of PMDD, the industry-enabled approval of drugs used in the treatment of PMDD is now used as the justification as to why PMDD is included as a psychiatric diagnosis in the DSM-5. The financial ties of industry and the support of both the APA and FDA is why disease mongering is called

into question for PMDD. By medicalizing menstruation, then making it pathological, beginning with LLPD, then to PMDD, illustrates how the truth of science is sacrificed for corporate gain. When industry dominates, medicalized diagnoses such as PMDD hides the social context and unequal power dynamics in which emotional anguish is entrenched.⁵⁶⁷

This calls into question if the cart is driving the horse in that the drug is providing a solution to a problem yet to exist. Rather than justify the DSM revisions using new evidence, the mood disorders work group used the development of new drugs to treat PMDD as rationale for its inclusion into the DSM, specifically stated:

The inclusion of PMDD as a diagnostic category may further facilitate development of treatments that are useful for PMDD and may encourage research into the biology, prevalence, as well as consequences of PMDD...It should be mentioned that there is already some accepted for PMDD as an independent category from Federal regulators in that desired medications have received an indication for treatment of PMDD (www.dsm-5.org).⁵⁶⁸

In addition to SSRI drugs, oral contraceptives are other drugs used in the treatment of PMDD.

5.16 Other treatment

There are a wide variety of oral contraceptives to choose from, and each new pill has limited improvements over its predecessor. Oral contraceptives are also a good example of drugs used to treat other conditions rather than prevention of unplanned pregnancy. Ortho Tri-Cyclen was the first oral contraceptive to be FDA approved for treating acne. While tested and approved for acne specifically, many others are not used for the same off-label purpose. When advertising ran for the benefits of the improvement of skin with use of Ortho Tri-Cyclen, sales doubled from \$225 million to \$493 million

and it became the most prescribed oral contraceptive in the United States.⁵⁶⁹ There are also concerns regarding the research that has been done on both PMS and PMDD.

5.17 Research limitations of PMDD

The majority of research conducted on PMS and PMDD has been done by researchers in Western countries (Australia, Canada, Germany, Great Britain, the US, Sweden, and the Netherlands). The majority of research study participants of PMS and PMDD research includes European, American, middle class, college students, or married women. Study participant recruitment often takes place from university psychology classes or private OB/GYN or psychiatric practices or university hospitals. Lower income women may not have access to these options. This methods limitation is rarely mentioned, but is an important consideration in whose experiences of PMS/PMDD has been medicalized. The World Health Organization's (WHO) surveys indicate menstrual cycle complaints, with the exception of cramps, are most often reported by women in the following locations: Western Europe, Australia, and North America. In mainland China and Hong Kong, fatigue, water retention, pain, and an increased sensitivity to cold are most often reported. Chinese women rarely reported negative affect. These results could further support the notion that culture shapes variation in mood and physical symptoms as to which are most noted as problematic.⁵⁷⁰ It is also a concern that PMDD medicalizes the menstrual cycle, making it an abnormal process that requires a medical solution for treatment.

5.18 Medicalizing normal functioning

PMDD was proposed to have a diagnostic threshold of five of its 11 symptoms being met during the week before menstruation and subside in the week that follows. The symptoms were supposed to have been present the week before onset of menses, improve during the onset, and are minimal or absent in the week that follows. Symptoms include mood swings, irritability, depressed mood, anxiety, decreased interest in activity, difficulty concentrating, fatigue, food cravings, sleep problems, feeling overwhelmed, and/or other physical symptoms, such as bloating or pain. These criteria should be confirmed over two menstrual cycles, without the use of oral contraceptives, not due to mental disorder or substance use, and cause significant impairment. This is controversial because claims were simple -PMDD makes pathological normal female biological functioning –into a disease. It is difficult to distinguish normal from psychiatrically abnormal perimenses. Another concern was distinguishing items such as an increase in interpersonal conflicts with those of normal relationship difficulties. The DSM workgroup acknowledged these concerns that a disorder that focuses on the premenstrual period can medicalize normal reproductive functioning of women. The group stated that most women would not fall into the category, and that prevalence rates suggest it impacts a small number of women. However, critics argue this answer is not sufficient because those who fall outside of criteria are considered “normal”, but doesn’t consider those who may be included in criteria can be normal too, and mistakenly labeled as disordered. There was concern of a high number of false positives.⁵⁷¹

5.19 PMDD and disease mongering associated with diagnosis

5.19.1 Medicalizing menstruation

The development of disorders surrounding the menstrual cycle is a classic case of medicalizing. Menstruation is an ordinary biological process. In 1986, the process began with controversy when PMS first had a place in the DSM. This stigmatized and portrayed the time of a women's menstrual cycle as rooted in mental illness. Then came the inclusion of PMDD. PMDD as a severe form of PMS paved the way for drug treatment, as SSRIs were approved for the use of this condition. There is debate if PMDD is a real condition, but regardless of that debate, the fact remains that medicalization has clearly redefined aspects of the menstrual cycle as symptoms of mental illness and there are now drug treatments available.⁵⁷²

PMDD began to be viewed as medicalization of the lives of women beginning in the 1970s. Women have demanded that some symptoms of PMS be given treatment, yet the medicalizing aspects of the lives of women can be disempowering. PMS can propagate the notion that women are emotionally unstable at the mercy of hormones. The natural process and associated features of menstruation with given more stigma when PMDD became a psychiatric condition.⁵⁷³

Classifying premenstrual syndrome into a disease status generates controversy because PMDD is now classified as a mental health problem. There is a lack of strong empirical support for PMDD as a separate disease and despite decades of research there are crucial methodological problems with research making claims the cause of PMDD is hormonal. Reliability of diagnosis remains a problem as well; there are no standardized assessments for PMDD. There are numerous challenges to the empirical basis for the

validity and reliability of the disorder, notwithstanding the hormonal and neurotransmitter model of PMDD is heavily marketed to be treated with SSRI drugs.⁵⁷⁴

All of this also contributes to the notion women in comparison to men are more emotionally unstable, PMDD affirms this notion. Women are encouraged to interpret their moods, anger, or frustration as being related to menstrual related problems. This line of thought preserves idealized constructs of femininity in that women should not be irritable. Despite all of the advances in neuroscience and brain imagining not one biological test is included in the DSM-5 disease criteria sets. This is what makes it susceptible to disease mongering. Eli Lilly developed the blockbuster drug Prozac. The company generated controversy for their marketing techniques of the drug when they took their blockbuster, changed the color of the pill to purple, and renamed the medication.⁵⁷⁵

Eli Lilly went on to rebrand and relicense the drug as Sarafem for PMDD, which occurred around time Prozac's patent expired which meant the company would lose millions of dollars. Before Sarafem was approved around table discussion article was published that stated the effectiveness of antidepressants to treat PMDD as well as it being a clinically distinct entity. Those who were included in the roundtable discussion included doctors, FDA representatives, and Eli Lilly staff. In fact, the majority of the DSM-5 panel members for PMDD also had financial ties to the drug company.⁵⁷⁶ The FDA issued a warning letter to Eli Lilly regarding Sarafem's television advertisements which portrayed marital discord and strained parenting citing it trivialized PMDD by making no distinction between clinically normal and abnormal behavior.⁵⁷⁷ Aside from

making turning the menstrual cycle into a diagnosable mental illness, there is thought that the whole concept of PMDD was an industry creation.

5.19.2 An industry creation

The pharmaceutical industry was heavily involved in defining and publicizing PMDD. In large part because they already had a solution in SSRI drug treatment. Drug companies often work to actively change and expand conditions, especially within mental health. The industry has great power and influence which makes them an influential agent of change when it comes to defining disease.⁵⁷⁸ The influence the industry had in aiding in PMDD becoming a medical condition is strong.

Indirect drug promotion is done through raising awareness of medical conditions. This was done heavily with PMDD. This process of “disease awareness” leads consumers to believe they may have the condition, but the dangers lies in *too* many people believing they have the condition. This took place with PMDD, in 2003 the Committee for Proprietary Medicinal Products in Europe removed license for using SSRI drugs to treat PMDD. The Committee stated that there was not enough evidence to support PMDD as a disease and there was concern that too many women would be given the diagnosis resulting in inappropriate use of the medication at a large scale.⁵⁷⁹

There is concern that due to pathologizing a large minority of women and having weak validity to the diagnosis, there will be many false positives in diagnosing PMDD. It is difficult to distinguish between the disorder and normal variations of perimenses. For example, qualifying symptoms include self-deprecating thoughts and insomnia, yet for women feeling physically uncomfortable these thoughts and physical occurrences can be

normal and distinguished from a psychiatric disorder. Additionally, diagnostic thresholds may be invalidly low in the context of normal symptom variations. For example the criteria states increased interpersonal conflict but this could be the normal part of any relationship. There is not a distinguishing characteristic exclusive to PMDD.⁵⁸⁰

This leads to concern how the industry incorporates gender into its techniques. Extending the patent of the drug Prozac into the same formula of Sarafem to treat women for PMDD is an example. Despite premenstrual symptoms being unremarkable in the rest of the world the US medical model frames them as a malfunction of female biology. The Sarafem ads targeted women showing marital discord and frayed mothers, which suggested that women could find solutions to domestic problems in a pill. This marketing tactic caused the FDA to issue a warning because it essentially trivialized PMDD by blurring the line between normal behaviors and “disease”.⁵⁸¹

The DSM is the most widely used psychiatric tool in North America and its use is required for insurance reimbursement, HMOs, hospitals and clinics in the US and in other countries throughout the world. The categories of the DSM are used in both criminal and civil lawsuits. Congress based their policies on mental health parity on the criteria of the DSM. The importance of PMDD in the DSM cannot be overstated. As the sensational news trials covering PMS as a defense of murder in the 1980s made PMS a serious threat to interpersonal relationship, the same can occur with PMDD. The DSM can now lead therapists to believe that PMDD is a mental illness. The errors in methodology in research ignore the cultural construction on mental illness. The line between normal and abnormal is blurry in regards to normal or abnormal menstruation conditions, comparing these from culture to culture or from one time period to the next is difficult. It is even

evidenced in the DSM itself as old “disorders” are removed, such as homosexuality and inadequate personality disorder are removed from the text. Now, PMDD is included. Even experts cannot precisely define what mental illness is, which leads to the conclusion that mental illness is what the experts define it to be.⁵⁸²

It is due to the number of concerns regarding criteria of PMDD. This includes its existence and also the medicalization of female biology. It also is of concern that pharmaceutical industry had strong influence on both of these areas on shaping this illness. This is why analyzing if disease mongering is occurring is necessary.

5.20 Analyzing disease mongering in PMDD using the UNESCO framework

5.20.1 Article 5 Autonomy and individual responsibility

Article 5 has a focus on autonomy and individual responsibility. Article 5 states, “the autonomy of persons to make decisions, while taking responsibility for those decisions and respecting the autonomy of others, is to be respected. For persons who are not capable of exercising autonomy, special measures are to be taken to protect their rights and interests.”⁵⁸³

When the drug Sarafem was first released to treat PMDD, the fact that it was just a different colored version of Prozac was not disclosed to women. Therefore, they were not made aware they were taking a more well-known drug that was an antidepressant. This lack of disclosure speaks to autonomous choice and informed consent. The collaborative nature of medical decision making between doctor and patient can only be valid if there is transparency and informed consent’s requirements are met. This includes disclosure, risk and benefits, as well as alternative treatment options. It can be argued that

a standard for informed consent was not met unless women were told that Sarafem was Prozac and if she had idiosyncrasies regarding the use of an antidepressant, and if women were given all risks, benefits, and alternatives. To take it one step further, what is the obligation to inform women that this “new” drug is not new; or that it was industry funded and researched in regards to safety and efficacy or even the controversy within the medical community in regards to the existence of PMDD.⁵⁸⁴

Prozac was a green and cream colored pill. Sarafem was pink and purple. The color of the pill was changed to discourage physician from prescribing the generic form of Prozac fluoxetine. Trade dress is a term used to distinguish the visual characteristics of a product, such as how a Coca Cola can is immediately recognized, so it can be immediately known to consumers. With drugs, the intention of trade dress has two parts. One part is to reduce the practice of palming-off. Palming off is an act where corrupt pharmacists substituted lesser quality or counterfeit drugs to unsuspecting consumers by passing them off as name brand drugs. The druggist charged a name brand price, the consumer received a cheaper drug, and the pharmacist pocketed the difference. Because of this, generic manufactures could not make pills that looked just like the brand names. The second reason was determined by courts to serve a public health function to prevent drug substitutes that were similar to name brand drugs. Today, trade dress is a critical part of the marketing of medications by the pharmaceutical company. An example is Nexium (stated in ads and well known by consumers as the purple pill) and Viagra, (the little blue pill), both of which widely included the visual of the pill in marketing campaigns.⁵⁸⁵ The drug Sarafem was promoted to patients and physicians using language that was deceptive. Physicians information stated, “Fluoxetine was initially developed

and marketed as an antidepressant (Prozac, fluoxetine hydrochloride)” while consumers read the following, “What is the active ingredient in Sarafem? Sarafem contains fluoxetine hydrochloride, the same active ingredient found in Prozac”. Both statements are true, however the language for patients appears intentionally misleading conveying a message it has the same ingredients so to speak, but is different.⁵⁸⁶

A drug already existed to effectively treat PMDD, which was Prozac. Prozac lost its patent. However, the generic fluoxetine was available and as a generic, at a lower cost to women. However, rather than encouraging the use of fluoxetine as effective treatment with the added benefit of lower cost, Sarafem was marketed as a seemingly new medication. The intentions were initially good, to protect consumers and prevent palming off, however with improved FDA standards for generics, consumers have the right to expect a generic drug will work just as effectively as a name brand.⁵⁸⁷ Knowledge of the generic drug being available, making a pink pill appear more attractive to treat a problem that only women will experience, and presenting misleading statements that made Sarafem appear unique for the exclusive treatment of PMDD violates patient autonomy.

The role industry has in medicine has made a standard format of informed consent corrupted. It is no longer enough to cite risks and benefits of drugs. A more dynamic model is needed that is a conversation over time where doctors and patients can talk about findings and critically think the evidence of new drugs. If evidence based medicine is to have any merit and real meaning research that has commercial ties must be evaluated. It is important for patients to be made aware of the role the industry has in the APA and the influence this has in medicine. Findings that only 11-14% of new drugs are

better than existing treatments and that the number of drugs that show no improvements has increased in the last decade, some even having a greater harm than benefit ratio.⁵⁸⁸

The lack of empirical data and no standardized assessment tool for PMDD's existence also pose concerns of legitimacy of disease and of a proper method of diagnosis. Insufficient information poses a threat to autonomy.⁵⁸⁹ This lack of a diagnostic tool also encourages self-diagnosis. If PMDD is genuinely a condition that affects few women, this can serve to have detrimental impacts for those who may "think" they have the condition and seek medical help from a physician who in turns lacks the proper means to diagnose anything with a reliable measure. Next, is Article 8.

5.20.2 Article 8: Respect for Human Vulnerability and Personal Integrity

Article 8 states, "In applying and advancing scientific knowledge, medical proactive and associated technologies, human vulnerability should be taken into account. Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected."⁵⁹⁰

The principle is violated for the fact that menstruation, a naturally occurring biological function for women, is now included as a mental illness, which seems to set forth notions that woman are more vulnerable simply due to being female. The notion of PMDD also sets forth a stereotype that women are in fact somehow vulnerable because they menstruate –they can have mood swings, they can be "crazy", or if they experience anger of any sort, it cycles back into the notion it is hormone related and minimized. These same qualities, if exhibited by a man, would likely not be linked to anything

testosterone related and somehow implying they are unstable or violent because they are male.

PMDD seeks to exploit menstruation to sell medication, a violation of human vulnerability. This is evidenced by the re-branding of Prozac at the time its patent was set to expire. In order for Lilly to use the drug for something else, there needed to be a condition prior to its FDA approval. This process of “putting the car before the horse” seems obvious when the drug Sarafem came on the market to treat a new condition of PMDD. The color of the pill was changed and a new market created. It was also not disclosed that this wasn’t something new, and that women could just ask for Prozac. Next, is Article 10.

5.20.3 Article 10: Equality, Justice, and Equity

Article 10 states, “the fundamental equality of all human beings in dignity and rights is to be respected so that they are treated fairly and justly.”⁵⁹¹

There is no evidence that PMS is a condition that it is problematic, PMS varies greatly from woman to woman, it lacks any form of a diagnostic tool, or treatment. By its very definition, it is a vague and unclear experience and almost impossible to accurately measure empirically. PMDD is an extension of the ambiguous phenomenon PMS in a more serious form. Yet, PMDD somehow manages to have stringent criteria when its predecessor has none. Lack of evidence that PMDD is a distinct condition and the heavy marketing of SSRI drugs, which existed before PMDD and for the use of treating depression, were again, an easy transition to continue profit from an expiring patent. This violates article 10.

Women are not being treated justly or fairly but rather as a new profit market feeding on age old notions the female gender can be unstable or acts “crazy” because menstruation is something unique to females. Justice is also called into question for placing a large group of women into a category of having a mental illness because they menstruate. Having certain mental health diagnoses can have impacts on a woman’s ability to be a fit parent should there be a divorce and her mental status is called into question. There could also be ethical issues surrounding a woman’s capacity to make decisions being questioned because of mental illness. With the newness of this diagnosis, only time will show if PMDD would have a roles in any such instances.

5.20.4 Article 11: Non-discrimination and non-stigmatization

Article 11 states, “no individual or group should be discriminated against or stigmatized on any grounds, in violation of human dignity, human rights and fundamental freedoms”.⁵⁹²

In popular culture women’s bodily products such as menstrual fluid or breast milk are often framed as disgusting. This type of framing has stigmatized many aspects of women’s bodies, including the menstrual cycle. Superstitious beliefs about menstruation were common which led to taboos that restricted women’s behavior during the menstrual cycle. These include notions that menstrual blood could kill plants and animals, women pumping well water could cause the well to become dry if they are menstruating, menstruating women have the ability to make men become ill by their touch, even foods and drink can go bad by a menstruating woman’s touch. In the not so distant past of the 1930s, scientists believed women exuded toxins from their bodies during menstruation.⁵⁹³

Menstruation is a benign process that is essential to the production of human life, yet it evokes fear, disgust, embarrassment, and shame. The menstrual cycle creates difference between the genders. When girls reach menarche, they are treated differently than prior to menstruation. Post-menarche girls are cautioned about sexuality, and often told they are now women or grown up, and to be ladylike. Menstruation marks women and girls as different compared to the privilege of a male body. If beliefs exist that because of menstruation, women are physically or emotionally disabled, the stigma of menstruation additionally marks women as being ill, out of control, or even crazy.⁵⁹⁴

The menstrual cycle is connected to out-of-control and erratic premenstrual women. Premenstrual women are stereotyped as moody, and even possibly dangerous. Take for example women in power, such as Hillary Clinton. Her name in conjunction with PMS produces a hearty number of internet search engine hits. Likewise, when G. Gordon Liddy stated “Let’s hope that the key conferences aren’t when she’s menstruating or something, or just before she’s going to menstruate. That would really be bad. Lord knows what we would get then!” regarding then Supreme Court nominee Supreme Court nominee Sonia Sotomayor.⁵⁹⁵

Anger, frustration, or aggression are all symptoms that surround the premenstrual period and these symptoms defy the norms of how women ought to behave, therefore become prima facie proof of a disorder. This can impact social control of a woman’s behavior (for example, “feminine” women do not get angry) and contribute to cultural views concerning the unchangeable differences between men and women. In turn, these beliefs can be used as justification for gender inequality within relationships, families, institutions, and society.⁵⁹⁶

PMDD as a mental health diagnosis exacerbates any stigma that is associated with menstruation and affirms stereotypes that women are not emotionally stable during the premenstrual time. The diagnosis has the ability to contribute to the discrimination of women in the workplace. Questions could arise in hiring a woman who is “crazy” once a month, or as to whether she is capable of performing her job effectively because of this mental health condition. Likewise, the diagnosis of PMDD could be used as validation as the source of problems in a woman’s personal relationships placing more responsibility on the woman because she has an illness, part of which involves mood swings that occur suddenly. Next, Article 14 examines social responsibility and health.

5.20.5 Article 14 on Social Responsibility and Health

Article 14 is on social responsibility and health, it reads:

“1. The promotion of health and social development for their people is a central purpose of governments that all sectors of society share. 2. Taking into account that the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition, progress in science and technology should advance: a. access to quality health care and essential medicines, especially for the health of women and children, because health is essential to life itself and must be considered to be a social and human good; b. access to adequate nutrition and water; c. improvement of living conditions and the environment; d. elimination of the marginalization and exclusion of persons on the basis of any grounds; e. reduction of poverty and illiteracy.”⁵⁹⁷

Overall, any condition that is being unnecessarily treated is placing a strain on the health care system which is a socially irresponsible waste of resources and burden to health care. With its inclusion as a mood disorder in DSM-5, the diagnosis of PMDD will increase further straining health care systems. It has a code in the DSM, this allows for a question that is suspect to be reimbursable in institutions and health insurance.

In addition, PMDD is subjecting more women to potentially unnecessary medication to a condition that is not abnormal. Some of the most common side effects of fluoxetine (Prozac/Sarafem) are anxiety, insomnia, nervousness, dizziness, headache, somnolence, tremor, which occur in 10% of those who take the drug. Drinking alcoholic beverages while taking the drug is discouraged as it can compound the side effects of dizziness, drowsiness, confusion, and difficulty concentrating. As an SSRI drug, risk cannot be ruled out during pregnancy. There are concerns such as higher rates of miscarriage particularly when taken in late pregnancy, may increase the risk of persistent pulmonary hypertension in newborns.⁵⁹⁸

Early research on the efficacy of SSRI treatment was a consideration to include PMDD in the DSM-5 as a distinct area. Four large trials did non-continuous dosing of SSRI drugs as opposed to continual treatment. It was reported that this could be just as beneficial because it is cheaper, and since the nature of PMDD is cyclical a targeted dose at the time of the menstrual cycle would be effective, and reduce frequency of side effects which is often cited as the reason SSRI medication is stopped. Interestingly, it was found that placebo effect was high in the trials regarding treatment of PMDD as well.⁵⁹⁹ However, this is never presented as an option that drug therapy may only be limited to the menstrual cycle, rather presented that SSRI treatment is the preference of treating PMDD.

This exposes them to not only possible serious side effects by iatrogenic harm of being labeled of having a mental illness that may not exist, which violates Article 14 calling attention to women's health specifically.

5.20.6 Article 15: Sharing of Benefits

Sharing of benefits, Article 14, states:

“1. Benefits resulting from any scientific research and its application should be shared with society as a whole and within the international community in particular with developing countries. In giving effect to this principle, benefits may take any of the following forms: a. special and sustainable assistance to, and acknowledgment of, the persons and groups that have taken part in the research; b. access to quality health care; c. provision of new diagnostic therapeutic modalities or products stemming from research; d. support for health services; e. access to scientific and technological knowledge; f. capacity-building facilities for research purposes, and g. other forms of benefit consistent with the principles set out in this Declaration. 2. Benefits should not constitute improper inducements to participate in research.”⁶⁰⁰

The new inclusion of PMDD as a mood disorder and the impact this new disease may have on the rest of the world that has not recognized it in the past remains unknown. Most of the non-Western world doesn't view the physical associations of menstruation as problematic. The behavioral components are unheard of. For the first time, PMDD is a legitimate mental illness.

The US medical model has spread globally via the DSM, which now includes PMDD. Only time will tell if there is a trend of more cases of PMDD being diagnosed and treated medically in other countries, perhaps on the US model. This too can contribute to other social factors that are ignored such as abuse in the home, or workplace problems that occur in the lives of some women –the greater structural issues that are ignored when a medical model is enacted. This could be especially harmful in nations where women have fewer rights and social standing than compared to men.

A focus on PMDD ignores more serious diseases women may experience such as genealogical or breast cancers, that have the potential to be life threatening, instead resources were directed to the development of a controversial condition despite many arguing against its existence. PMDD relies heavily on self-report. If a US model is used

and spreads globally how will cultural components of symptoms be included or should they be excluded? –This question remains unknown. If PMDD is the product of the US and its notion of disease surrounding menstruation this must be considered into the impact the byproducts of research on PMDD, (e.g. questionnaires, self-report measures) in countries who do not view PMDD as existing. The impact that PMDD has on future generations is the final Article to be examined.

5.20.7 Article 16 Protecting Future Generations

The articles states, “The impact of life sciences on future generations, including on their genetic constitution, should be given due regard.”⁶⁰¹

There is a need to recognize what impacts making menstruation pathological will have on normal female biological function for future generations. The topic of menstruation remains a socially offensive topic that is focused on a biological process. For women, the notion that the menstrual cycle is a biological process is further reinforced by PMDD as a disease, a mental illness. Women are to believe that something went wrong and that having any unpleasant events surrounding menstruation is abnormal, or “might” be abnormal and having a conversation with a physician about possible treatments for this “problem” is warranted.

Young girls will grow up to be socialized that PMDD can happen as the result of having a menstrual period due to a biological flaw having never known a time before this disorder existed. The disorder of PMDD overlooks other social variables that she may also experience such as outside stress and anger and frustration that results which may just be minimized as “hormonal” and written off. Even those who may not meet criteria

for PMDD will become aware that menstruation is volatile and can make some women “crazy”. It also is yet to be determined how this label can have impacts remaining in a woman’s medical record and what sort of areas this could negatively impact.

5.21 Conclusion

PMDD as we know it today has come a long way from a little known condition of the past. It is now psychiatric diagnosis with symptoms that are physical and psychological that begin shortly before menses and subside at the onset.⁶⁰²

However, the problem with PMDD is that as a diagnostic category, great controversy erupted. Few nations feel the premenstrual symptoms are abnormal.⁶⁰³ There is controversy that PMDD was an industry creation designed to sell a drug by medicalizing a normal process that is not considered to be pathological by branding it a mental illness. PMDD is a severe form of premenstrual syndrome and treatment includes SSRIs and oral contraceptives.⁶⁰⁴ It is included in the most current version of the DSM. In the past, PMDD was only included in the appendix of the DSM. The move to the body of the manual generated great debate.⁶⁰⁵

PMDD is ethically troublesome because of the disease mongering associated with creating the condition and extending a patent for a highly profitable drug for this new “disease”. The drug to treat it, Sarafem, was Prozac, however this was never disclosed to women.⁶⁰⁶ The pharmaceutical industry has a heavy hand in the development of PMDD because its drug treats it.⁶⁰⁷ It is because of these concerns, that it is necessary to examine if PMDD violates ethical principles and examine the suspicions of disease mongering that surround PMDD.

Article 5 is violated due the true nature of autonomy being undermined by the failure to disclose that Sarafem was simply Prozac. Disclosure as an element of informed consent is critical to making a truly informed consent. In addition, if women had been made aware that PMDD was not a disease that was greatly accepted within the mental health community, this too may have had an impact on their decisions to seek treatment and be diagnosed essentially as having a mood disorder.

Article 8 is violated for the fact that menstruation is normal. Any discomfort associated with a normal process isn't outstanding. Thus, by the nature of menstruation woman are more vulnerable to be considered mentally ill. The industry perpetrates this notion by advertising premenstrual discomfit as a problem to which they have a solution. Broader, it reinforces stereotypes that women are somehow more volatile due to their gender.

Article 10 is violated because most healthy women in their childbearing years menstruate. To make connections that changes in mood or behavior surrounding menstruation is an unfair assumption it is a due to disease and not other outside factors such as work or domestic issues creating tensions. A sole focus on a disease model does not account for these important variables in the lives of women.

Article 11 is violated because a diagnosis of PMDD can contribute to the stigmatization of women who menstruate. Menstruation has long been a forbidden topic with negative associations; women who menstruate are dirty or are bad luck, for example. PMDD affirms old notions that menstruation makes women mentally unstable as well. This could lead to discriminatory practices in the workforce or women absorbing an unfair burden of responsibility for any discord in marital or family relationships as well.

Article 14 is violated because of the highly suspect nature of PMDD. Women are being treated for this condition medically. The drugs have side effects. The drugs also can have an impact on woman who are pregnant. This is a risk to women, their child, and places a strain on the healthcare systems with cost. In addition, the weight of being labeled with a mental illness because of the symptoms that are associated with having menstrual cycle is harmful iatrogenically.

Article 14 is violated because of the effects the fruits of this diagnosis may have on the rest of the world's woman. PMDD is mainly unique to the Western world, as is the diagnostic tool. It has never before been validated by inclusion as a full category in the DSM. Therefore, what impact this will have in global rates of diagnosis remain unknown, as is the degree the tools to diagnose are sensitive to non-Western values and norms.

Article 16 speaks to protecting future generations. Another unknown to the inclusion of a medicalized disorder being in the DSM is the role it will have on women. Questions may arise surrounding their menstrual cycles –Is this normal? –Is it me? Thus, not accounting any other factors which may be contributing. For younger girls, a medical model of PMDD will be something that is simply associated as a problem that can happen as they approach puberty, justified by being in a medical bible of sorts, the DSM. How might this impact them as they mature into believe anything surrounding menstruation is abnormal and beyond their control is unknown.

The UNESCO model when used brings to light the ethical issues that surround PMDD. PMDD is troubling because of the medicalization on menstruation. Now, menstruation can lead to a diagnosis of a mental illness. Because of its relatively new inclusion in the DSM, it remains unknown how this will impact woman and as well as

future generations. In summary, the construction of PMDD as mental illness from the broader ethical view is not acceptable as examined in the UNESCO ethical framework model.

Chapter 6: Conclusion

Drug companies have an active role informing society and health professionals about their drugs and the conditions the drugs are used to treat.⁶⁰⁸ The media hails medical breakthroughs, but behind the scenes exists a tarnished reputation that includes profit as the end goal and tactless marketing aimed at consumers.⁶⁰⁹ The most central principle of medicine for all physicians from those who work as researchers, physicians, editors of medical journals, academic institutions, or pharmaceutical companies is do no harm. Yet, problems frequently arise with some drugs that compromise patients.⁶¹⁰

Corporate motives prove to be more of a force than scientific or ethical principles.⁶¹¹ Much is at stake in pharmaceuticals and there are many people who can benefit from the success of a profitable drug. Currently, most published literature on disease mongering focuses on descriptive reports as well as critical commentary on suspected cases of disease mongering. Other literature focuses on aggressive product promotion and general critique on industry marketing practices.⁶¹² Conducting an ethical assessment of disease mongering is important. Disease mongering is often suspected but an ethical framework provides a tool of measurement for analyzing the phenomenon which to date is lacking.

The problem of disease mongering is global. Most drug research and companies are based in the US, but the conditions branded by these companies and treatments affect the world. The US medical model is expanding across the world, which puts more people at risk. This medical model ignores cultural variations, social conditions, and other factors that may contribute to illness. In the mental health field, this is especially

concerning because the majority of illnesses lack any form of biological testing and symptoms are predominately treated with prescription drugs.

This makes a global framework an ideal fit for examining disease mongering and determining if it occurs. The UNESCO framework was used to ethically analyze disease mongering for two conditions, Attention Deficit Hyperactivity Disorder (ADHD) and Premenstrual Dysphoric Disorder (PMDD).

6.1 Ethical Summaries

6.1.1 ADHD

As analyzed in the UNESCO ethical model framework, the practice of disease mongering occurs with ADHD. The history of ADHD is extensive, it began as strictly a childhood disorder for children. Currently, the DSM-5 has lowered the age of onset and included an adult population as well. The concerns associated with disease mongering and ADHD are that ADHD is being over-diagnosed, expanded to include adults, and turning childhood into a disease.

In summary, the articles 5, 8, 10, 14, 15, and 16 of the *Universal Declaration on Bioethics and Human Rights* are violated when ADHD is examined in the UNESCO model. Autonomy is undermined by deceptive or misleading pharmaceutical company promotional materials intended to sell drugs more so than educate and inform. The concept of autonomy is promoted by the drug industry to consumers by the suggestion to ask their physician about treatment options, which will likely be a drug. Children rely on adults; their parents, their doctors, and their teachers, and the role the industry aggressively takes at promoting their behaviors as abnormal medicalizes childhood.

Children are a vulnerable group who should have their interest protected. Yet, the pharmaceutical industry instead targets parents, teachers, and physicians to notice symptoms of ADHD and encourages them to use medication. Embedded in this message is the fear of negative outcomes by letting ADHD go untreated, such as school failure or even future criminal behavior. Other alternatives are not suggested. The broader social contexts that may contribute to negative behaviors associated with ADHD are ignored.

Ignoring alternative options violates justice for those with ADHD. Mediation doesn't solve the broader problems that may also contribute to inattentive or hyperactive symptoms such as poor school systems for children or unsatisfying relationships for adults. The US model of the DSM has become the world standard in psychiatry replacing instruments such as the stricter diagnostic instrument of the ICD in diagnosing ADHD. ADHD diagnosis can be applied not only to broader populations in criteria but now the trend to global spread of the DSM model.

Last, the predominantly target population of ADHD is children. This creates concern for future generations and the impacts that powerful stimulant medications may have on growth and development as the age of diagnosis is at its lowest. Even toddlers are being treated, which is an age group that is outside of treatment guidelines. Incredibly high rates of diagnosis already exist and now even more children can be medicated for this disorder.

6.1.2 PMDD

In summary, the articles 5, 8, 10, 11, 14, 15, and 16 of the *Universal Declaration on Bioethics and Human Rights* are violated when PMDD is examined in the UNESCO

model. The mental health diagnosis of PMDD also has a long history evolving from a benign form of premenstrual syndrome, which was a cluster of symptoms associated with the menstrual cycle, to a full-blown psychiatric diagnosis.

Few places outside of the US view the physical symptoms that co-occur with the timeframe surrounding menstruation as abnormal let alone any form of a mental health issue. There was a great deal of controversy to include PMDD in the DSM-5 and the ties that members of the APA and DSM workgroups had with the pharmaceutical industry added to these concerns. Despite this, PMDD as a distinct category was included for the first time. The disease mongering associated with PMDD is that it was an industry creation designed to sell a drug coming off patent, and that it medicalizes a normal biological process for women in their child bearing years.

The menstrual cycle may not be pleasant for all women, but it is a normal function. The physical associations such as bloating or abdominal cramps may be unpleasant, but they are not abnormal. PMDD suggests otherwise, they are in fact abnormal and the symptoms are indicative of a mood disorder. Menstruation became a medicalized condition.

The drug to treat PMDD was Sarafem, which was Prozac. A drug that was coming off of its highly profitable patent. In order to have the patent extended, there must first be a condition for which a drug will treat, and shortly after came the condition of PMDD. The drug Sarafem was used to treat it. Yet, it was no chemically different than Prozac, it was only re-colored pink or purple. The pharmaceutical industry has a heavy hand in the development of PMDD in drug promotion and propelling the diagnosis. It is because of these concerns an ethical assessment.

Autonomy was undermined by not disclosing that Sarafem was simply Prozac, which would have been just as effective to treat PMDD, and less expensive in its generic form. Women were not informed that Sarafem was an antidepressant either. Menstruation is normal. Most discomfort associated with it is not abnormal. PMDD makes women a vulnerable group more apt to be mentally ill because of the menstrual cycle.

Pathologizing normal function is harmful to women. PMDD as a mental illness reinforces antiquated stereotypes that women are moody or emotional. PMDD places the blame of mood solely on a biological function and internalizes the problem to the individual woman. This allows greater external difficulties to be ignored that could be contributing to hostile feelings, such as troubles at home or at work. Medicalizing menstruation ignores these variables.

PMDD can contribute to the stigmatization of women. Menstruation has a long history of negative associations for women. PMDD affirms outdated notions that menstruation makes women crazy. Having a menstrual cycle could lead to discriminatory practices in the workforce, in child custody battles, or for women seeking positions of authority.

PMDD is based off of PMS. PMS has no valid measures, varies from woman to woman and cycle to cycle. Medically, PMS is a mystery. Yet, for PMDD, women are being treated for this condition medically with a stringent set of criteria from a non-empirical base of PMS. Treatment is with SSRI drugs. The drugs have side effects to women, unborn children, and financial impacts on the health insurance; all of these may be unnecessary risks and burdens for a highly questionable condition. In addition, a mental illness carries the risk of iatrogenic harm as well.

PMDD is a new psychiatric diagnosis. How it progresses in diagnostic rates or further DSM changes in impending revisions remains unknown. For future generations of women, a medical model of PMDD may serve to affirm society's and even women's own self-doubts that some problems are menstruation-related. Women may be inclined to accept it because now these feelings or experiences are a medical problem confirmed by PMDD. Women may find themselves wondering if it is an emotionally unstable time, or think "maybe it *is* just me", and wonder if they should be treated. PMDD reinforces ideas that there is some sort of a *problem* with a woman who menstruates, rather than a normal function.

The UNESCO model when used brings forward the ethical issues that surround ADHD and PMDD with more clarity. PMDD is new to the DSM and ADHD has been significantly revised. The impact that disease mongering has on both of these areas will become more known in time. In summary, the expansion of ADHD and the construction of PMDD as mental illness, are not ethically acceptable when examined in the UNESCO ethical framework model. Addressing the ethical problems of disease mongering in the future is the final topic.

6.2 Future considerations

Questions may arise on how to incorporate a generalized normative framework into practice. One way is to incorporate this framework into the teaching of professionals, such as doctors and scientists.⁶¹³ A key element to address disease mongering is education to those who have the ability to confront it. The influence of the industry permeates the medical field starting in medical school and into physicians' practices. It is

critical to address industry influence in medical schools. Not only the sponsorship that occurs, but to raise awareness how this type of industry influence affects medicine and research overall. For physicians who practice or go into medical research, the same holds true. Implicit bias the industry has on medical professionals may not be apparent and financial disclosures may not be enough to combat disease mongering. For an ethical approach to medicine, industry influence is a fundamental problem.

An interesting approach by Cosgrove and Wheeler regards the informed consent process. Rather than the disclosure of risks and benefits, industry affiliations are a consideration for patients to be made aware of as well. This allows for independent decisions and consideration be made for each individual, which would support true autonomy.⁶¹⁴

The general public blindly accepts medical conditions and treatments because “doctor knows best” and if a drug or condition exists, it must be real. Physicians too should investigate conditions and treatments that extend beyond detailing that is done by pharmaceutical company employed drug representatives and demand more answers. For “do no harm” to be ethically upheld, the pharmaceutical industry’s vital role in the development of disease must be addressed.

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